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ROLE OF MIR-29B-1 AND MIR-29A IN ENDOCRINE-RESISTANT BREAST CANCER

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DEDICATION

This dissertation is dedicated to my parents for their constant love, encouragement and support over the course of my life and my Ph.D. program. Also, I would like to dedicate this to my siblings Ateh, Lum, Francine, Ambe, Bernard, Benise, Rose-Mary and Abongwa for their constant love and prayers. Finally I will want to also dedicate this to my friend Anye and the Wamucho family for their constant advice and motivation.

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ABSTRACT

ROLE OF MIR-29B-1 AND MIR-29A IN ENDOCRINE-RESISTANT BREAST CANCER

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Therapies targeting estrogen receptor α (ERα) including selective estrogen receptor modulators (SERMs), *e.g.*, tamoxifen (TAM); selective estrogen receptor downregulators (SERDs), *e.g.*, fulvestrant (ICI 182,780); and aromatase inhibitors (AI), *e.g.*, letrozole, are successfully used in treating breast cancer patients whose initial tumor expresses ERα. Unfortunately, the effectiveness of endocrine therapies is limited as ~ 40% of breast cancer patients will eventually acquire resistance to them. The role of miRNAs in the progression of endocrine-resistant breast cancer is of keen interest in developing biomarkers and therapies to counter metastatic disease. This dissertation begins with a review on miRNAs implicated in breast cancer, their *bona fide* gene targets, and associated pathways promoting endocrine resistance.

Although microRNAs are dysregulated in breast cancer, their contribution to endocrine-resistance is not yet fully understood. Previous microarray analysis identified miR-29a and miR-29b-1 as repressed by TAM in MCF-7 endocrine-sensitive breast cancer cells but stimulated by TAM in LY2 endocrine-resistant breast cancer cells. Here we examined the mechanism for the differential regulation of these miRs by TAM in MCF-7 *versus* TAM-resistant LY2 and LCC9 breast cancer cells and the functional role of these microRNAs in these cells. Knockdown studies revealed that ERα is responsible for TAM regulation of miR-29b-1/a transcription. Transient overexpression of miR-29b-1/a decreased MCF-7, LCC9, and LY2 proliferation and inhibited LY2 cell migration and colony formation but did not sensitize LCC9 or LY2 cells to TAM. Furthermore, TAM reduced DICER1 mRNA and protein in LY2 cells, a known target of miR-29. Supporting this observation, anti-miR-29b-1 or anti-miR-29a inhibited the suppression of DICER by 4-OHT. These results suggest that miR-29b-1/a have tumor suppressor activity in TAM-resistant cells and do not appear to play a role in mediating TAM resistance.

The target genes mediating miR-29b-1/a tumor suppressor activity were unknown. Here, using RNA sequencing, we identify miR-29b-1 and miR-29a target transcripts in both MCF-7 and LCC9 cells. We find that miR-29b-1 and miR-29a regulate common and unique transcripts in each cell line. The cell-specific and common downregulated genes were characterized using the MetaCore Gene Ontology (GO) enrichment analysis algorithm. LCC9-sepecific miR-29b-1/a-regulated GO processes include oxidative phosphorylation, ATP metabolism, and apoptosis. Extracellular flux analysis of cells transfected with anti- or pre- miR-29a confirmed that miR-29a inhibits mitochondrial bioenergetics in LCC9 cells. qPCR and luciferase reporter assays also verified the ATP synthase subunit genes *ATP5G1* and *ATPIF1* as *bona fide* miR29b-1/a targets. Our results suggest that miR-29 repression of TAM-resistant breast cancer cell proliferation is mediated in part through repression of genes important in mitochondrial bioenergetics.

There is a critical need to develop sensitive circulating biomarkers that accurately identify signaling pathways altered in breast cancer patients resistant to endocrine therapies. Serum miRNAs have the potential to serve as biomarkers of the progression of endocrine-resistant breast cancer due to their cancer-specific expression and stability. Exosomal transfer of miRNAs has been implicated in metastasis and endocrine-resistance. This dissertation ends with a review on miRNAs in breast tumors and in serum, including exosomes, from breast cancer patients that are associated with resistance to tamoxifen.

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CHAPTER I: INTRODUCTION[1]

BREAST CANCER SUBTYPES

Breast cancer (BC) is the most common malignant disease among women worldwide [1] with an estimated 1.7 million new cases diagnosed in 2012 according to GLOBOCAN statistics. In 2017 about 255,180 new cases will be diagnosed in the US and approximately 41,070 women are projected to die from the disease [2]. These data underscore the need to improve and/or develop better preventive, diagnostic, and therapeutic strategies addressing BC. Mortality from BC is decreasing in part due to early diagnosis and implementation of advanced therapies including adjuvant chemo- and hormone-therapies [3].

BC is a heterogeneous disease characterized by distinct molecular and morphological traits that inform prognosis and therapy. BC is classified into five subtypes based on distinct gene expression profiles: luminal A, luminal B, basal, human epidermal growth factor receptor 2 (HER2/ERBB2)-positive (+), and normal breast-like tumors [4-8]. Most tumors are classified as luminal [7] and express estrogen receptor α (ERα), progesterone receptor (PR), and the luminal cytokeratins (CK) 8 and 18. Luminal B tumors have higher Ki67 expression than luminal A [9]. Ki67 is a nuclear protein

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associated with cellular proliferation, disease recurrence, relapse, and poor survival in BC patients [10-12]. ERα+ tumors are associated with smaller, low grade tumors and are often lymph node negative [13, 14]. HER2+, basal and 'normal breast-like' tumors are ERα/PR negative (ERα-/PR-). HER2 is constitutively active and predicts reduced disease-free survival [15]. Triple negative breast cancer (TNBC, *i.e.*, ER-/PR-, and HER2-) is a highly diverse group of breast cancers with poor prognosis [16]. The origins of TNBC are debated. One model from murine mammary tumors suggests that *in vivo* tumor heterogeneity of luminal A tumors gives rise to claudin-low tumors, basal-like tumors and HER2+ tumors [17]. The expression profiles of 'normal breast-like' tumors are more varied and are similar to adipose tissue, basal epithelial cells, and other non-epithelial components of the breast [4, 5]. The HER2+, basal-like, and TNBC tumors are associated with more advanced stage at presentation [18] and patients have reduced disease-free survival [19]. In this chapter, I will focus on luminal A and B tumors and resistance to endocrine therapy

ER PATHWAYS IN BREAST TUMORS

Estrogens are steroid hormones whose effects mediate cellular processes including cell proliferation, cell survival and apoptosis [20]. In addition to their roles in breast and reproductive tract development and homeostasis, estrogens are involved in a variety of physiological processes including skeletal homeostasis, maintenance of the cardiovascular and central nervous systems, lipid and carbohydrate metabolism, and electrolyte balance [21]. Estrogens are central in the maintenance and development of female physiology, reproduction, and behavior [21, 22]. The most potent estrogen is 17β-estradiol (E_2). The biological effects of estrogens, including E_2, are mediated by binding to nuclear receptors ERα and ERβ and their splice variants, *e.g.*, ERα36 (reviewed in [23] and ERα46 [24], and to G-protein coupled ER (GPER) [25]. The ERα activation initiated by E_2 binding and consequent conformational changes results in "nuclear/genomic" or "non-genomic/membrane-initiated" responses [26, 27]. ERα is upregulated in breast tumors [28]. It is the target for therapeutic agents originally termed antiestrogens because they compete with E_2 for ERα binding, but now termed SERMs and SERDs because of our greater understanding of their molecular actions [29]. Because the role of ERβ in breast cancer remains to be clearly established (reviewed in [30]) and because ERα expression is higher than ERβ in breast tumors and is thus the target of therapeutic intervention, this dissertation will focus primarily on ERα activities related to miRNA expression and activity in endocrine-resistance.

The ERα activation initiated by E_2 binding and consequent conformational changes results in 'nuclear/genomic' or 'non-genomic/membrane-initiated responses [26, 27]. In the nuclear/genomic response, ERα serves as ligand-activated transcription factor that dimerizes either within the nucleus or translocates to the nucleus where, in combination with coregulators/coactivators which remodel chromatin, it binds to estrogen response elements (EREs) in promoter regions of estrogen-regulated genes [31]. Genome-wide chromatin immunoprecipitation (ChIP) for ERα binding sites revealed ERα binding sites in the 3' UTR of target genes as well as in interchromatin regions [32, 33]. The ERE is a short palindromic inverted repeat 5'-AGGTCAnnnTGACCT-3' where n = any nucleotide [34]. Extension of this repeat in the 3' and 5' direction, flanking ATrichness, number of nucleotides separating the inverted repeat, and nucleotide changes in each half-site (5'-AGGTCA-3') determines the affinity for ERα binding to ERE [35, 36]. ERα also binds imperfect, non-palindromic EREs in E_2-regulated genes, usually in collaboration with other transcription factors [37]. The transcriptional activity of ERα is also mediated by 'tethering' involving protein:protein interaction of ERα with other transcription factors including activator protein-1 (AP-1) and specificity protein (Sp1) at cognate DNA-responsive sites [38]. Coactivators including AIB1 (SRC-3), which is overexpressed in TAM-resistant tumors and cell lines [39], enhance ERα transcriptional activity [40]. The end result is an increase or decrease in gene transcription resulting in the physiological outputs associated with estrogen signaling, including tissue- and cell-specific changes in cell cycle, proliferation, apoptosis, invasion, angiogenesis, and survival [41].

In the non-nuclear/membrane-initiated ER pathways, E_2 rapidly alters intracellular signaling pathways culminating in changes in gene transcription by a processes mediated by plasma membrane-associated ERα, ERβ, or GPER/GPR30 (reviewed in [26, 27, 42-44]). These rapid responses include E_2 activation of PI3K and Src in the plasma membrane (PM) which then activate mTOR through PI3K-mediated AKT phosphorylation. Membrane ER and GPER activate epidermal growth factor receptor (EGFR) with downstream signaling through Ras/Raf and mitogen-activated protein kinase (MAPK) [45]. E_2 activation of EGFR can increase ERα phosphorylation (reviewed in [44, 46, 47]). These signaling pathways subsequently regulate ER transcriptional activity. Despite the numerous studies on ERα, the events and overall processes including their regulated gene targets are not completely understood.

MECHANISMS OF ENDOCRINE THERAPY IN BREAST CANCER

Antiestrogen therapies function by two main mechanisms: targeting ERα activity and/or stability. SERMs, *e.g.*, TAM, raloxifene (RAL), and toremifene, compete with E_2 for binding the ligand binding domain (LBD) of ERα and inhibit ERα transcriptional activity in a gene- and cell-specific manner. SERMs can be agonists or antagonists depending on the tissue and gene. For example, SERMs are agonists for ERα in the endometrium and increase endometrial tumor incidence [48, 49]. As antagonists, SERMs are used in the treatment of breast cancer patients with ERα+ breast tumors [50]. SERDs, *e*.g., fulvestrant (ICI 182,780, Faslodex), not only alters the ERα conformation, but stimulate ER protein degradation [51-53]. Aromatase inhibitors (AIs) inhibit the activity of aromatase (CYP19A1), thus reducing estrogen synthesis in peripheral adipose tissues and within the tumor [51]. Examples of AIs include letrozole and anastrozole, which are steroidal/irreversible inhibitors, and exemestane, a non-steroidal/reversible inhibitor [51].

For postmenopausal women with ERα+ primary tumors, ASCO guidelines recommend AI therapy, and for premenopausal women, TAM for 10 years is recommended [54]. Adjuvant therapy with TAM for postmenopausal women with endocrine responsive breast tumors effectively reduced the odds of recurrence by 40% and death from breast cancer after 5 years by 20% [55]. Unfortunately, 40-50% of patients initially responsive to TAM develop TAM resistance [56]. Likewise, a similar proportion of patients develop AI-resistance [57, 58]. This indicates additional mechanisms evolve to promote breast cancer progression in the absence of estrogen signaling.

MECHANISMS OF ENDOCRINE RESISTANCE

A number of molecular mechanisms have been implicated in promoting endocrine resistance (Fig. 1) [56, 59, 60]. For example, ERα expression is silenced by DNA methylation, resulting in reduced ERα protein [61]. Mutations in ERα [62] or increased expression of truncated forms of ERα, including ERα36 [63], are potential mechanisms in acquired resistance. Alterations in ERα coregulators, *e.g.*, increased expression of AP1 and nuclear factor-κB (NF-κB) are associated with endocrine resistance [64, 65]. Crosstalk between ERα and amplification or activation of receptor tyrosine kinases (RTKs), including EGFR and insulin-like growth factor receptor (IGFR), have also been implicated in endocrine resistance [44]. Overexpression of HER2 (ERBB2) can elicit TAM resistance [44], although HER2+ tumors are of a distinct molecular genotype from luminal A/ERα + breast tumors [66]. Apoptotic and cell survival signals are also dysregulated in TAM-resistant cells [42]. A more extensive review of mechanisms promoting endocrine resistance can be found in [51, 60, 67].

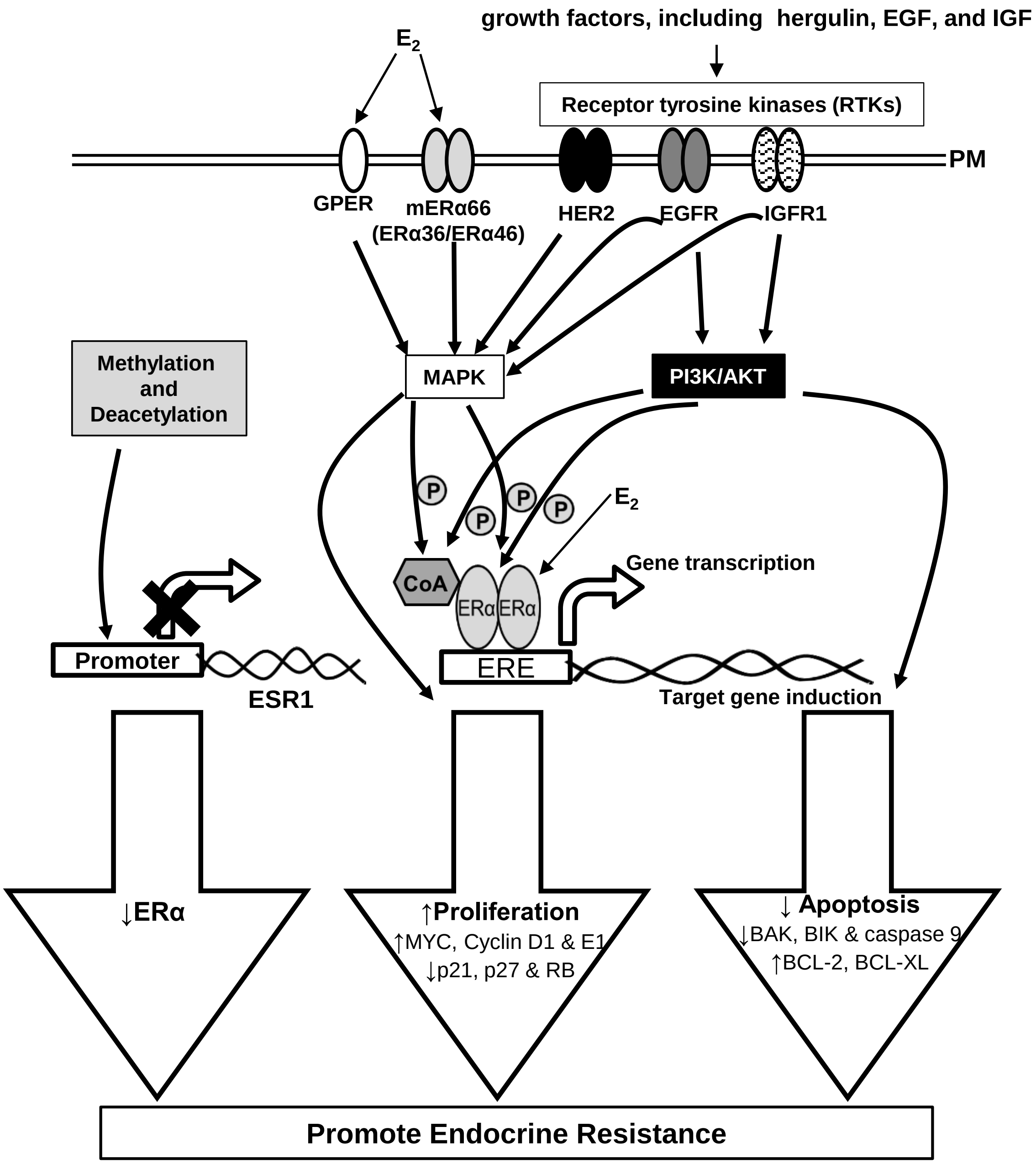
growth factors, including hergulin, EGF, and IGF
E2
Receptor tyrosine kinases (RTKs)
PM
GPER
mERα66
(ERα36/ERα46)
HER2
EGFR
IGFR1
Methylation and Deacetylation
MAPK
PI3K/AKT
P
P
P
P
E2
CoA
ERα
ERα
Gene transcription
Promoter
ESR1
ERE
Target gene induction
↓ERα
↑Proliferation
↑MYC, Cyclin D1 & E1
↓p21, p27 & RB
↓ Apoptosis
↓BAK, BIK & caspase 9
↑BCL-2, BCL-XL
Promote Endocrine Resistance

Figure 1. Summary of the molecular mechanisms promoting acquired endocrine resistance.

Activation and/or amplification of receptor tyrosine kinases (RTKs) including insulin-like growth factor receptor (IGFR), epidermal growth factor receptor (EGFR), and HER2 have been detected in tamoxifen-resistant breast cancer cells and endocrine-resistant patient tumors. Plasma membrane-associated GPER and ERα, including splice variants ERα36 ERα46, are increased in endocrine-resistant breast cancer cells and tumors. Activation of these receptors activate intracellular signaling cascades including MAPK and PI3K/AKT pathways that ultimately increase transcription of genes that promote growth and survival, and resistance to apoptosis. Additionally, these pathways increase ligand-independent ERα activation by phosphorylation. Alternatively, MAPK and PI3K/AKT can directly promote expression of non-ERE responsive genes by activating other transcription factors, *e.g.*, AP-1, not shown here. Promoter methylation of CpG islands and histone deacetylation have been shown to repress ERα expression and promote endocrine resistance. *Abbreviations:* Estrogen receptor α (ERα), estrogen response element (ERE), G protein-coupled estrogen receptor (GPER), plasma membrane (PM), retinoblastoma (RB), V-Myc Avian Myelocytomatosis Viral (MYC), B-cell lymphoma (BCL), homologous antagonist killer (BAK), BCL-2-interacting killer (BIK)

CHAPTER II: SIGNIFICANCE OF MICRORNA EXPRESISON IN ENDOCRINE/TAMOXIFEN-RESISTANT BREAST CANCERS

MICRORNA BIOGENESIS

miRNAs are evolutionarily conserved, small, non-coding, 22 nt RNAs that post-transcriptionally regulate gene expression by binding to the 3' untranslated region (3'UTR) of mRNAs to repress translation or promote degradation [68]. There are an estimated 2,588 miRNAs arising from intragenic or intergenic regions of the human genome (June 2014; http://www.mirbase.org/) [69]. Intragenic, *i.e.*, intronic or exonic, miRNAs, which constitute about half of all miRNAs [70], originate from within protein coding genes and can therefore have a shared promoter (and/or transcriptional start site (TSS)) and are expressed simultaneously with their host protein-coding transcript [71, 72]. However, later findings suggest this may not be the case and regulation of intronic miRNA transcription can occur independent from the host gene [73, 74]. Intergenic miRNAs tend to have their own promoters [74]. Determining these TSSs will be essential in understanding the regulation of miRNA expression. Sixty percent of all human protein coding genes are regulated by miRNAs [75] and because miRNAs regulate multiple mRNAs, they are implicated as key regulators in a variety of cellular processes including cell differentiation, cell death development, proliferation, and metabolism [76].

miRNA biogenesis occurs through canonical and non-canonical pathways. In the canonical pathway of miRNA biogenesis, the primary RNA transcript (pri-miRNA) is transcribed from DNA by RNA polymerase II. Pri-miRNA is further processed to a hairpin precursor transcript (pre-miRNA; ~70 nt) by a microprocessor complex comprised of Drosha (RNase III enzyme) and associated DiGeorge syndrome critical region gene 8 (DGR8) [77]. DGR8 anchors and recognizes the miRNA region for endonuclease cleavage by Drosha [78, 79]. The Drosha microprocessor complex is also implicated in miRNA-independent functions including regulation of heteronuclear ribonucleoproteins (hnRNPs) and alternative splicing [80]. Pre-miRNA is exported from the nucleus by Exportin 5 (a RanGTP-dependent dsRNA-binding protein [81]) to the cytoplasm where it is further processed by another RNase III enzyme, DICER, in conjugation with trans-activation response (TAR) RNA binding protein (TRBP) and protein activator of the interferon-induced protein kinase (PACT; also known as PRKRA) results in a small dsRNA duplex (~22 nt) [78, 82]. One of the duplex strands is included in the RNA-induced silencing (RISC) complex where it recognizes and binds mRNA resulting in mRNA degradation or translational repression depending on the extent of complementarity [83]. The core RISC complex is composed of four Argonaute (Ago) proteins with AGO2 endonuclease activated upon recruitment of target mRNAs [84].

In the non-canonical pathway, miRNAs (miRtrons) are processed by spliceosomes in an RNase III (Drosha)-independent manner (reviewed in [85]). The intermediate generated is further processed by lariat debranching enzyme resulting in products that appear as pre-miRNA mimics. These mimics then enter the canonical pathway as Exportin 5 or DICER substrates.

miRNAs are considered to be key players in cellular transformation and in the initiation and progression of cancer [86]. Selected miRNA signatures have been recognized in categorizing developmental lineages and differentiation states of different tumors [87, 88]. In these roles miRNAs may function as oncomiRs (oncogenic miRNAs) or oncosuppressor miRNAs, although there is an overall downregulation of miRNAs in tumors compared to normal tissues [87]. Substantial effort is currently underway to understand the molecular mechanisms associated with miRNA dysregulation to assist in early diagnosis and management of breast cancer patients.

MICRORNA AND BREAST CANCER

Since 2005, when miRNA deregulation was first reported in breast cancer [89], over 1000 studies have been published identifying and examining the role of miRNAs in this disease. Some of these miRNAs are regulated by E_2 and/or influence expression of estrogen-responsive genes [90-92]. miRNAs have been implicated in regulating hallmarks of breast cancer (reviewed in [93]) including cell proliferation, cell death, apoptosis, immune response, cell cycle energetics, metabolism, replicative immortality, senescence, invasion, metastasis (reviewed in [94-97], and angiogenesis (reviewed in [93, 98]).

MODELS FOR MICRORNA INVESTIGATION

The process of investigating miRNAs involved in endocrine resistance usually begins with an initial profiling of miRNA differences between endocrine-sensitive *versus* endocrine-resistant breast cancer cell lines or between breast tumors from patients responsive and non-responsive to endocrine therapies. Methods used in these studies have included microarrays, RNA sequencing (RNA-seq), and the relatively recent high-throughput sequencing of RNA isolated by crosslinking immunoprecipitation (HITS-CLIP) method with confirmation by qPCR. These methods result in the acquisition of huge amounts of data that require integrative analysis and further confirmation. Computational approaches are then utilized to predict possible targets and signaling pathways that are aberrantly regulated by the identified miRNAs. Functional analysis utilizing ectopic expression and forced repression of miRNA expression are performed to validate the role of deregulated miRNAs in tumorigenesis and/or endocrine resistance *in vivo* and *in vitro*. The targets of miRNAs are further confirmed by cloning the target 3'-UTR downstream of a luciferase reporter, transfecting a cell line with this reporter plasmid to validate direct inhibition; western blots and qPCR. Target validation in clinical samples provide human significance to the study. These models have identified miRNAs involved in endocrine resistance that are summarized in Tables 1 and 2.

There are limitations to these approaches. For example, integrative analysis for identifying aberrantly expressed miRNAs is limited by the set of computational parameters used in the study, and rarely are these parameters applied to other studies. Functional investigations need to be performed for each miRNA and its target. The acquisition of massive amounts of information, which though relevant, does not often translate to physiological significance. This necessitates further studies within clinical settings. HITS-CLIP is technically challenging and complex. It requires great skill but has the advantage of capturing interactions ‘frozen’ by UV-crosslinking under physiological conditions without the use of exogenous crosslinking agents which can lead to artificial interactions [99].

MICRORNAs REGULATING ERα PROTEIN AND SIGNALING

The role of miRNAs in promoting endocrine resistance is exemplified by, but not limited to, their involvement in regulating ERα (Fig. 2). Decreased ERα expression is involved in endocrine-resistant breast cancer progression. miRNAs including miR-221/222 [100], miR-342-3 p [101], miR-873 [102] and Let7b/Let-7i [103] downregulate ERα protein expression (Table 1). miR-221 and miR-222 are overexpressed in TAM-resistant and ERα-negative breast cancer cell lines and tumors [100, 104, 105]. miR-221/222 directly target the 3’UTR of ERα. This results in a decrease ERα protein but not mRNA [100]. Transient overexpression of miR-221/222 in TAM-sensitive MCF-7 and T47D cells resulted in TAM resistance whereas downregulation of miR-221/222 in ERα negative/TAM-resistant MDA-MB-468 cells restored ERα expression and sensitized cells to TAM-induced cell cycle arrest and apoptosis [100]. ERα is not a direct target of miR-342-3p, but loss miR-342-3p was associated with a concomitant loss in ERα expression and resulted in TAM resistance [101]. Conversely, forced overexpression of miR-342-3p sensitized MCF-7 cells to TAM-induced apoptosis [101]. The exact mechanism promoting loss of ERα expression upon downregulation of miR-342-3p is yet to be determined [106].

Increased expression of ERα splice variants have also been reported to be associated with poor prognosis and contribute to endocrine resistance [107, 108]. ERα36 is an N-terminal truncated 36 kDa variant of full-length ERα (ERα66) [109]. ERα36 lacks AF-1 and AF-2 of ERα66, retains DNA binding and dimerization domains, binds E_2, but is not inhibited by TAM or fulvestrant [109]. ERα36 is expressed in ERα-negative breast cancer cells and tumors [110] and overexpressed in TAM-resistant breast cancer cells [108]. Increased ERα36 protein expression is proposed to be mediated by decreased let-7 levels, since transfection of let-7b and let-7i mimics repressed ERα36 expression and sensitizes TAM-resistant MCF-7 cells to TAM growth inhibition [103]. Let-7 family members are downregulated in breast cancer tissues and TAM-resistant MCF-7 cells [103, 111].

ERα is regulated by post-translational modifications including phosphorylation, methylation, sumoylation, and palmitoylation [112-116]. These modifications influence ERα interaction with other molecules, including transcriptional coregulators, hence regulating gene transcription (Fig. 1). These post-translational events also contribute to endocrine resistance [117]. miRNAs are implicated in altering post-translational ERα modifications to promote TAM resistance [114]. For example, miR-873 targets CDK3, which phosphorylates ERα at Ser104/116 and Ser118 [114]. miR-873 expression was downregulated in TAMR/MCF-7 breast cancer cells, and forced overexpression of miR-873 in these cells reversed TAM resistance and decreased xenograft tumor growth. The authors postulated that the decrease in miR-873 resulted in enhanced ERα phosphorylation and ligand-independent activity in TAMR/MCF-7 cells [114].

Table 1: miRNA associated with antiestrogen-resistance in breast cancer

Experimentally proven *bona fide* targets and method used in confirming target are indicated. Proposed pathways associated with endocrine-resistance are included. Method of identification of targets: 3’-UTR luciferase reporter assay (L), downregulation of protein shown by western blot (W), and downregulation of target in quantitative real-time PCR assay (Q).

miRNA	**Treatment/Human Cell line/ tissue**	**Comments**	**Targets** (method of identification)	**Pathway**
Putative oncomiRs based on experimental data				
miR-101	0, 1, 2, 3, 4 µM 4-OHT 4 d in MCF-7 cells	miR-101 infected cells promote growth stimulatory activity in medium lacking E$_2$ and TAM resistant. miR-101 has growth inhibitory activity in E$_2$-containing medium [118] .	MAGI-2 ((membrane-associated guanylate kinase) (L, W) [118]	Growth factor receptor (GFR) Cytoplasmic signaling
miR125b-5p	0.001- 10 µM anastrozole or letrozole in LET-R MCF-7 ANA-R MCF-7 vs MCF-7aro cells; Primary breast tumors	Upregulated in LET-R MCF-7 cells, ANA-R MCF-7 compared to MCF-7aro; high miR-125b-5p correlated with earlier relapse in ER+/PR+ patients [119]		
miR-128a	TAM+LET-R MCF-7 cells, MCF-7aro cells	Upregulated in TAM+LET-R MCF-7 cells vs MCF-7aro cells [120]	TGF-βRI (L, W) [120]	GFR Cytoplasmic signaling

MiR-181b	Human breast samples; 1 µM 4-OHT, for 0, 24, 48 and 72 h, 50 nM 4-OHT, 0, 3, 5 min T47D, TAM-R MCF-7 vs TAM-S MCF-7	Enhanced expression in TAM-R MCF-7 cells [121] Anti-miR-181b suppressed TAM-R xenograft tumor growth in TAM treated mice.	TIMP3 (L W, Q) [121]	GFR Cytoplasmic signaling
miR-205-5p	1, 10, 100 nM, 1, 10 µM anastrozole, 1, 10, 100 nM, 1, 10 µM letrozole; LET-R MCF-7 cells, ANA-R MCF-7 vs MCF-7aro Primary breast tumors	Upregulated in LET-R MCF-7 cells, ANA-R MCF-7 compared to MCF-7aro cells; High miR-125b-5p correlated with earlier relapse in ER+/PR+ patients [119]		
miR-210	Patient samples, 100 nM 4-OHT, 0, 1, 2, 3, 4 d, MCF-7, MDA-MB-231	Increased miR-210 with breast tumor histological grade. Higher in MDA-MB-231 compared to MCF-7 cells [102]		
miR-222	Human breast samples 1 µM 4-OHT, for 0, 24, 48 and 72 h; 50 nM 4-OHT, 0, 3, 5 min	Anti-miR-222 suppressed TAM-resistant xenograft tumor growth in TAM treated mice [121]	TIMP3 (L W, Q) [121]	GFR Cytoplasmic signaling

	T47D, TAM-R MCF-7 vs TAM-S MCF-7			
miR-221/222	0-65 µM 4-OHT, 6 d MCF-7/TAM-R vs MCF-7 measured in conditioned media [122]	Six-fold increase in exosomes in MCF-7/ TAM-S vs MCF-7/TAM-R cells [122]	P27 and ERα (W, Q) [122]	ERα signaling /cell cycle
	0, 15, and 20 µM TAM, 16 h TAM-S vs TAM-R MCF-7 cells, HER2/neu (+) vs HER2/neu (-) human breast tissue	TAM increased miR-221/222 in TAM-R cells and HER2/neu (+) breast tumors compared to TAM-S MCF-7and HER2/neu (-) tumors, respectively [104]	p27(Kip1) (W, Q)[104]	GFR Cytoplasmic signaling/ cell cycle
	0, 5, 10, 20 µM 4-OHT, 12, 24, 48 h, MCF-7 and MDA-MB-231		TIMP3 (W, Q) [123]	GFR Cytoplasmic signaling
	10 µM 4-OHT, -/+1 nM E_2, 48 h MCF-7 mammosphere transformed vs MCF-7 cells as xenografts in SCID mice	Higher in MCF-7 mammospheres compared to MCF-7 cells [124]	ERα (W)	EMT
	100 nM fulvestrant;	Overexpressed in Ful-R MCF-7 cells. Indirect activation of β-catenin		GFR Cytoplasmic signaling

	TAM-R MCF-7, Ful-R MCF-7, MCF-7, MCF-7-Mek5, MCF-7 TNR	Repression of TGF-β mediated growth inhibition [125]		
	0, 5, 10, 20 µM, 10, 20, nM 4-OHT, 72 h MCF-7, T47D vs MDA-MB-468 cells Breast tumor tissue	Higher in ERα negative MDA-MB-468 breast cancer cells and primary breast tumors vs ERα positive MCF-7 and T47D cells [100]	ERα (L, W) [100]	ERα signaling
	100 nM 4-OHT, 100 nM fulvestrant, 6 h, 2 d, TAM-sensitive MCF-7 vs TAM-resistant LY2 cells	4-OHT upregulates miR-221/222 in LY2 TAM-resistant cells and down regulates miR-221/222 in MCF-7 cells [105]	ERBB3, ERα (Q) [105]	ERα signaling/ GFR Cytoplasmic signaling

miR-301	300 nM 4-OHT, 24, 48, 72 h MCF-7, MDA-MB-231	Higher in MCF-7, T47D, MDA-MB-231, and MDA-MB-231 compared to MCF-7 10A. Higher expression in lymph node negative (LNN) invasive ductal breast cancer [126]	FOXF2, BBC3, PTEN, (L, W, Q), COL2A1 (L,Q) [126]	GFR Cytoplasmic signaling
miR-519a	0, 5, 10 µM 4-OHT, 3 h , 72 h TAM-R MCF-7 vs MCF-7, HEK 293FT, breast cancer patient datasets	Upregulated in TAM-resistant MCF-7 cells compared to TAM-sensitive MCF-7 cells [127]	CDKNIA, RB1 and PTEN (L, W, Q) [127]	Cell cycle
miR-1280	Patient blood samples	Higher in blood from patients with metastatic breast cancer after cytotoxic chemotherapy or undefined endocrine therapy [128]		
Putative oncosuppressor miRNAs based on experimental data				
Let-7b/Let-7i	TAM-R MCF-7, MCF-7, MDA-MB-231 Breast cancer tissues	Overexpression of Let-7b/Let-7i enhanced sensitivity of TAM-R MCF-7 cells to TAM only in hormonal withdrawal medium and not in normal growth medium [103]	ERα36 (L, W, Q) [103]	ERα signaling
Let-7i	5, 10, 15 and 20 µM 4-OHT, 48 h, ZR-75-1 cells	Overexpression of Let-71 increased TAM-sensitivity in ZR-75-1 cells		Apoptosis/cell survival signaling

		Inverse correlation of Let-7i and TNF receptor associated factor (TRAF)1 [129]		
miR-10a	Primary breast tumors	Higher expression in patient tumors was associated with longer relapse-free time. Increased expression predicted tumor relapse in TAM-treated ER+ postmenopausal breast cancer patients [130]		
miR-15a/16	100 pM E$_2$, 1 µM 4-OHT, 100 nM fulvestrant, E2+4-OHT, E2+ICI, for 24 h, 24 h, 72 h TAM-R MCF-7/HER2Δ16 vs MCF-7/HER2 cells [131]	Suppressed expression of miR-15a and miR-16 in HER2Δ16 mutant cells associated with inverse expression of BCL-2 protein and mRNA and decreased sensitivity to TAM and ICI [131]		Apoptosis/cell survival signaling
miR-30a-3p	Patient samples [132]	Increased expression in ER+ primary breast tumors of patients who received TAM and showed longer progression-free survival; Inverse correlation with HER2 and RAC1 cell motility signaling pathways [132]		
miR-126	Primary breast tumors	Higher expression in patient tumors was associated with longer relapse-free time. Increased expression		

		predicted tumor relapse in TAM-treated ER+ postmenopausal breast cancer patients [130]		
miR-200b/200c	100 nM 4-OHT, 100 nM fulvestrant, 6 h, 2 d, TAM-S MCF-7 vs TAM-R LY2 [133]	Decreases in TAM-resistant LCC1, LCC2, LCC9 and LY2 cells vs MCF-7 cells [133]	ZEB1/2 (W, Q) [133]	EMT
	100 nM 4-OHT, 100 nM ICI, 6 h, 2 d, TAM- sensitive MCF-7 vs TAM-resistant LY2	Increased in TAM-sensitive MCF-7 and decreased in TAM-resistant LY2 cells [105]	CYP1B1(Q) [105]	
miR-342-3p	24h 100 pM E_2, 1µM 4-OHT, E_2+4-OHT in TAM-R MCF-7/HER2Δ16, MCF-7/HER2, TAMR1, LCC2 cells, Breast tumors [134]	Downregulated in TAM-R MCF-7/HER2Δ16 cell, TAMR1, LCC2 cells and TAM refractory human breast tumors vs MCF-7 cells and TAM-S tumors. TXNIP is an indirect target of miR-342 [134]	BMP7, GEMIN4 (microarray, L, Q,) SEMAD(microarray, Q) [134]	GFR Cytoplasmic signaling
	Primary breast tumors 10 nM E_2, 20 µM 4-OHT, 72 h, MCF-7 vs SKBR-3 & MDA-MB-231 cells	Decreased in ERα (-) SKBR-3 and MDA-MB-231 cells vs MCF-7 cells. Direct correlation between miRNA-342 expression and ERα expression [101]		ERα signaling

miR-375	5 µM 4-OHT TAM- resistant MCF-7 cells vs TAM-sensitive MCF-7 cells	Lower in TAM-R MCF-7 vs MCF-7 cells [135]	MTDH (L, W, Q) [135]	EMT
miR-424-3p	0.001-10 µM anastrozole or letrozole; LET-R MCF-7 cells, ANA-R MCF-7 vs MCF-7aro Primary breast tumors	Downregulated in LET-RMCF-7 cells, ANA- R MCF-7 compared to MCF-7aro [119]		
miR-451	1 µM 4-OHT for 0 h, 4 h, 8 h 24h TAM-R MCF-7 vs TAM-S MCF-7 cells	Reduced levels in TAM-R vs TAM-S MCF-7 cells [136]	14-3-3ς (W, Q) [136]	GFR Cytoplasmic signaling
miR-574-3p	1µM 4-OHT, MCF-7 cells/ tissue sample	Lower in TAM-R MCF-7 cells and clinical breast cancer tissues compared to TAM-S MCF-7cells and adjacent normal control, respectively [137]	Clathrin heavy chain (CLTC) (L, W, Q) [137]	GFR Cytoplasmic signaling
miR-873	1, 10, 100 nM, 1, 5 µM 4-OHT, 7 d MCF-7/TAM-R vs MCF-7 cells and xenograft tumors	Downregulated in TAM-R MCF-7 and breast tumors compared to TAM-S and normal tissues, respectively.	cyclin-dependent kinase 3 (CDK3) (L, W, Q) [114]	Repressed ERα transcriptional activity [114].

Abbreviations: 4-hydroxytamoxifen (4-OHT); TAM-sensitive (TAM-S); TAM-resistant (TAM-R); letrozole-resistant (LET-R), Anastrozole-resistant (ANA-R); Fulvestrant-resistant (Ful-R). MCF-7aro cells are MCF-7 cells stably overexpressing aromatase

MICRORNA REGULATION OF ERα PATHWAYS IN BREAST CANCER

ERα interacts with other transcription factors, *e.g.,* AP-1, Sp-1, NF-κB, and forkhead transcription factor (FOXM1), to regulate gene expression [138-140]. Increased activity of these transcription factors is associated with endocrine resistance [64, 65, 141, 142]. FOXM1 is overexpressed in many cancers, including breast cancer, and its ectopic expression promotes cell invasiveness [142]. Repression of FOXM1 was associated with increased miR-211 [143] and miR-23a [144], and repressed breast cancer cell growth, migration and invasion in animal models.

Activation of NF-κB contributes to endocrine-resistance in breast cancer [145]. A genome-wide miRNA screen in HEK-293T cells identified 13 miRNAs regulating NF-κB transcriptional activity [145]. Subsequent studies in MDA-MB-231 TNBC cells demonstrated that miR-570 and miR-373 inhibited TGFα-activation of NF-κB-induced transcription of pro-inflammatory cytokines, *e.g.*, IL-6, IL-8, CXCL1 and ICAM-1, and TGF-β signaling by direct targeting of RELA and TGFBR2. The authors reported that transient overexpression of miR-520 or miR-373 inhibited TGF-β induced MDA-MB-231 cell invasion. While they did not detect miR-373 in human breast tumors, a correlation of higher miR-520c expression in ERα- tumors and lower *TGFBR2* transcript expression was observed, allowing the authors to suggest loss of miR-520 expression may play a role in ERα-tumor progression via altered NF-κB signaling [145].

The nuclear receptor coactivator proline glutamic acid leucine rich protein (PELP1) interacts with ERα [146] to modulate genomic [147] and nongenomic functions of ERα [148, 149]. As a proto-oncogene, PLEP1 is upregulated during breast cancer metastasis and promotes human breast tumor xenograft growth in nude mice [149-151]. In MCF-7 cells, cytoplasmic localization of PELP1 conferred resistance to TAM [149]. Although the mechanisms of PELP1 promotion of TAM resistance is not fully known, the binding of PELP to the proximal promoters of the oncosuppressors miR-200a and miR-141 recruited histone-deacetylase 2 (HDAC2) and repressed their transcription [152]. The attendant decrease in miR-200a and miR-141 was suggested to stimulate metastatic growth [153].

ERα coactivator nuclear receptor co-activator 3 (*NCOA3*, also known as SRC-3 [154] and AIB1 [155]) is overexpressed in 50% breast tumors [156]. Targeting SRC-3 is of clear clinical interest [157]. SRC-3 overexpression results in constitutive activation of ERα-mediated transcription, breast tumor growth, and resistance to TAM *in vivo* and in xenograft models [56, 158]. SRC-3 translation is repressed by miR-17-5p. Overexpression of miR-17-5p in MCF-7 cells repressed E_2-induced proliferation and endogenous cyclin D1 transcription [159]. MiR-195 negatively regulates SRC-3 in human hepatoma cells [160], but whether it does so in breast cancer is unknown.

ERα corepressors including nuclear receptor co-repressor 1 (NCoR1) influence gene transcription by recruiting HDAC complexes to promote chromatin condensation and repression of gene transcription [56, 161]. NCoR1 is reduced in TAM-resistant MCF-7 xenograft tumors grown in nude mice [161]. However, both NCoR and the corepressor SMRT stimulated 4-OHT-ERα agonist activity on an ERE-driven luciferase reporter in transiently transfected Rat-1 cells. Blockage of NCoR1 promoted the agonistic activity of TAM [161]. To our knowledge, there are no reports of miRNA regulation of NCoR1. However, inhibition of miRNA synthesis by knocking down

DICER in LNCaP prostate cancer cells increased NCoR1 transcription and likewise, NCoR1 increased in the prostate of DICER$^{-/-}$ mice [162]. Conversely ectopic expression of DICER mediates metastasis and TAM resistance in breast cancer cells [163].

MICRORNA ACTIVATION OF GROWTH FACTOR RECEPTOR SIGNALING

Endocrine resistant breast cancer cells and tumors show increased EGFR signaling [164]. Although trastuzimab is a targeted therapy widely used in patients whose breast tumors overexpress HER2, these patients also benefit from TAM [165]. Unfortunately, overexpression of an isoform of HER2, HER2Δ16, which is associated with metastasis [166], also promotes TAM resistance [131, 134]. Decreased expression of miR-15a, miR-16, and miR-342-3p contribute to endocrine resistance in TAM-resistant MCF-7/HER2Δ16 breast cancer cells [131, 134]. miR-342 was also downregulated in TAM-non-responsive breast tumors and HER2 negative, TAM-resistant TAMR1 and LCC2 cells [134]. Transient overexpression of miR-342 resensitized TAM-resistant MCF-7/HER2Δ16 and TAMR1 cells to TAM-induced apoptosis; decreased BMP7, GEMIN4, and SEMAD are proposed as direct miR-342 targets mediating this response. However, the role of these targets in directly promoting TAM resistance was not examined.

Decreased miR-451 also regulates mitogenic signaling to promote TAM resistance [136]. TAM, but not raloxifene or fulvestrant, downregulates miR-451 in TAM- resistant cells [136]. Downregulation of miR-451 was associated with upregulation of its target protein 14-3-3ζ, a scaffolding protein whose high expression is correlated with early time to disease recurrence in patients treated with TAM. Overexpression of miR-451 in MCF-7 cells decreased 14-3-3ζ and reduced activation of HER2, EFGR, and MAPK signaling, resulting in decreased cell proliferation and migration and increased apoptosis. In addition, overexpression of miR-451 restored the inhibitory effectiveness of SERMs in TAM-resistant cells.

Ujihira, *et al*. used a miRNA library screen to identify miRNAs associated with TAM sensitivity in MCF-7 cells [137]. The authors identified miR-105-2, miR-877, let-7f, miR-125a and miR-574-3p as “dropout” miRNAs that were downregulated in 4-OHT-treated compared to vehicle control-treated MCF-7 cells. Of these miRNAs, miR-574-3p was found to be downregulated in breast cancer tissue samples compared to adjacent normal tissue samples. Luciferase reporter assays and knockdown or overexpression of miR-574-3p identified clathrin heavy chain (CLTC) as a *bona fide* miR-574-3p target. Low *CLTC* transcript levels were correlated with better survival in breast cancer patients. This study outlines a new role of miR-574-3p in mediating TAM responses: however, whether upregulation of miR-574-3p will sensitize TAM-resistant cells to TAM remains to be determined.

Earlier, we discussed downregulation of ERα protein by increased miR-221/222 in endocrine-resistant breast cancer. Dysregulation of miR-221/222 was also reported to regulate multiple stages of RTK pathways to promote anti-endocrine resistance. *In vitro* analysis confirmed miR-221/222 was increased in endocrine resistant HER2 positive primary human breast cancer tissues compared to HER-2 negative tissue samples [104]. Overexpression of miR-221/222 made TAM-sensitive MCF-7 cells resistant to TAM and decreased protein expression of its known target p27. Overexpression of p27 enhanced

TAM-induced cell death in TAM-resistant MCF-7 cells [104]. The same lab reported that repression of miR-222 and miR-181b suppressed growth of TAM-resistant MCF-7 tumor xenografts in mice [121]. Reduced expression of tissue metalloproteinase inhibitor 3 (TIMP3), a common target of miR-221 /222/181b, in primary breast carcinomas was also reported to mediate TAM resistance by relieving repression of ADAM10 and AMAM17. ADAM10 and AMAM17 are critical for growth of TAM-resistant cells [121]. Ectopic expression of TIMP3 repressed growth of TAM-resistant cells and reduced phosphoMAPK- and EGF- induced phosphoAKT levels. Conversely, repression of TIMP3 in TAM-sensitive MCF-7 promoted phosphorylation of MAPK and AKT, and desensitized the cells to growth inhibition by TAM *in vitro* and *in vivo*. In another study, the same group showed that sensitivity to TAM upon inhibition of miR-221/222 was unique to ERα positive MCF-7 cells and not ERα-negative MDA-MB-231 cells, although TIMP3 was a miR-221/222 target in both cells [123].

By promoting cell growth, miR-221/222 also promotes resistance to fulvestrant [125]. Ectopic expression of miR-221/222 in TAM-resistant MCF7 and TAM-resistant BT474 cells increased β-catenin and relieved TGF-β-mediated growth inhibition. Inhibition of β-catenin decreased estrogen-independent growth in pre-miR-221/222-transfected MCF-7 cells [125]. The TGF-β signaling pathway was inhibited in letrozole-resistant, aromatase-stably transfected MCF-7 (T+LET R) breast cancer cells and miR-128a was upregulated in these cells [120]. miR-128a targeted and repressed TGF-βR1 (TGF-β receptor 1) protein expression in T+LET R cells compared to the parental MCF-7 cells stably transfected with aromatase (MCF-7aro). Repression of miR-128a re-sensitized T+LET R cells to TGF-β growth inhibition.

Loss of PTEN is associated with poor outcome in HER2+ breast tumors [167]. PTEN is downregulated by miR-101 [118]. Overexpression of miR-101 promotes MCF-7 cell growth and TAM resistance in estrogen-free growth medium but suppressed cell growth in E_2-containing medium [118]. TAM resistance was mediated by AKT activation and was independent of ERα expression. miR-101 repressed its target MAGI-2 (membrane associated guanylate kinase), a scaffolding protein required for PTEN activity, thus reducing PTEN activity leading to activation of AKT. *PTEN* is also a *bona fide* target of the oncomiR miR-301 [126]. Transient repression of miR-301 in MCF-7 cells decreased cell viability and sensitized cells to TAM [126].

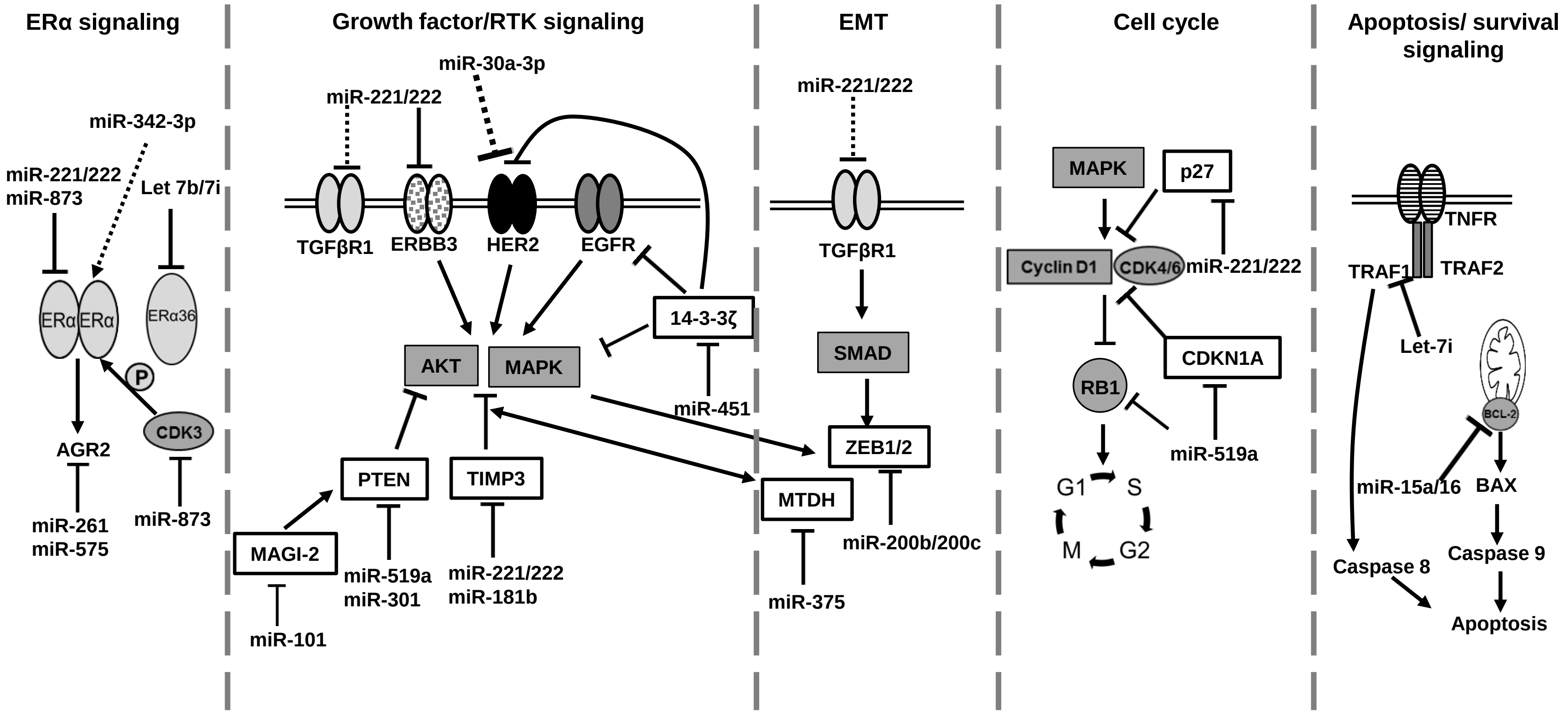
ERα signaling
Growth factor/RTK signaling
EMT
Cell cycle
Apoptosis/ survival signaling
miR-342-3p
miR-221/222
miR-873
Let 7b/7i
ERα
ERα
ERα36
P
CDK3
AGR2
miR-261
miR-575
miR-873
miR-30a-3p
miR-221/222
TGFβR1
ERBB3
HER2
EGFR
14-3-3ζ
miR-451
AKT
MAPK
PTEN
TIMP3
MAGI-2
miR-101
miR-519a
miR-301
miR-221/222
miR-181b
miR-221/222
TGFβR1
SMAD
ZEB1/2
MTDH
miR-375
miR-200b/200c
MAPK
p27
Cyclin D1
CDK4/6
miR-221/222
CDKN1A
RB1
miR-519a
G1
S
G2
M
TNFR
TRAF1
TRAF2
Let-7i
BCL-2
miR-15a/16
BAX
Caspase 8
Caspase 9
Apoptosis

Figure 2. Established targets of miRNAs in endocrine resistant breast cancer. miRNAs associated with ERα signaling, growth factor/RTK signaling, EMT, dysregulation of cell cycle kinetics, and apoptosis and their targets in these pathways involved in endocrine resistance are shown. The miRNAs and their targets are described in the text and summarized in Tables 1 and 2. The *bona fide* targets are indicated with solid black lines. The dotted arrows indicate observed correlations with unknown mechanisms

MICRORNAs AS CELL CYCLE REGULATORS

SERMs can be cytostatic and cytotoxic by promoting G1-phase cell cycle arrest [168]. miR-221/222 [104] and miR-519a [127] have been implicated in altering expression of molecular regulators of the cell cycle to promote endocrine resistance. miR-221/222 represses p27 to promote TAM resistance in breast cancer cells [104, 122].

Recently, miR-519a was reported as a novel oncomiR by increasing cell viability and cell cycle progression [127]. miR-519a was upregulated in TAM- resistant MCF-7 cells compared with TAM-sensitive MCF-7 cells. Elevated levels of miR-519a in primary breast tumors were associated with reduced disease-free survival in ERα+ breast cancer patients and miR-519a was suggested to contribute to TAM resistance. Knockdown of miR-519a in TAM-resistant MCF-7 cells sensitized the cells to TAM growth inhibition. Concordantly, overexpression of miR-519a in TAM-sensitive MCF-7 cells desensitized the cells to TAM by preventing growth inhibition while promoting caspase activity and apoptosis. Tumor suppressor genes (TSGs) involved in PI3K signaling CDKNIA (which encodes p21), RB1, and PTEN, were reported to be *bona fide* targets of miR-519a, although the role of these targets in mediating TAM-resistance have not been explored.

MICRORNAs IN EPITHELIAL-TO-MESENCHYMAL TRANSITION (EMT)

Changes involved in tumor progression include acquisition of migration/invasion, gain of front-rear polarity, resistance to anoikis, and mesenchymal transition [169]. Genetic changes that occur during EMT include but are not limited to activation of

SNAIL, increased Zinc-finger E-box-binding 1 (ZEB1), reduced E-cadherin, and increased vimentin and N-cadherin [170]. EMT is also implicated as a mechanism by which tumors enact resistance to TAM [171].

To identify miRNAs that mediate TAM resistance, we used a microarray to identify miRNAs differentially regulated between endocrine-sensitive MCF-7 cells and an endocrine-resistant MCF-7 variant LY2 cells, with selected results confirmed by qPCR [105]. Among these, miR-200a, miR-200b, and miR-200c were found to be downregulated in LY2 cells and other TAM-resistant breast cancer cell lines (LCC9) compared with parental TAM-sensitive MCF-7 cells [105, 133]. The decrease in miR-200 family expression was associated with increase in ZEB1. ZEB1 is an EMT-inducing transcription factor that represses E-cadherin [172]. Ectopic expression of miR-200b and/or miR-200c altered LY2 morphology to a more epithelial-like phenotype and inhibited cell migration. These phenotypic changes were associated with repression of the mesenchymal markers N-cadherin, vimentin, and ZEB1 and an increase in the epithelial marker E-cadherin. Further, upregulation of miR-200b/200c or ZEB1 knockdown sensitized LY2 cells to TAM- and fulvestrant-induced growth inhibition. However, overexpression of miR-200b/200c in MCF-7 cells did not promote resistance to TAM or fulvestrant, indicating that cellular changes in addition to downregulation of miR-200 family members are involved in TAM resistance in LY2 cells.

In another miRNA microarray study, miR-375 was found to be downregulated in a mesenchymal TAM-resistant MCF-7 cell line model [135]. Re-expression of this miR-375 sensitized TAM-resistant cells to TAM and reduced invasiveness by decreasing expression of mesenchymal markers fibronectin, ZEB1, and SNAI2 while increasing the epithelial markers E-cadherin and ZO-1. This resulted in partial reversal of EMT called MET (mesenchymal-to-epithelial transformation). Metadherin (MTDH), a cell surface protein upregulated in breast tumors that mediates metastasis [173], was identified as a direct, *bona fide* miR-375 target mediating this response. TAM- treated patients whose primary tumor presented with high MTDH showed shorter-disease-free survival and a higher risk of relapse. This study exemplifies the role of miRNAs in mediating cellular transformations that foster tumor progression and TAM resistance.

EMT allows the emergence of cancer stem cells (CSCs) that have properties including self-renewal potential and tumorigenicity [135, 174]. Mammosphere culture is widely utilized to enrich the population of mammary epithelial stem cells and breast CSCs *in vitro* [175, 176]. Mammosphere culture of MCF-7 cells (MCF-7_M cells) resulted in permanent EMT with increased miR-221/222 and loss of their target ERα mRNA expression [124]. MCF-7_M cells were also characterized by downregulation of epithelial-associated tumor suppressor miRNAs including miR-200c, miR-203 and miR-205. MCF-7_M cells were resistant to TAM-induced cell death. These data reinforce other studies discussed above demonstrating a role for increased expression of miR-221/222 in driving TAM-resistance.

MICRORNAs AS REGULATORS OF APOPTOSIS/CELL SURVIVAL SIGNALING

Tumor growth reflects a balance between cell growth and cell death. Endocrine inhibitors activate apoptotic and stress signals to inhibit breast cancer cell growth [42, 60, 177]. However, the molecular mechanisms behind these observations are yet to be fully defined. Activation of antiapoptotic proteins such as BCL-2, crosstalk between apoptotic effects of antiestrogens and the TNF-α pathway, and promotion of survival signals including PI3K-AKT and NF-κB have been documented to promote resistance endocrine therapy [42]. MiRNAs can directly target antiapoptotic transcripts or regulate mediators of the survival signaling pathways. For example, low miR-15a/16 expression correlated with upregulation of BCL-2 in TAM- and fulvestrant- treated TAM-resistant MCF-7/HER2Δ16 cells and xenograft tumor promotion *in vivo* [131]. RNAi targeting of BCL-2 or reintroduction of miR-15a/16 decreased TAM-induced BCL-2 expression in TAM-resistant MCF-7/HER2Δ16 cells resulting in TAM-induced decrease in cell growth and promotion of apoptosis. Conversely, repression of miR-15a/16 in TAM-sensitive MCF-7/vector or MCF-7/HER2 increased BCL-2 expression and promoted resistance to TAM by inhibiting apoptosis and preventing growth inhibition.

To identify potentially ethnic group-specific TAM sensitivity biomarkers, Weng *et al*. performed an integrative genomic analysis on 58 African-derived HapMap YRI lymphoblastoid cell lines (YRI LCLs; breast cancer cells) [178]. Genetic variants (including 50 SNPs with effects on 34 genes and 30 miRNAs) were identified to be sensitive to endoxifen, an active metabolite of TAM. Among the genes identified, increased TNF receptor-associated factor 1 (TRAF1) and decreased let-7i expression correlated with endoxifen resistance in 44 YRI LCLs. TRAFs are intracellular signal transducers for death receptor superfamily TNF receptor (TNFR) [178]. TRAF1 associates with TRAF2 to form a protein complex that interacts with inhibitor-of-apoptosis protein (IAP) to mediate anti-apoptotic signals (MAPK8/JNK and NF-κB) from the TNF receptor [179, 180]. Repression of TRAF1 or overexpression of let-7i in ZR-75-1 luminal breast cancer cells enhanced sensitivity to TAM and decreased the number of viable cells. These data show that by regulating death signals, miRNAs can also mediate response to antiestrogens.

EXTRACELLULAR VESICULAR (EXOSOME) TRANSPORT OF MICRORNAs

Extracellular vesicles (EVs), produced by outward budding of the PM, contain proteins and nucleic acids that can be transported in blood between tissues and cells [181, 182]. The contents of EVs can facilitate tumor growth including angiogenesis, invasion, metastasis, and immune suppression. They also play a role in reducing effectiveness of drugs [183]. Exosomes are smaller EVs of endosomal origin and formed by the fusion of multivesicular bodies with PMs [184, 185]. Exosomes transport miRNAs in circulation. Mechanisms of exosomal formation and delivery are cell-specific and display proteins from their tissue of origin and are specific to the target cells [186-188]. It was initially reported that miRNAs were randomly packaged into exosomes with no specific miRNA preferentially incorporated [189, 190]. Studies now indicate different miRNAs are associated with specific customized exosomes [191]. However, the selection mechanism for incorporating miRNAs into exosomes is yet to be elucidated.

EVs or exosomal delivery of miRNAs is thought to play roles in breast tumorigenesis and metastasis (Table 2). Cell culture studies showed that exosomes secreted by TAM-sensitive MCF-7 cells were larger in size and number compared to TAM-resistant MCF-7 cells [122]. This study showed that miR-221/222 released in

TAM-resistant exosomes were taken up by TAM-sensitive MCF-7 cells resulting in reduction of their target genes p27 and ERα, and enhanced TAM resistance. Transfection of a miR-221/222 inhibitor in MCF-7 cells treated with TAM-resistant MCF-7 exosomes reduced TAM-resistance. These data again support the importance of miR-221/222 in TAM resistance in MCF-7 cells. The potential use of exosomal miRNAs as candidate biomarkers for cancer diagnosis and prognosis remains to be definitively proven. The manipulation of exosomal miRNAs suggest a new therapeutic approach for drug delivery, but requires further research.

Table 2: Exosomal miRNAs described in breast cancer

↑ Increased expression; ↓ Reduced expression. Method of identification of targets: 3'-UTR luciferase reporter assay (L), downregulation of protein shown by western blot (W), and downregulation of target in quantitative real-time PCR assay (Q)

Extravesicular (EV) miRNA composition	**Direction of miRNA expression**	**Sample source**			**Time in culture prior to harvesting exosome**	**comments**	**Targets analyzed in study**	**Reference**
		Cell line	**Patient**	**Xenograft**				
miR-21, let-7a, miR-100, miR-125b, miR-720, miR-1274a, and miR-1274b miR-205	↑ ↓	MCF-7 MCF10A	No	No	72 h			[192]
miR-10a, miR155, miR-373, miR-10b, miR-21, miR-27a	↑	MCF-7 MCF-10A NMuMG MDA-MB-231	Yes	Yes	24 h 72 h	OncomiRs miR-10b and miR-21 confirmed by northern blot.		[193]

miR-10b and miR-10a, miR-218, miR10a, miR-99a, miR-142-3p; miR-32, miR-138, miR-7e, miR-106b	↑	MCF-7 MDA-MB-231 MCF-10A HMLE HEK-293T	No	No	48 h	OncomiR	HOXD10 and KLF4 (L, W; targets for miR-10b)	[194]
miR-140 miR-29a, and miR-21	↓ ↑	MCF-10DCIS MCF-7 MDA-MB-231 HEK-293T	No	No	3 d			[195]
miR-373, miR-101, and miR-372	↑	MCF-7	Yes (Serum)	No	Serum used	High in TNBC; Over-expression of miR-373 promotes loss of ER and resistance to Camptothecin		[196]

miR-221/222	↑	MCF-7 TAM-R/MCF-7	No	No	72 h	Exosomal transport may be an additional mechanism by which miR-221/222 promote TAM-R	P27 (Q, W), ERα (Q, W)	[122]
miR-23a, miR1246	↑	MCF-7 MCF-7/Doc	No	No	12 h 24 h	May contribute to Cisplatin resistance		[197]
miR-100, miR-17, miR-222, miR-342-3p,miR-451 and miR-30a	↑	MCF-7 MCF-7/Adr MCF-7/Doc	No	No	72 h		PTEN (Q; target for miR-222)	[198]
let-7a, miR-328, miR-130a, miR-149, miR-602, and miR-92b miR-198	↑ ↓	MCF-7, MDA-MB-231	No	No				[199]

miR-16	↑	MSCs 4T1 SVEC	No	No	48 h		VEGF (Q)	[200]
miR-16, miR-720, miR-451, miR-1246	↑	MCF-7 MDA-MB-231	No	No	5 d			[191]
miR-451, miR-1246	↑	MCF-7 MDA-MB-231 SKBR3 BT-20	No	No	5 d			[201]
miR-223	↑	Macrophages SKBR3 MDA-MB-231	No	No	24 to 48 h	Released by macrophages and promotes breast cancer cell invasion	Mef2c (L,W)	[202]

miR-210	↑	MCF7	No	No	48 h	Released in response to hypoxia		[203]

Abbreviations: Adriamycin (Adr), Docetaxel (Doc), Mesenchymal stem cells (MSCs), Mouse breast cancer cell line (4T1), mouse endothelial cell line (SVEC), nontumorigenic mouse mammary epithelial cells (NMuMG), human mammary epithelial (HMLE) cell line, MCF-10 ductal carcinoma *in situ* cells (MCF-10DCIS).

MICRORNAs OF UNKNOWN FUNCTION IN ENDOCRINE-RESISTANT BREAST CANCER

Other microRNAs identified by microarray or library screen and confirmed by qPCR to promote antiestrogen resistance in breast cancers, but having undetermined functional roles include: miR-10a, miR-21, miR-22, miR-29a, miR-181a, miR-125b, miR-205 which mediate resistance to TAM [105]; and miR-125a and miR-877 which also mediate TAM resistance [137] Other miRNAs identified by integrative analysis to make up network clusters that contribute to antiestrogen resistance include: miR-146a, miR-27a, miR-145, miR-21, miR-155, miR-125b, and let-7s [204].

ROLES OF DROSHA, DICER, AND AGO2 IN ENDOCRINE-RESISTANT BREAST CANCER

As described earlier in this review, Drosha and DICER function in miRNA processing. The role of Drosha in endocrine resistance has not been ascertained, despite the observation that reduced cytoplasmic Drosha is predictive of better endocrine therapy response [205]. Loss of DICER is predictive of a better response to endocrine therapy [206]. Elevated DICER was associated with TAM resistance in metastatic breast tumors and tumor xenografts [163]. DICER-overexpressing cells were enriched with the breast cancer resistance protein (BCRP), a member of the ATP-binding cassette (ABC) transporter superfamily that causes resistance to several chemotherapeutic agents [207]. Increased BCRP resulted in a more efficient efflux of TAM in DICER-overexpressing cells compared to control cells. Inhibition of BCRP inhibited TAM efflux and restored

TAM sensitivity in DICER-overexpressing cells. In ERα negative breast cancer cells, DICER is targeted by oncogenic miRNAs including miR-103/107 [208], let-7, miR-222/221, and miR-29a [209]. Whether repression of DICER by these miRNAs mediates endocrine resistance is yet to be determined.

AGO2 recruits mRNA and miRNA into the RISC complex and is the catalytic component of the RISC complex. AGO2 is elevated in ERα negative compared to ERα positive breast cancer cell lines and tumors [210]. Expression of AGO2 is mediated by ERα/estrogen signaling and epidermal growth factor (EGFR)/ mitogen-activated protein kinase (MAPK) signaling pathways [210]. Ectopic expression of full length AGO2 in MCF-7 cells promoted cell proliferation, reduced cell-cell adhesion, and increased cell migration [210]. Whether AGO2 plays a role in endocrine resistance is yet to be determined.

We examined the association of AGO2 expression and overall survival rate in breast cancer patients using the online survival analysis tool, Kaplan–Meier Plotter (http://kmplot.com/backup/breast) [211]. It assesses the association of gene expression on breast cancer prognosis using microarray data from 3554 patients. The patient data are from GEO. Higher AGO2 expression correlates with reduced relapse-free survival in all breast cancer patients and those whose primary tumors are ER+/PR+ (Fig. 3).

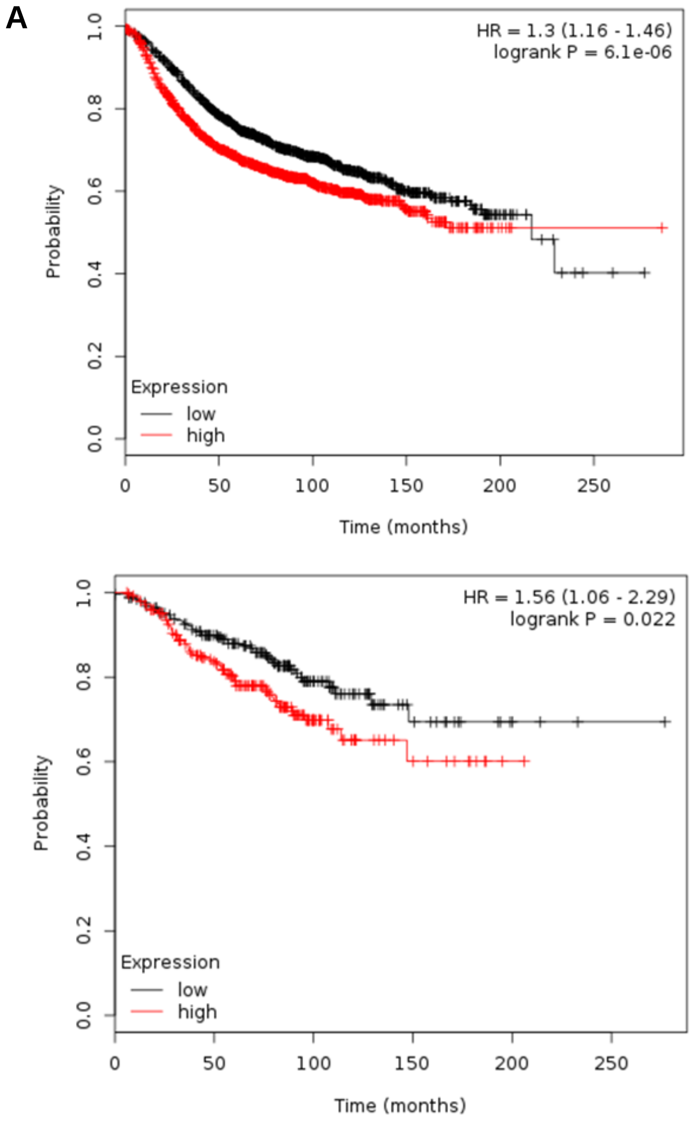

Figure 3. Higher expression of AGO2 is statistically associated with decreased relapse-free survival in all breast cancer and in patients whose primary tumors are ERα+/PR+.

The Kaplan-Meier plots of AGO2 expression in breast tumors with breast cancer survival were generated using http://kmplot.com/analysis/index.php?p=service [212]. A) All breast tumors, n = 3557; B) ERα+/PR+, n = 701.

CONCLUSIONS

miRNAs are dysregulated in endocrine-resistant breast cancer and these miRNAs regulate specific genes in growth-promoting, apoptosis-resistant, and EMT pathways that result in TAM- and AI- resistance (Tables 1 and 2). The involvement of exosomes containing miRNAs in mediating endocrine resistance provides a new target for biomarker identification and therapeutic intervention to block metastatic spread. Although identifying new miRNAs mediating endocrine resistance is important, research effort is needed to determine the mechanisms and functional roles of already identified miRNAs with unknown roles in endocrine resistance and to develop “targeted” therapeutics to counter miRNA dysregulation and enhance hormonal sensitivity.

DISSERTATION HYPOTHESIS AND SPECIFIC AIMS

Despite initial sensitivity to TAM and other antiestrogens, ~40-50% of patients develop acquired endocrine resistance, relapse, and eventually die from their disease [56, 213]. These observations underscore a need to identify and target mechanisms promoting endocrine-resistance of ERα+ breast cancers.

Previous microarray analysis identified [105] and quantitative real time PCR (qPCR) confirmed microRNAs (miR) miR-29b-1 and miR-29a to be downregulated in estrogen/tamoxifen sensitive (TAM-S) MCF-7 and upregulated in estrogen-independent/TAM resistant (TAM-R) LCC2, LCC9, and LY2 human breast cancer cells treated with 4-hydoxytamoxifen (4-OHT, a bioactive TAM metabolite). miR-29b-1/a are encoded by a single primary miR (pri-miR) transcript and share a promoter. Depending on the cell type, miR-29b-1/a serve as oncosuppressor miRNAs or oncomiRs. For example, miR-29b-1 upregulation in a triple negative breast cancer (TNBC) cell line increased cell migration and invasion [214]. However, the role of miR-29b-1/a in endocrine-resistant breast cancer is unknown. The research performed here tested the hypothesis that miR- 29b-1/a promotes TAM-resistance by recruiting ERα to its promoter to stimulate its transcription, consequently resulting in downregulation of miR-29b-1/a specific targets that mediate TAM responses.

SPECIFIC AIM 1: Determine the role of ERα in modulating miR-29b-1/a expression in response to tamoxifen in TAM-S MCF-7 cells and TAM-R LCC9 cells. ERα regulates cell proliferation and survival by binding estrogen response elements (EREs) in the promoter or enhancer regions of target genes [92]. I hypothesized that ERα normally regulates miR-29b-1/a expression and that 4-OHT treatment alters ERα occupancy at the miR-29b-1/a promoter. Experiments examined whether ERα knockdown and/or overexpression modulate miR-29b-1/a transcription in 4-OHT- treated cells.

SPECIFIC AIM 2: Determine if upregulation of miR-29b-1/a in endocrine sensitive and knockdown of miR-29b-1/a in endocrine-resistant breast cancer cells alters cellular responses to antiestrogens *in vitro*. The role of miRNAs, including miR-29b-1/a, in acquired endocrine resistant breast cancer was unknown. I hypothesized that the opposite regulation of miR-29b-1/a in TAM-S MCF-7 and TAM-R LCC9 and LY2 cells in response to 4-OHT corresponds to functional outcomes that promote TAM-resistance and cell migration, invasion, and hence disease dissemination. Experiments examined whether overexpression of miR-29b-1/a in MCF-7 cells or knockdown of miR-29b-1/a in LCC9 and LY2 cells have functional outcomes on cell proliferation, migration and colony formation, and whether blocking 4-OHT-induced miR-29b-1/a upregulation in TAM-R cells sensitizes the cells to 4-OHT.

SPECIFIC AIM 3: Identify miR-29b-1/a targets differentially regulated in response to tamoxifen in TAM-S MCF-7 and TAM-R LCC9 cells. Differential regulation of miRNAs and concomitant inverse expression of their target genes are reported in several cancers [215, 216]. However, the identity of miR-29b-1/a target genes specifically found in TAM-resistant breast cancer were unknown. I hypothesized that changes in miR-29b-1/a expression were associated with inverse changes in target gene expression. To identify miR-29b-1/a targets specific to TAM-R breast cancer cells, RNA sequencing (RNA-Seq) was performed in MCF-7 and LCC9 cells transfected with pre-miR-b-1/a and anti-miR-29a. Selected targets were verified by qPCR. Luciferase reporter assays was used to ascertain the authenticity of mRNAs directly regulated by miR29b-1/a while bioinformatics analysis was used examine signaling pathways regulated by identified mRNA targets.

CHAPTER III: TAMOXIFEN DIFFERENTIALLY REGULATES MIR-29B-1 AND MIR-29A EXPESSION DEPENDING ON ENDOCRINE-SENSITIVITY IN BREAST CANCER[2]

INTRODUCTION

Breast cancer is the second leading cause of cancer-related deaths in women in the US [3]. Seventy percent of breast tumors express estrogen receptor α (ERα) [56, 217], making these patients eligible for endocrine therapies including aromatase inhibitors (AIs), *e.g.*, letrozole, and selective estrogen receptor modulators (SERMs), *e.g.*, tamoxifen (TAM). Unfortunately ~40% of patients initially responsive to endocrine therapies acquire resistance to TAM or AI therapy [55]. The selective estrogen receptor down regulator (SERD) fulvestrant (ICI 182 780) is used for the treatment of patients who relapse on AIs or TAM [50, 51, 53, 218]. New clinical studies show that patients treated with AIs who have metastatic tumors with ERα ligand binding domain mutations show increased disease-free and overall survival with fulvestrant treatment [219]. These and other data implicate ERα as an important target in endocrine resistance. While still not completely understood, a variety of mechanisms play a role in endocrine resistance including increases in coactivators SRC-1 (NCOA1) and/or SRC-3 (NCOA3), activation of receptor tyrosine kinases (TRKs, *e.g.*, epidermal growth factor receptor (EGFR)) that crosstalk with ERα, and deregulation of apoptotic or cell survival signals [56, 59, 220].

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[2] The text of this chapter was published in Can. Lett. 2017 388: 230-238. doi: 10.1016/j.canlet.2016.12.007

MicroRNAs are 22 nucleotide (nt) noncoding RNA molecules that bind to the 3'-UTR region of target mRNAs to cause mRNA degradation or translational repression [221, 222]. microRNAs are dysregulated in breast tumors resulting in aberrant expression of target proteins involved in cellular processes including proliferation, apoptosis, and migration. A number of microRNAs play a role in mediating endocrine resistance (reviewed in [218, 220]); however, it is likely that additional microRNAs contribute to the emergence of endocrine-resistance. Previously we used microarray analysis to identify microRNAs that are differentially regulated between estradiol (E_2)- and TAM-sensitive MCF-7 and endocrine-resistant LY2 human breast cells that were derived by long-term incubation of MCF-7 cells with a precursor to raloxifene and which are cross-resistant resistant to TAM and fulvestrant [223, 224]. Several microRNAs, including miR-29b-1 and miR-29a, were identified to be differentially regulated by 4-hydroxytamoxifen (4-OHT, the active metabolite of TAM) between MCF-7 and LY2 cells. However, the role of miR-29b-1/a in breast cancer remains unclear and the relationship between increased miR-29b-1 and miR-29a in 4-OHT-treated LY2 cells and TAM resistance is unknown.

The miR-29 family includes 4 members encoded at two genomic sites. miR-29b-2 and miR-29c are encoded on chromosome 1q32.2 separated by 502 base pairs (bp) with miR-29b-2 upstream of miR-29c [225, 226]. miR-29b-1 and miR-29a are located on chromosome 7q32.3, separated by 652 bp, with miR-29b-1 upstream of miR-29a [227-229]. Each pair (miR-29b-2/c and miR-29b-1/a) is postulated to share a promoter and be transcribed as a single primary-microRNA, *i.e.*, pri-miR-29b-2/c and pri-miR-29b-1/a. All four miR-29s have the same seed sequence [226]. Interestingly, miR-29 family members have higher expression in Luminal A and B breast tumors compared with basal and HER2+ tumors [230].

Both oncogenic and tumor suppressive roles have been ascribed to miR-29 in breast cancer progression (summarized in SupplementaryTable1) [231-233]. Forced overexpression of miR-29b and miR-29a promoted an epithelial-to-mesenchymal transition (EMT) in MCF-7 and T47D cells while miR-29a repression reduced invasiveness of MDA-MB-231 triple negative breast cancer (TNBC) cells [234]. However, other studies indicate that miR-29a and miR-29b act as oncosuppressors in breast cancer cells by repressing cell proliferation, differentiation, and metastasis [230, 235, 236]. These conflicting studies underscore the need to further elucidate the role of miR-29b-1/a in breast cancer.

In the current study, we confirmed the opposing regulation of miR-29b-1 and miR-29a transcription by 4-OHT seen in the original microarray studies in MCF-7 and LY2 cells [223] using quantitative realtime PCR (qPCR). We examined the mechanism for this opposite regulation by 4-OHT in these cells and in additional TAM- and fulvestrant-resistant cell lines derived from MCF-7 cells: LCC2 and LCC9. Transient overexpression of miR-29b-1 and miR-29a decreased cell proliferation in all 3 cell lines and inhibited migration and colony formation of LY2 cells. Inhibition of miR-29b-1/a did not sensitize TAM-resistant LCC9 or LY2 cells to TAM. The increase in miR-29b-1/a in LY2 cells was associated with decreased protein expression of DICER, a *bone fide* target of miR-29b-1/a. Knockdown of miR-29b-1/a blocked 4-OHT mediated repression of DICER. Our results suggest that miR-29b-1/a do not appear to play a role in acquired tamoxifen-resistance in breast cancer cells.

MATERIALS AND METHODS

Cell culture/treatments

MCF-7 (purchased from American Type Culture Collection (ATTC, Manassas, VA, USA), LCC2, LCC9 and LY2 (provided by Robert Clarke, Georgetown University) [224, 237, 238] cells were grown in phenol red IMEM supplemented with 5% fetal bovine serum (FBS, Atlanta Biologicals, Lawrenceville, GA, USA) and 1% penicillin/streptomycin (Invitrogen, Carlsbad, CA, USA). These cells represent a model of progression to endocrine/TAM- resistance [239]. For the experiments described here, cells were grown in hormone depleted medium: phenol red-free IMEM supplemented with 5% dextran-coated charcoal-stripped fetal bovine serum(DCC-FBS, Atlanta Biologicals, Lawrenceville, GA, USA) for 48 h prior to experiments to reduce basal hormone-related activities [240]. Where indicated, cells were pretreated with 10 μg/ml actinomycin D (ACTD, a transcriptional inhibitor, Sigma, St. Louis, MO, USA) or 100 nM fulvestrant (ICI 182,780; Tocris, Ellisville, MO, USA) for 6 h prior to treatment. Treatments included vehicle control (ethanol (EtOH) or DMSO) or 100 nM 4-hydroxytamoxifen, (4-OHT; Sigma St Louis, MO, USA).

Transfection

MCF-7, LCC9, and LY2 cells were transiently transfected for 48 h with miR-29b-1/a inhibitor (Anti-miR^{TM}s, Ambion, Austin, TX, USA), siERα (Silencer$^{®}$, Ambion), pre-miR-29b-1/a precursor (Pre-miR^{TM}s, Ambion), using Lipofectamine RNAiMAX (Invitrogen, Carlsbad, CA, USA) and Opti-MEM® Reduced Serum Medium (Invitrogen, Carlsbad, CA). Negative controls were Anti-miR ™ negative control #1 (Ambion), Pre-miR™ negative control #1 (Ambion), or Negative Control #1 (Silencer®, Ambion). Treatments were performed following transfections.

Quantitative real-time PCR (qRT-PCR)

RNA was isolated using the miRCURY RNA isolation kit (Exiqon, Vedbaek, Denmark) according to manufacturer's instructions. RNA concentration and quality was assessed using a NanoDrop spectrophotometer (Thermo Scientific, Rockford, IL, USA). The TaqMan® MicroRNA Reverse Transcription Kit (Applied Biosystems) and the High Capacity cDNA Reverse Transcription kit for RNA (PE Applied Biosystems, Carlsbad, CA, USA) were used to make cDNA for microRNA and mRNA respectively. Quantitative real-time PCR (qPCR) for pri-miR-29b-1/a, miR-29b-1/a, (Applied Biosystems) and *DICER1* [241] (IDT), was performed using TaqMan (Applied Biosystems/Life Technologies) or SYBR green (QIAGEN). Normalizers included *RNU6B*, *RNU48* or *RNU38, PPIA*, *18S* rRNA (Applied Biosystems) or *GAPDH* (SYBR green). qPCR was performed in the ABI Viia 7 (LifeTechnologies) with each reaction run in triplicate. Fold change was determined using the comparative threshold cycle (Ct) method relative to vehicle control [242].

Luciferase assay

To examine ERα regulation of miR-29b-1/a promoter, CHO-K1 cells were transiently transfected in triplicate in 24 well plates with pGL3 -1530/+165 miR-29b-1/miR-29a promoter fragment [227] and pGL4-hRluc-TK (*Renilla*, Promega, Madison, WI, USA) using FuGENE HD (Roche, Indianapolis, IN, USA) for 48 h as per the manufacturer's protocol. 18 h post transfection, cells were either not pre-treated or pre-treated for 6 h and then treated for 24 h prior to performing dual luciferase assay (Promega). Relative expression was determined by dividing averaged values from DMSO treated values.

Cell proliferation (BrdU), colony formation, and migration (wound healing) assays

MCF-7, LCC9 and LY2 cells were placed in hormone-depleted medium and transfected with precursor microRNA or anti-miR transcripts or 48 h and the following assays performed: For <u>BrdU assays</u>, cells were treated with 100 nM 4-OHT for 48 h and cell proliferation quantified using BrdU ELISA assay (Roche). For <u>colony formation</u>, following transfection, LY2 cells were counted and transferred to agarose plates and allowed to grow for 14 days to form colonies. Colonies were stained with crystal violet (0.005% w/v, Sigma) and counted using an inverted Nikon microscope (x10 objective). For <u>cell migration assays</u>, LY2 cells grown in hormonally depleted medium and transfected in six well plates for 24 h. Cells were wounded by scratching with a p20 pipette tip, and treated with 100 nM 4-OHT for up to 8 h. Images were captured at each time point at 4X magnification using an EVOS microscope (Thermo Fisher

Scientific Waltham, MA, USA). NIH Image J software (http://imagej.nih.gov/ij/) was used to analyze percent wound area.

Western blot

Whole cell extracts (WCE) were prepared in RIPA buffer (Sigma) with added phosphatase and complete protease inhibitors (Roche). Protein concentration was determined using the Bio-Rad DC protein assay (Bio-Rad). Where indicated, 10 or 15 μg of protein was boiled for 5 min, electrophoresed on 10% SDS-PAGE gels and electroblotted on PVDF membranes (Bio-Rad) for western blotting with the following antibodies: ERα (G-20, Santa Cruz Biotechnology, Santa Cruz, CA, USA), DICER1, PTEN (Cell Signaling, Danvers, MA, USA) and β-actin (loading control; Sigma). Bands were visualized using Carestream Image Station 4000R PRO with Carestream Molecular Imaging Software Version 5.0.2.30 (Carestream Health, Inc., New Haven, CT, USA) and quantified by UN-SCAN-IT Graph Digitizer Software 7.1 (Silk Scientific, Orem, UT, USA). The values were normalized to loading control and the normalized values for vehicle-treated and/or control-transfected cells were set to 1 for comparison within each cell line.

Statistical analysis

Statistical evaluations were performed using Student's t-test or one-way ANOVA followed by Tukey test in GraphPad Prism (La Jolla, CA, USA).

RESULTS

4-OHT reduces expression of miR-29b-1/a in TAM-sensitive (TAM-S) MCF-7 cell and increases miR-29b-1/a expression in TAM-resistant (TAM-R) LCC2, LCC9 and LY2 human breast cancer cells

Our previous microarray analysis of microRNA expression revealed that 4-OHT reduced expression of miR-29b-1 and miR-29a in endocrine sensitive MCF-7 breast cancer cells and increased expression in endocrine resistant LY2 cells [223]. As a follow up on these initial observations, qPCR was performed to examine the effect of 4-OHT on miR-29b-1 and miR-29a expression in MCF-7 cells and a panel of MCF-7-derived cells lines showing progressive resistance to TAM and fulvestrant: LCC2, LCC9 and LY2 cells [224, 237]. For these experiments, cells were grown in hormone-depleted medium *i.e.*, incubated with phenol-red free IMEM + 5% DCC-stripped FBS + 1% P/S, for 48 h to reduce basal hormone-related activities [240] and then treated with 100 nM 4-OHT for 6 h. Confirming the microarray data [223], 4-OHT decreased the expression of miR-29b-1 and miR-29a in MCF-7 cells, but increased miR-29b-1 and miR-29a expression in the three endocrine-resistant cell lines: LCC2, LCC9 and LY2 cells (Fig. 4A). miR-29b-1/a-3p expression levels were higher than miR-29b-1/a-5p expression levels (Supplementary Fig. 1). Thus, we examined miR-29b-1-3p and miR-29a-3p in all subsequent experiments.

miR-29b-1 and miR-29a are transcribed from a common promoter as a single primary transcript [227]. Pri-miR-29b-1 and pri-miR-29a expression was reduced by 4-OHT in MCF-7 cells and increased by 4-OHT in LCC2 and LCC9 cells (Fig. 4B). These data suggest 4-OHT regulates pri-miR-29b-1/a transcription.

To examine if the 4-OHT regulation of miR-29b-1/a expression was mediated at the level of transcription, cells were preincubated with the transcriptional inhibitor actinomycin D (ACT D; Fig. 4C and D). While ACT D inhibited basal expression of miR-29b-1 and miR-29a in all cells (data not shown), ACT D further inhibited miR-29b-1 and miR-29a expression in 4-OHT-treated MCF-7 cells. Also, ACT D inhibited the 4-OHT-induced miR-29b-1 (Fig. 4C) and miR-29a (Fig. 4D) expression in LCC9 and LY2 cells, suggesting a primary transcriptional response.

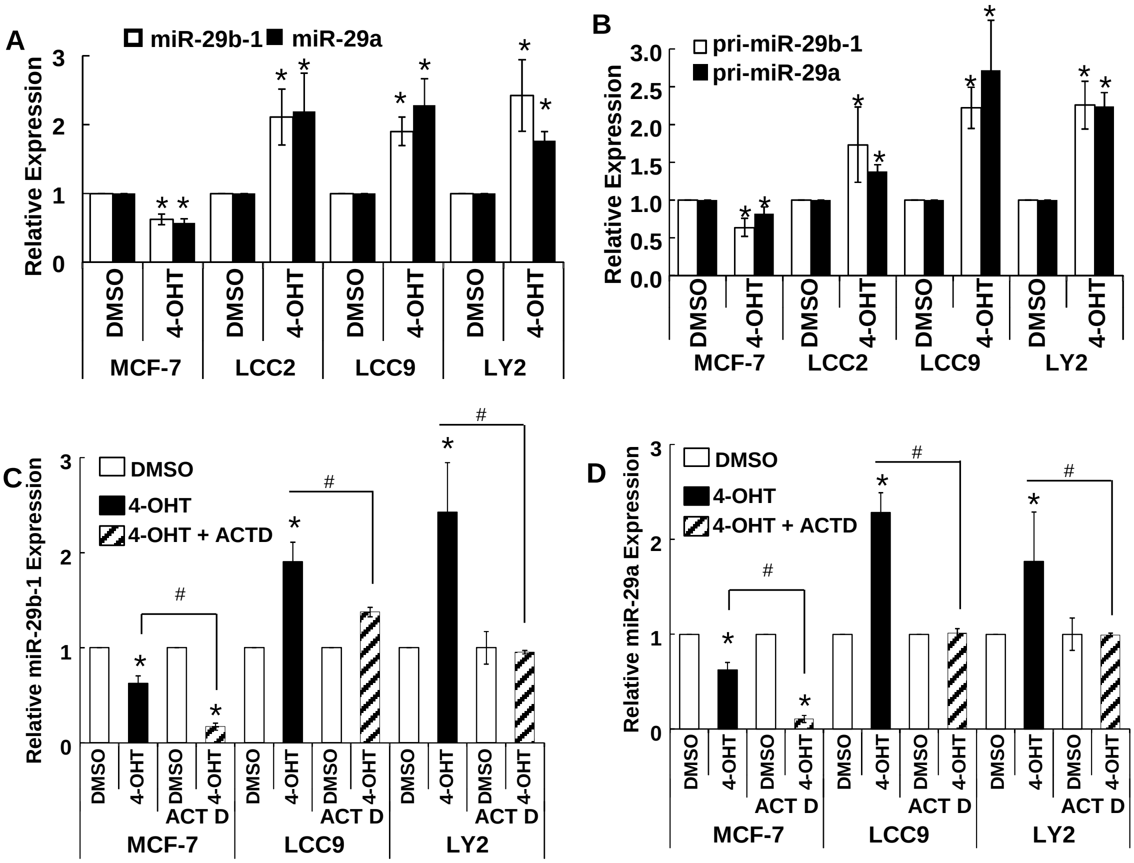


Figure 4. Differential regulation of miR-29b-1/a expression by 4-OHT in MCF-7, LCC2, LCC9, and LY2 breast cancer cells.

Cells were grown in hormonally depleted medium for 48 h and treated with vehicle control (DMSO) or 100 nM 4-OHT for 6 h. A, C, and D) miR-29b-1 and miR-29a expression was normalized to *RNU38* or *RNU48*. B) pri-miR-29b-1 and pri-miR-29a expression was normalized to *GAPDH*. C and D) Cells were pre-incubated with 10 µg/ml actinomycin D (ActD) for 1 h prior to 6 h treatment. Values are the average of 4-20 (A), 3-9 (B), and 3 (C, D) separate experiments ± SEM. *p < 0.05 *versus* control; #p<0.05 *versus* 4-OHT in the same cell line.

ERα mediates 4-OHT regulation of miR-29b-1/a transcription

The observed 4-OHT regulation of miR-29b-1/a transcription in these ERα+ breast cancer cells suggests a possible role of ERα, and/or ERβ, in mediating these effects. MCF-7 and LCC9 cells have higher ERα than ERβ and higher ERα protein levels than LY2 [239]. To evaluate ERα's role in mediating 4-OHT-regulation of miR-29b-1/a expression, MCF-7 and LCC9 cells were transfected with siERα or siControl. siERα reduced ERα protein levels by ~ 70% in MCF-7 and ~90% in LCC9 cells, respectively (Fig. 5A). *ESR1* mRNA levels were decreased by siERα in both cell lines (Fig. 5B). ERα knockdown had no significant effect on basal pri-miR-29b-1/a expression in MCF-7 or LCC9 cells (Fig. 5C). ERα knockdown inhibited the decrease in pri-miR-29b-1/a (Fig. 5C), as well as the reduction in miR-29b-1 and miR-29a seen with 4-OHT treatment in MCF-7 cells (Fig. 5D).

Although ERα knockdown did not affect basal pri-miR-29b/1a expression in LCC9 cells (Fig. 5C), there was a significant increase in miR-29a (Fig. 5D). Knockdown of ERα blocked 4-OHT stimulation of pri-miR-29b-1/a (Fig. 5C) and mature miR-29b-1 and miR-29a expression (Fig. 5D). Comparable results were seen with ERα knockdown in LY2 cells (Supplementary Fig. 2). Together, these data suggest that ERα plays a role in mediating 4-OHT suppression of miR-29b-1/a expression in MCF-7 cells and 4-OHT stimulation of miR-29b-1/a expression in LCC9 and LY2 cells.

4-OHT regulates miR-29b-1/a promoter activity

To examine the direct effect of 4-OHT on the 5' promoter of miR-29b-1/a, CHO-K1 cells were transiently transfected with an ERα expression vector [243] and a luciferase reporter containing –1530 to +165 of the human miR-29b-1/a promoter [227]. 4-OHT reduced luciferase activity and this was inhibited by fulvestrant (Supplementary Fig. 3). These data support the model that 4-OHT inhibits miR-29b-1/a promoter activity through ERα.

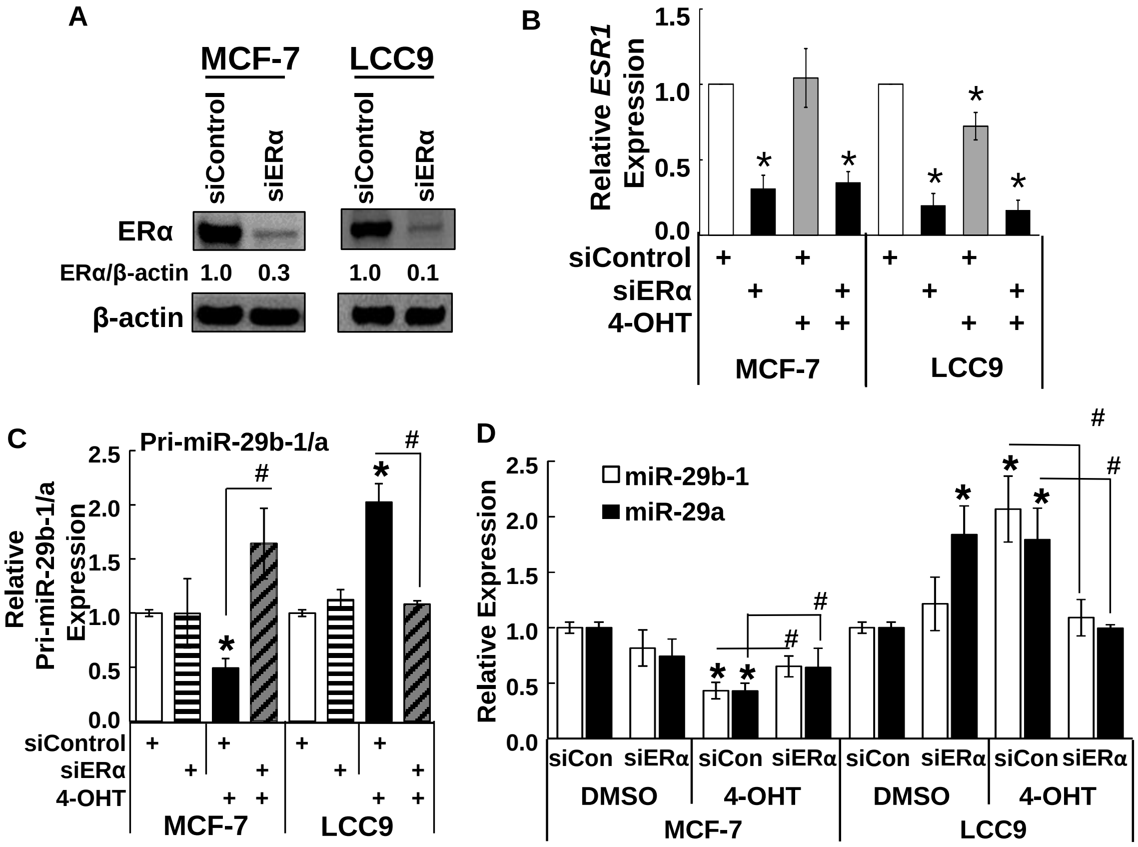


Figure 5. ERα regulates miR-29b-1/a expression in MCF-7 and LCC9 cells. Cells were grown in hormonally depleted medium and transfected with siControl or siERα. 48 h post transfection, cells were treated for 6 h with EtOH or 100 nM4-OHT. (A) ERα protein was examined in WCE and the blot was stripped and re-probed for β-actin for normalization. Values are the ERα/β-actin with siControl set to one for each cell line. Q-PCR for *ESR1* (B); pri-miR-29b-a and pri-miR-29a (C); and mR-29b-1 and miR-29a (D). Values are the average of 4-6 separate experiments ± SEM. *p < 0.05 *versus* control-transfected cells. #p < 0.05 *versus* 4-OHT-treated Control-transfected cells.

miR-29b-1/a inhibit cell proliferation but do not sensitize cells to 4-OHT inhibition

To examine the functional roles of miR-29b-1 and miR-29a in sensitivity to TAM, we evaluated how overexpression or inhibition of miR-29b-1 and miR-29a affected MCF-7, LCC9, and LY2 cell proliferation. Successful repression or overexpression of miR-29b-1 and miR-29a was confirmed by qPCR up to 6 d post transfection (Supplementary Fig. 9). Anti-miR-29b-1 or anti-miR-29a transfection had no effect on basal cell proliferation (Fig. 6A-C). However, inhibition of miR-29a blocked 4-OHT inhibition of MCF-7 proliferation (Fig. 6A). Further, the combined inhibition of miR-29b-1 and miR-29a resulted in 4-OHT stimulating MCF-7 cell proliferation, effectively reversing the normal antiestrogenic pharmacology of 4-OHT in MCF-7 cells (Fig. 6A). These data are commensurate with the inhibition of miR-29b-1/a expression by 4-OHT in MCF-7 cells (Fig. 4), suggesting a possible role for miR-29b-1 and miR-29a in 4-OHT's antiproliferative activity in MCF-7 cells.

Since 4-OHT stimulated miR-29b-1/a in TAM-resistant LCC9 and LY2, cells, we anticipated that inhibiting miR-29b-1 and/or miR-29a might sensitize these cells to 4-OHT inhibition. However, inhibition of miR-29b-1/a did not result in 4-OHT inhibiting cell proliferation (Fig. 6B, 6C). In contrast, inhibiting miR-29b-1 and/or miR-29a resulted in a stimulation of LCC9 cell proliferation with 4-OHT treatment (Fig. 6B). There was no significant effect of anti- mR-29b-1 or miR-29a on 4-OHT-stimulated LY2 cell proliferation (Fig. 6C).

Transfection of pre-miR-29b-1 and/or pre-miR-29a inhibited basal MCF-7 and LCC9 cell proliferation (Fig. 6A, 6B). In LCC9 cells, the inhibition by pre-miR-29b-1/a transfection was reduced by 4-OHT, although the effect was not statistically significant for miR-29a (Fig. 6B). Transfection of pre-miR-29a, alone or in combination with pre-miR-29b-1, inhibited LY2 cell proliferation, but did not sensitize the cells to further inhibition by 4-OHT (Fig. 6C).

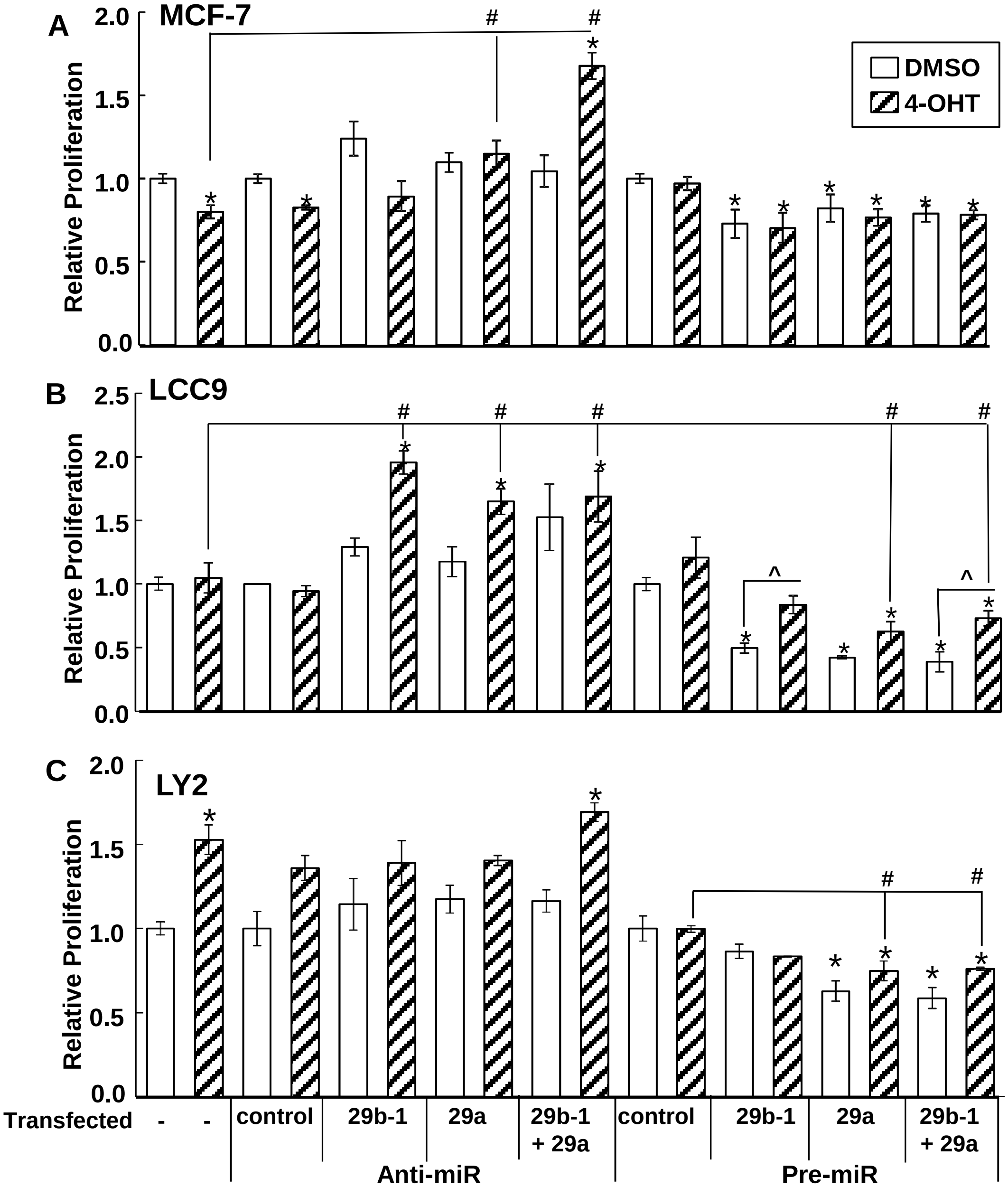


Figure 6. Overexpression of miR-29b-1 /a decreases cell proliferation.
Cells were grown in hormonally depleted medium and transfected with anti-miR-control, anti-miR-29b-1/a, pre-miR control, or pre-miR-29b-1/a for 48 h prior to treatment with DMSO (vehicle control) or 100 nM 4-OHT for 48 h prior to BrdU assay. Values are the ± SEM of 3 separate experiments *$p < 0.05$ *versus* vehicle control-transfected cells; #$p < 0.05$ *versus* 4-OHT-treated control transfected cells, ^$p < 0.05$ *versus* DMSO-treated miRNA transfected cells, as indicated.

miR-29b-1/a inhibit LY2 cell migration and colony formation

Transfection of MDA-MB-231 triple negative breast cancer (TNBC) cells with pre-miR-29b increased invasion, whereas anti-miR-29b inhibited invasion [214]. To further elucidate the possible functional role of miR-29b-1/a in ER-positive breast cancer cells, cell migration and colony formation experiments were performed with LY2 cells. We chose LY2 cells because they are invasive whereas MCF-7 and LCC9 cells are not [244, 245]. In accordance with our observation for an antiproliferative role for miR-29b-1 and miR-29a in LY2 cells, transfection of LY2 cells with pre-miR-29b-1 and pre-miR-29a inhibited cell migration (Fig. 7A, 7B). 4-OHT inhibited LY2 cell migration by ~ 5% after 8 h; however, this inhibition was not detected in cells transfected with pre-miR-29b-1 or pre-miR-29a.

4-OHT inhibited LY2 colony formation. Transfection of LY2 cells with pre-miR-29b-1 and pre-miR-29a inhibited colony formation and these transfections enhanced 4-OHT inhibition of colony formation (Fig. 7C). Together, these data suggest that miR-29b-1 and miR-29a stimulate anti-migratory and anti-colony-forming activity in LY2 cells. It appears that overexpression of miR-29b-1 and miR-29a enhance LY2 cell responses to 4-OHT's antiestrogen activity on cellular migration and invasion.

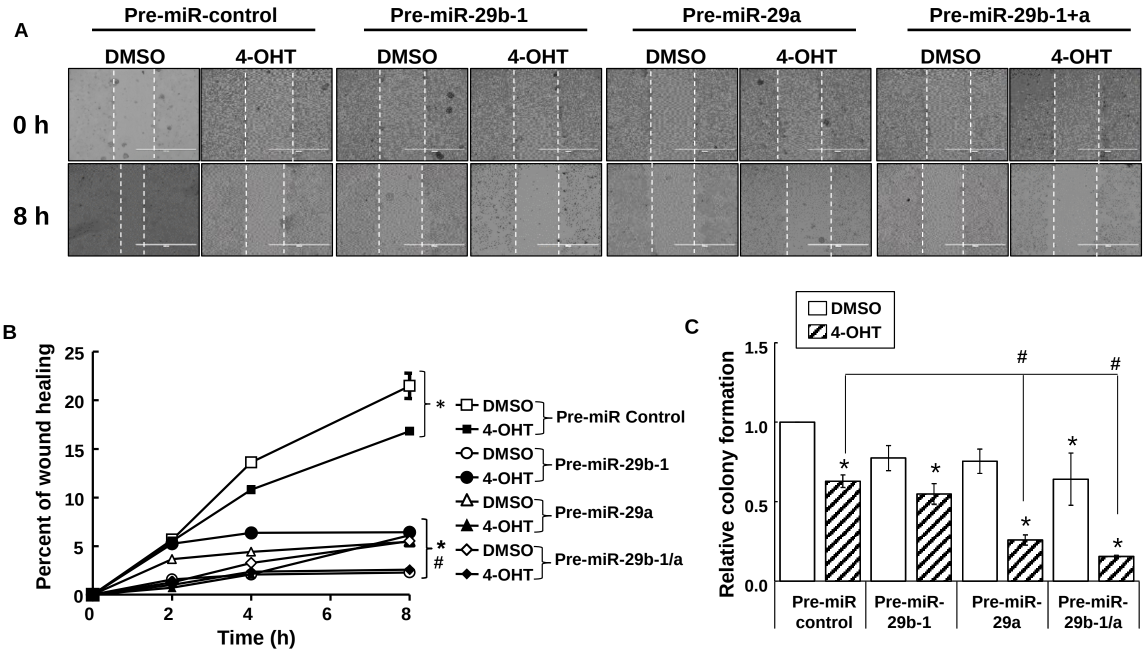


Figure 7. Overexpression of miR-29b-1 /a decreases LY2 cell migration.
LY2 cells were grown in hormonally depleted medium and transfected with pre-miR control or pre-miR-29b-1/a .(A-B) Twenty-four h post transfection cells were treated with DMSO (vehicle) or 4-OHT for up to 8 h and images taken at indicated time points. (C) Two d post transfection, colony formation assay was performed for 14 d. (B) Values are the ± SEM of 3 separate measurements within an experiment. (C) Values are the ± SEM of 6 replicates. *p < 0.05 *versus* vehicle control-transfected cells; #p < 0.05 *versus* control transfected + 4-OHT-treated cells

miR-29b-1/a decrease DICER in LY2 cells.

Next it was important to examine how 4-OHT's regulation of miR-29b-1/a transcription affected a *bona fide* target of miR-29b-1/a in these cells. To address the identity of such miR-29b-1/a targets, we searched online databases (mirdb.org[246]; microrna.org [247])) and identified DICER1 as one such candidate [209]. There are no previous reports of TAM-regulation of DICER1 transcription. Although DICER1 expression is upregulated in TAM-R MCF-7 cells [163], the mechanism was not examined. Transfection of LY2 cells with pre-miR-29b-1 or pre-miR-29a, individually or together, reduced DICER1 protein (Fig. 8A). Conversely, transfection with either anti-miR-29b-1 or anti-miR-29a, alone or in combination, increased DICER1 protein expression (Fig. 8A), suggesting that DICER1 is a target of miR-29b-1/a in LY2 cells. Similar results were observed for another *bona fide* target of miR-29b-1/a: tumor suppressor PTEN [248] (Supplementary Fig. 5). RNA-seq data (GSE81620) show lower transcript levels of PTEN in LCC9 *versus* MCF-7 cells (Supplementary Fig. 6A). However, qPCR for PTEN reveal no difference in basal PTEN transcript levels in MCF-7 and LCC9 cells grown in hormonally depleted medium (5% DCC-FBS, phenol-red free IMEM) for 48 h and treated with DMSO (vehicle control) or 100 nM 4-OHT (Supplementary Fig. 6B). Significantly higher PTEN transcript levels were found in LY2 cells under these experimental conditions. We note that while 'serum starvation' in 0.5% FBS had no effect on PTEN in MCF-7 cells, PTEN was increased in more aggressive adenocarcinoma cell lines including MDA-MB-468 TNBC cells [249]. Our data indicate that 4-OHT increased PTEN in MCF-7 cells but not in LCC9 or LY2 cells, commensurate with the TAM-resistant phenotype of these cells.

To determine whether 4-OHT would decrease DICER1 by increasing miR-29b-1/a in LY2 cells, cells were treated with 100 nM 4-OHT for 24 h following 48 h growth in hormone-depleted medium. Indeed, 4-OHT decreased *DICER1* mRNA (Fig. 8B) and protein (Fig. 10C). Next, we examined if anti-miR-29b-1 and anti-miR-29a would block 4-OHT downregulation of DICER1 expression. Anti-miR-29b-1/a transfection blocked 4-OHT downregulation of DICER protein (Fig. 10C) and transcript (Supplementary Fig. 7). We also show that 4-OHT downregulation of *DICER1* mRNA expression is mediated through ERα since knockdown of ERα blocked 4-OHT inhibition of DICER1 mRNA (Supplementary Fig. 8). These results suggest that the 4-OHT-stimluated increase in miR-29b-1/a in LY2 cells results in decreased DICER1 expression.

4-OHT-increased miR-29b-1/a in LY2 suppresses DICER1, we would anticipate lower overall miRNA expression in 4-OHT-treated LY2 cells relative to 4-OHT-treated MCF-7 cells in which miR-29b-1/a is repressed. We examined data from the miRNA microarray study and note that indeed, we detected lower expression overall of miRNAs in 4-OHT-treated LY2 cells compared to 4-OHT-treated MCF-7 cells [223]

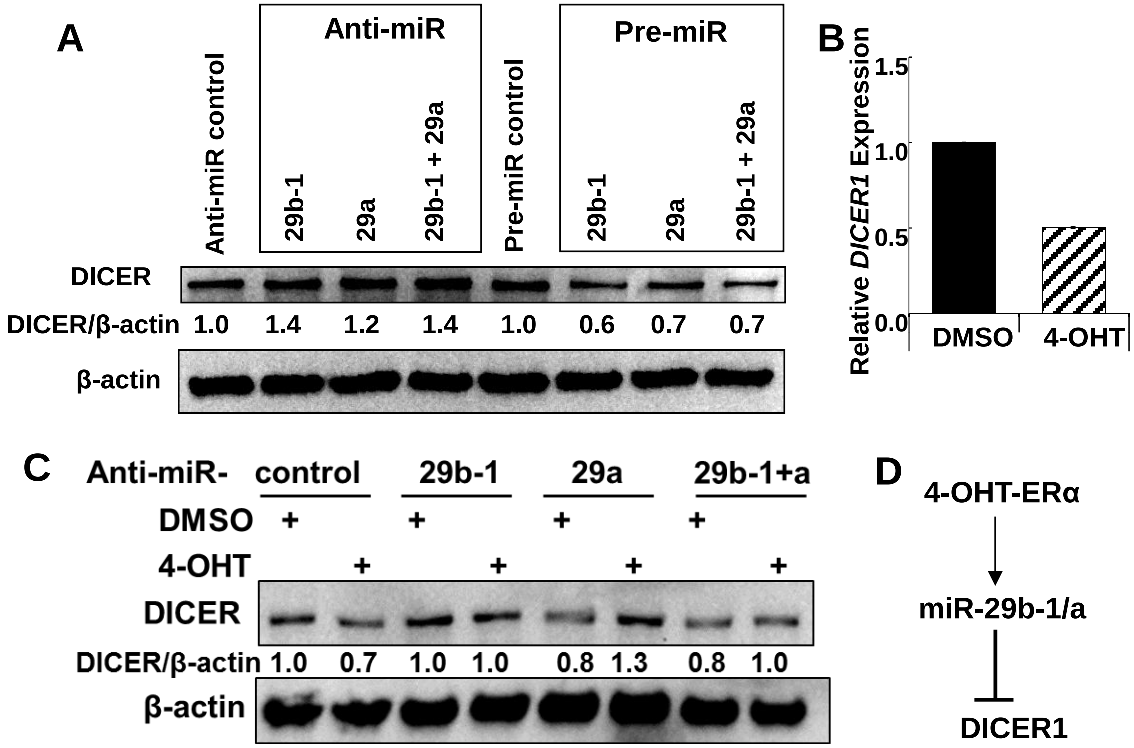


Figure 8. miR-29b-1/a downregulate DICER in LY2 cells and 4-OHT decreases DICER1 mRNA and protein in LY2 cells.

A) LY2 cells were transfected with Anti-miR-control, Anti-mIR-29b-1, AS-miR-29a, or the combination for 48 h. B and C) LY2 cells were grown in hormonally depleted medium for 48 h and treated for 24 h with vehicle control (DMSO) or 100 nM 4-OHT. B) qPCR for *DICER1* relative to *18S*. Values are the average of triplicate determinations ± SEM in one experiment. For A and C, the blots were striped and reprobed for β-actin. Values are the ratio of DICER/β-actin from the experiment shown. All experiments were repeated 3-4 times and representative data is shown. D) Model of suggested pathway for decreased DICER1 in 4-OHT-treated LY2 cells.

DISCUSSION

In this study, we demonstrated that ERα-mediates the 4-OHT-induced decrease in miR-29b-1 and miR-29a expression in endocrine-sensitive MCF-7 cells and the 4-OHT-induced increase in the transcription of these microRNAs in LCC2, LCC9 and LY2 cells. This supports our findings in a microarray analysis of 4-OHT-regulated microRNAs in MCF-7 and LY2 cells [223]. These 4-OHT-induced changes in mature miR-29b-1/a expression were initiated at the level of ERα-regulated transcription of pri-miR-29b-1/a. However, knockdown of ERα had no effect on basal pri-miR-29b-1/a transcription, or mature miR-29b-1 or miR-29a levels, suggesting the importance of the ligand 4-OHT in the ERα transcriptional response. A recent study identified a positive roles for Oct-4 (POU5F1 gene) and the E3 ubiquitin ligase SKP2 and a negative role for NKX3-1 in TAM-ERα stimulated gene transcription in MCF-7 cells [250]. This study did not examine regulation of miRNAs. The authors provided evidence for a 4-OHT-ERα/SKP2 complex and postulate this complex collaborates with Oct-4 to increase transcription of TAM-stimulated genes. To our knowledge, there are no reports of Oct-4 regulation of miR-29 family members. Oct-4 was increased and NKX3-1 decreased in TAM-R MCF-7 cells compared to parental MCF-7 cells [250]. We found no difference in *Oct-4* (*POU5F1*) transcript levels between MCF-7 and LCC9 cells whereas *SKP2* was increased and *NKX3-1* decreased in LCC9 compared to MCF-7 cells (Supplementary Fig. 9). Future studies will be required to elucidate the role of these factors in 4-OHT-ERα stimulated miR-29b-1/a transcription in LCC9 cells.

We observed that transfection of both TAM-S MCF-7 and its TAM-R cell line derivatives with miR-29b-1 or miR-29a repressed cell proliferation. Transient overexpression of miR-29a also inhibited the growth of MDA-MB-453 TNBC cells

[236], implying repression of cell growth by miR-29a is not dependent on ERα. If the 4-OHT-induced increase in miR-29b-1/a in TAM-R cells is involved in resistance, then we would expect that inhibiting miR-29-b-1/a should enhance 4-OHT inhibition of cell proliferation. However, inhibition of miR-29b-1 or miR-29a did not enhance the sensitivity of the TAM-R cells to 4-OHT.

Likewise, transient overexpression of either miR-29b-1 or miR-29a in TAM-R LY2 cells decreased cell migration and colony formation. Interestingly, overexpression of miR-29a alone or in combination with miR-29b-1 enhanced 4-OHT inhibition of LY2 colony formation. These data suggest that the 4-OHT-induced increase in miR-29b-1/a in LY2 may be involved in TAM-sensitivity, not resistance. Future studies will address if a combination of miR-29a and 4-OHT may lead to mesenchymal-to-epithelial transition (MET) in LY2 cells, although other gene expression changes are likely to contribute. The inhibitory effect of miR-29b-1 and miR-29a on LY2 cell migration and colony formation are the opposite of the effect of overexpression of these miRs in MDA-MB-231 TNBC cells. Overexpression of miR-29b enhanced the mesenchymal-like phenotype in MDA-MB-231 whereas transient transfection of antisense miR-29b decreased MDA-MB-231 cell migration [214]. The expression of ERα and other genes in LY2 cells may mediate the observed phenotypic difference in cellular responses to manipulation of miR-29b-1/a expression as TNBCs, by definition, lack ERα.

miR-29 family members contribute to resistance of chemotherapeutic agents [251-254]. For example, miR-29a contributes to resistance to Adriamycin and Docetaxel in breast cancer by repressing the tumor suppressor PTEN [251], fostering cell proliferation and inhibiting apoptosis. Transient overexpression of miR-29b increased

MCF-7 cell migration and invasion by repressing the PTEN [214]. Upregulation of miR-29b was recently reported to enhance sensitivity of gastric cancer cells to cisplatin, while knockdown enhanced cisplatin resistance [252]. Likewise, loss of miR-29 inhibits cisplatin-induced cell death in ovarian cancer through upregulation of collagen type I alpha 1 (COL1A1) and inactivation of glycogen synthase kinase beta (GSKβ) [253]. In pancreatic cancer, miR-29a contributes to resistance of gemcitabine through upregulation of the Wnt/β-catenin signaling pathway [254]. These studies implicate the miR-29 family as mediators of drug resistance and sensitivity in several cancers through mechanisms that may be drug and cancer-type-specific. It is therefore essential to identify the deregulated pathways mediating responses to miR-29 in each disease type.

Although miR-29b-1 and miR-29a originate from the same primary transcript, sharing the same promoter and seed sequence [226, 227], they had similar but not identical functional outcomes in our study. This difference can be explained in part by nucleotide differences adjacent to the seed sequence which contribute to target specificity and posttranscriptional processing, including subcellular localization and stability [232, 255]. Specifically, a hexanucleotide terminal localization motif present in miR-29b-1 and not in miR-29a targets miR-29b-1 for nuclear enrichment, while miR-29a and other vertebrate microRNAs are predominantly cytoplasmic [255, 256]. The nuclear localization of miR-29b appears to depend on the cell type, suggesting cell-specific expression of the machinery involved in miR-29b nuclear import [257]. We speculate this difference in subcellular localization may cause differential gene regulation and hence, differences in the functional outcomes between miR-29b-1 and miR-29a. Further studies are needed to examine the subcellular distribution of miR-29a and miR-29b-1 in breast cancer cells.

miR-29b-1 and miR-29a downregulate DICER1 protein levels in LY2 breast cancer cells. Because of its role in microRNA processing from pre-miRs to mature microRNAs, DICER1 regulates cellular processes including cell differentiation, programmed cell death, senescence, DNA repair, and chromatin remodeling [258-262]. DICER1 expression was reported to be downregulated in breast cancer cells exhibiting mesenchymal phenotypes and in primary breast tumors of patients with lower disease free survival [263]. However, a larger study of primary breast tumors reported that DICER1 staining was associated with ER negativity, HER2+, high Ki67, and expression of basal-like biomarkers [264]. Our observation that 4-OHT reduced DICER1 by increasing miR-29b-1/a and the reported increase in DICER1 in ERα-negative breast tumors suggest a possible role for ERα in DICER1 regulation, although further experiments are needed to validate this suggestion. Further DICER1 expression was associated with reduced overall survival, except in HER2+ patients where moderate or strong DICER1 expression was associated with improved disease free survival [264] .

DICER1 mRNA expression was decreased in breast cancer tissues [265] and in invasive ductal breast carcinomas [258]. In ERα negative breast cancer cells, DICER1 is repressed by tumor promoting microRNAs including miR-103/107 [208], miR-222/221 [209], and miR-18a [266]. The differing reports on the role of DICER1 deregulation underscore the limited current knowledge of its role in cellular processes and mechanism of action. These discrepancies can, in part, be explained by heterogeneity and genetic diversity of cancers and cell types [267], target expression status, the cell type and the microenvironment of each cell [234].

We observed that TAM decreased DICER1 protein expression in the TAM-R breast cancer cells by upregulating miR-29b-1/a, suggesting a decrease in DICER1 may play a role in promoting TAM resistance. This is contrary to a previous report that stable DICER1-overexpression in MCF-7 breast cancer cells conferred TAM resistance by increasing breast cancer resistance protein (BCRP) [163]. However, miR-29b-1/a regulation of DICER1 was not examined. In prostate tumors, DICER1 mRNA levels were negatively correlated with miR-29b-1 [268]. Further studies are needed on the impact of DICER1 in TAM resistance. Increased expression of miR-29b-1 and miR-29a in 4-OHT-treated TAM-R cells also suggest that this microRNA family could target transcripts of tumor suppressor proteins. Indeed, we observed downregulation of the tumor suppressor PTEN, another *bona fide* target of miR-29 regulation [248]. Certainly additional miR-29 targets may contribute to the response of TAM-R cells to TAM.

CONCLUSIONS

Mechanisms for endocrine resistance in breast cancer are multifactorial (reviewed in [269]). Here we identified miR-29b-1/a as regulated in opposite direction by 4-OHT in TAM-S MCF-7 cells *versus* TAM-R LCC2, LCC9, and LY2 cells. We show that the TAM regulation of miR-29b-1/a is mediated by ERα in opposite direction, *i.e.*, stimulation in LCC9 and LY2 *versus* inhibition in MCF-7 cells. We found that inhibiting miR-29b-1/a in TAM-R LCC9 and LY2 cells did not increases their sensitivity to 4-OHT inhibition. Further studies to identify other targets of these microRNAs are needed. It is perhaps not surprising that miR-29b1/a has a complicated set of effects, given that there are 632 predicted gene targets for has-miR-29a-3p and has-miR-29b-3p in the microRNA data base (http://mirdb.org/miRDB/). Examining the role of microRNAs in mediating endocrine resistance will provide new insights in elucidating defective cellular pathways and improving therapeutics for cancer patients.

CHAPTER IV: THE MIR-29 TRANSCRIPTOME IN ENDOCRINE-SENSITIVE AND RESISTANT BREAST CANCER CELLS

INTRODUCTION

microRNAs (miRNA, miRs) are 22 nt non-coding RNAs that recognize and bind complementary seed sequences in the 3’-UTR region of a target messenger RNA (mRNA) [221, 222] . This results in translational repression and/or transcriptional degradation of the target gene. By targeting several mRNAs, miRNAs regulate several cellular and biological processes including cell cycle, cell proliferation and cell differentiation, apoptosis, cellular respiration and glycolysis (reviewed in [94-97]). Aberrant miRNA expression mediates disease initiation and progression in breast and other cancers [86].

Seventy percent of breast tumors express estrogen receptor alpha (ERα) implying eligibility for endocrine therapies including selective estrogen receptor modulators (SERMs), e.g., Tamoxifen (TAM), and aromatase inhibitors (AI), e.g., letrozole. The efficacy of endocrine therapy is limited by relapse in ~40% of patients [56, 270]. Endocrine resistance is mediated by multiple mechanisms depending on the type of therapy used (reviewed in [40, 156, 271-273]). Alterations in miRNA expression are also implicated in endocrine-resistance (reviewed in [220, 274]).

Previously, we reported miR-29b-1 and miR-29a were downregulated by TAM in TAM- sensitive (TAM-S) MCF-7 BC cells and upregulated in TAM-resistant (TAM-R)

LCC2, LCC9, and LY2 BC cells [275]. There are four miR-29 family members in the human genome: miR-29b-2 and miR-29c (chromosome 1q32.2) and miR-29b-1 and miR-29a (chromosome 7q32.3). miR-29b-1 and miR-29a are separated by ~652 bp on the same pri-miRNA transcript [226-229]. Upon processing, mature miR-29b-1 preferentially localizes to the nucleus, while mature miR-29a localizes to the cytoplasm [255]. miR-29 family members have been reported to exhibit both tumor suppressive and oncogenic roles in breast cancer [231-233, 275].

We recently reported that ERα mediates 4-hydroxyTAM (4-OHT) repression of miR-29b-1/a in MCF-7 and upregulation in TAM-R LCC9 and LY2 BC cells. However, inhibition of miR-29b-1 and miR-29a did not sensitize LCC9 or LY2 cells to TAM [275]. Ectopic expression of miR-29b-1/a did not drive TAM resistance in MCF-7 cells, but it did significantly repress proliferation of TAM-R LCC9 and LY2 cells as compared to TAM-S MCF-7 cells. This suggests that miR-29b-1/a may regulate different transcripts, and thus pathways, in TAM-R cells and TAM-S cells. To identify and quantitate mRNA targets regulated by miR-29, we performed RNA-sequencing (RNA-seq) in MCF-7 and LCC9 BC cells transiently transfected with anti-miR-29a, pre-miR-29b-1 or pre-miR-29a. MetaCore™ functional analysis of the RNA-seq data identified several metabolic processes including oxidative phosphorylation (OXPHOS) uniquely regulated by both miR-29b-1 and miR-29a in LCC9 cells. We observed that miR-29a overexpression inhibited mitochondrial bioenergetic function in LCC9 cells, thus correlating function with identified Gene Ontology (GO) processes. We used qPCR and a luciferase reporter assay to validate that two subunits of ATP synthase (Complex V in the oxidative phosphorylation respiratory chain), *ATP5G1* and *ATPIF1*, are *bona fide* miR-29b-1/a targets.

MATERIALS AND METHODS

Cell lines and reagents

The following cells and reagents were used: HEK-293 (ATCC® CRL-1573™) and MCF-7 cells were purchased from ATCC. LCC9 cells are ERα+/progesterone receptor (PR)+ cells resistant to antiestrogens (tamoxifen and fulvestrant) and were kindly provided by Dr. Robert Clarke, Georgetown University [238]. Transfection reagents included anti-miR-29a (Anti-miR™s, Ambion), pre-miR-29b-1-3p or pre-miR-29a-3p precursor (Pre-miR™s, Ambion), miR-29a mimic or miR-29b-1 mimic (miR-Vana™, Ambion), Lipofectamine RNAiMAX (Invitrogen), FuGENE® HD (Promega), Pre-miR™ negative control #1 (Ambion), Anti-miR™ negative control #1(Ambion), miR-Vana™ negative control (Ambion), pEZX-MT06_ATP5G1 wild type (WT), pEZX-MT06_ATPIF1 (WT), pEZX-MT06_negative control (miTarget™ miRNA 3' UTR, GeneCopoeia).

Transient transfection of miRNAs and anti-miRNAs

Cells were grown as previously described in [275]. Briefly, MCF-7 and LCC9 cells were grown in hormone-depleted medium: phenol-red free IMEM (Gibco, Thermo Fisher) supplemented with 5% dextran-coated charcoal-stripped fetal bovine serum (DCC-FBS, Atlanta Biologicals) [275] and concomitantly transfected with either anti-miR-29a, pre-miR-29b-1-3p, pre-miR-29a-3p, pre-miR™ negative control #1 or anti-miR ™ negative control #1 for a 48 h, as indicated.

RNA-sequencing

RNA-sequencing was previously described in [276]. In brief, MCF-7 and LCC9 breast cancer cells were plated in 100 mm plates, hormone-depleted and transfected in triplicate with either pre-miR-29b-1, pre-mir-29a and anti-miR-29a using Lipofectamine (Ambion) and OPTI-MEM® I (Gibco: Life technologies). Twenty-four h post transfection, RNA was isolated using miRCURY RNA isolation kit (Exiqon) according to manufacturer's instructions and RNA concentration and quality assessed with a NanoDrop spectrophotometer. Using TruSeq Stranded mRNA kit (Illumina, San Diego, CA, USA), mRNA libraries were made using 2 μg of RNA and validated with an Agilent 2100 Bioanalyzer (Santa Clara (CA). After further library quantification with the Illumina Library Quantification Kit, RT-PCR was performed using the ABI Prism qPCR Mix (Kapa Biosystems) on an ABI17900HT real-time PCR instrument. Single read sequencing (75-76 cycles) was then performed using the 500 High-output v2 (75cycle) sequencing kit on an Illumina NextSeq500 instrument. Obtained read sequences were mapped to the human reference genome version GRCh37.1 using the mapping algorithm tophat [277] version 2.0.2. Using cufflinks version 2.2.1 and annotations found at ENSEMBL, Homo_sapiens GRCh37.73.gtf expression levels at loci were quantified. Raw sequencing data files obtained from our analysis are available at Gene Expression Omnibus (GEO) database: accession number GSE81620. Entrez gene identifiers for significantly expressed genes had a q-value cutoff of 0.05. Samples were then divided into fastq single end sequencing files representing comparisons of pre-miR-29b-1 vs anti-miR-29a and anti-miR-29a vs pre-miR-29a in MCF-7 and LCC9 cells.

In silico network analysis

Data from RNA-seq was analyzed such that transcripts selected had a log2 fold-change greater than 0.34 (or -0.34 for repressed transcripts) and a statistical significant threshold q value less than 0.05. Pathway and network analysis of differentially expressed genes was determined using the web-based software MetaCore™ version 6.27 (GeneGO, Thomson Reuters, New York, N.Y). MetaCore™ is a manually curated data base of over 6 million experimental findings interactions including protein-protein, protein-DNA, protein-RNA, and protein-compounds; metabolic and signaling pathways; and other additional information [278].

Metabolic analysis with the Seahorse XF24 extracellular flux analyzer

Metabolic profiles were performed as previously described in [276, 279]. Briefly, LCC9 cells were plated at 25,000 cells/well in XF24 plates. Twenty-four h post plating, cells were transfected with either anti-miR-29a or pre-miR-29a for 48 h. One hour prior to running the Seahorse Mito Stress Test assay, the media was replaced with DMEM assay media containing 1 mM sodium pyruvate, 25 mM glucose, and 1.85 g/L NaCl (all from Sigma), 2 mM Glutamax (Thermo Fisher), pH 7.4, and maintained at 37ºC in an non-CO_2 incubator. Sensor cartridges were incubated in XF24 calibrant solution (Agilent Technologies) at least 6 h prior to running assay. Initial measurement of basal ECAR (mpH/min) and OCR (pmol O_2/min) were taken prior to determining mitochondrial function using sequential injections of oligomycin A (1.5 μM), FCCP (0.5 μM) and combination of antimycin A (10 μM) and rotenone (2 μM) [276]. The protein concentration in each well was determined using the BioRad DC™ Protein Assay (BioRad, Hercules, CA, USA). OCR and ECAR values were normalized to protein concentration/well. Each experimental condition was run in quadruplicate within one experiment and separate experiments were run 3-4 times for statistical evaluation.

quantitative real-time PCR (qRT-PCR)

RNA isolation, RT-PCR and qPCR were performed as previously described in [275]. TaqMan (Thermo Fisher Scientific) master mix was used for miR-29b-1/a primers (Thermo Fisher Scientific) and SYBR green (QIAGEN) master mix was used for *LDHA* [280], *ENO1* [281], *CYCS* [282], *ATP5G1* [283], *ATP5C1* [284], *ATPIF1* [285], *ATP5G3* [283], *NDUFS6* [286], *NDUFC2* [287]. Normalizers included RNU6B or U48 (Thermo Fisher Scientific) for miRNA and *GAPDH* (SYBR green) [288] and *18S* (TaqMan; Thermo Fisher) for mRNA.

Site-directed mutagenesis, transient transfection of HEK-293 cells, and Dual luciferase assay

Mutation of the predicted 3’UTR binding site of miR-29b-1/a on pEZX-MT06 miRNA 3' UTR target dual luciferase expression vectors was performed using the GeneArt® Site-Directed Mutagenesis PLUS Kit (Thermo Fisher Scientific) according to manufacturer’s instructions. Where indicated, HEK-293 cells were plated in 24 well plates and co-transfected with 200 ng of wild type (wt) or mutant (mut) vectors plus a 20 nM final concentration of miR-29b-1/a mimic, anti-miR-29a or negative control mimic using FuGENE HD (Promega) according to manufacturer's protocol. Twenty-four h post transfection, a dual luciferase assay (Promega) was performed. Luciferase expression was determined relative to negative control mimic and statistical evaluation performed using GraphPad Prism Software (Graph Pad Software, San Diego, CA).

Statistics

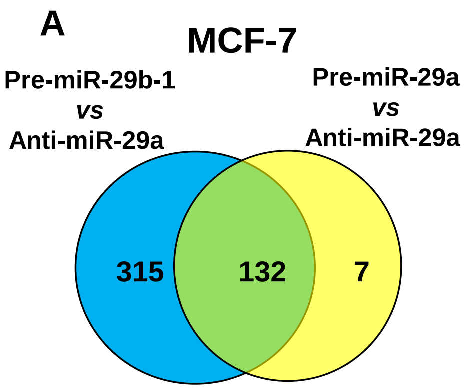
Data are represented as mean ± standard error of the mean (SEM) of at least three independent experiments. Statistical analyses were performed using GraphPad Prism 5 (Graph Pad Software, Inc.). One-way analysis of variance (ANOVA) was followed by Tukey's or Newman-Keuls multiple comparison *post hoc* tests where indicated [275].

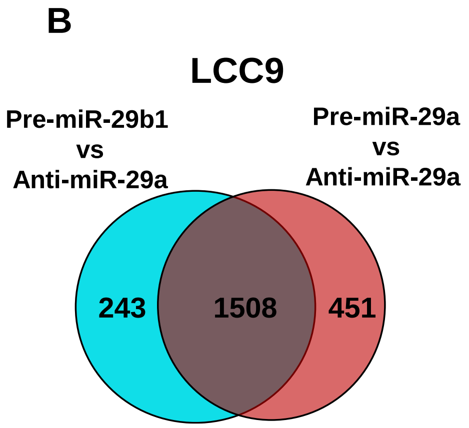
RESULTS

Identification and characterization of the miR-29b-1 and miR-29a transcriptome in MCF-7 and LCC9 cells

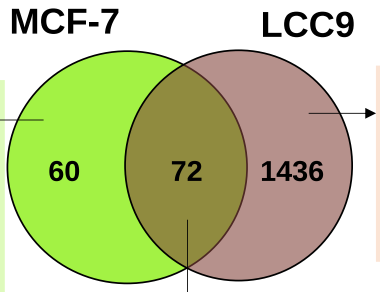
To identify potential miR-29b-1 and miR-29a targets in breast cancer cells and their possible role in tumor suppression, TAM-S MCF-7 and TAM-R LCC9 cells were grown in hormonally depleted medium and transfected with anti-miR-29a (that inhibits both miR-29b-1 and miR-29a expression) and pre-miR-29b-1 or pre-miR-29a (Supplementary Fig. 10). The strategy of comparing the transcriptome of cells transfected with anti-miR-29a *versus* pre-miR-29b-1 and anti-miR-29a *versus* pre-miR-29a was selected to enrich for direct miR-29b-1 and miR-29a targets. As miRNAs historically repress target transcript translation and/or mRNA expression, we focused on genes downregulated with pre-miRNA treatment and upregulated with anti-miR treatment for transcriptome analysis.

miR-29b-1 and miR-29a downregulated 447 and 139 genes in MCF-7 cells respectively (Fig. 9A) and 1,751 and 1959 genes in LCC9 cells (Fig. 9B; $p < 0.05$), respectively. The identity of these genes with MetaCore pathway analysis is provided in Supplementary Tables 2 and 3. These data suggest that miR-29b-1 and miR-29a regulate more transcripts in TAM-R LCC9 cells compared to TAM-S MCF-7 cells.





C Common miR-29b-1 and miR-29a targets



Uniquely downregulated genes in MCF-7 cells

1. Cell cycle: Chromosome condensation in prometaphase
2. Translation: Non-genomic (rapid) action of Androgen Receptor
3. Regulation of metabolism: Triidothronine and Thyroxine signaling
4. Aberrant lipid trafficking and metabolism in age-related macular degeneration pathogenesis
5. Glutathione metabolism

Uniquely downregulated genes in LCC9 cells

1. Oxidative phosphorylation
2. dATP/dITP metabolism
3. ATP/ITP metabolism
4. Apoptosis and survival role: Role of IAP-proteins in apoptosis
5. NETosis in SLE

Commonly DOWNREGULATED top 10 pathways

1. Neurophysiological Process
2. Immune response:IL-6 signaling
3. Development: Role if CNTF and LIF in regulation of oligodendrocyte
4. Development: EGFR signaling via small GTPases
5. Cell adhesion: Plasmin signaling
6. Cell adhesion: Tight junctions
7. Glycine, serine, cysteine and threonine metabolism
8. Main growth factor signaling cascades in multiple myeloma cells
9. Development: Neurotrophin family signaling
10. Development: EPO-induced MAPK pathway

Figure 9. Enrichment analysis of RNA-seq data.

Differentially expressed genes were identified in pairwise comparisons: Pre-miR-29b-1 vs. Anti-miR-29a and Anti-miR-29a vs. Pre-miR-29a using tophat and cufflink-cuff diff2. The Venn diagrams show the number of differentially and commonly regulated genes identified. GeneGo Pathways Software (MetaCore™) was then used to identify genes significantly downregulated by miR-29b-1 and miR-29a in A) MCF-7 and B) LCC9 cells. C) Pathway analysis of the downregulated genes was performed using MetaCore™. The order of the pathways identified for each comparison are listed in the order provided by MetaCore™ analysis.

In MCF-7 cells, 132 genes were identified as common targets of both miR-29b-1 and miR-29a (Fig. 9A). In LCC9 cells, 1,508 genes were common targets to both miR-29b-1 and miR-29a (Fig. 9B). MetaCore™ pathway analysis of the common and uniquely regulated genes is provided in Supplementary Fig. 11 and Supplementary Fig. 12. Of the common targets, 60 were unique to MCF-7 and 1,436 were unique to LCC9 (Fig. 9A, Supplementary Tables 4). Seventy-two targets were common to both MCF-7 and LCC9 cells (Fig. 9C). Together, these data confirm that miR-29b-1 and miR-29a regulate common and unique targets in MCF-7 and LCC9 cells. MetaCore™ pathway enrichment analysis was performed for each dataset and the top pathways identified are listed in Fig. 9C.

Gene ontology (GO) analysis of the uniquely downregulated transcripts by both miR-29b-1 and miR-29a in LCC9 cells (Fig. 9C) identified organonitrogen compound metabolic and biosynthetic processes and cotranslational protein targeting to the membrane as the top three regulated processes (Supplementary Fig. 13A). The top five regulated process networks included translation initiation, elongation, termination, and cell cycle S phase (Supplementary Fig. 13B).

Pathway enrichment analysis of the uniquely downregulated miR-29b-1/a target genes in LCC9 cells identified pathways including oxidative phosphorylation, ATP metabolism, apoptosis, and cell survival. MetaCore™ network analysis on mitochondrial respiratory complex genes downregulated by miR-29b-1/a is shown in Supplementary Fig. 13C. Several genes including components of respiratory Complex II and III, Cytochrome *c* oxidase, and ATP synthase (Complex IV) were uniquely downregulated by miR-29b-1/a in LCC9 cells (Supplementary Fig. 13C). We previously reported that six genes encoding subunits of ATP synthase that are not regulated by miR-29 were more highly expressed in LCC9 than MCF-7 cells [276]. The role of these genes in endocrine resistance will require further evaluation.

miR-29a regulates mitochondrial bioenergetics in tamoxifen-resistant LCC9 cells

Because OXPHOS was identified as the top enrichment pathway modulated by miR-29b-1/a in LCC9 cells, and not in MCF-7 cells (Fig. 9C), we postulated that miR-29a regulates mitochondrial bioenergetics activity in LCC9 cells. We focused on miR-29a because its basal expression is higher in LCC9 and other breast cancer cells compared to miR-29b-1 [275]. To examine the impact of miR-29a on mitochondrial respiration, MCF-7 and LCC9 cells were transfected with either anti-miR-29a or pre-miR-29a, *versus* control, and grown in hormonally depleted phenol red-free medium for 48 h prior to determining oxygen consumption rate (OCR) and extracellular acidification rate (ECAR; reflects glycolytic rate) [279] using the Seahorse extracellular flux assay [276, 279] (Supplementary Fig. 14).

In agreement with our previous work [276], TAM-R LCC9 cells grown in hormonally depleted medium have increased basal OCR *versus* MCF-7 cells (Fig. 10A). Transfection of LCC9 cells with anti-miR-29b-1 increased while pre-miR-29a repressed basal OCR, ATP-linked OCR (which measures the rate of mitochondrial ATP synthesis) and mitochondrial reserve (also known as reserve respiratory capacity) [289] (Fig. 10A). Similar results were seen in pre-miR-29a-transfected MCF-7 cells except that growth in hormonally depleted medium ablates reserve capacity, and thus, no effect of miR-29a on reserve capacity was detected (Fig. 10A). The changes in basal OCR suggest that miR-

29a modulates metabolic rate in part through electron flow. The regulation of reserve capacity, which is a measurement of the ability to respond to increased energy demand after injection of the uncoupler FCCP, suggests that miR-29-regulated genes adversely impact LCC9's mitochondrial ability to mitigate cellular stress. Inverse changes, albeit of lesser magnitude, were seen in LCC9 cells transfected with anti-miR-29a.

Compared to MCF-7 cells, LCC9 cells have higher basal proton leak. Proton leak is required for protecting against cellular oxidative damage through lowering ROS produced by the electron transport chain (ETC) [290]. Pre-miR-29a transfection repressed proton leak in LCC9 cells (Fig. 10A). Non-mitochondrial activity, which is attributed to cytoplasmic oxidases, was lower in LCC9 cells transfected with pre-miR-29a (Fig. 10A). Transfection of LCC9 cells with anti-miR-29a increased while pre-miR-29a transfection decreased maximal mitochondrial (mt) capacity (Fig. 10B). The maximal mitochondrial capacity is the OCR measured after injection of the uncoupler FCCP and is indicative of the mt ability to take up substrates [291].

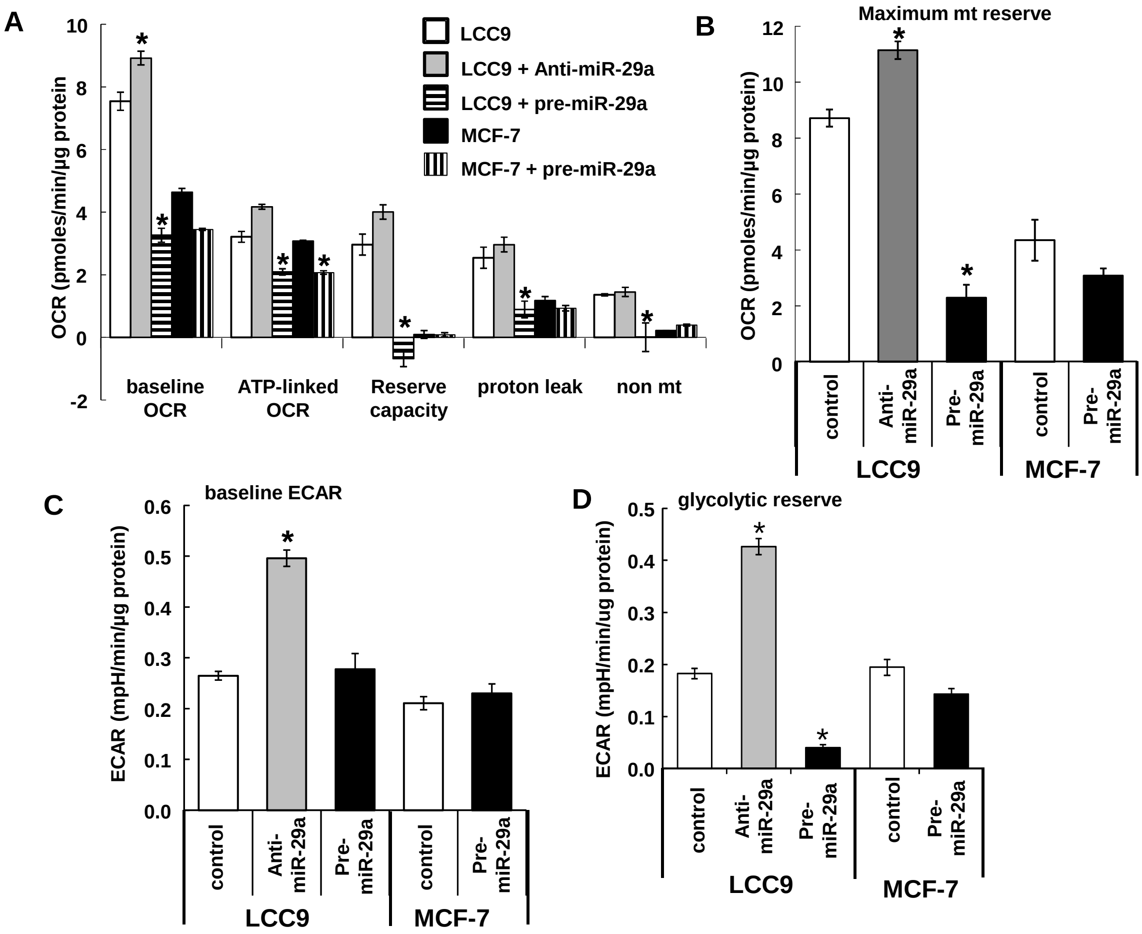


Figure 10. Upregulation of miR-29a represses mitochondrial function in MCF-7 and LCC9 cells.

MCF7 and LCC9 cells were plated in XF-24 plates in hormonally-depleted medium and transfected with control, anti-miR-29a, or pre-miR-29a for 28 h prior to running the Seahorse extracellular flux assay to determine mitochondrial activity. A and B) OCR parameters; C and D) ECAR parameters. Each bar is an average of 4 separate wells ±SEM in one experiment. *p <0.05 *versus* LCC9 or MCF-7 control for the indicated parameter. For LCC9, data were analyzed by one-way ANOVA followed by Tukey's test. For MCF-7, two-tailed Student's t-test was performed (NS).

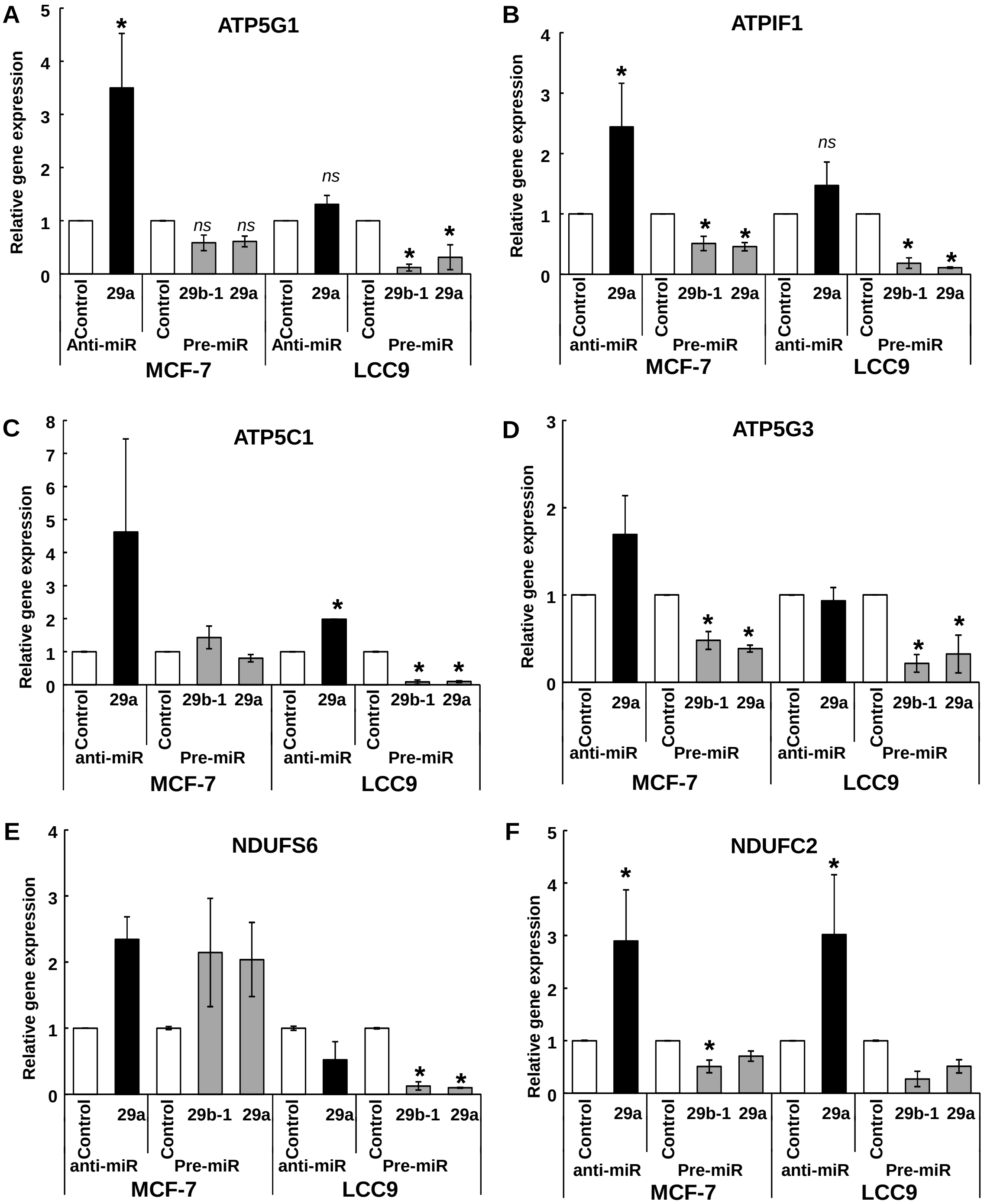
We previously reported that ECAR measurements agree with conversion of radio-labelled glucose to H_2O in MCF-7 and T47D breast cancer cells, demonstrating that ECAR is a reliable measure of glycolysis [279]. LCC9 cells alone or upon transfection with anti-miR-29a had increased basal ECAR than MCF-7 cells (Fig. 10C). The glycolytic response to oligomycin, considered as the glycolytic reserve [292], was increased by miR-29a repression and reduced by miR-29a overexpression in LCC9 cells (Fig. 10D). These data suggest that miR-29a regulates genes with roles in glycolysis in LCC9 cells. Examination of the RNA-seq data identified *TPI1*, *PGAM1*, *ENO1*, and *LDHA* as possible targets of miR-29b-1/a (Supplementary Fig. 15A). qPCR analysis confirmed that overexpression of miR-29b-1/a inhibited *ENO1* and *LDHA* transcript expression in MCF-7 and LCC9 cells (Supplementary Fig. 15B). Future studies will further evaluate these observations.

Validation of ATP5G1 and ATPIF1 as bona fide targets of miR-29b-1 and miR-29a.

miR-29a regulation of mitochondrial activity is suggestive of direct regulation of mitochondrial complex genes. Analysis of our RNA-seq data revealed miR-29 regulation of mitochondrial genes including *ATP5G1*, *ATP5C1*, *ATPIF1*, *ATP5G3*, *NDUFS6* and *NDUFC2* (Supplementary Fig. 16). To confirm miR-29 regulation of the putative target transcripts, qPCR was performed for these genes in MCF-7 and LCC9 cells transfected with either anti-miR-29a, pre-miR-29b-1, pre-miR-29a or their negative controls (Fig. 11, Supplementary Fig. 17). Anti-miR-29a transfection increased *ATP5G1* and *ATPIF1* mRNA expression in MCF-7 and LCC9 cells (Fig. 11A & 11B). Conversely, pre-miR-

29b-1 and pre-miR-29a transfection repressed *ATP5G1* in LCC9 cells alone and *ATPIF1* mRNA expression in both MCF-7 and LCC9 cells (Fig. 11A & 11B).

In LCC9 cells, anti-miR-29a transfection increased *ATP5C1* and *NDUFC2* while pre-miR-29b-1 and pre-miR-29a transfection repressed *ATP5C1*, *ATP5G3*, *NDUFS6* and *NDUFC2* transcript expression (Fig. 11C-11F). In MCF-7 cells anti-miR-29a transfection increased *NDUFC2* mRNA expressions while pre-miR-29b-1 and pre-miR-29a transfection repressed expression of *ATP5G3* and *NDUFC2* transcripts (Fig 11D & 11F). Taken together, these data suggest cell line specific differential regulation of miR-29 targets between MCF-7 and LCC9 cells. Notably, *ATP5G1* and *ATP1F1* were downregulated by miR-29b-1/a in both LCC9 and MCF-7 cells (Fig. 11A & 11B). Further, basal mRNA expression of *ATP5G1*, *ATP5IF1* and *ATP5G3* were higher (lower CT) relative to *ATP5IC1*, *NDUFS6*, and *NDUFC2* in both MCF-7 and LCC9 BC cells, (Supplementary Fig. 17). Hence we selected *ATP5G1* and *ATP5IF1* for further study.


A
ATP5G1
Relative gene expression
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Control
29b-1
29a
anti-miR
Pre-miR
anti-miR
Pre-miR
MCF-7
LCC9

Figure 11. miR-29b-1/a regulates mRNA expression of putative targets in MCF-7 and LCC9 cells.
MCF-7 and LCC9 cells were grown in hormone-depleted media and transfected with anti-miR-control, anti-miR-29a (3p), pre-miR control or pre-miR-29b-1/a (3p), as indicated. Twenty-four h post transfection, RNA was isolated and qPCR performed. Values were normalized to *18S*. Values are the mean ± SEM of 3 independent experiments. Within each experiment, each sample was run in triplicates. Statistical evaluation was performed using one-way ANOVA followed by Tukey's test. *$p<0.05$ *versus* control transfected cells.

To determine whether ATP5G1 and ATPIF1 are *bona fide* miR-29 targets, we tested the ability of miR-29 to repress the luciferase activity from reporter vectors containing wild type (WT) or mutant (mut) 3’ UTRs of these genes. The miR-29 binding region at the 3’UTR region of *ATP5G1* and *ATPIF1* are conserved across species (Fig. 12A). We created mutations in the miR-29 recognition sequence in *ATP5G1* (Fig. 12A). Cotransfection of miR-29b or miR-29a mimics with the luciferase reporter containing *ATP5G1* 3’ UTR WT sequence repressed luciferase activity (Fig. 12B). Mutation of the *ATP5G1* 3’ UTR (Mut) abrogated repression by the miR-29b and miR-29a mimics (Fig. 12B). These data demonstrate that *ATP5G1* is a *bona fide* direct target of miR-29b and miR-29a. Additionally, miR-29b and miR-29a mimics repressed luciferase activity from the *ATPIF1* 3’ UTR WT luciferase vector and repression was abrogated when cells were cotransfected with anti-miR-29a (Fig. 12C). These data suggest that *ATPIF1* is also a *bona fide* direct target of miR-29b and miR-29a.

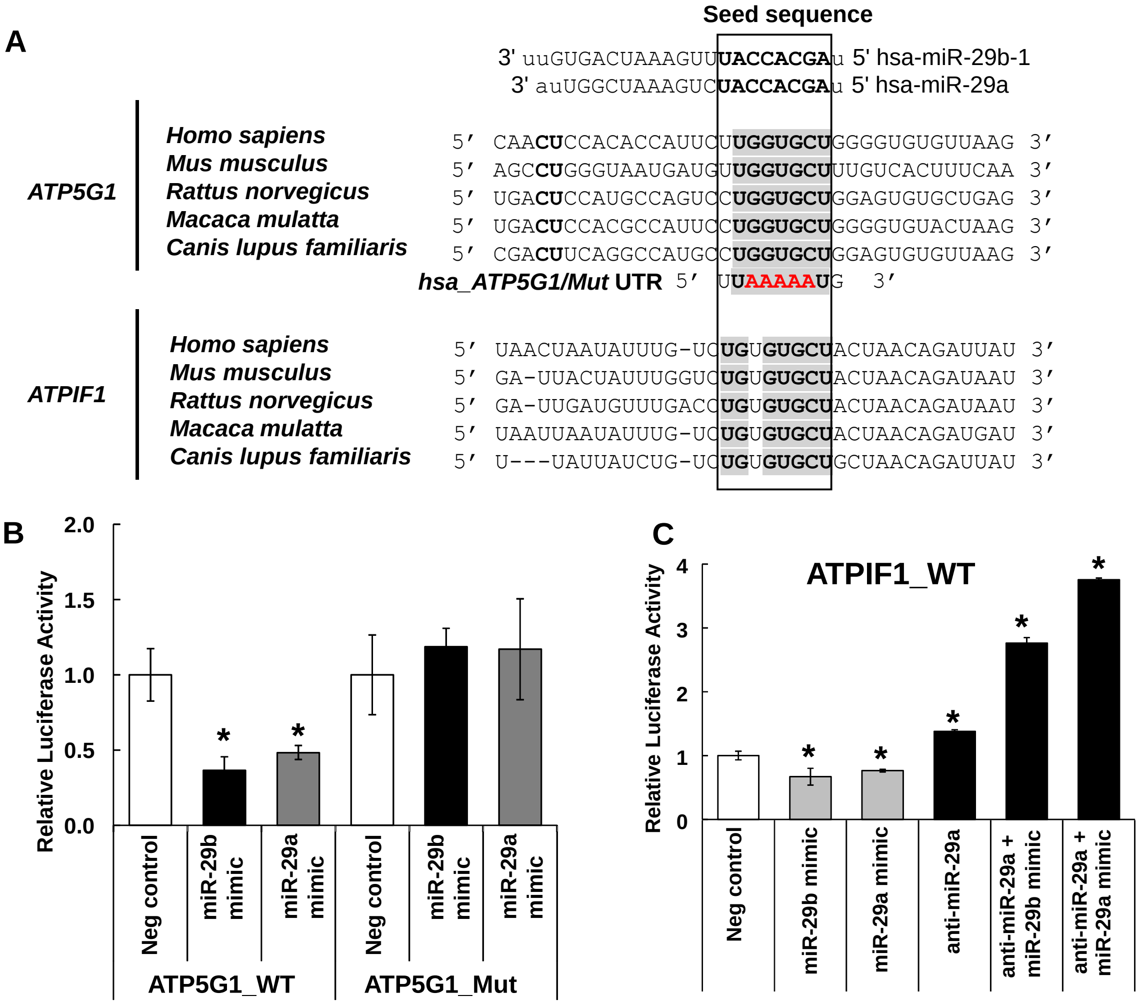

Figure 12. miR-29b-1/a regulate *ATP5G1* and *ATPIF1* 3'-UTRs luciferase reporter activity.

A) Alignment of miR-29b-1 and miR-29a, their seed elements (**in bold**) and the 3'-UTRs of *ATP5G1* and *ATPIF1*. The mutated seed element in *ATP5G1* used in luciferase assay is indicated in red. miR-29 family members have the same seed sequence and their binding sites in the 3'UTRs of *ATP5G1* and *ATPIF1* are conserved across several species. B and C) HEK-293 cells grown in hormonally depleted medium were transiently transfected with pEZ-MT10 dual luciferase reporter containing the 3'UTR of ATP5G1 wildtype (WT), ATPIF1 WT, miR-29 seed element mutated (Mut) constructs and an RNA mimic negative control or miR-29b or miR-29a mimics +/- Anti-miR-29a for 24 h prior to dual luciferase assay. Data are the avg. of three replicate wells ± SEM. *$p < 0.05$ *versus* negative control. Statistical analysis used one-way ANOVA followed by Newman-Keuls Multiple Comparison Test.

DISCUSSION

Dysregulation of the miR-29 family members plays a role in breast cancer progression, metastasis, and endocrine resistance [160, 275]. However, the precise mechanism(s) and targets of miR-29 in breast cancer are not fully elucidated. Here we identified the miR-29b-1 and miR-29a transcriptomes in MCF-7 TAM-S and LCC9 TAM-R breast cancer cells. Although miR-29b-1 and miR-29a have commonly regulated transcripts, they also have uniquely regulated transcripts. We observed that miR-29 regulates more transcripts in LCC9 than MCF-7 cells, and MetaCore™ enrichment analysis of unique miR-29 target transcripts in LCC9 cells identified GO pathways involved in oxidative phosphorylation, ATP metabolism, apoptosis and survival. In agreement with this literature-based association, ectopic miR-29a expression resulted in an inhibition of mitochondrial bioenergetics in LCC9 cells. Further, we demonstrate for the first time that *ATP5G1* and *ATPIF1* are *bona fide* miR-29b-1/a targets.

Dysregulation of mitochondrial bioenergetics is common in cancer cells [290]. Thus, identifying impaired mitochondrial pathways is of pathological and therapeutic relevance [293]. Mitochondria dysregulation results from alterations in mitochondrial function and ultrastructure [294], overproduction of reactive oxygen species (ROS) [295], and mitochondrial DNA (mtDNA) mutations and deletions [295, 296]. miRNA regulation of mitochondria has previously been reported (reviewed in [297, 298]). However, this is the first report that miR-29b-1/a regulate genes in ATP synthase (Complex V).

In agreement with the MetaCore pathway enrichment identification of OXPHOS as the top enriched pathway among miR-29b-1/a regulated genes in LCC9 cells, we observed that pre-miR-29a decreased basal OCR, ATP-linked OCR, and mt reserve. Concordantly, anti-miR-29a increased OCR and mt reserve, suggesting that repression of miR-29a may serve as an adaptive response to meet the increased energy demand of cancer cells and promote survival. Basal-like human breast tumors have lower levels of miR-29a, miR-29b, and miR-29c compared with Luminal A and B tumors [230]. Repression of miR-29a increased basal ECAR (glycolysis) in LCC9 cells (Fig. 10C), a finding in agreement with the Warburg effect of increased glycolysis seen in basal-like tumors [299, 300]. Overall changes in OCR and ECAR suggest overexpression of miR-29a has a greater impact on OXPHOS while repression of miR-29a increases both glycolytic activity and mitochondrial activity (OXPHOS) in LCC9 cells. Pre-miR-29a transfection repressed proton leak in LCC9 cells to levels below those seen in MCF-7 cells with hormone deprivation, suggesting miR-29a overexpression depletes mitochondrial OXPHOS, which could lead to activation of apoptosis or other cell death pathways.

LCC9 cells alone or when transfected with anti-miR-29a had a higher maximum mitochondrial capacity than the hormonally depleted MCF-7 cells, suggesting increased bioenergetics reserve. Indeed repression of miR-29a in LCC9 cells increased the glycolytic reserve. This may be attributable in part to the higher non-mitochondrial activity in LCC9 cells. Further metabolomics studies will be required to further assess changes in cellular metabolism with changes in miR-29b/a expression.

We identify several ETC proteins including ATP synthase genes ATP5G1 and ATPIF1 as targets of miR-29b-1/a. We experimentally validated that *ATP5G1* and *ATPIF1* are *bona fide* targets of miR-29b and miR-29a. Inhibition of ATP synthase in

MCF7, T47D and MDA-MB-231 BC cells induced cell cycle arrest, decreased colony formation, and inhibited cell proliferation [301]. The targeting of ATP synthase complex subunits may account for miR-29's repression of OCR and of BC cell proliferation [275]. Additional studies are warranted to confirm this suggestion.

CONCLUSIONS

Our RNA-seq transcriptome analysis revealed that miR-29b-1 and miR-29a regulate common and unique gene targets in TAM-S MCF-7 and TAM-R LCC9 BC cells. We focused on common miR-29b-1 and miR-29a targets downregulated uniquely or in common in MCF-7 and LCC9 cells. We report that miR-29b-1 and miR-29a regulate more transcripts in LCC9 than MCF-7 cells. MetaCore™ pathway enrichment analysis identified OXPHOS as the top GO pathway regulated by miR-29b-1/a target transcripts in LCC9 cells and cell cycle: chromosome condensation in prometaphase as the top GO pathway in MCF-7 cells. Seahorse extracellular flux analyses of LCC9 and MCF-7 cells confirmed regulation of cellular bioenergetics by miR-29a including repression of OXPHOS by ectopic miR-29a expression. We experimentally validated *ATP5G1* and *ATPIF1* as new miR-29 *bona fide* targets suggesting that these targets play a role in mediating miR-29's anti-proliferative effects in LCC9 and MCF-7 breast cancer cells.

CHAPTER V: FUTURE PERSPECTIVE-MICRORNAS AS POTENTIAL BIOMARKERS FOR ACQUIRED ENDOCRINE RESISTANCE IN BREAST CANCER[3]

miRNAs from metastases and in the serum of BC patients resistant to endocrine therapies has the potential to serve as selective biomarkers. These miRNA biomarkers can help identify patients with endocrine-resistant disease who could benefit from early intervention using an alternative therapeutic modality. Here, we will summarize what is known about miRNAs with predictive and prognostic potential in endocrine-resistant BC.

DYSREGULATED MICRORNAs THAT REGULATE ERα SIGNALING

ERα signaling is critical for response to endocrine therapy. miRNAs serve as predictive signatures for ER status [302] and regulate ERα protein expression to mediate endocrine resistance [91, 218, 220]. For example, miR-221/222 [100], miR-342-3 p [101], miR-873 [114] and Let7b/Let-7i [103] downregulate ERα protein expression (Fig. 13; Table 3). Lower ERα provides less target for endocrine therapies and thus, in combination with other deregulated miRNAs, serves as a mechanism for resistance.

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[3] The text of this chapter was published in Mol Cell Endocrinol. 2017 Feb 2. pii: S0303-7207(17)30080-1. doi: 10.1016/j.mce.2017.02.004

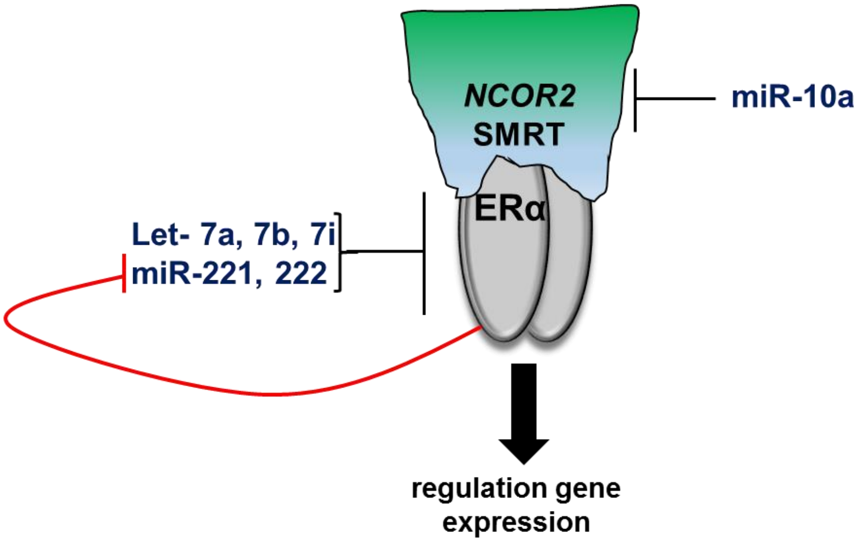

Figure 13. miRNAs that regulate ERα signaling that have been identified in human breast tumors and serum as potential biomarkers.
As described in the text, breast tumors have higher let-7a, 7b, and 7i [303], higher miR-221 [100, 304] and miR-222 [100, 304] compared to normal breast tissue. Each targets ERα. E_2-ERα represses miR-222 [100] and miR-222 [100]. As summarized in Table 3, elevated miR-10a was reported in breast tumors but its predictive role remains unclear. The corepressor SMRT (NCOR2) is a *bona fide* target of miR-10 [305]. As indicated in Table 4, miR-10a has been identified in exosomes [193].

Table 3. miRNA associated with endocrine-resistance in human breast tumors or patient samples
Experimentally proven *bona fide* targets and the method used to confirm the target are indicated. Methods of identification of the miRNA gene targets: 3’-UTR luciferase reporter assay (L), downregulation of protein shown by western blot (W), and downregulation of target in quantitative real-time PCR assay (Q) or Northern blot (N). Proposed pathways associated with endocrine-resistance are included. LET-R: letrozole-resistant; ANA-R: anastrozole-resistant. TAM-R: tamoxifen-resistant

miRNA	**Sample source**	**Comments**	**Targets (method of identification; L,W, Q)**	**Indicator**
miRNAs with increased expression (Putative oncomiRs) and their suggested targets in endocrine-resistance.				
miR125b-5p	Human breast tumors [119]	Upregulated in LET-R MCF-7 cells, ANA-R MCF-7 compared to MCF-7aro (aromatase-overexpressing MCF-7 cells). High miR-125b-5p correlated with earlier relapse in ER+/PR+ patients [119].	ERBB2, ERBB3(L, W, N) [306]	Increased expression is prognostic for lower relapse-free survival
miR-205-5p	Human breast tumors [119]	Upregulated in LET-R MCF-7 and ANA-R MCF-7 cells. [119].	ERBB2 (L,W, Q) [307]	Increased expression is a biomarker of poor prognosis and predictive for AI resistance

miR-210	Human breast tumors [102]	Increased miR-210 with breast tumor histological grade [102]	ISCU (iron-sulfur cluster scaffold homolog) and COX10 (cytochrome c oxidase assembly protein) (L, W) [308]	Increased expression is predictive of TAM resistance
miR-221/222	Human breast tumors [104]	TAM increased miR-221/222 in TAM-R cells and HER2+ breast tumors compared to TAM-S MCF-7 and HER2-tumors, respectively [104].	p27(Kip1) (W, Q) [104]	Increased expression is predictive for endocrine (TAM) resistance
	Human breast tumors [100]	Higher in ERα negative MDA-MB-468 BC cells and primary breast tumors vs ERα positive MCF-7 and T47D cells [100].	ESR1/ERα (L, W) [100]	
miR-301	Human breast tumors [126]	Higher expression in lymph node negative (LNN) invasive ductal BC [126].	FOXF2, BBC3, PTEN, (L, W, Q), COL2A1 (L,Q) [126]	Increased expression is predictive for patient tumor relapse to TAM
miR-375	Patient whole blood [309]	Increased circulating levels are associated with disease recurrence [309].	MMP13 (L, W) [310]	Increased expression is

				prognostic for disease recurrence
miR-519a	BC patient datasets [127]	High expression correlated with decreased disease-free survival in ERα-positive BCs. Upregulated in TAM-resistant MCF-7 cells and in ERα-negative breast tumors compared to TAM-sensitive MCF-7 cells and ERα-positive tumors, respectively [127].	CDKNIA, RB1 and PTEN (L, W, Q) [127]	Increased expression is prognostic for lower disease-free survival
miR-1266	Human breast tumors	Upregulation was indicative of lower disease-free survival and prognostic for recurrence.	IL17BR (Q)[311]	Increased expression is indicative of poor prognosis
miR-1280	BC patient blood samples [128]	Higher in blood from patients with metastatic BC after cytotoxic chemotherapy or undefined endocrine therapy [128].	ERα [312]	Decreased expression was predictive for response to systemic treatment
miRNAs with decreased expression (putative tumor suppressor) and their suggested targets in endocrine-resistance.				
Let-7b/Let-7i	Human breast tumors [103]	Overexpression of Let-7b/Let-7i enhanced sensitivity of TAM-R MCF-7 cells to TAM only in	ERα36 (L, W, Q) [103] ERα (L, W, Q) [303] (serves a putative	Decreased expression is

		hormone-depleted medium and not in normal growth medium [103].	oncomiRs in targeting ERα)	indicative of poor prognosis
miR-10a	Human breast tumors [130]	Higher expression in tumors was associated with longer relapse-free survival. Increased expression predicted tumor relapse in TAM-treated ER-positive postmenopausal BC patients [130]	SMRT/NCOR2 [305]	Increased expression is predictive for longer relapse-free survival
miR-30a-3p miR-30c miR-182	Human breast tumors [132]	Increased expression in ER-positive primary breast tumors of patients who received TAM and showed longer progression-free survival; Inverse correlation with HER2 and RAC1 cell motility signaling pathways [132].	AVEN (L, W, Q: miR-30 target)[313]	Increased expression is predictive for response to endocrine therapy
miR-126	Human breast tumors [130]	Higher tumor expression was associated with longer relapse-free time. Increased expression predicted tumor relapse in TAM-treated ER+ postmenopausal BC patients [130]	ADAM9 (W) [314]	Increased expression is predictive for longer relapse-free survival
miR-342-3p	Human breast tumor samples [134]	Downregulated in TAM-R MCF-7/HER2Δ16 cell, TAMR1, LCC2 cells and TAM refractory	BMP7, GEMIN4 (microarray, L, Q,)	Decreased expression is

		human breast tumors vs MCF-7 cells and TAM-responsive tumors. TXNIP is an indirect target of miR-342 [134]	SEMAD(microarray, Q) [134]	predictive of TAM resistance
	Human breast tumors [101]	Decreased in ERα (-) SKBR-3 and MDA-MB-231 cells vs MCF-7 cells. Direct correlation between miRNA-342 expression and ERα expression [101]		
miR-574-3p	Human breast tumors [137]	Downregulation in TAM-resistant MCF-7 cells and clinical breast tumors compared to TAM-sensitive MCF-7cells and adjacent normal control respectively [137]	Clathrin heavy chain (CLTC) (L, W, Q) [137]	Lower expression is predictive for endocrine resistance

Low let-7a, b, and c family members were associated with high recurrence scores (RS) score in human breast tumors [315]. One validated target of let-7b-5p and let-7i-5p is ERa36 [103]ERα36 is an ERα splice variant that is associated with poor prognosis and contributes to endocrine resistance [107, 108]. Let-7 family members are downregulated in breast tumors and TAM-resistant MCF-7 cells [103, 111]. However, meta-analysis identified let-7b-5p as upregulated in ductal carcinoma *in situ* (DCIS) [316], indicating the need for further study on let-7's function in BC.

miR-221 and miR-222 are overexpressed in TAM-resistant and ERα- BC cell lines and tumors [100, 104, 105]. Inhibition of miR-221/222 restored TAM inhibition only to ERα positive MCF-7 cells and not ERα-negative MDA-MB-231 TNBC cells [123]. Higher miR-222 was associated with ERα+, high Ki67 proliferation index, and tumor grade but was not associated with EMT expression markers (increased vimentin, smooth muscle actin (SMA), osteonectin and N-cadherin; loss of E-cadherin) in breast tumors suggesting increased miR-222 as a marker related to aggressiveness and endocrine resistance in ERα+ primary tumors [317]. Identification of increased expression of ERα targeting miRNAs, e.g., miR-222, may predict unfavorable outcomes to endocrine and other therapies [318]. Interestingly E2-ERα inhibits miR-221 [319] and miR-222 [125, 319] expression in ERα positive MCF-7 cells (Fig 13).

miRNAs may also affect ERα-regulated gene transcription in breast tumors by targeting coregulators, i.e., coactivators and corpressors (reviewed in [91]). For this review, we will summarize only those miRNAs that regulate ERα and have been reported to be associated with endocrine-resistance in breast tumors or blood samples (Table 3). For example, miR-10a and miR-10b repress SMRT/NCOR2 [305]. As summarized in

Table 3, the precise role of miR-10a in breast tumors remains to be defined since it has been reported to correlate with both longer relapse-free survival and tumor relapse in TAM-treated patients [130]. Serum levels of miR-10a-5p were reported to be associated with poorer overall survival in acute myeloid leukemia (AML) [320]. miR-10b is considered a metastasis-regulating miRNA in breast and other cancers [321]. Of course since each miRNA regulates hundreds of targets, these miRNAs regulate targets in addition to ERα that are involved in breast tumorigenesis and metastasis.

MICRORNA REGULATION OF ERα COACTIVATOR SRC-3 IN BREAST CANCER

ERα interacts with coactivators and corepressors in a ligand-dependent manner. These coregulators regulate ERα's transcriptional activity by promoting changes in chromatin. ERα coactivator nuclear receptor co-activator 3 (NCOA3), also referred to as SRC-3 [154] and AIB1 [155], is overexpressed in ~ 50% breast tumors [156]. SRC-3 overexpression activates ligand-independent ERα transcription, breast tumor growth, and resistance to TAM [56, 158]. SRC-3 is a direct target of miR-17-5p and overexpression of miR-17-5p in MCF-7 cells repressed E_2-induced proliferation [159]. This suggests that miR-17-5p would be a biomarker of endocrine-sensitivity and a meta-analysis revealed upregulation of miR-17-5p in luminal BC [316].

MICRORNAs AS BIOMARKERS

MammaPrint, Oncotype DX and PAM50 gene arrays are used in ERα+ BC diagnostics, but are limited by cost and inability to predict recurrence beyond 5 years [322-324]. None of these tests currently includes miRNAs. To date, there is one study correlating miRNA expression with RS from Oncotype DX on 23 human BC tumors [315]. That study reported reduced expression of Let-7 family members in cases with high RS and high expression of miR-377-5p, miR-663b and miR 3648 were associated with high RS scores.

Circulating miRNAs as signatures for distinguishing histopathological features and molecular BC subtypes have been reviewed in [8]. Important for biomarker measurement, circulating miRNAs are usually very stable [325]. Moreover, as a potential tool for personalized BC management, serum miRNAs are easily accessible [8]. These features suggest miRNAs as practical for clinical applications. However, discrepancies in miRNA signatures resulting from clinicopathological variables and intrinsic heterogeneity of BC are challenges remaining to be resolved [8].

MICRORNAs AS BIOMARKERS TO TAM RESPONSE AND RESISTANCE

Ideally, miRNA biomarkers would be used to track BC patient response to adjuvant endocrine therapy and thus be predictive of relapse. Endocrine resistant BC cells and tumors show increased epidermal growth factor receptor (EGFR) signaling [164]. TAM, but not raloxifene or fulvestrant, downregulates miR-451 in TAM-R cells [136]. Downregulation of miR-451 upregulates its target protein 14-3-3ζ, a scaffolding protein correlated with early disease recurrence in patients treated with TAM. Overexpression of miR-451 in MCF-7 TAM-resistant BC cells decreased 14-3-3ζ and reduced activation of HER2, EFGR and MAPK signaling, resulting in decreased cell proliferation and migration and increased apoptosis [136]. In addition, overexpression of miR-451 restored the inhibitory effectiveness of SERMs in TAM-resistant cells. In another study, lower circulating miR-451 levels was a predictor to resistance in BC patients who underwent neoadjuvant chemotherapy [326]. These findings suggest that miR-451 may be a biomarker of resistance to both endocrine and chemotherapy. Importantly, higher serum miR-341 levels in patients with locally advanced BC receiving neo-adjuvant chemotherapy were associated with improved clinical and pathological responses and disease-free survival [327].

miR-105-2, miR-877, let-7f, miR-125a and miR-574-3p were associated with a loss of inhibition by TAM in MCF-7 cells [137]. Of these miRNAs, miR-574-3p was also reduced in BC tissue samples compared to adjacent normal breast tissue. This report suggests that miR-574-3p may serve both as a diagnostic biomarker of BC and a predictive biomarker of endocrine-resistance. Increased miR-125b was associated with lower relapse-free survival, poor prognosis and their repression was suggestive as therapeutic targets to overcome letrozole resistance [119]. Indeed we reported higher miR-125b expression in TAM-R LY2 compared to TAM-S MCF-7 cells [223]. Thus reduced expression of miR-125 family members may serve as biomarkers of endocrine response.

To identify miRNAs that promote TAM resistance, Miller et al. used microarray analysis to show increased expression of miR-221, miR-222, and miR-181 and decreased expression of miR-21, miR-342, and miR-489 in TAM-resistant *versus* TAM-sensitive MCF-7 cells [104]. miR-221/222 was higher in endocrine resistant, HER2+ primary BC tumors [104]. Overexpression of miR-221/222 made TAM-sensitive MCF-7 cells resistant to TAM. This finding makes sense because, as reviewed above, miR-221 and miR-222 target ERα [100]. Moreover, these result correlate with our observation of higher expression of miR-221 and miR-222 in TAM-R LY2 cells *versus* TAM-S MCF-7 cells [223].

miR-375 was downregulated in a mesenchymal TAM-resistant MCF-7 cell line [328]. Re-expression of miR-375 sensitized TAM-resistant cells to TAM and reduced invasiveness by decreasing expression of mesenchymal markers fibronectin, ZEB1, and SNAI2 while increasing epithelial markers E-cadherin and Tight Junction Protein 1 (TJP1, ZO-1). This resulted in partial reversal of EMT which is called MET (mesenchymal-to-epithelial transformation). Metadherin (MTDH), a cell surface protein upregulated in breast tumors that mediates metastasis [173], was identified as a direct, *bona fide* miR-375 target mediating this response [328]. TAM- treated patients whose primary tumor had high MTDH showed shorter-disease-free survival and a higher risk of relapse. Thus, reduced miR-375 may be a biomarker of poor prognosis and TAM-resistance. Indeed, a recent report identified upregulation of circulating miR-375 in BC patients with recurrence [309]. It is uncertain why up or down regulation of miR-375 is associated with TAM resistance in BC however, it should be noted that miR-375 dysregulation in many cancers is due to several factors including aberrant promoter methylation and dysregulation of transcription factors [329]. miR-375 serves a tumor suppressor role in other cancers [329].

Huo *et al*. identified four miRNAs to be upregulated in the serum of BC patients with recurrent disease: miR-21-5p, miR-375, miR-205-5p, and miR-194-5p and three miRNAs to be downregulated: miR-382-5p, miR-376c-3p, and miR-411-5p) [309]. Upregulation of miR-205 was previously reported to mediate AI resistance in aromatase-overexpressing MCF-7 cells and was associated with poor prognosis in breast tumors [119]. These studies suggest increased miR-205 may serve as a marker of poor prognostic in BC patient serum and may be indicative of AI resistance. Additional studies are required to validate the other miRNAs identified in [309] as biomarkers of endocrine resistance.

High breast tumor expression of miR-30a-3p, miR-30c, and miR-182 were identified as predictors of clinical benefit from TAM for patients with ERα positive primary breast tumors [132]. Global testing pathway analysis associated miR-30c with low HER and RAC1 signaling pathways, but other targets are likely involved. High expression of miR-30e* was associated with favorable prognosis in luminal tumors from BC patients receiving adjuvant trastuzumab treatment [330]. These reports suggest miR-30 family may be a biomarker for benefit to both endocrine and chemotherapy. However, miR-30 is upregulated in tumor-initiating cells (T-ICs); a sub-population of cancer cells mediating tumor initiation, tumor progression, metastasis and post-treatment relapse [331] suggesting that depending on BC stage, miR-30 may switch form an oncogenic miRNA to a tumor suppressor miRNA. There are no reports of miR-30 as a BC biomarker in human serum.

High levels of miR-26a in breast tumors were associated with low levels of Enhancer of Zeste Homolog (EZH) and a favorable outcome in BC patients on TAM

[332, 333]. EZH is a conserved chromatin modifier required for epigenetic memory and maintenance of cellular characteristics [334]. Low levels of cell cycle regulators CCNE1 and CDC2 were also associated with high levels of miR-26a, although they were not shown by authors to be direct targets of miR-26a [333]. There are no reports of miR-26a as a BC biomarker in human serum.

High tumor expression of miR-210 was associated with increased risk of BC recurrence [102]. Increased expression of miR-210 was associated with poor clinical outcome to TAM treatment. Serum miR-210 was not found to be a predictive serum marker in HER2+ BC patients receiving trastuzumab or lapatinib [335]

miRNA screening of recurrent *versus* recurrent-free primary ERα+ breast tumors from postmenopausal BC patients treated with adjuvant TAM identified increased miR-126 and miR-10a as predictive of longer relapse-free survival [130]. A meta-analysis of 30 studies supported increased miR-126 as predicting favorable survival in various cancers [336].

Upregulation of miR-1266 is indicative of lower disease-free survival and prognostic for BC recurrence, metastasis and TAM response in ER+ BC patients [311]. miR-1266 was predicted to target the 3’ UTR region of Homeobox B13 (HOXB13) and Interleukin 17 Receptor B (IL17BR). The HOXB13 to IL17BR expression ratio is a potential biomarker for TAM response [337-339]

EXOSOMAL MICRORNAs AS POSSIBLE BIOMARKERS OF ENDOCRINE-RESISTANT BREAST CANCER

Exosomes are small extracellular vesicles of endosomal origin that are formed by the fusion of multivesicular bodies with plasma membrane (PM) [184, 185]. The content of exosomes reflects their tissue/cell type of origin [193, 340]. Exosomes contain mRNA, miRNA, and small regulatory RNAs as well as Dicer, TRBP, and AGO2 to process pre-miRNAs into mature miRNAs [193], which are protected from ribonucleases in circulation [183]. Current studies indicate different miRNAs are associated with specific endogenous exosomes [191]. There is much excitement about the exploration of exosomes in the liquid biopsy field as biomarkers of cancer diagnosis and monitoring therapy [341]. Tumor-derived exosomes (TDEs) are thought to play a role in drug resistance by exporting drugs, neutralizing antibody-based drugs including trastuzumab used in HER2+ BC, and exosome-mediated transfer of miRNAs (reviewed in [342]). Exosomal delivery of miRNAs is thought to be important in breast tumorigenesis and metastasis. One of the areas of challenge in miRNAs in exosomes or in blood samples as biomarkers is a lack of a standardized approach and which blood fraction is best for identifying cancer-related miRNAs is unclear (reviewed in [343]). Further, various techniques are used for isolating exosomes and quantifying exosome-associated proteins, *e.g.*, CD9, CD63, as markers (Reviewed in [343]). Quantitative realtime PCR is used for miRNA detection in exosomes.

Exosomal transfer of miRNAs to cells is implicated in antiestrogen resistance [122] (Fig. 14, Table 4). Wei *et al.*, reported that addition of labelled exosomes from TAM-R MCF-7 cells into the culture medium of TAM-S MCF-7 cells resulted in uptake of the labelled exosomes by the TAM-S cells [122]. Moreover, miR-221/222 were released from exosomes into TAM-S MCF-7 cells resulting in concomitant reduction in the expression of their target genes p27 and ERα, and enhanced TAM resistance. Transfection of miR-221/222 inhibitor into the MCF-7 TAM-S cells that were incubated with the TAM-R MCF-7 exosomes reduced TAM-resistance. These data support the importance of miR-221/222 in TAM-resistance in MCF-7 cells and a possible role for exosomal transfer of miRNAs in TAM-resistance. The authors also observed that the exosomes secreted by TAM-S MCF-7 cells were larger in size and number compared to TAM-R MCF-7 cells [122].

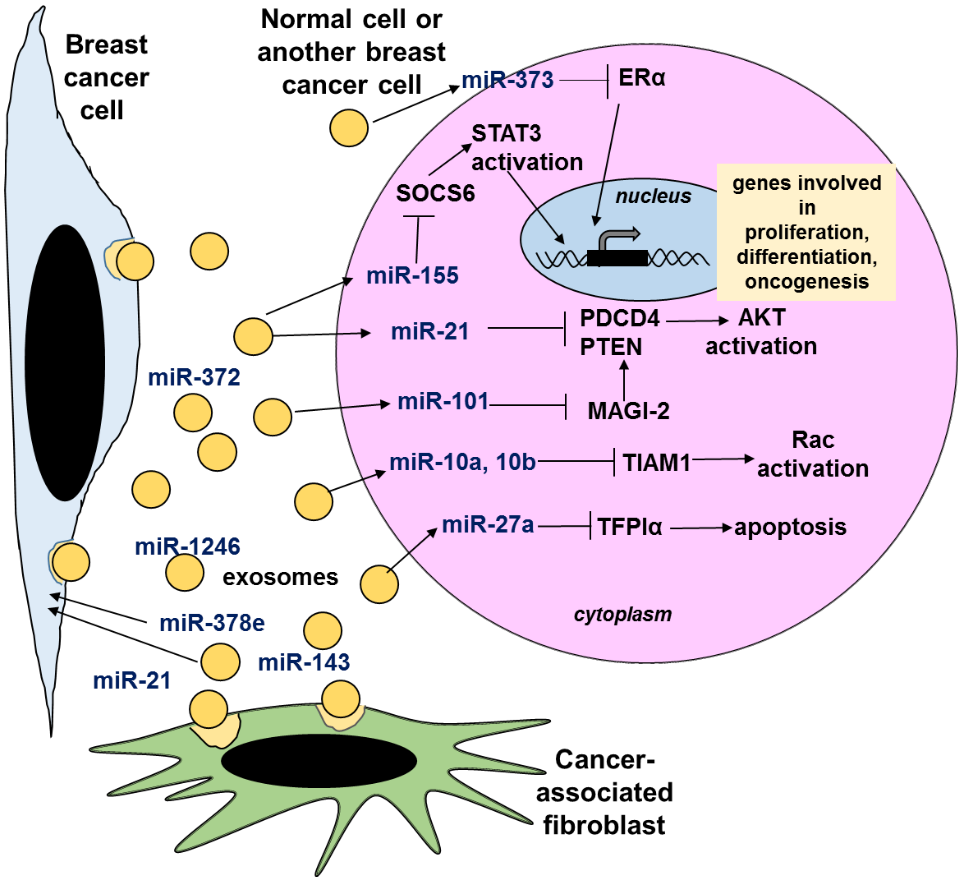
Breast cancer cell
Normal cell or another breast cancer cell
miR-373
ERα
STAT3 activation
SOCS6
nucleus
genes involved in proliferation, differentiation, oncogenesis
miR-155
miR-21
PDCD4
PTEN
AKT activation
miR-372
miR-101
MAGI-2
miR-10a, 10b
TIAM1
Rac activation
miR-27a
TFPIα
apoptosis
miR-1246
exosomes
cytoplasm
miR-378e
miR-143
miR-21
Cancer-associated fibroblast

Figure 14. Exosome Transfer of miRNAs from breast cancer cells to normal cells may play a role in tumor progression and metastasis.
Exosomal miRNAs are from Table 2**.** While targets of these exosomal miRNAs have not been established, experimentally validated by 3’UTR luciferase reporter assay (*bona fide*) targets of these miRNAs have been shown to be involved in breast or other cancers:

- T-lymphoma invasion and metastasis inducing factor 1 (TIAM1) is inversely correlated with miR-10a expression [344]
- TIAM1 is a *bona fide target* of miR-10b which results in inhibition of TIAM1-mediated RAC activation [345]
- Tissue factor pathway inhibitor (TFPI) α is a *bona fide* target of miR-27a [346]
- MAGI-2 is a *bona fide* target of miR-101 [118]
- ERα protein expression was repressed by miR-373 in MCF-7 cells [196]
- Verified targets of miR-373 include LATS2, CD44, DCH1, RAD52, MBD2, NFIB, PPP6C, TXNIP, RElA, TGFBR2, mTOR, SIRT, DKK1, BTG1, RNFAIP1, TP52INP1, IRAK2, LAMP1, MMP14, JAK1, IRF9, and PIK3CA [347]
- Programmed cell death protein 4 (PDCD4) and Phosphatase and tensin homolog (PTEN) are *bona fide* targets of miR-21 [348]
- Suppressor of cytokine signaling 6 (SOCS6) is *bona fide* target of miR-155 [349]
- miR-372 and miR-1246 have no confirmed targets in BC, although miR-1246 was shown to promote growth and metastasis of colon cancer by directly targeting CCNG2 [350].

Table 4. Exosomal miRNAs described in human breast cancer cell lines and tumors

↑ Increased expression; ↓ Reduced expression. Abbreviations: nontumorigenic mouse mammary epithelial cells (NMuMG)

Extravessicular (EV) miRNA composition	Direction of miRNA expression	Sample source			Time in culture prior to harvesting exosome	comments	Reference
		Cell line	Patient	Xenograft			
miR-10a, miR-155, miR-373, miR-10b, miR-21, miR-27a	↑	MCF-7 MCF-10A NMuMG MDA-MB-231	Yes (serum)	Yes	24 h 72 h	OncomiRs miR-10b and miR-21 were confirmed by northern blot. miR-10b deficient mice have normal development but miR-10b deletion inhibited polyomavirus middle t oncogene-induced (PyMT) mammary tumorigenesis, progression, and metastasis [321]	[193]
miR-373, miR-101, miR-372	↑	MCF-7	Yes (Serum)			High in TNBC. Overexpression of miR-373 promotes loss of ERα	[196]

						and resistance to Camptothecin	
miR-1246, miR-21	↑	MCF7, ZR-75-1, T47D, MDA-MB-231, BT-20, BT-474, and SK-BR-3	Yes (plasma)	Yes (PDX mouse plasma)		Higher in plasma exosomes of 16 BC patients compared to healthy controls	[351]

A miRNA array identified exosomal miR-27a and miR-155 from cultured MCF-7 and MDA-MB-231 cells [193]. miR-155 acts as an oncomiR and mediates TAM-resistance by reducing SOCS6 leading to STAT3 activation and increased expression of genes involved in proliferation and differentiation in MCF-7 and SKBR3 cells [349]. MiR-27a/b were reported to negatively regulate TFPIα expression in MCF-7 cells [346] and TFPIα induces apoptosis in breast cancer cells [352]. We have modeled these potential pathways for exosomal miR-27a and miR-155 in Figure 14.

High miR-101, miR-372, and miR-282 were identified in the serum of BC patients compared to healthy women or those with benign breast disease [196]. MAGI-2 (membrane-associated guanylate kinase), a scaffold protein required for PTEN activity, is a *bona fide* target of miR-101 [118]. A decrease in MAGI-2 by miR-101 increased PTEN and PDCD4 leading to AKT activation [118]. This activity of miR-101 is modeled in Figure 14. Higher exosomal levels of miR-373 in serum from BC patients was indicative of a TNBC phenotype [196]. Further, miR-10 and miR-21 were significantly increased in exosomes from BC cells and patients sera [193]. miR-10 and miR-21 initiate tumor formation in mice [193]. miR-1246 and miR-21 were significantly higher in the exosomes from plasma of 16 BC patients compared to the plasma exosomes of healthy control subjects [351]. These studies suggest that exosomal miR-10, miR-1246 and miR-21 are diagnostic biomarkers to distinguish BC patients from healthy controls.

Exosomal transfer of miR-21 in breast cancer has recently been supported by recent studies [353]. These authors demonstrated that exposure of T47D, BT549 and MDA-MB-231 breast cancer cells to exosomes (containing miR-21, miR-378e, and miR-143-3p) from cancer-associated fibroblasts (CAFs) containing miR-21, miR-378e, and miR-143-3p induced stemness and EMT phenotypes in the cancer cells [353]. Upon evaluating 744 Breast Invasive Carcinoma patients from The Cancer Genome Atlas (TCGA) database, lower miR-378 expression was associated with longer overall survival [353]; suggesting a prognostic role of low miR-378. Increased miR-143 expression was associated with higher (III/IV) compared to lower (I/II) breast cancer stages [353]. Further, a positive correlation between miR-143 and -378 and between miR-143 and miR-21 expression was observed [353]. Thus higher exosomal expression of miR-21, miR-378e, and miR-143-3p may suggest progression toward metastasis in breast cancer.

Overall, the clinical use of exosomal miRNAs as candidate biomarkers for cancer diagnosis and prognosis remains to be proven [91]. Moreover, the ability manipulate exosomes to deliver antitumor agents including doxorubicin [354] and miRNAs such as let 7a [355] suggests a new therapeutic approach for drug delivery. Clearly, additional studies encompassing the packaging, formation, and the delivery of exosome-containing miRNAs is warranted [186].

CLINICAL TRIALS OF MICRORNAs AS BIOMARKERS IN BREAST CANCER

There are two ongoing clinical trials assessing the potential use of miRNA as biomarkers. NCT01612871 focuses on identifying circulating miRNAs in patients with metastatic invasive BC or locally advanced BC for which TAM or AIs are indicated. NCT01722851 aims to identify miRNAs that could be used to monitor a patient’s response to chemotherapy and hormonal therapy. The limited number of miRNA clinical trials on endocrine therapy and/or resistance suggest that although miRNAs are promising markers for clinical practice, further research is warranted to understand molecular mechanisms of already identified miRNAs and move miRNAs into clinical application.

CONCLUSIONS

miRNAs are dysregulated in endocrine-resistant BC. Identifying miRNAs that will be useful as predictive serum biomarkers of developing endocrine resistance and in identifying individuals who will benefit from endocrine therapy is critical for improving management for BC patients with ERα+ primary tumors. No reports have identified miR-29 family members as a prognostic or predictive markers of endocrine resistance. Nonetheless, low miR-29 expression correlates with poor overall survival in ERα+ breast cancer patients (Supplementary Fig. 18)[356]. It is beyond the scope of this chapter to detail the genes and pathways involved in each dysregulated miRNA, and much has been reviewed in Chapter II and elsewhere [218, 220]. The possibility of using exosomes as a biomarkers for endocrine resistance is a promising idea, but additional studies are warranted to standardized exosomal isolation techniques for significant progress to be made in this area of research. The ability to design synthetic exosomes carrying tumor suppressor miRNAs that can be targeted to metastatic cells to inhibit metastasis warrants more research. Future studies are also needed to elucidate the mechanisms behind miRNA dysregulation and to develop ‘targeted’ therapeutics to counter miRNA dysregulation and enhance endocrine sensitivity.

CHAPTER VI: RESEARCH IMPLICATIONS

The sustained exposure to endogenous estrogens is involved in the initiation and progression of breast cancer [357]. The cellular effects of estrogens are mediated by ERα and ERβ and their splice variants [62]. Approximately 70% of primary breast tumors express ERα [56, 358], providing the rationale for the successful use of targeted endocrine therapies in breast cancer progression (Reviewed in [29]).

Endocrine therapies including SERMs *e.g.*, tamoxifen (TAM); SERDs, *e.g.*, fulvestrant (ICI 182,780), and aromatase (CYP19A) inhibitors (AI), *e.g.*, anastrozole and letrozole, are the frontline adjuvant therapies in treatment of women with ERα positive breast tumors [359]. These therapies have resulted in substantial improvements in overall survival fand quality of lives of breast cancer survivors [360]. Unfortunately, the effectiveness of TAM and AI therapy is limited as seen in relapse of ~ 40% of patients [55]. When resistance occurs, it is unclear which subsequent endocrine therapy is most appropriate [361]. Overall, the mechanisms of endocrine resistance are many and include mutations in the ligand binding domain of ERα [62], increased expression of truncated forms of ERα (including ERα36) [63], amplification of multiple growth signaling pathways [42, 56, 362-364], and dysregulation of miRNAs [68]. In this dissertation, I described the role of miR-29b-1 and miR-29a in breast cancer and endocrine resistance.

In chapter III, I reported that miR-29b-1 and miR-29a expression in response to TAM is dependent on endocrine sensitivity of the breast cancer cell line studied. miR-29b-1 and miR-29a are members of the miR-29 family and with the same seed sequence [227-229]. They are co-transcribed as a single primary transcript, sharing the same promoter, with miR-29b-1 upstream of miR-29a [227-229]. Using qPCR, I confirmed the original microarray study [223] that 4-OHT decreased miR-29b-1 and miR-29a expression in endocrine-sensitive MCF-7 breast cancer cells and 4-OHT increased transcription of both microRNAs in MCF-7 derivative, TAM-R LCC2, LCC9 and LY2 cells [275]. Similar observations were made at the primary (pri-miR) transcript level. As TAM exerts its effects, in part, through ERα, I examined the role of ERα in 4-OHT-induced regulation of miR-29b-1 and miR-29a. Using knockdown studies, ERα was shown to mediate 4-OHT regulation of the primary and mature transcripts of miR-29b-1 and miR-29a in MCF-7 and LCC9 cells [275].

I then sought to determine whether ectopic expression of miR-29b-1/a in TAM-S MCF-7 cells will desensitize cells to 4-OHT and whether inhibiting miR-29-b-1/a in TAM-R LY2 will enhance 4-OHT inhibition of cell proliferation, cell migration and colony formation. Transfection of TAM-S MCF-7 with miR-29b-1 or miR-29a did not result in endocrine resistance, but it did repress cell proliferation in both TAM-S MCF-7 and its TAM-R cell line derivatives [275]. Previously, transient overexpression of miR-29a also inhibited the growth of MDA-MB-453 TNBC cells [236], implying repression of cell growth by miR-29b-1 and miR-29a is not dependent on ERα. Inhibition of miR-29b-1 or miR-29a did not enhance the sensitivity of the TAM-R LCC9 and LY2 cells to 4-OHT. In TAM-R LY2 cells, overexpression of miR-29b-1 and miR-29a decreased cell migration and colony formation. Interestingly, overexpression of miR-29a alone or in combination with miR-29b-1 enhanced 4-OHT inhibition of LY2 colony formation [275]. These data suggest that the 4-OHT-induced increase in miR-29b-1/a in LY2 may be involved in TAM-sensitivity, not resistance

Also in Chapter III, I reported DICER1 protein levels to be down regulated by miR-29b-1 and miR-29a in LY2 cells [275]. DICER1 is a validated target of miR-29 family members [209]. DICER1 regulates cellular processes including cell differentiation, programmed cell death, senescence, DNA repair, and chromatin remodeling [258-262]. In TAM-R LY2 breast cancer cells, TAM decreased DICER1 protein expression by upregulating miR-29b-1/a [275], suggesting a decrease in DICER1 mediates resistance to TAM. A decrease in DICER1 would be expected to result in lower miRNA expression. In fact, we observed lower overall miRNA expression of 4-OHT-treated LY2 cells compared with 4-OHT-treated MCF-7 cells ([223]; Klinge, unpublished, GSE28267)

In Chapter VI, RNA-seq was used to identify miR-29b-1 and miR-29a transcriptomes in TAM-S MCF-7 and TAM-R LCC9 breast cancer cells. miR-29b-1 and miR-29a have common and unique regulated transcripts. Commonly regulated transcripts can be attributed to both miRNAs having the same seed sequences. Uniquely regulated transcripts can be due to differences in sequences adjacent to the seed sequence and the predominant nuclear localization of miR-29b-1 *versus* cytoplasmic localization of miR-29a [255, 256]. However, miR-29b-1/a can also indirectly regulate transcripts by regulating transcription factors. Overall, miR-29b-1/a regulated more transcripts in LCC9 than MCF-7 cells. Enrichment analysis of unique miR-29 target transcripts in LCC9 cells identified top regulated pathways including oxidative phosphorylation (OXPHOS), ATP metabolism, apoptosis and survival.

To examine involvement of miR-29 in regulation of OXPHOS, I studied mitochondrial bioenergetics in LCC9 cells. Pre-miR-29a transfection in LCC9 cells repressed mitochondrial activity by decreasing basal OCR, ATP-linked OCR, and mitochondrial (mt) reserve. This suggests that repression of cell proliferation, migration and colony formation upon ectopic miR-29b-1/a expression (observed in Chapter VII) may in part be due to repression of mitochondrial activity. Repression of miR-29a increased OCR and mt reserve, suggesting that repression of miR-29a may serve as an adaptive response to meet increased energy demand of cancer cells and promote survival. Repression of miR-29a also increased basal ECAR (glycolysis) in LCC9 cells. RNA-seq data identified and qPCR confirmed electron transport chain (ETC) proteins including ATP synthase genes *ATP5G1* and *ATPIF1* as targets of miR-29. Luciferase assay confirmed *ATP5G1* and *ATPIF1* as *bona fide* miR-29 targets. It will be interesting to further investigate the roles of *ATP5G1* and *ATPIF1* in breast cancer

In conclusion, this study has provided important insights into the role of miR-29b-1 and miR-29a in endocrine resistant breast cancer cells. The suggestion that a 4-OHT-induced increase in miR-29b-1/a in LY2 may be involved in TAM-sensitivity, not resistance warrants further research. The identification of miR-29 targets mediating specific cellular processes in MCF-7 TAM-S and LCC9 TAM R cells offers clues for additional research on the impact of miR-29 regulation in breast cancer.

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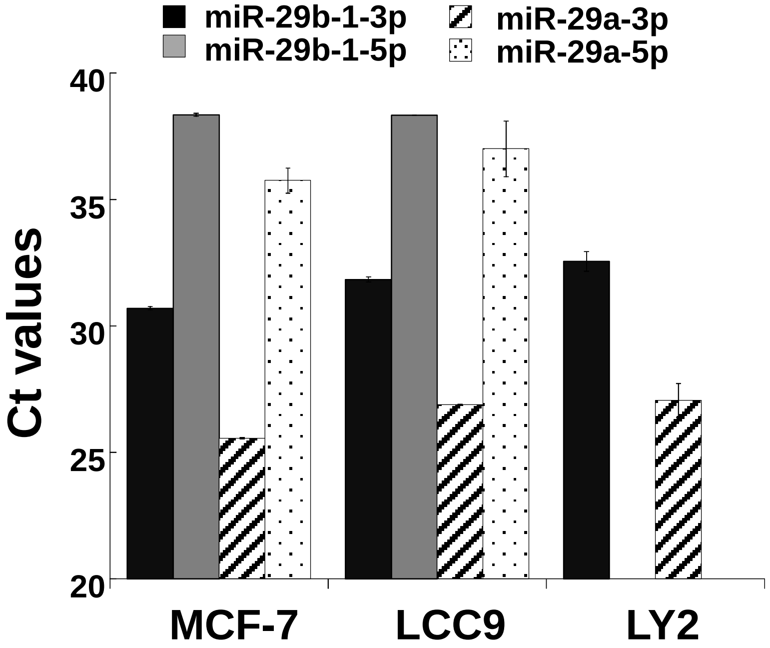
APPENDIX I: SUPPLEMENTARY MATERIAL

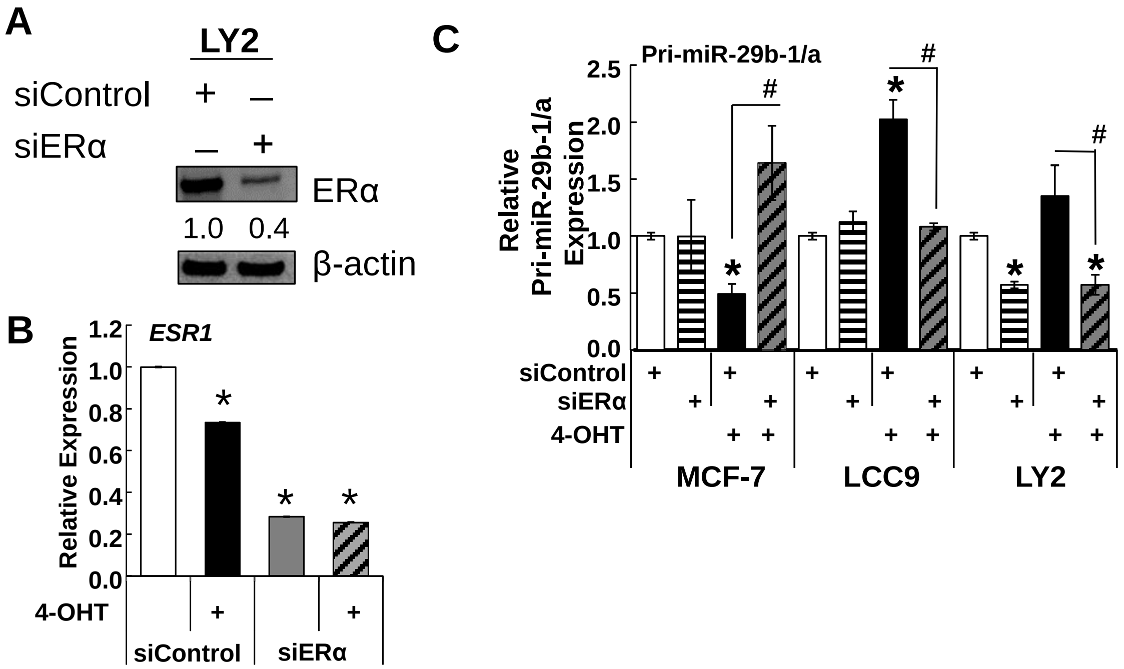
Supplementary Table 1: miR-29 targets experimentally validated in breast cancer

miRNA	**Function**	**Process**	**Target**	**Cell lines**	**Method of target confirmation**	**Reference**
miR-29a	OncomiR	Metastasis (EMT)	Tristetraprolin (TTP)	Epithelial EpRas (mouse breast) cells Mesenchymal RasXT (mouse breast) cells Human breast cancer patients	Luciferase reporter assay Western blot qPCR	Gebeshuber *et al*., 2009 [365]
miR-29b	OncomiR	Cell proliferation	Phosphatase and Tensin Homolog (PTEN)	MCF-7 cells MDA-MB-231 Patient sample	Western blot	Wang *et al*., 2011[366]
miR-29a	No causal effect of miR-29a on breast cancer progression through ATPB1		ATPase, Na(+)/K(+) transporting, beta 1 polypeptide (ATP1B1)	T47D	Luciferase reporter assay Western blot	Cochrane *et al*., 2012 [367]
miR-29a,b,c	Onco suppressor	Cell differentiation	Kruppel-like factor 4 (KLF4)	T47D BT474 (ER+ breast cancer cell)	Luciferase reporter assay Western blot	Citterlly *et al*., 2013 [235]
miR-29a	Onco suppressor	Cell proliferation	V-Myb Avian Myeloblastosis Viral Oncogene	T-47D, MDA-MB-453 MCF-7	Luciferase reporter assay Western blot	Wu *et al*., 2013 [236]

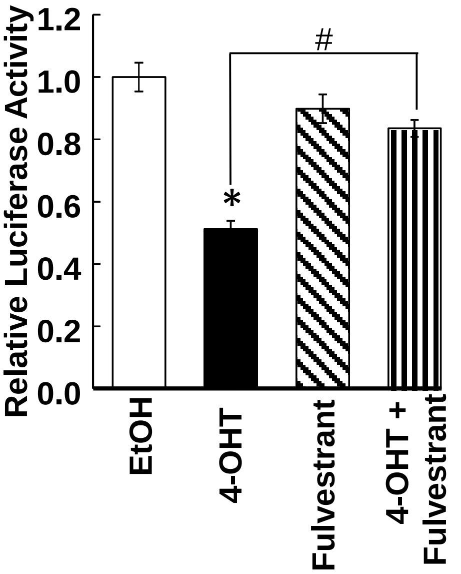
			Homolog-Like 2 (B-myb)	MCF-10A HMEC		
miR-29a	OncomiR	Drug resistance (to Adriamycin (Adr) and docetaxel (Doc))	PTEN	MCF-7/Adr MCF-7/Doc	Western blot qPCR	Zhong *et al*., 2013 [251]
miR29b	Onco suppressor	Cell differentiation and metastasis	ANGPTL4, LOX, MMP9, PDGFC and VEGFA	MDA-MB-231 MDA-MB-231-GATA3	Luciferase reporter assay qPCR	Chou *et al*., 2013 [230]
miR-29a,b	OncomiR	Metastasis (EMT)	N-myc interactor (NMI)	MCF-7 T47D MDA-MB-231 MDA-MB-435	Luciferase reporter assay Western blot	Rostas *et al*., 2014[234]
miR-29b,c	No causal effect of miR-29a on breast cancer progression through ADAM12-L		A Disintegrin And Metalloproteinase 12) ADAM12-L	SUM159PT, BT549	Luciferase reporter assay Western blot qPCR	Duhachek-Muggy *et al*., 2015 [368]
miR-29c	Onco suppressor	Cell differentiation	Kruppel-like factor 4 (KLF4)	$ALDH^{-}$ MCF10A	qPCR	Vares *et al*., 2015 [369]
miR-29b	Onco suppressor	Cell proliferation, breast cancer development and progression	Chaperone protein Hsp47	MDA-MB-231	Luciferase reporter assay Western blot	Zhu *et al*., 2015 [370]



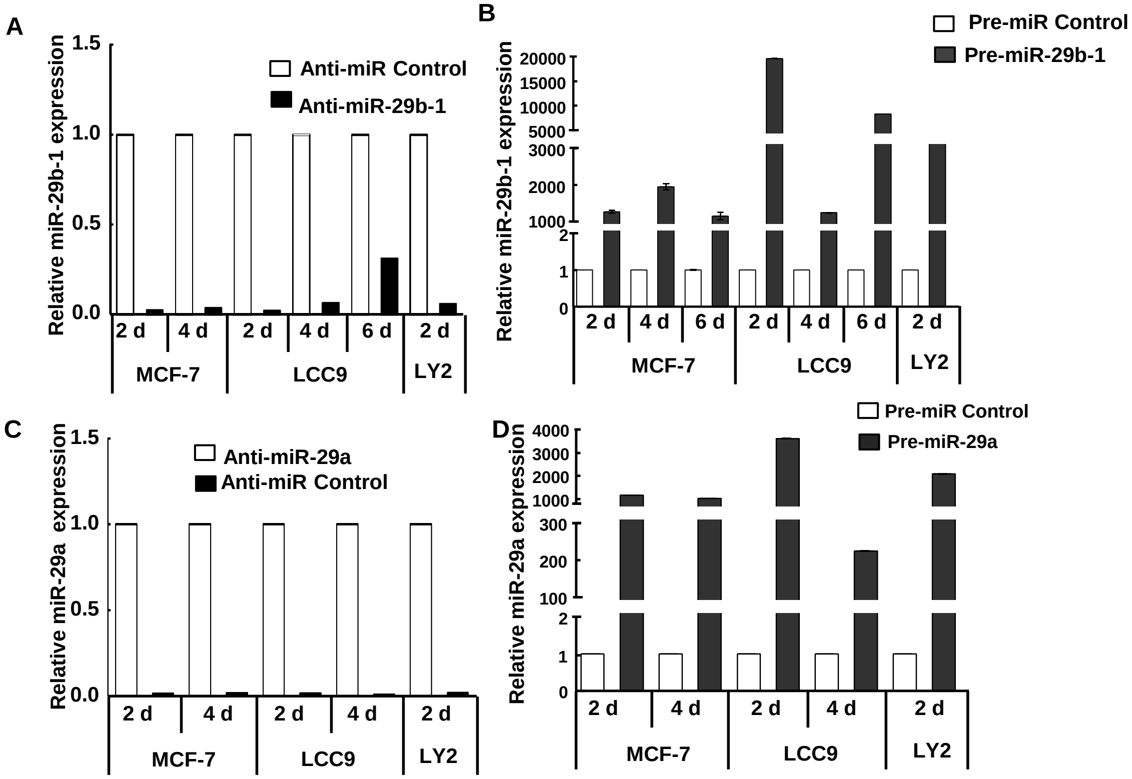
Supplementary Figure 1. Basal expression of miR-29b-1-3p, miR-29b-1-5p, miR-29a-3p and miR-29a-5p in MCF-7, LCC9 and LY2 breast cancer cells. Cells were grown in hormonally depleted medium for 48 h and miRNA expression was determined by qPCR. Each sample was run in triplicates. miR-29a-5p and miR-29b-1-5p CT values were not examined for LY2 cells.



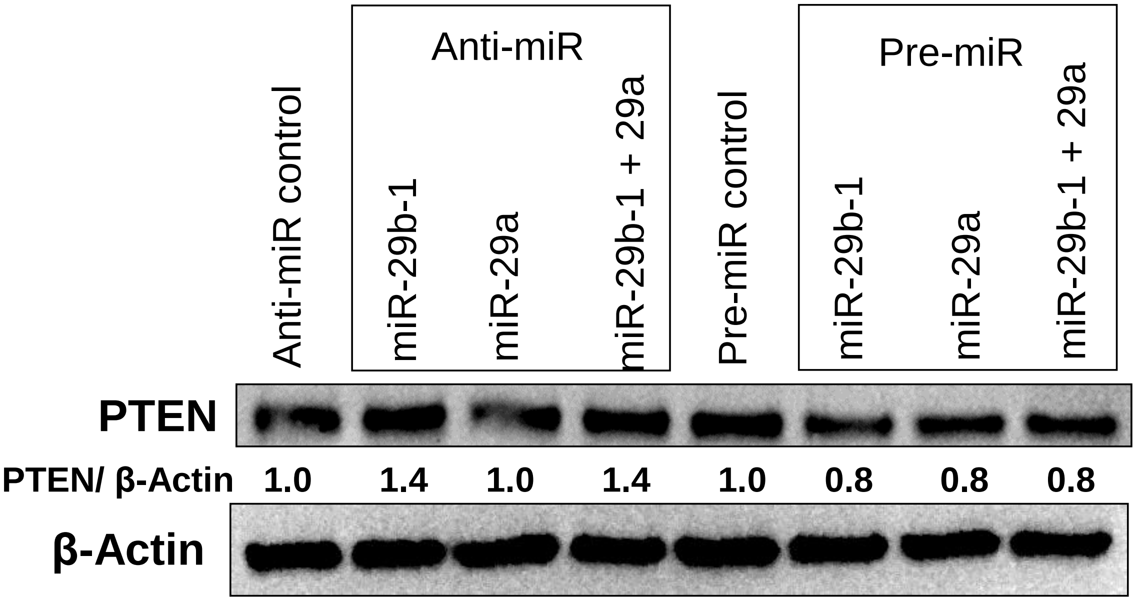
Supplementary Figure 2. Knockdown of ERα inhibits pri-miR-29b-1/a transcription in LY2 cells. LY2 cells were grown in hormonally depleted medium and transfected with siControl or siERα. 48 h post transfection, cells were treated for 6 h with DMSO or 100 nM 4-OHT. (A) ERα protein was examined in WCE and the blot was stripped and re-probed for β-actin for normalization. Values are the ERα/β-actin with siControl set to one. Q-PCR for ESR1 (B); pri-miR-29b-1 and pri-miR-29a (C). Data for MCF-7 and LCC9 in panel C are identical to those in Fig. 5C. *p < 0.05 *versus* control-transfected cells. #p < 0.05 *versus* 4-OHT-treated Control-transfected cells.



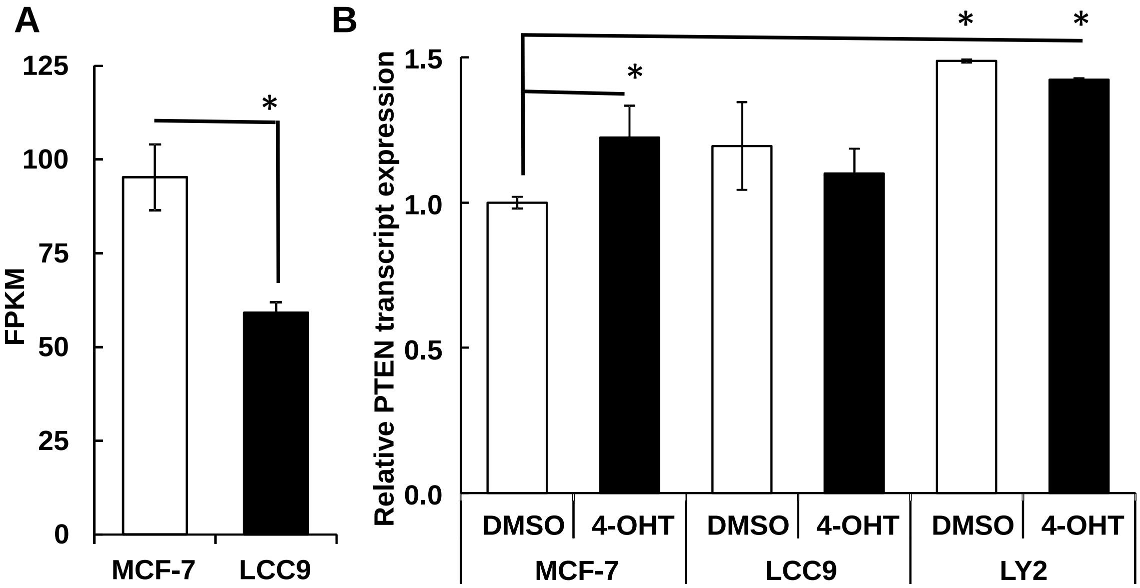
Supplementary Figure 3. 4-OHT-ERα regulates miR-29b-1/a promoter activity. CHO-K1 cells were transfected with a miR-29b-1/a luciferase reporter and an ERα expression vector. Cells were treated with EtOH (vehicle control), 100 nM 4-OHT, 100 nM fulvestrant, or both 100 nM 4OHT+ 100 nM fulvestrant for 24 prior to dual luciferase assay. Relative luciferase expression for EtOH was set to 1. Values are the average ± of 4 separate wells in one experiment. *p < 0.05 *versus* EtOH; #p < 0.05 *versus* 4-OHT-treated cells



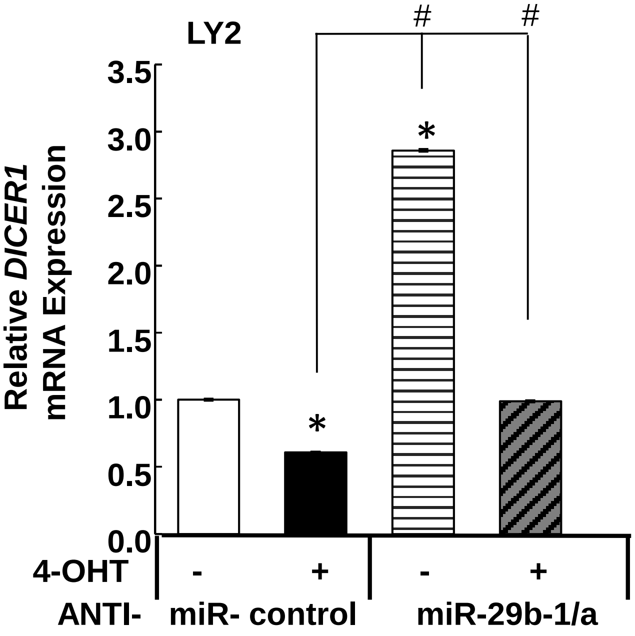
Supplementary Figure 4. Successful knockdown and overexpression of miR-29b-1 /a. (A &C) Demonstrates the knockdown of miR-29b-1/a for up to 6 days after transfection. (B &D) Demonstrates the knockdown of miR-29b-1/a for up to 6 days after transfection. Q-PCR was performed and miR-29b-1/a was normalized to RNU48 or RNU6B. Values are the mean ± SEM of 1-3 independent experiments. Within each experiment, each sample was run in triplicates.



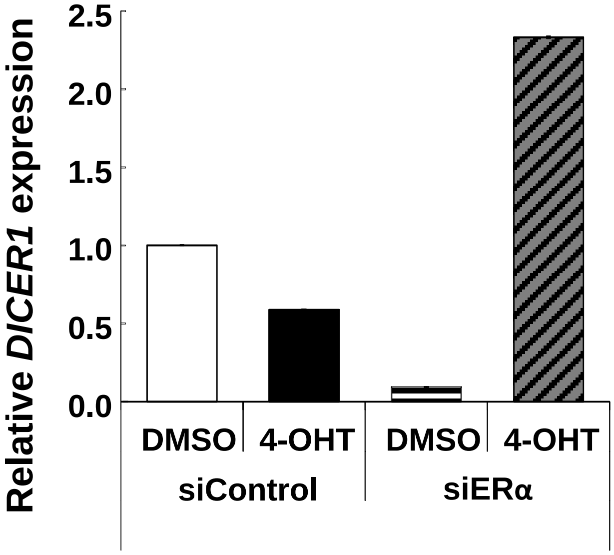
Supplementary Figure 5. miR-29b-1/a downregulates PTEN in LY2 cells. LY2 cells were transfected with anti-miR control, anti-mIR-29b-1, anti-miR-29a, or the combination for 48 h. The blot was probed for PTEN and then for β-actin. Values are the ratio of PTEN/ β-actin from the experiment shown. This is the same blot used for DICER1 in Fig. 10A and thus the β-actin blot is identical.



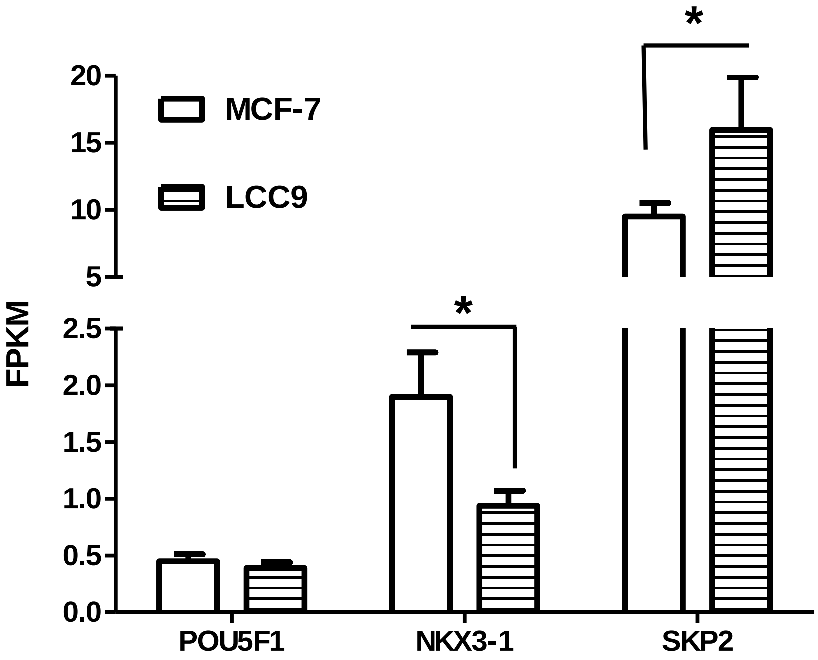
Supplementary Figure 6. Relative basal and 4-OHT-regulated *PTEN* expression. A) *PTEN* expression data (FPKM = fragments per kilobase of exon per million fragments mapped) from RNA-seq (GSE81620) in MCF-7 and LCC9 cells. *P < 0.01 *versus* MCF-7 cells. B) Cells were grown in hormonally depleted medium for 48 h and treated with vehicle (DMSO) or 100 nM 4-OHT for 6 h. *PTEN* mRNA expression was determined by qPCR relative to *18S* or *GAPH*. Values are the mean ± SEM of 3 separate experiments. P < 0.05 *versus* MCF-7 DMSO.



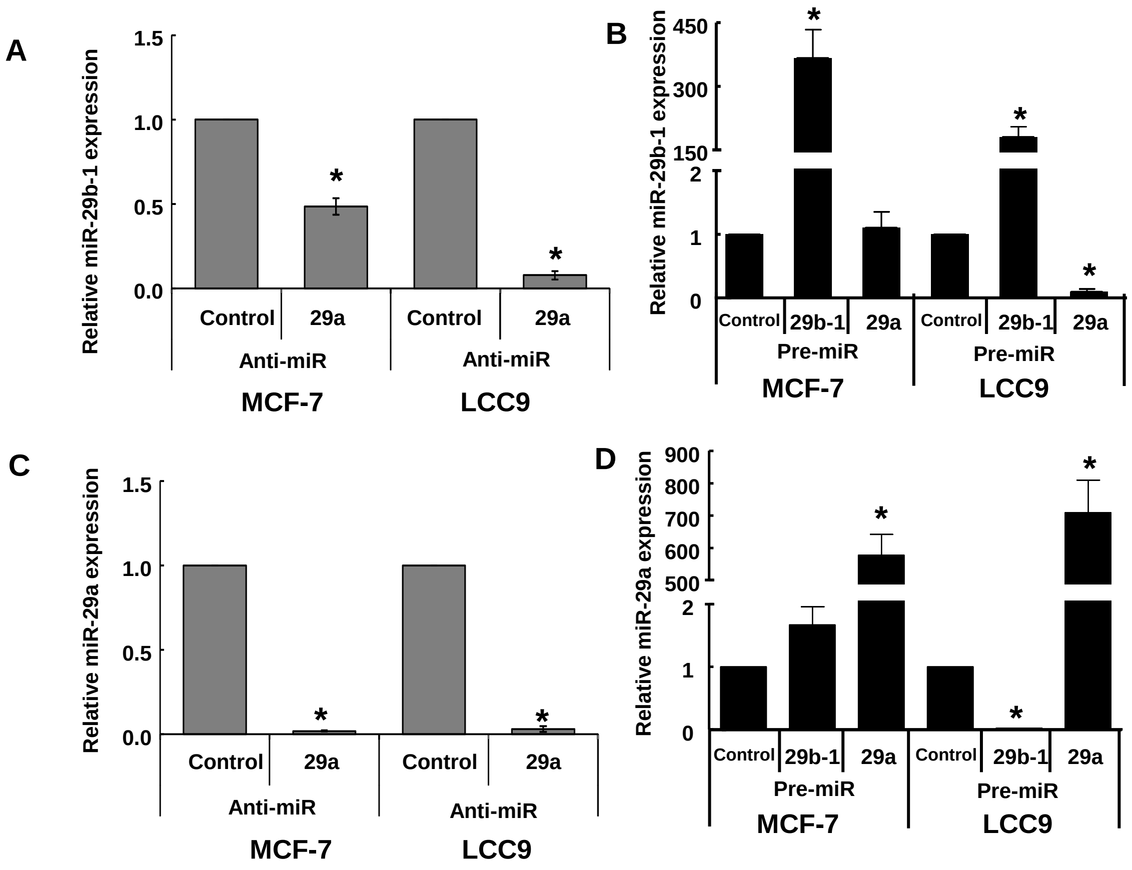
Supplementary Figure 7. LY2 cells were grown in hormonally depleted medium and transfected with Anti- miR-Control, Anti-miR-29b-1 + Anti-miR-29a. 48 h post transfection, cells were treated for 6 h with DMSO or 100 nM 4-OHT. Q-PCR was performed to determine *DICER* mRNA expression relative to *18S*. Values are the mean ± SEM of three separate wells in one experiment. *p < 0.05 *versus* vehicle control-transfected cells. #p < 0.05 *versus* 4-OHT-treated Control-transfected cells.



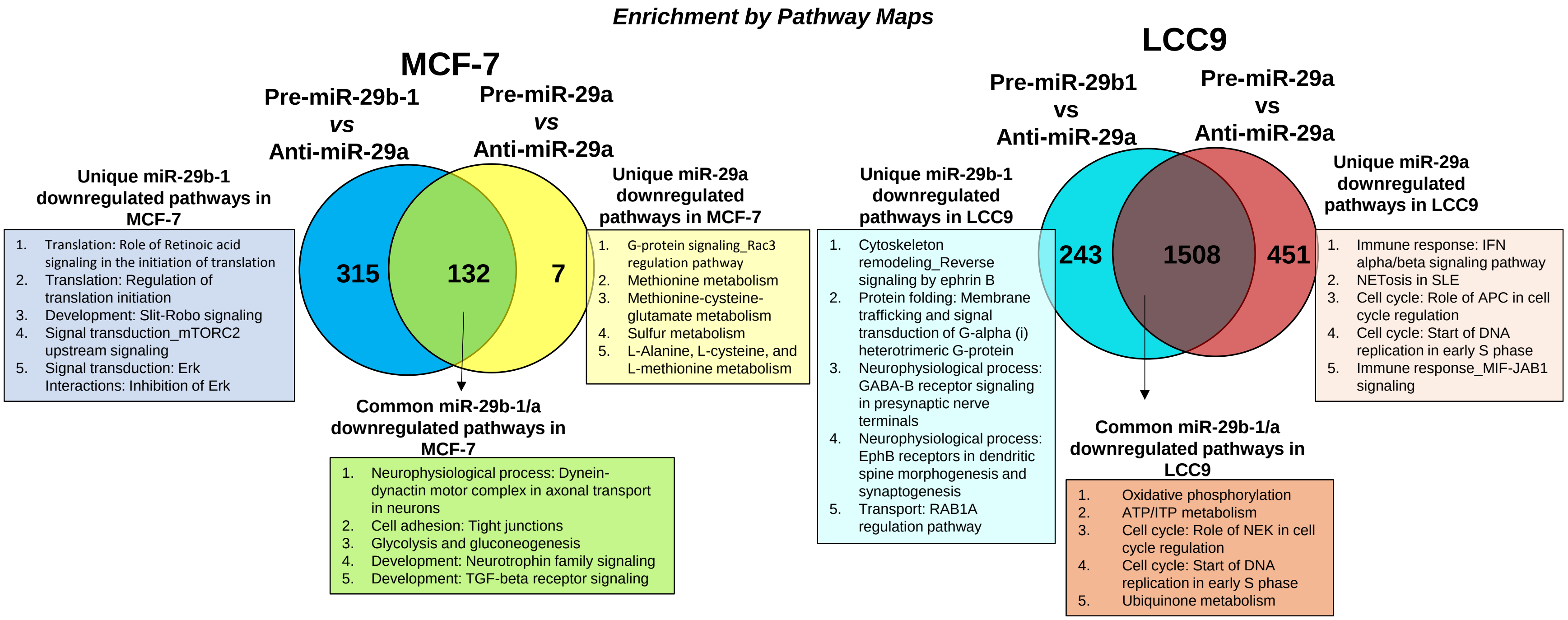
Supplementary Figure 8. Knockdown of ERα inhibits 4-OHT repression of DICER transcript expression in LCC9. LCC9 cells were grown in hormonally depleted medium and transfected with siControl or siERα. 48 h post transfection, cells were treated for 6 h with DMSO or 100 nM 4-OHT. Q-PCR was performed to determine *DICER* mRNA expression relative to 18S. Values are the mean ± SEM of three separate wells in one experiment. *p < 0.05 *versus* control-transfected cells. #p < 0.05 *versus* 4-OHT-treated Control-transfected cells.



Supplementary Figure 9. Expression of *NKX3-1* and *SKP2* are significantly different in between MCF-7 TAM-sensitive and LCC9 TAM-resistant cells. Values are FPKM = Fragments Per Kilobase of transcript per Million mapped reads and are from GSE81620. *****p < 0.05 (Two way ANOVA, Bonferroni post hoc test). *POU5F1* is the gene for Oct-4.



Supplementary Figure 10. Successful knockdown and upregulation of miR-29b-1 /a in MCF-7 and LCC9 cells. Cells were grown in hormone-depleted media and transfected with anti-miR-control, anti-miR-29a (3p), pre-miR control or pre-miR-29b-1/a (3p) as indicated. RNA was extracted 48 h post transfection and qPCR performed. Values were normalized to *RNU6B*. Values are the mean ± SEM of 3 independent experiments. Within each experiment, each sample was run in triplicate. *p<0.05 *versus* control transfected cells. Statistical evaluation was performed using one-way ANOVA followed by Newman-Keuls Multiple Comparison Test.



Unique miR-29b-1 downregulated pathways in MCF-7

1. Translation: Role of Retinoic acid signaling in the initiation of translation
2. Translation: Regulation of translation initiation
3. Development: Slit-Robo signaling
4. Signal transduction_mTORC2 upstream signaling
5. Signal transduction: Erk Interactions: Inhibition of Erk

Unique miR-29a downregulated pathways in MCF-7

1. G-protein signaling_Rac3 regulation pathway
2. Methionine metabolism
3. Methionine-cysteine-glutamate metabolism
4. Sulfur metabolism
5. L-Alanine, L-cysteine, and L-methionine metabolism

Common miR-29b-1/a downregulated pathways in MCF-7

1. Neurophysiological process: Dynein-dynactin motor complex in axonal transport in neurons
2. Cell adhesion: Tight junctions
3. Glycolysis and gluconeogenesis
4. Development: Neurotrophin family signaling
5. Development: TGF-beta receptor signaling

Unique miR-29b-1 downregulated pathways in LCC9

1. Cytoskeleton remodeling_Reverse signaling by ephrin B
2. Protein folding: Membrane trafficking and signal transduction of G-alpha (i) heterotrimeric G-protein
3. Neurophysiological process: GABA-B receptor signaling in presynaptic nerve terminals
4. Neurophysiological process: EphB receptors in dendritic spine morphogenesis and synaptogenesis
5. Transport: RAB1A regulation pathway

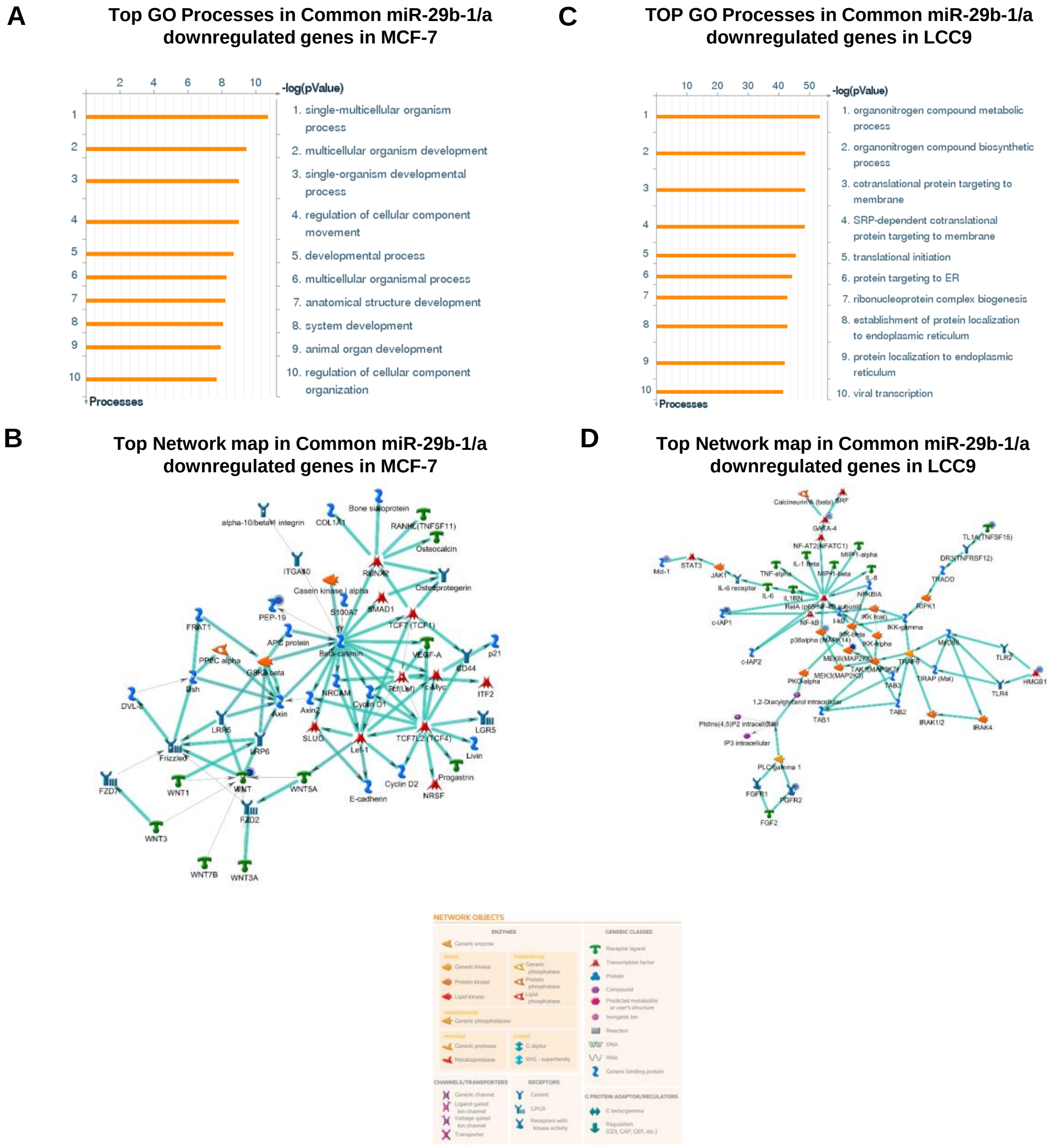
Unique miR-29a downregulated pathways in LCC9

1. Immune response: IFN alpha/beta signaling pathway
2. NETosis in SLE
3. Cell cycle: Role of APC in cell cycle regulation
4. Cell cycle: Start of DNA replication in early S phase
5. Immune response_MIF-JAB1 signaling

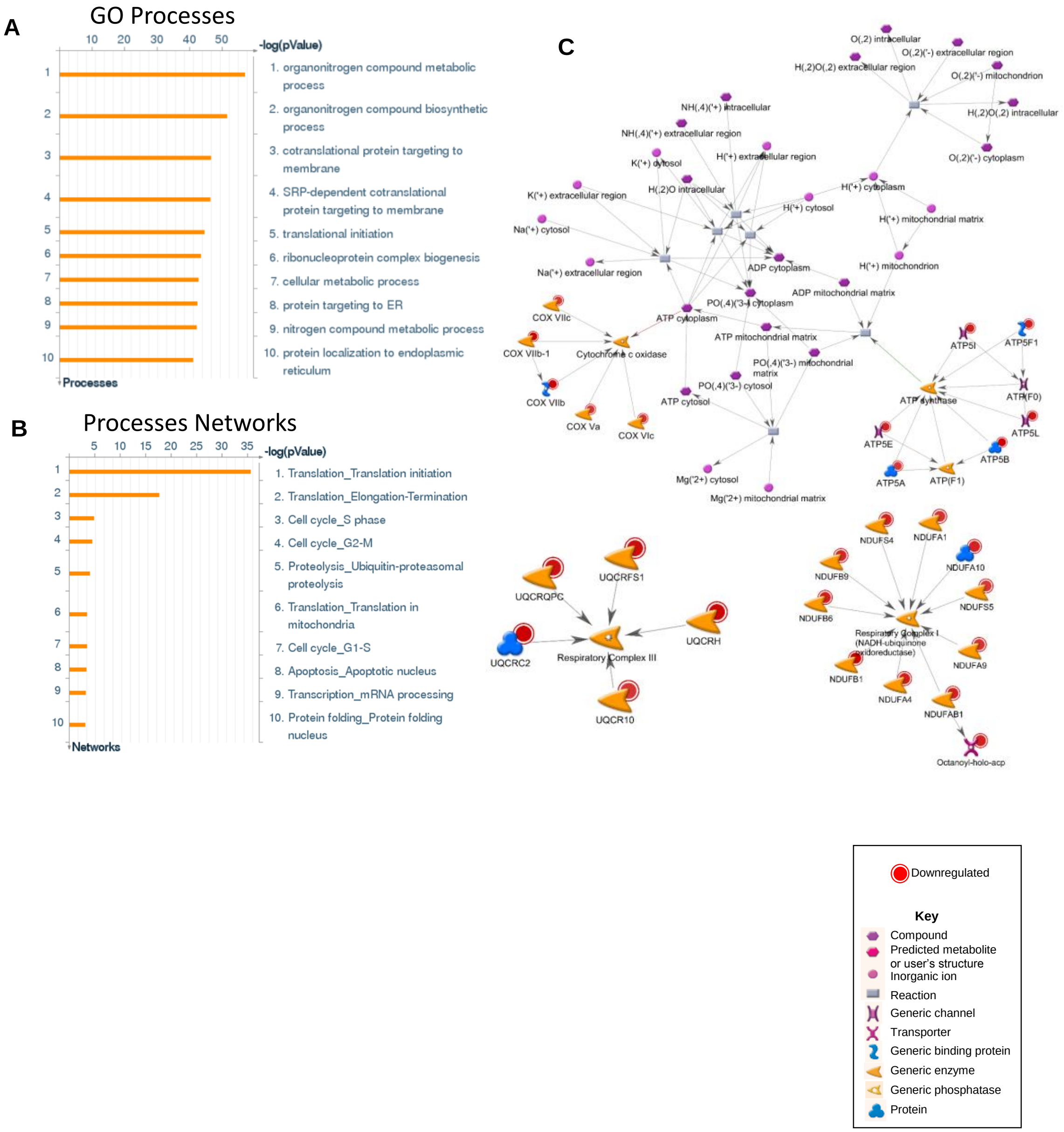
Common miR-29b-1/a downregulated pathways in LCC9

1. Oxidative phosphorylation
2. ATP/ITP metabolism
3. Cell cycle: Role of NEK in cell cycle regulation
4. Cell cycle: Start of DNA replication in early S phase
5. Ubiquinone metabolism

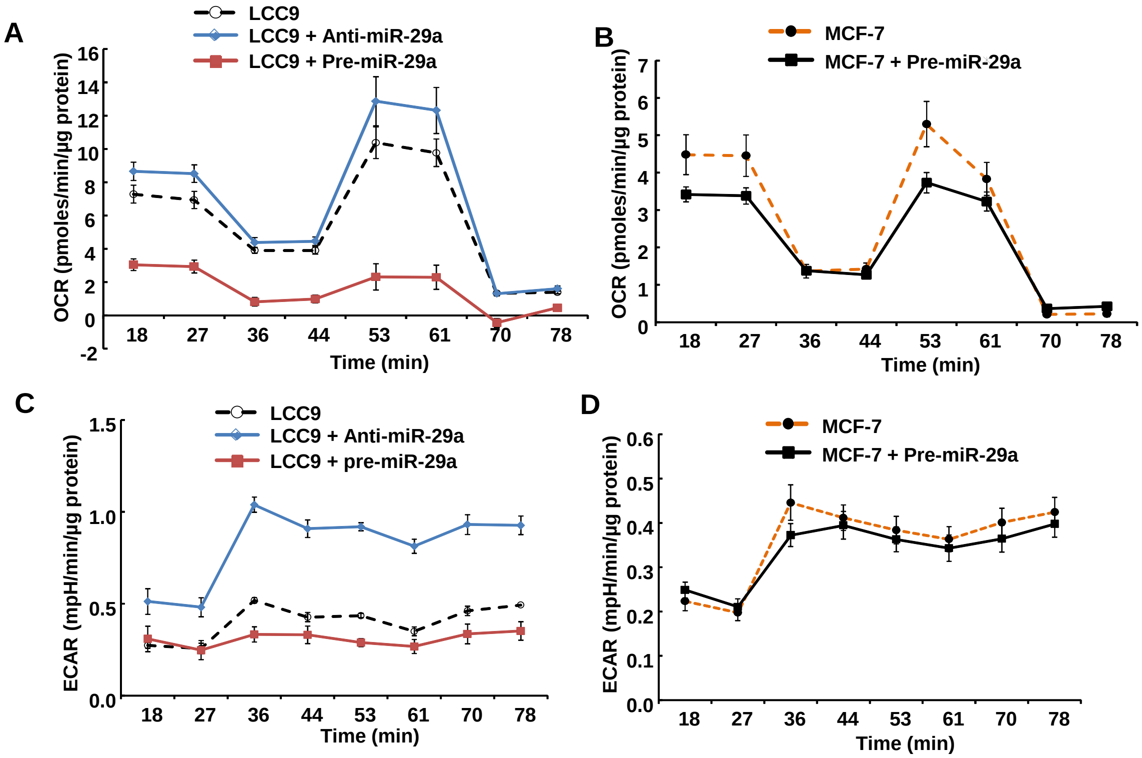
Supplementary Figure 11. Enrichment analysis of RNA-seq data in MCF-7 and LCC9 cells. Data are the same as Fig. 9A and B with an inclusion of pathways identified. The Venn diagrams show the number of differentially expressed genes identified in pairwise comparisons: Pre-miR-29b-1 *vs.* Anti-miR-29a and Anti-miR-29a *vs.* Pre-miR-29a using tophat and cufflink-cuff diff2. GeneGo Pathways Software (MetaCore™) was then used to obtain the number of common and uniquely expressed genes significantly downregulated by miR-29b-1 a.



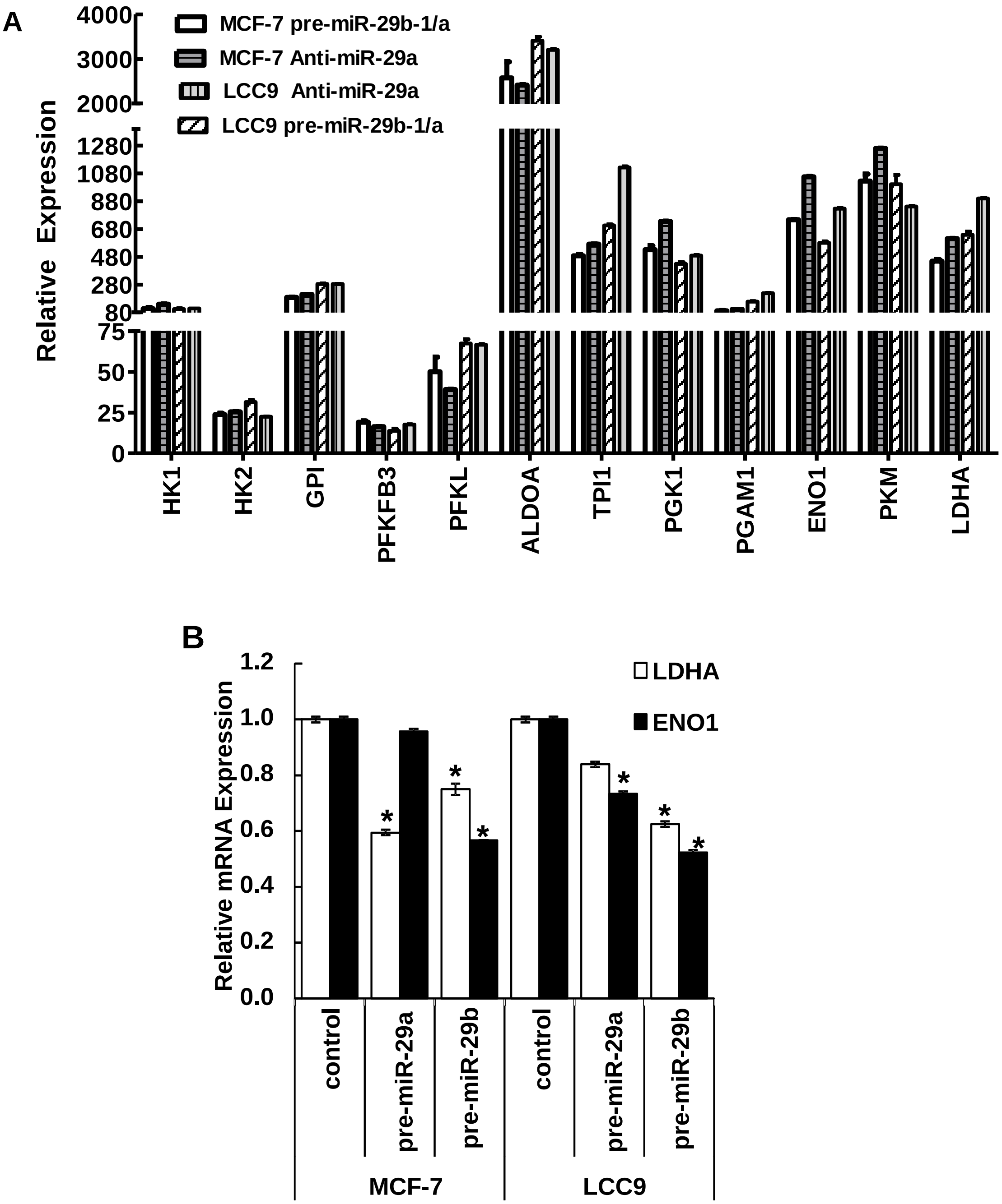
Supplementary Figure 12. Enrichment onthologies of genes regulated by miR-29b-1/a in MCF-7 and LCC9 cells. A, C) Gene Ontology (GO) cellular processes. B, D) The top scored GO network processes determined using Analyze Networks algorithm with default settings in MetaCore™. Thick cyan lines indicate canonical pathways. Items with blue circles indicate downregulated genes.



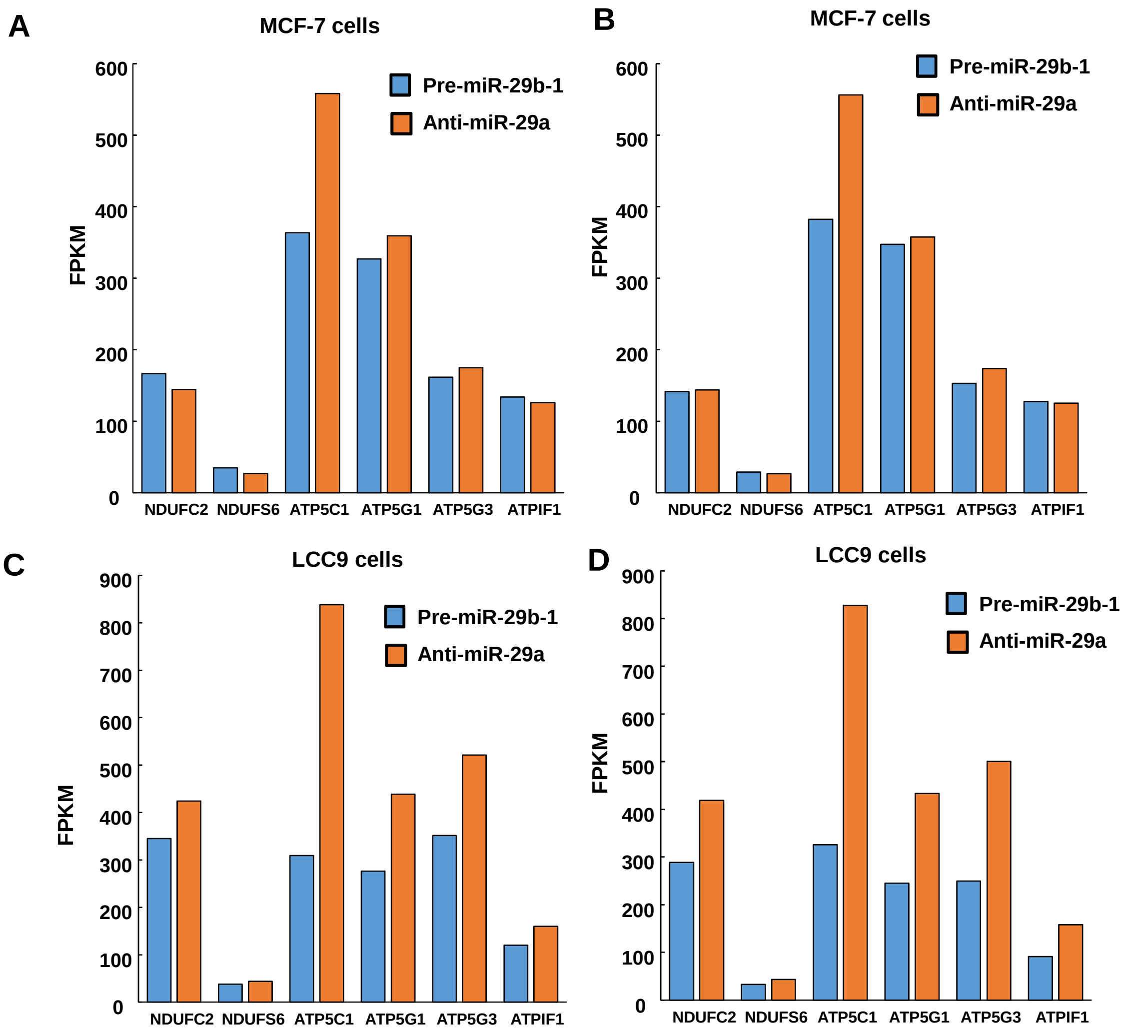
Supplementary Figure 13. Enrichment onthologies of genes uniquely downregulated in LCC9 cells. Differentially expressed genes unique to LCC9 cells identified in pairwise comparisons using cufflink-cuff diff2. MetaCore™ was then used to determine A) top Gene Ontology (GO) cellular processes and B) top Process Networks. C) Network analysis of genes mediating mitochondrial ATP synthesis coupled proton transport. miR-29 downregulated target genes are indicated by the red circle.



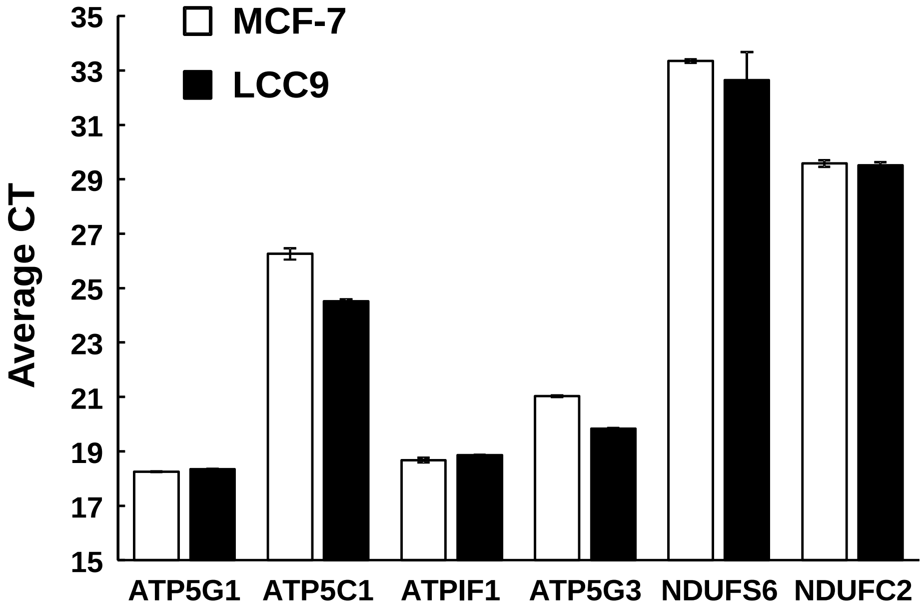
Supplementary Figure 14. miR-29a regulates mitochondrial function of MCF-7 and LCC9 BC cells. MCF-7 and LCC9 cells were plated in XF-24 plates, 'hormone-deprived' and transfected with anti-miR-29a or pre-miR-29a, *versus* control, as indicated, for 28 h prior to running extracellular flux assay to determine mitochondrial activity. Each point is the avg of 4 separate wells ± SEM.


A
Relative Expression
4000
3000
2000
1280
1080
880
680
480
280
80
75
50
25
0
MCF-7 pre-miR-29b-1/a
MCF-7 Anti-miR-29a
LCC9 Anti-miR-29a
LCC9 pre-miR-29b-1/a
HK1
HK2
GPI
PFKFB3
PFKL
ALDOA
TPI1
PGK1
PGAM1
ENO1
PKM
LDHA
B
Relative mRNA Expression
1.2
1.0
0.8
0.6
0.4
0.2
0.0
LDHA
ENO1
*
control
pre-miR-29a
pre-miR-29b
control
pre-miR-29a
pre-miR-29b
MCF-7
LCC9

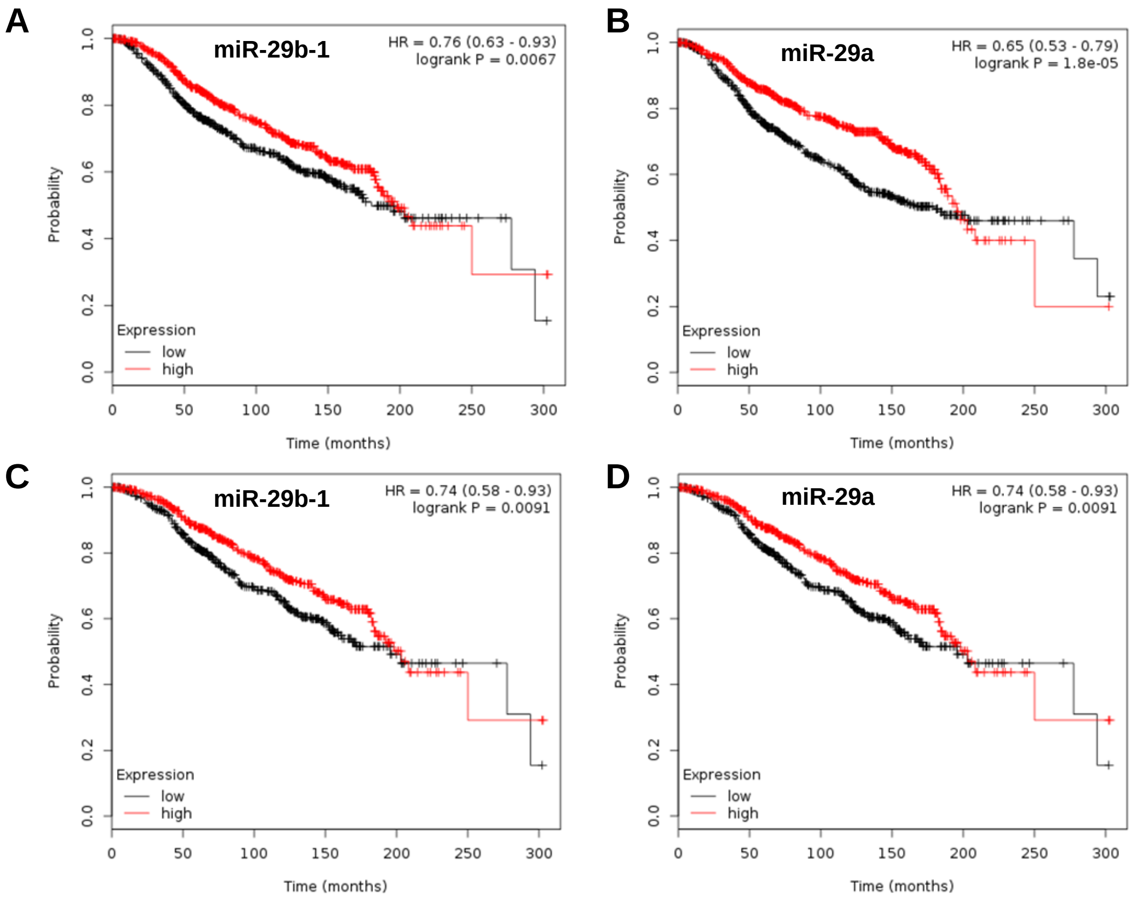
Supplementary Figure 15. Glycolytic gene expression in MCF-7 and LCC9 BC cells. MCF-7 and LCC9 cells were 'hormone-deprived' and transfected with pre-miR-29a, pre-miR-29b-1, or anti-miR-29a. A) Values are the FPKM (Fragments Per Kilobase of transcript per Million mapped reads) from GSE81620 RNA-seq dataset. Bars for pre-miR-29b-1/a are the average of 6 separate experiments and bars with Anti-miR-29a are the average of 3 experiments. B) qPCR of *LDHA* and *ENO1* mRNA transcript expression in MCF-7 and LCC9 cells transfected as indicated. Values are the mean ± SEM of 3 samples in one experiment. *$p<0.05$ *versus* control transfected cells. Statistical evaluation was performed using Student's t test.



Supplementary Figure 16. RNA-seq expression profiles of *ATP5G1*, *ATP5C1*, *ATPIF1*, *ATP5G3*, *NDUFS6* and *NDUFC2* in MCF-7 and LCC9 breast cancer cells. Values are FPKM (Fragments Per Kilobase of transcript per Million mapped reads) from GSE81620 RNA-seq dataset. Each bar is the average of 3 separate experiments.



Supplementary Figure 17. Basal expression levels of putative miR-29b-1/a targets in breast cancer cells. MCF7 and LCC9 cells were grown in hormone-depleted media for 48 h. RNA was isolated and qPCR performed to determine expression levels. Each bar is the avg. ± SEM of triplicate samples in one experiment.



Supplementary Figure 18. Lower expression of miR-29b-1 and miR-29a is statistically associated with decreased relapse-free survival in all breast cancer and in patients whose primary tumors are ERα+. Kaplan-Meier (KM) plots of A) miR-29b-1 and B) miR-29a expression in all tumors (n = 1262). KM plots of C) miR-29b-1 and D) miR-29a in ER+ tumors (n = 996). Plots were generated using www.kmplot.com/mirpower [371]

Supplementary Table 2: miR-29 targets in MCF-7 cells

Supplementary Table 2A: miR-29a unique targets in MCF-7 cells

					MCF-7 Pre-miR-29b-1 vs Anti-miR-29a
	Gene Symbol	**Entrez Gene IDs**	**OMIM IDs**	**Gene Name**	**log$_2$(fold change)**
1.	HIBADH	11112	608475	3-hydroxyisobutyrate dehydrogenase	0.463839
2.	EIF4EBP2	1979	602224	eukaryotic translation initiation factor 4E binding protein 2	0.503226
3.	ABCB7	22	300135;301310	ATP binding cassette subfamily B member 7	0.503745
4.	ADAMTS19	171019	607513	ADAM metallopeptidase with thrombospondin type 1 motif 19	0.895057
5.	ADAM9	8754	602713;612775	ADAM metallopeptidase domain 9	0.538095
6.	ADH5	128	103710	"alcohol dehydrogenase 5 (class III), chi polypeptide"	0.569996
7.	AHNAK	79026	103390	AHNAK nucleoprotein	0.71501
8.	AIF1L	83543	No ID	allograft inflammatory factor 1 like	0.441216
9.	AK4	205	103030	adenylate kinase 4	0.779273
10.	ALDH7A1	501	107323;266100	aldehyde dehydrogenase 7 family member A1	0.609418
11.	FAM117B	150864	No ID	family with sequence similarity 117 member B	0.495994
12.	AMIGO2	347902	615690	adhesion molecule with Ig like domain 2	0.361687
13.	GNA14	57037	No ID	ankyrin repeat and MYND domain containing 2	0.838909
14.	ANO6	196527	262890;608663	anoctamin 6	0.504893
15.	SLC25A5	292	300150	solute carrier family 25 member 5	0.531863
16.	APLP2	334	104776	amyloid beta precursor like protein 2	0.634654
17.	APP	351	104300;104760;605714	amyloid beta precursor protein	0.591877
18.	NCAM2	401	602078;602753	paired like homeobox 2a	0.793964
19.	ARL5B	221079	608909	ADP ribosylation factor like GTPase 5B	0.526453
20.	ARNT	405	126110	aryl hydrocarbon receptor nuclear translocator	0.516884
21.	ACTR2	10097	604221	ARP2 actin related protein 2 homolog	0.388238
22.	ATP11B	23200	605869	ATPase phospholipid transporting 11B (putative)	0.79681
23.	ATP1B1	481	145500;182330	ATPase Na+/K+ transporting subunit beta 1	0.460634
24.	ATP5A1	498	164360;615228;616045	"ATP synthase, H+ transporting, mitochondrial F1 complex, alpha subunit 1, cardiac muscle"	0.4749
25.	ATP5B	506	102910	"ATP synthase, H+ transporting, mitochondrial F1 complex, beta polypeptide"	0.526923
26.	ATP5EP2	432369	No ID	"ATP synthase, H+ transporting, mitochondrial F1 complex, epsilon subunit pseudogene 2"	0.690007
27.	ATP6V1A	523	607027	ATPase H+ transporting V1 subunit A	0.786597
28.	ADK	132	102750;614300	adenosine kinase	0.421368
29.	ADIPOR2	79602	607946	adiponectin receptor 2	0.489597
30.	SGCE	8910	159900;604149	sarcoglycan epsilon	1.66249
31.	PTPLAD1	51495	615940	3-hydroxyacyl-CoA dehydratase 3	0.559162
32.	B3GNT5	84002	615333	"UDP-GlcNAc:betaGal beta-1,3-N-acetylglucosaminyltransferase 5"	0.885252
33.	SMARCC1	6599	601732	"SWI/SNF related, matrix associated, actin dependent regulator of chromatin subfamily c member 1"	0.67286
34.	BCAS1	8537	602968	breast carcinoma amplified sequence 1	0.598178
35.	DBT	1629	248600;248610	dihydrolipoamide branched chain transacylase E2	0.560221
36.	BCKDHB	594	248600;248611	branched chain keto acid dehydrogenase E1 subunit beta	0.648202
37.	GLB1	2720	230500;230600;230650;253010;611458	galactosidase beta 1	0.728066
38.	BRI3BP	140707	615627	BRI3 binding protein	0.55248
39.	BTF3	689	602542	basic transcription factor 3	0.481856
40.	CTNNB1	1499	114500;114550;116806;132600;1552	catenin beta 1	0.506777

			55;156240;167000;181030;615075		
41.	APMAP	57136	615884	adipocyte plasma membrane associated protein	0.401089
42.	LINC00205	102723489	No ID	long intergenic non-protein coding RNA 205	0.5533
43.	CADPS2	93664	609978	calcium dependent secretion activator 2	0.738824
44.	CALCOCO1	57658	No ID	calcium binding and coiled-coil domain 1	0.58291
45.	SLC7A2	6542	601872	solute carrier family 7 member 2	0.448744
46.	CBLN4	140689	615029	cerebellin 4 precursor	0.974278
47.	CD302	9936	612246	CD302 molecule	0.766404
48.	CD44	960	107269;172290;609027	CD44 molecule (Indian blood group)	0.780123
49.	CDC42	998	116952;616737	cell division cycle 42	0.484322
50.	CHP1	11261	606988	calcineurin like EF-hand protein 1	0.466563
51.	CHSY1	22856	605282;608183	chondroitin sulfate synthase 1	0.45663
52.	GNS	2799	252940;607664	glucosamine (N-acetyl)-6-sulfatase	0.758816
53.	CLEC3A	10143	613588	C-type lectin domain family 3 member A	1.36846
54.	CMTM4	146223	607887	CKLF like MARVEL transmembrane domain containing 4	0.845446
55.	CMTM6	54918	607889	CKLF like MARVEL transmembrane domain containing 6	0.527145
56.	CREG1	8804	No ID	cellular repressor of E1A stimulated genes 1	0.546034
57.	EMB	7514	602559	exportin 1	0.636447
58.	SCP2	10106	608711	CTD small phosphatase 2	0.553321
59.	SPANXA2-OT1	619455	No ID	SPANXA2 overlapping transcript 1	1.15675
60.	CYP1B1	1545	137750;137760;231300;600975;601771;604229	cytochrome P450 family 1 subfamily B member 1	0.589318
61.	ATP2A2	488	101900;108740;124200	ATPase sarcoplasmic/endoplasmic reticulum Ca2+ transporting 2	0.486506
62.	CLSTN2	64084	611323	calsyntenin 2	0.820318
63.	CETN2	1069	300006	centrin 2	0.545244
64.	MPP7	8208	601245	chromatin assembly factor 1 subunit B	0.669472
65.	CLTC	1213	118955	clathrin heavy chain	0.518539
66.	COL12A1	1303	120320;616470;616471	collagen type XII alpha 1 chain	0.997639
67.	COL14A1	7373	120324	collagen type XIV alpha 1 chain	1.07939
68.	CUL4B	8450	300304;300354	cullin 4B	0.423513
69.	CCNG2	901	603203	cyclin G2	0.608184
70.	CCNI	10983	No ID	cyclin I	0.704477
71.	CD55	1604	125240;613793	CD55 molecule (Cromer blood group)	0.445821
72.	DAZAP2	9802	607431	DAZ associated protein 2	0.471512
73.	OSTC	58505	No ID	oligosaccharyltransferase complex non-catalytic subunit	0.72726
74.	DCLK1	9201	604742	doublecortin like kinase 1	0.709475
75.	PTPRJ	5795	600925	"protein tyrosine phosphatase, receptor type J"	0.58445
76.	GLUD1	2746	138130;606762	glutamate dehydrogenase 1	0.534844
77.	DIO2	1734	601413	"deiodinase, iodothyronine, type II"	1.43126
78.	ENSG00000264364	140735	608942	dynein light chain LC8-type 2	0.449333
79.	DNAJC25	548645	No ID	DnaJ heat shock protein family (Hsp40) member C25	0.668936
80.	METTL9	51108	609388	methyltransferase like 9	0.574265
81.	DSP	1834	125420;125485;125490;125500;605594	dentin sialophosphoprotein	0.456755
82.	DSTN	11034	609114	"destrin, actin depolymerizing factor"	0.521062
83.	EEF1A1P5	158078	No ID	eukaryotic translation elongation factor 1 alpha 1 pseudogene 5	0.643883
84.	EEF1A1P9	441032	No ID	eukaryotic translation elongation factor 1 alpha 1 pseudogene 9	0.712999
85.	EIF3L	51386	No ID	eukaryotic translation initiation factor 3 subunit L	0.67883
86.	ELOVL5	60481	611805;615957	ELOVL fatty acid elongase 5	0.424171

87.	ENPP1	5167	125853;173335;208000;601665;602475;613312;615522	ectonucleotide pyrophosphatase/phosphodiesterase 1	0.6384
88.	ETNK2	55224	609859	ethanolamine kinase 2	0.768113
89.	RUNX1T1	862	133435	RUNX1 translocation partner 1	1.0154
90.	HSP90B1	7184	191175	heat shock protein 90 beta family member 1	0.483563
91.	EPCAM	4072	185535;613217;613244	epithelial cell adhesion molecule	0.437596
92.	EFNB3	1949	602297	ephrin B3	0.479075
93.	EPS15	2060	600051	epidermal growth factor receptor pathway substrate 15	0.470549
94.	ERGIC3	51614	616971	ERGIC and golgi 3	0.570885
95.	EXT2	2132	133701;601224;608210;616682	exostosin glycosyltransferase 2	0.687945
96.	FBXO21	23014	609095	F-box protein 21	0.455003
97.	TMEM150C	441027	No ID	transmembrane protein 150C	0.490383
98.	FRAT2	23401	605006	frequently rearranged in advanced T-cell lymphomas 2	0.467266
99.	FUCA1	2517	230000;612280	"fucosidase, alpha-L- 1, tissue"	0.487582
100.	FUT8	2530	602589	fucosyltransferase 8	0.594184
101.	FZD6	8323	603409;614157	frizzled class receptor 6	0.421184
102.	PLS1	5357	602734	plastin 1	0.599518
103.	FRAS1	80144	219000;607830	Fraser extracellular matrix complex subunit 1	0.69899
104.	FUT9	10690	606865	fucosyltransferase 9	0.59
105.	GNG12	55970	615405	G protein subunit gamma 12	0.612162
106.	GDE1	51573	605943	glycerophosphodiester phosphodiesterase 1	0.537638
107.	GFRA3	2676	605710	GDNF family receptor alpha 3	1.04305
108.	GPD1L	23171	272120;611777;611778	glycerol-3-phosphate dehydrogenase 1-like	0.41666
109.	GPNMB	10457	604368	glycoprotein nmb	0.744162
110.	TMEM181	57583	613209	transmembrane protein 181	0.553905
111.	GSTA4	2941	605450	glutathione S-transferase alpha 4	0.934667
112.	GLO1	2739	138750	glyoxalase I	0.402551
113.	AGR2	10551	606358	"anterior gradient 2, protein disulphide isomerase family member"	0.467375
114.	HINT3	135114	609998	histidine triad nucleotide binding protein 3	0.476442
115.	HIPK1	204851	608003	homeodomain interacting protein kinase 1	0.559793
116.	BRK1	55845	611183	"BRICK1, SCAR/WAVE actin nucleating complex subunit"	0.475471
117.	HEATR5B	54497	No ID	HEAT repeat containing 5B	0.587967
118.	H3F3A	3020	601058;601128	H3 histone family member 3A	0.414925
119.	IGBP1	3476	300139;300472	immunoglobulin (CD79A) binding protein 1	0.415533
120.	IGSF1	3547	300137;300888	immunoglobulin superfamily member 1	0.733403
121.	IL1R1	3554	147810	interleukin 1 receptor type 1	0.78683
122.	IL13RA1	3597	300119	interleukin 13 receptor subunit alpha 1	0.618167
123.	IL1RAPL2	26280	300277	interleukin 1 receptor accessory protein like 2	1.43643
124.	IL23R	149233	605606;607562;612261	interleukin 23 receptor	0.643553
125.	INSIG1	3638	602055	insulin induced gene 1	0.423326
126.	ITGA6	3655	147556;226730	integrin subunit alpha 6	0.884631
127.	ARL6IP5	10550	605709	ADP ribosylation factor like GTPase 6 interacting protein 5	0.590619
128.	PRDX1	56659	607367	potassium two pore domain channel subfamily K member 13	0.489384
129.	KCTD20	222658	615932	potassium channel tetramerization domain containing 20	0.604093
130.	KCTD3	51133	613272	potassium channel tetramerization domain containing 3	0.691036
131.	FAM168A	23201	616316	family with sequence similarity 168 member A	0.502726
132.	KIAA1244	57221	No ID	ARFGEF family member 3	0.440378
133.	KIAA1324	57535	611298	KIAA1324	0.548838
134.	TXNDC16	57544	616179	thioredoxin domain containing 16	0.69446
135.	EPG5	57724	242840;615068	ectopic P-granules autophagy protein 5 homolog	0.619241
136.	KIAA2018	205717	No ID	upstream transcription factor family member 3	0.447222
137.	KIF1B	23095	118210;171300;256700;605995	kinesin family member 1B	0.540446

138.	KIF3B	9371	603754	kinesin family member 3B	0.526819
139.	FERMT2	10979	607746	fermitin family member 2	0.588173
140.	LAMP2	3920	300257;309060	lysosomal associated membrane protein 2	0.463606
141.	RPSA	3921	150370;271400	ribosomal protein SA	0.444295
142.	LANCL1	10314	604155	LanC like 1	0.573726
143.	LAPTM4B	55353	613296	lysosomal protein transmembrane 4 beta	0.683263
144.	ARHGEF12	23365	604763	Rho guanine nucleotide exchange factor 12	0.500601
145.	LDHA	3939	150000;612933	lactate dehydrogenase A	0.484053
146.	LDOC1	23641	300402	leucine zipper down-regulated in cancer 1	0.464045
147.	LRRFIP1	9208	603256	LRR binding FLII interacting protein 1	0.420842
148.	LSM11	134353	No ID	"LSM11, U7 small nuclear RNA associated"	0.491352
149.	LRRC58	116064	No ID	leucine rich repeat containing 58	0.483267
150.	MAN1A1	4121	604344	mannosidase alpha class 1A member 1	0.666365
151.	MAML2	84441	607537	mastermind like transcriptional coactivator 2	0.631339
152.	MAOB	4129	309860	monoamine oxidase B	0.878248
153.	MAP2	4133	157130	microtubule associated protein 2	0.770299
154.	MBOAT2	129642	611949	membrane bound O-acyltransferase domain containing 2	0.764623
155.	MCCC2	64087	210210;609014	methylcrotonoyl-CoA carboxylase 2	0.586974
156.	SLC16A7	9194	603654	solute carrier family 16 member 7	0.753861
157.	ME1	4199	154250	malic enzyme 1	0.482464
158.	MAP3K1	4214	600982;613762	mitogen-activated protein kinase kinase kinase 1	0.465687
159.	MEST	4232	601029	mesoderm specific transcript	0.752552
160.	MGST3	4259	604564	microsomal glutathione S-transferase 3	0.545689
161.	DUSP4	1846	602747	dual specificity phosphatase 4	0.405569
162.	MMP16	4325	602262	matrix metallopeptidase 16	1.14912
163.	MORF4L2	9643	300409	mortality factor 4 like 2	0.413342
164.	MTMR2	8898	601382;603557	myotubularin related protein 2	0.65462
165.	MUCL1	118430	610857	mucin like 1	0.762445
166.	MUT	4594	251000;609058	methylmalonyl-CoA mutase	0.487788
167.	PAM	23077	610392	"MYC binding protein 2, E3 ubiquitin protein ligase"	0.934899
168.	MYO1B	4430	606537	myosin IB	0.632889
169.	MYOF	26509	604603	myoferlin	0.462151
170.	MYO6	4646	600970;606346;607821	myosin VI	0.654896
171.	N4BP2	55728	No ID	NEDD4 binding protein 2	0.685434
172.	NCKAP5	344148	608789	NCK associated protein 5	1.05894
173.	SLC8A1	6546	182305	solute carrier family 8 member A1	0.551218
174.	NDRG3	57446	605273	NDRG family member 3	0.666619
175.	NEBL	10529	605491	nebulette	0.609686
176.	NEK6	10783	604884	NIMA related kinase 6	0.502781
177.	BNIP3L	665	605368	BCL2 interacting protein 3 like	0.588141
178.	NPC2	10577	601015;607625	NPC intracellular cholesterol transporter 2	0.423578
179.	NQO1	1728	125860	NAD(P)H quinone dehydrogenase 1	0.46134
180.	MAGED1	9500	300224	MAGE family member D1	0.787782
181.	NRCAM	4897	601581	neuronal cell adhesion molecule	0.717003
182.	NRK	203447	300791	Nik related kinase	1.47776
183.	REST	5978	600571;616806	RE1 silencing transcription factor	0.481066
184.	IVNS1ABP	10625	609209	influenza virus NS1A binding protein	0.366829
185.	PRDX6	9588	602316	peroxiredoxin 6	0.390866
186.	NRG3	10718	605533	neuregulin 3	1.70994
187.	NBEA	26960	604889	neurobeachin	0.768566
188.	NUS1	116150	610463;617082	NUS1 dehydrodolichyl diphosphate synthase subunit	0.412875
189.	P4HA1	5033	176710	prolyl 4-hydroxylase subunit alpha 1	0.456554
190.	PABPC1	26986	604679	poly(A) binding protein cytoplasmic 1	0.624322
191.	PABPC4L	132430	No ID	poly(A) binding protein cytoplasmic 4 like	0.881233
192.	PAPSS1	9061	603262	3'-phosphoadenosine 5'-phosphosulfate synthase 1	0.637146
193.	PCDHB16; ME1	57717	604967;606345	protocadherin beta 16	0.666527
194.	PCDHB3	56132	604967;606329	protocadherin beta 3	0.596374
195.	PCDHB16; PCDHB8	56128	604967;606334	protocadherin beta 8	0.82234
196.	PCYOX1	51449	610995	prenylcysteine oxidase 1	0.669556

197.	PDE4B	5142	600127	phosphodiesterase 4B	1.3981
198.	PGK1	5230	300653;311800	phosphoglycerate kinase 1	0.542224
199.	PGM1	55276	172000	phosphoglucomutase 2	0.744899
200.	PHLDA1	22822	605335	pleckstrin homology like domain family A member 1	0.438257
201.	PHTF2	57157	616785	putative homeodomain transcription factor 2	0.763051
202.	PIR	11025	604820	leukocyte immunoglobulin like receptor B3	0.681574
203.	PJA2	9867	No ID	praja ring finger ubiquitin ligase 2	0.408532
204.	PRKACA	5566	601639;615830	protein kinase cAMP-activated catalytic subunit alpha	0.544697
205.	PLCXD3	345557	617016	phosphatidylinositol specific phospholipase C X domain containing 3	0.475518
206.	PLOD2	5352	601865;609220	"procollagen-lysine,2-oxoglutarate 5-dioxygenase 2"	0.631555
207.	PLXDC2	84898	606827	plexin domain containing 2	0.481995
208.	PPP2R2B	5521	604325;604326	protein phosphatase 2 regulatory subunit Bbeta	1.6416
209.	PPM1H	57460	616016	"protein phosphatase, Mg2+/Mn2+ dependent 1H"	0.51243
210.	PRICKLE2	166336	607459;608501;613832	prickle planar cell polarity protein 2	0.384805
211.	PRR11	55771	615920	proline rich 11	0.602035
212.	PSD3	23362	614440	pleckstrin and Sec7 domain containing 3	0.758157
213.	PTPLA	9200	255310;610467	3-hydroxyacyl-CoA dehydratase 1	0.703489
214.	PTDSS1	9791	151050;612792	phosphatidylserine synthase 1	0.457234
215.	RABL5	64792	No ID	intraflagellar transport 22	0.534114
216.	GNB2L1	10399	176981	receptor for activated C kinase 1	0.346332
217.	SMS	10743	182290;607642	retinoic acid induced 1	0.406627
218.	REG4	83998	609846	regenerating family member 4	0.92634
219.	RNF130	55819	No ID	ring finger protein 130	0.61701
220.	ROBO1	6091	602430	roundabout guidance receptor 1	1.05768
221.	ROCK1	6093	601702	Rho associated coiled-coil containing protein kinase 1	0.448331
222.	RPL11	6135	604175;612562	ribosomal protein L11	0.456786
223.	RPL17	6139	603661	ribosomal protein L17	0.388701
224.	RPL23A	6147	602326	ribosomal protein L23a	0.372125
225.	RPL24	6152	604180	ribosomal protein L24	0.342158
226.	RPL34	6164	616862	ribosomal protein L34	0.423911
227.	RPL35A	6165	180468;612528	ribosomal protein L35a	0.364678
228.	RPL39	6170	300899	ribosomal protein L39	0.429273
229.	RPL4	6124	180479	ribosomal protein L4	0.428614
230.	RPL41	6171	613315	ribosomal protein L41	0.532606
231.	RPL5	6125	603634;612561	ribosomal protein L5	0.538675
232.	RPL6	6128	603703	ribosomal protein L6	0.626526
233.	RPL7A;RPL7	6129	604166	ribosomal protein L7	0.47839
234.	RPL7A	6130	185640	ribosomal protein L7a	0.453726
235.	RPL9	6133	603686	ribosomal protein L9	0.479611
236.	RPS15A	6210	603674	ribosomal protein S15a	0.516768
237.	RPS17	6218	180472;612527	ribosomal protein S17	0.865613
238.	RPS4X	6191	312760	"ribosomal protein S4, X-linked"	0.495312
239.	RPS6	6194	180460	ribosomal protein S6	0.460106
240.	RPS7	6201	603658;612563	ribosomal protein S7	0.360347
241.	RAB13	5872	602672	"RAB13, member RAS oncogene family"	0.389677
242.	SASH1	23328	607955	SAM and SH3 domain containing 1	0.535221
243.	SETD7	80854	606594	SET domain containing lysine methyltransferase 7	0.39308
244.	SH3BGRL	6451	300190	SH3 domain binding glutamate rich protein like	0.771522
245.	SH3BGRL2	83699	615678	SH3 domain binding glutamate rich protein like 2	0.741634
246.	SIDT2	51092	No ID	SID1 transmembrane family member 2	0.837797
247.	SLC19A2	10560	249270;603941	solute carrier family 19 member 2	0.463341
248.	SLC25A15	10166	238970;603861	solute carrier family 25 member 15	0.477293
249.	SLC25A24	29957	608744	solute carrier family 25 member 24	0.375516
250.	SLC25A3	5250	600370;610773	solute carrier family 25 member 3	0.544249
251.	SLC25A43	203427	300641	solute carrier family 25 member 43	0.609365
252.	SLC38A1	81539	608490	solute carrier family 38 member 1	0.655669
253.	SLC39A6	25800	608731	solute carrier family 39 member 6	0.512706

254.	SLC44A1	23446	606105	solute carrier family 44 member 1	0.57194
255.	SLC4A10	57282	605556	solute carrier family 4 member 10	0.74709
256.	SLC4A7	9497	603353	solute carrier family 4 member 7	0.695701
257.	SLIT2	9353	603746	slit guidance ligand 2	1.11886
258.	SNX4	8723	605931	sorting nexin 4	0.522873
259.	SOX2-OT	347689	616338	SOX2 overlapping transcript	1.37425
260.	SEC11A	23478	No ID	"SEC11 homolog A, signal peptidase complex subunit"	0.460174
261.	SRD5A1	6715	184753	steroid 5 alpha-reductase 1	0.655391
262.	SSR2	6746	600867	signal sequence receptor subunit 2	0.479507
263.	NSD1	64324	117550;130650;606681	nuclear receptor binding SET domain protein 1	0.571588
264.	SUCLG2	8801	603922	succinate-CoA ligase GDP-forming beta subunit	0.520378
265.	SULF1	23213	610012	sulfatase 1	0.824325
266.	SUMF1	285362	272200;607939	sulfatase modifying factor 1	0.552387
267.	SEC24D	9871	607186;616294	"SEC24 homolog D, COPII coat complex component"	0.544885
268.	KIAA1598	57698	611171	shootin 1	0.644697
269.	SPAST	6683	182601;604277	spastin	0.461301
270.	STC1	6781	601185	stanniocalcin 1	0.480749
271.	TANC1	85461	611397	"tetratricopeptide repeat, ankyrin repeat and coiled-coil containing 1"	0.46755
272.	TC2N	123036	No ID	"tandem C2 domains, nuclear"	0.538673
273.	TET2	54790	263300;612839;614286	tet methylcytosine dioxygenase 2	0.526523
274.	TFPI	7035	152310	tissue factor pathway inhibitor	0.696434
275.	TGFB2	7042	190220;614816	transforming growth factor beta 2	0.983306
276.	TIMP2	7077	188825	TIMP metallopeptidase inhibitor 2	0.451907
277.	TLE4	7091	605132	transducin like enhancer of split 4	0.807059
278.	TM9SF2	9375	604678	transmembrane 9 superfamily member 2	0.499806
279.	TMEM2	23670	605835	transmembrane protein 2	1.03637
280.	TMEM59	9528	617084	transmembrane protein 59	0.557126
281.	TMEM65	157378	616609	transmembrane protein 65	0.57703
282.	TMEM66	51669	614768	store-operated calcium entry associated regulatory factor	0.480183
283.	LINC00052	145978	No ID	long intergenic non-protein coding RNA 52	0.38313
284.	TPT1	7178	600763	"tumor protein, translationally-controlled 1"	0.449878
285.	TRIB2	28951	609462	tribbles pseudokinase 2	0.548341
286.	TRPS1	7227	150230;190350;190351;604386	transcriptional repressor GATA binding 1	0.702954
287.	TSPAN6	7105	300191	tetraspanin 6	0.473511
288.	TTC3	7267	602259	tetratricopeptide repeat domain 3	0.809686
289.	TUG1	55000	614971	taurine up-regulated 1 (non-protein coding)	0.603472
290.	TUSC3	7991	601385;611093	tumor suppressor candidate 3	0.545792
291.	TSPAN3	10099	613134	tetraspanin 3	0.410548
292.	TMTC1	83857	615855	transmembrane and tetratricopeptide repeat containing 1	0.673343
293.	MARVELD2	153562	610153;610572	MARVEL domain containing 2	0.511093
294.	TSPAN32	10077	603853	tetraspanin 32	1.96707
295.	TUBA1A	7846	602529;611603	tubulin alpha 1a	0.784308
296.	TUBD1	51174	607344	tubulin delta 1	0.463035
297.	UBL3	5412	604711	ubiquitin like 3	0.437758
298.	UCP2	7351	601693;607447	uncoupling protein 2	0.494843
299.	UGDH	7358	603370	UDP-glucose 6-dehydrogenase	0.5911
300.	UGT1A6	54657	143500;191740;218800;606429;606785	UDP glucuronosyltransferase family 1 member A4	0.684012
301.	CSDE1	7812	191510	cold shock domain containing E1	0.572963
302.	SLC27A6	28965	604196	solute carrier family 27 member 6	0.686412
303.	DCAF12	25853	No ID	DDB1 and CUL4 associated factor 12	0.64399
304.	WSB2	55884	No ID	WD repeat and SOCS box containing 2	0.591227
305.	XYLT1	64131	264800;608124;615777	xylosyltransferase 1	0.664025
306.	YES1	7525	164880	"YES proto-oncogene 1, Src family tyrosine kinase"	0.484034
307.	YPEL2	388403	609723	yippee like 2	0.691608

308.	MLTK	51776	609479;616890	sterile alpha motif and leucine zipper containing kinase AZK	0.481224
309.	ZFP91	80829	No ID	ZFP91 zinc finger protein	0.48339
310.	ZNF652	22834	613907	zinc finger protein 652	0.397467
311.	ITGB1	3688	135630	integrin subunit beta 1	0.816957
312.	EEF1G	1937	130593	eukaryotic translation elongation factor 1 gamma	0.53172
313.	EIF3F	8665	603914	eukaryotic translation initiation factor 3 subunit F	0.563518
314.	EIF3E	3646	602210	eukaryotic translation initiation factor 3 subunit E	0.566074
315.	EIF4B	1975	603928	eukaryotic translation initiation factor 4B	0.595304

Supplementary Table 2B: Common miR-29b-1 and miR-29a targets in MCF-7 cells

					MCF-7_Pre-miR-29b1 vs Anti-miR-29a	**MCF-7 Pre-miR-29a vs Anti-miR-29a**
	Gene Symbol	**Entrez Gene IDs**	**OMIM IDs**	**Gene Name**	**log$_2$ (fold change)**	**log$_2$(fold change)**
1.	VAT1L	57687	No ID	vesicle amine transport 1 like	1.16268	1.0319
2.	AIM1	202	601797	absent in melanoma 1	0.778095	0.658569
3.	AKR1C3	8644	603966	aldo-keto reductase family 1 member C3	0.885048	0.645128
4.	ANKRD50	57182	No ID	ankyrin repeat domain 50	0.73071	0.554446
5.	ARL4C	10123	604787	ADP ribosylation factor like GTPase 4C	0.554121	0.695993
6.	ARPC5	10092	604227	actin related protein 2/3 complex subunit 5	0.586134	0.607786
7.	ATP1A1	476	182310	ATPase Na+/K+ transporting subunit alpha 1	0.64489	0.431066
8.	ATP5C1	509	108729	"ATP synthase, H+ transporting, mitochondrial F1 complex, gamma polypeptide 1"	0.6197	0.540511
9.	ATP7A	538	300011;300489;304150;309400	ATPase copper transporting alpha	0.798753	0.616152
10.	TMSB4X	7114	300159	"thymosin beta 4, X-linked"	0.559619	0.483911
11.	PGM5	5239	600981	phosphoglucomutase 5	2.04583	1.71094
12.	ANXA1	301	151690	annexin A1	0.86142	0.786981
13.	ANXA5	308	131230;614391	annexin A5	0.553169	0.52333
14.	ATRN	8455	603130	attractin	0.717643	0.492748
15.	BAK1P1	600	No ID	BCL2 antagonist/killer 1 pseudogene 1	0.72886	0.853615
16.	BMP5	653	112265	bone morphogenetic protein 5	0.836287	0.658327
17.	XXYLT1	152002	614552	xyloside xylosyltransferase 1	0.716947	0.799999
18.	CCDC167	154467	No ID	coiled-coil domain containing 167	0.573969	0.620072
19.	GINM1	116254	No ID	glycoprotein integral membrane 1	0.688129	0.599535
20.	CD276	80381	605715	CD276 molecule	0.6514	0.687137
21.	CD36	948	173510;248310;608404;610938;611162	CD36 molecule	0.991681	1.19904
22.	SCUBE2	57758	611747	"signal peptide, CUB domain and EGF like domain containing 2"	0.935904	0.815793
23.	CSGALNACT1	55790	616615	chondroitin sulfate N-acetylgalactosaminyltransferase 1	1.41892	1.27735
24.	CMBL	134147	613379	carboxymethylenebutenolidase homolog	0.765169	0.549379
25.	CRISP3	10321	No ID	cysteine rich secretory protein 3	1.1613	0.739149
26.	TET1	80312	607790	tet methylcytosine dioxygenase 1	1.14532	1.06875
27.	CYP19A1	1588	107910;139300;613546	cytochrome P450 family 19 subfamily A member 1	2.32583	2.35814
28.	RCN2	10231	604876	regulator of calcineurin 2	0.531026	0.452163
29.	CAV1	857	601047;606721;612526;615343	caveolin 1	1.16046	1.01584
30.	PPIC	5480	123842	peptidylprolyl isomerase C	1.21937	1.17803
31.	MIB1	57534	608677;615092	mindbomb E3 ubiquitin protein ligase 1	0.73351	0.521844
32.	DNAJC28	54943	No ID	DnaJ heat shock protein family (Hsp40) member C28	1.06775	0.92687
33.	FILIP1L	11259	612993	filamin A interacting protein 1 like	0.667145	0.583131
34.	DSC2	1824	125645;610476	desmocollin 2	1.29529	1.10679

35.	DYNLT1	6993	601554	dynein light chain Tctex-type 1	0.498623	0.60201
36.	CLEC7A	64581	606264;613108;614079	C-type lectin domain family 7 member A	1.28516	1.75287
37.	DSG2	1829	125671;610193;612877	desmoglein 2	0.743464	0.481257
38.	VOPP1	81552	611915	"vesicular, overexpressed in cancer, prosurvival protein 1"	0.476688	0.451507
39.	EPB41L4B	54566	610340	erythrocyte membrane protein band 4.1 like 4B	0.59199	0.530691
40.	ELF5	2001	605169	E74 like ETS transcription factor 5	1.20403	1.00089
41.	ENO1	2023	172430	enolase 1	0.499112	0.49841
42.	ERMP1	79956	611156	endoplasmic reticulum metallopeptidase 1	0.939574	0.679547
43.	EPHA6	285220	600066	EPH receptor A6	1.03363	0.877418
44.	EPHA7	2045	602190	EPH receptor A7	0.879505	0.701687
45.	FBP1	2203	229700;611570	fructose-bisphosphatase 1	0.45042	0.490642
46.	FAM102B	284611	No ID	family with sequence similarity 102 member B	0.61018	0.463769
47.	FAM127C	441518	No ID	family with sequence similarity 127 member C	0.511481	0.559729
48.	FECH	2235	177000;612386	ferrochelatase	1.03486	0.802485
49.	FKBP1A	2280	186945	FK506 binding protein 1A	0.72236	0.541505
50.	C4orf32	132720	No ID	chromosome 4 open reading frame 32	0.716821	0.62176
51.	EFEMP1	2202	126600;601548	EGF containing fibulin like extracellular matrix protein 1	0.943595	0.981479
52.	FREM2	341640	219000;608945	FRAS1 related extracellular matrix protein 2	1.2842	1.13966
53.	GALNT1	2589	602273	polypeptide N-acetylgalactosaminyltransferase 1	0.95207	0.767107
54.	GCSH	2653	238330;605899	glycine cleavage system protein H	0.812153	0.678064
55.	GSTM3	2946	138380	glutathione S-transferase mu 2	0.603347	0.474469
56.	HEPHL1	341208	No ID	hephaestin like 1	1.38329	1.14249
57.	MAP4K4	9448	604666	mitogen-activated protein kinase kinase kinase kinase 4	0.6531	0.563603
58.	HMGCLL1	54511	No ID	3-hydroxymethyl-3-methylglutaryl-CoA lyase like 1	1.15732	1.03274
59.	S100A16	388697	616293	hornerin	0.669323	0.682906
60.	HOXC13	3229	142976;614931	homeobox C13	0.546096	0.67975
61.	IGFBP5	3488	146734	insulin like growth factor binding protein 5	0.52921	0.390971
62.	IGSF3	3321	149700;603491	immunoglobulin superfamily member 3	0.98228	1.12764
63.	ACO1	48	100880	aconitase 1	0.950629	0.626089
64.	ISOC1	51015	No ID	isochorismatase domain containing 1	0.720805	0.671419
65.	ITGB1	3688	135630	integrin subunit beta 1	0.816957	0.659117
66.	F11R	50848	605721	F11 receptor	0.829893	0.805344
67.	JARID2	3720	601594	jumonji and AT-rich interaction domain containing 2	0.474666	0.444702
68.	KCNJ8	3764	239850;272120;600935	potassium voltage-gated channel subfamily J member 8	0.940332	0.848572
69.	KDELC1	79070	611613	KDEL motif containing 1	1.0655	1.27176
70.	KIAA1161	57462	No ID	KIAA1161	0.708471	0.59354
71.	KIAA1549	57670	613344	KIAA1549	0.770061	0.663556
72.	KLHDC3	116138	611248	kelch domain containing 3	0.612973	0.698181
73.	KLHL4	56062	300348	kelch like family member 4	1.07248	0.81465
74.	KLHL5	51088	608064	kelch like family member 5	0.756199	0.602252
75.	KRT23	25984	606194	keratin 23	0.859914	0.780114
76.	KRT80	144501	611161	keratin 80	0.387774	0.516173
77.	LTBP1	4052	150390	latent transforming growth factor beta binding protein 1	1.32021	0.921458

78.	MALL	7851	602022	"mal, T-cell differentiation protein like"	1.60014	1.58334
79.	MBTD1	54799	No ID	mbt domain containing 1	0.616126	0.501719
80.	SLC16A2	6567	300095;300523	solute carrier family 16 member 2	1.25596	0.854277
81.	MAP2K6	5608	601254	mitogen-activated protein kinase kinase 6	1.35071	1.27931
82.	METTL7A	25840	No ID	methyltransferase like 7A	0.81592	0.96939
83.	MIR17HG	407975	609415;614326	miR-17-92a-1 cluster host gene	2.37174	2.2729
84.	MPZL3	196264	611707	myelin protein zero like 3	0.796882	0.842667
85.	MRFAP1	93621	616905	Morf4 family associated protein 1	0.465383	0.536648
86.	MORF4L1	10933	607303	mortality factor 4 like 1	0.614757	0.563526
87.	NRAS	4893	114500;137550;162900;163200;164790;188470;249400;607785;613224;614470	neuroblastoma RAS viral oncogene homolog	0.552152	0.43652
88.	NAALADL2	254827	608806	N-acetylated alpha-linked acidic dipeptidase like 2	0.69365	0.67568
89.	SLC24A3	57419	609839	solute carrier family 24 member 3	0.589257	0.4987
90.	STK38	11329	606964	serine/threonine kinase 38	0.455075	0.426797
91.	NPNT	255743	610306	nephronectin	0.774074	0.579707
92.	NANOS1	340719	608226;615413	nanos C2HC-type zinc finger 1	0.858277	0.9082
93.	GS1-358P8.4;PDK3	5165	300905;300906	pyruvate dehydrogenase kinase 3	0.771457	0.564068
94.	PCP4	5121	601629	Purkinje cell protein 4	0.864802	0.712848
95.	PERP	64065	609301	"PERP, TP53 apoptosis effector"	0.587256	0.421452
96.	PIK3R3	8503	606076	phosphoinositide-3-kinase regulatory subunit 3	0.801967	0.829185
97.	C7orf73	647087	No ID	chromosome 7 open reading frame 73	0.803039	0.703753
98.	KDM5B	10765	605393	lysine demethylase 5B	0.98413	0.779044
99.	BPGM	669	222800;613896	bisphosphoglycerate mutase	0.744332	0.734537
100.	PPT1	5538	256730;600722	palmitoyl-protein thioesterase 1	0.742549	0.688119
101.	PRMT6	55170	608274	protein arginine methyltransferase 6	0.576114	0.729643
102.	PSG9	5678	176398	pregnancy specific beta-1-glycoprotein 9	0.84128	0.757355
103.	PANX1	24145	608420	pannexin 1	0.666987	0.487432
104.	PKP1	5317	601975;604536	plakophilin 1	1.25349	1.28295
105.	RPS24	6229	602412;610629	ribosomal protein S24	0.555705	0.488549
106.	RPS3A	6189	180478	ribosomal protein S3A	0.687786	0.491714
107.	RTN3	10313	604249	reticulon 3	0.612048	0.503042
108.	S100A10	6281	114085	S100 calcium binding protein A10	0.574568	0.414773
109.	SERINC5	256987	614551	serine incorporator 5	0.805837	0.548127
110.	SESTD1	91404	No ID	SEC14 and spectrin domain containing 1	1.10416	1.06537
111.	SLITRK6	84189	221200;609681	SLIT and NTRK like family member 6	0.786628	0.553729
112.	TMTC3	160418	No ID	transmembrane and tetratricopeptide repeat containing 3	0.828496	0.643048
113.	SCIN	85477	613416	scinderin	1.3387	1.19559
114.	SEMA3C	10512	602645	semaphorin 3C	0.865222	0.66281
115.	SEMA3D	223117	609907	semaphorin 3D	1.48777	1.16477
116.	SORT1	6272	602458;613589	sortilin 1	0.749978	0.522416
117.	STON1	11037	605357	stonin 1	1.5401	1.4028
118.	TBC1D7	51256	248000;612655	TBC1 domain family member 7	0.921924	0.83745
119.	RCC2	55920	609587	regulator of chromosome condensation 2	0.401982	0.591432
120.	TDG	6996	601423	thymine DNA glycosylase	0.815785	0.81763

121.	TET3	200424	613555	tet methylcytosine dioxygenase 3	0.923868	1.01061
122.	TMEM117	84216	No ID	transmembrane protein 117	1.76039	1.52825
123.	TMEM164	84187	No ID	transmembrane protein 164	0.8879	0.803582
124.	TMEM45B	120224	No ID	transmembrane protein 45B	0.797278	0.752252
125.	TOP2B	7155	126431	topoisomerase (DNA) II beta	0.707055	0.519007
126.	NTRK2	4915	600456;613886	neurotrophic receptor tyrosine kinase 2	0.987398	1.21638
127.	UBTD2	92181	610174	ubiquitin domain containing 2	0.753085	0.627815
128.	UNC5C	8633	603610	unc-5 netrin receptor C	1.2494	1.47876
129.	VAMP7	6845	300053	vesicle associated membrane protein 7	0.950366	0.81555
130.	WNT2B	7482	601968	Wnt family member 2B	1.1319	1.0473
131.	TRAK2	66008	607334	trafficking kinesin protein 2	0.706495	0.568506
132.	KIT	3815	154800;164920;172800;273300;601626;606764	KIT proto-oncogene receptor tyrosine kinase	1.99239	1.71144

Supplementary Table 2C: miR-29a unique targets in MCF-7 cells

					MCF-7 Pre-miR-29a vs Anti-miR-29a
	Gene Symbol	**Entrez Gene IDs**	**OMIM IDs**	**Gene Name**	**$\log_2$(fold change)**
1.	CDR1	1038	302650	cerebellar degeneration related protein 1	1.25927
2.	CASP14	23581	605848	caspase 14	3.26142
3.	DNMT3B	1789	242860;602900	DNA methyltransferase 3 beta	0.592581
4.	SGK196	84197	615247;615249;616094	protein-O-mannose kinase	0.792492
5.	SERPINH1	871	600943;610504;613848	serpin family H member 1	0.691306
6.	NRBP1	29959	606010	nuclear receptor binding protein 1	0.446701
7.	ZNF469	84627	229200;612078	zinc finger protein 469	0.819815

Supplementary Table 3: miR-29 targets in LCC9 cells

Supplementary Table 3A: miR-29b-1 unique targets in LCC9 cells

				LCC9 Pre-miR-29b-1 vs Anti-miR-29a
	Input IDs	**Gene Symbol**	**Gene Name**	**log$_2$(fold change)**
1.	ENSG00000106049	HIBADH	3-hydroxyisobutyrate dehydrogenase	0.491816
2.	ENSG00000150756	FAM173B	family with sequence similarity 173 member B	0.610799
3.	ENSG00000204574	ABCF1	ATP binding cassette subfamily F member 1	0.404991
4.	ENSG00000197150	ABCB8	ATP binding cassette subfamily B member 8	0.490734
5.	ENSG00000060971	ACAA1	acetyl-CoA acyltransferase 1	0.400058
6.	ENSG00000141385	AFG3L2	AFG3 like matrix AAA peptidase subunit 2	0.728778
7.	ENSG00000188266	HYKK	hydroxylysine kinase	0.511482
8.	ENSG00000155085	AK9	adenylate kinase 9	0.652831
9.	ENSG00000187134	AKR1C1	aldo-keto reductase family 1 member C1	0.648362
10.	ENSG00000196139	AKR1C3	aldo-keto reductase family 1 member C3	0.556808
11.	ENSG00000172339	ALG14	ALG14, UDP-N-acetylglucosaminyltransferase subunit	0.826509
12.	ENSG00000137760	ALKBH8	alkB homolog 8, tRNA methyltransferas"	0.63568
13.	ENSG00000088448	ANKRD10	ankyrin repeat domain 10	0.692931
14.	ENSG00000132623	ANKEF1	ankyrin repeat and EF-hand domain containing 1	0.491522
15.	ENSG00000116819	TFAP2E	transcription factor AP-2 epsilon	1.24266
16.	ENSG00000149089	APIP	APAF1 interacting protein	0.585429
17.	ENSG00000169621	APLF	aprataxin and PNKP like factor	0.666282
18.	ENSG00000113966	ARL6	ADP ribosylation factor like GTPase 6	0.590646
19.	ENSG00000143437	ARNT	aryl hydrocarbon receptor nuclear translocator	0.576123
20.	ENSG00000130707	ASS1	argininosuccinate synthase 1	0.569205
21.	ENSG00000176208	ATAD5	ATPase family, AAA domain containing 5	0.409172
22.	ENSG00000115966	ATF2	activating transcription factor 2	0.636007
23.	ENSG00000122507	BBS9	Bardet-Biedl syndrome 9	0.732789
24.	ENSG00000236824	BCYRN1	brain cytoplasmic RNA 1	0.733708
25.	ENSG00000136573	BLK	BLK proto-oncogene, Src family tyrosine kinase	1.73238
26.	ENSG00000184992	BRI3BP	BRI3 binding protein	0.388747
27.	ENSG00000074317	SNCB	synuclein beta	1.28303
28.	ENSG00000122378	FAM213A	family with sequence similarity 213 member A	0.500409
29.	ENSG00000022277	RTFDC1	replication termination factor 2 domain containing 1	0.382306
30.	ENSG00000184809	B3GALT5-AS1	B3GALT5 antisense RNA 1	1.15966
31.	ENSG00000172478	C2orf54	chromosome 2 open reading frame 54	1.28875
32.	ENSG00000196821	C6orf106	chromosome 6 open reading frame 106	0.542815
33.	ENSG00000203778	FAM229B	family with sequence similarity 229 member B	0.720804
34.	ENSG00000147894	C9orf72	chromosome 9 open reading frame 72	0.647372
35.	ENSG00000003989	SLC7A2	solute carrier family 7 member 2	0.476024
36.	ENSG00000172785	CBWD1	COBW domain containing 1	0.417456
37.	ENSG00000163001	CFAP36	cilia and flagella associated protein 36	0.533663
38.	ENSG00000109881	CCDC34	coiled-coil domain containing 34	0.651414
39.	ENSG00000141519	CCDC40	coiled-coil domain containing 40	1.16175
40.	ENSG00000173588	CEP83	centrosomal protein 83	0.710338
41.	ENSG00000081377	CDC14B	cell division cycle 14B	0.657699
42.	ENSG00000100526	CDKN3	cyclin dependent kinase inhibitor 3	0.378184
43.	ENSG00000166446	CDYL2	chromodomain Y-like 2	0.756545
44.	ENSG00000114107	CEP70	centrosomal protein 70	0.527855
45.	ENSG00000188153	COL4A5	collagen type IV alpha 5 chain	1.26463
46.	ENSG00000138663	COPS4	COP9 signalosome subunit 4	0.575052
47.	ENSG00000111652	COPS7A	COP9 signalosome subunit 7A	0.470495
48.	ENSG00000096006	CRISP3	cysteine rich secretory protein 3	0.74899
49.	ENSG00000049656	CLPTM1L	CLPTM1 like	0.516426
50.	ENSG00000145681	HAPLN1	hyaluronan and proteoglycan link protein 1	4.09352
51.	ENSG00000124207	CSE1L	chromosome segregation 1 like	0.396727
52.	ENSG00000150527	CTAGE5	"CTAGE family member 5, ER export factor"	0.479836
53.	ENSG00000137770	CTDSPL2	CTD small phosphatase like 2	0.660265
54.	ENSG00000111249	CUX2	cut like homeobox 2	0.772002
55.	ENSG00000161921	CXCL16	C-X-C motif chemokine ligand 16	0.654154

56.	ENSG00000174437	ATP2A2	ATPase sarcoplasmic/endoplasmic reticulum Ca2+ transporting 2	0.464372
57.	ENSG00000152495	CAMK4	calcium/calmodulin dependent protein kinase IV	1.09332
58.	ENSG00000132906	CASP9	caspase 9	0.586727
59.	ENSG00000150764	DIXDC1	DIX domain containing 1	0.874583
60.	ENSG00000167670	CHAF1A	chromatin assembly factor 1 subunit A	0.759801
61.	ENSG00000111907	TPD52L1	tumor protein D52-like 1	0.484994
62.	ENSG00000134107	BHLHE40	basic helix-loop-helix family member e40	0.5102
63.	ENSG00000155792	DEPTOR	DEP domain containing MTOR-interacting protein	1.01048
64.	ENSG00000136044	APPL2	"adaptor protein, phosphotyrosine interacting with PH domain and leucine zipper 2"	0.847216
65.	ENSG00000126698	DNAJC8	DnaJ heat shock protein family (Hsp40) member C8	0.444634
66.	ENSG00000189212	DPY19L2P1	DPY19L2 pseudogene 1	0.557364
67.	ENSG00000165891	E2F7	E2F transcription factor 7	0.580426
68.	ENSG00000164330	EBF1	early B-cell factor 1	2.01344
69.	ENSG00000109381	ELF2	E74 like ETS transcription factor 2	0.584111
70.	ENSG00000138185	ENTPD1	ectonucleoside triphosphate diphosphohydrolase 1	0.51802
71.	ENSG00000187672	ERC2	ELKS/RAB6-interacting/CAST family member 2	0.765149
72.	ENSG00000170515	PA2G4	proliferation-associated 2G4	0.534069
73.	ENSG00000185900	POMK	protein-O-mannose kinase	0.865861
74.	ENSG00000133216	EPHB2	EPH receptor B2	0.546443
75.	ENSG00000031003	FAM13B	family with sequence similarity 13 member B	0.523452
76.	ENSG00000154511	FAM69A	family with sequence similarity 69 member A	0.569141
77.	ENSG00000158169	FANCC	Fanconi anemia complementation group C	0.900585
78.	ENSG00000160752	FDPS	farnesyl diphosphate synthase	0.65476
79.	ENSG00000169018	FEM1B	fem-1 homolog B	0.807097
80.	ENSG00000197296	FITM2	fat storage inducing transmembrane protein 2	0.374061
81.	ENSG00000198468	FLVCR1-AS1	FLVCR1 antisense RNA 1 (head to head)	0.934593
82.	ENSG00000138759	FRAS1	Fraser extracellular matrix complex subunit 1	0.825708
83.	ENSG00000150667	FSIP1	fibrous sheath interacting protein 1	4.68256
84.	ENSG00000114450	GNB4	G protein subunit beta 4	0.651437
85.	ENSG00000242616	GNG10	G protein subunit gamma 10	0.677874
86.	ENSG00000172380	GNG12	G protein subunit gamma 12	0.792578
87.	ENSG00000164949	GEM	GTP binding protein overexpressed in skeletal muscle	0.570737
88.	ENSG00000198814	GK	glycerol kinase	1.29919
89.	ENSG00000130309	COLGALT1	collagen beta(1-O)galactosyltransferase 1	0.676398
90.	ENSG00000073605	GSDMB	gasdermin B	0.835803
91.	ENSG00000226259	GTF2H2B	general transcription factor IIH subunit 2B (pseudogene)	1.24475
92.	ENSG00000234741	GAS5	growth arrest specific 5 (non-protein coding)	0.584347
93.	ENSG00000179409	GEMIN4	gem nuclear organelle associated protein 4	0.498702
94.	ENSG00000175697	GPR156	G protein-coupled receptor 156	0.564154
95.	ENSG00000249115	HAUS5	HAUS augmin like complex subunit 5	0.562282
96.	ENSG00000048052	HDAC9	histone deacetylase 9	1.17183
97.	ENSG00000206053	HN1L	hematological and neurological expressed 1 like	0.716046
98.	ENSG00000149428	HYOU1	hypoxia up-regulated 1	0.37912
99.	ENSG00000146674	IGFBP3	insulin like growth factor binding protein 3	1.78987
100.	ENSG00000032742	IFT88	intraflagellar transport 88	0.561653
101.	ENSG00000243646	IL10RB	interleukin 10 receptor subunit beta	1.09275
102.	ENSG00000016402	IL20RA	interleukin 20 receptor subunit alpha	0.687926
103.	ENSG00000148950	IMMP1L	inner mitochondrial membrane peptidase subunit 1	1.24312
104.	ENSG00000240682	ISY1	ISY1 splicing factor homolog	0.766524
105.	ENSG00000082781	ITGB5	integrin subunit beta 5	0.537403
106.	ENSG00000140057	AK7	adenylate kinase 7	0.986999
107.	ENSG00000140854	KATNB1	katanin regulatory subunit B1	0.560459
108.	ENSG00000122778	KIAA1549	KIAA1549	0.738185
109.	ENSG00000102271	KLHL4	kelch like family member 4	0.978512
110.	ENSG00000118162	KPTN	"kaptin, actin binding protein"	0.648915
111.	ENSG00000102781	KATNAL1	katanin catalytic subunit A1 like 1	0.545075
112.	ENSG00000170523	KRT83	keratin 83	0.821228
113.	ENSG00000170745	KCNS3	potassium voltage-gated channel modifier subfamily S member 3	0.504918
114.	ENSG00000131023	LATS1	large tumor suppressor kinase 1	0.454589
115.	ENSG00000134333	LDHA	lactate dehydrogenase A	0.556593
116.	ENSG00000179241	LDLRAD3	low density lipoprotein receptor class A domain containing 3	0.659617
117.	ENSG00000117114	ADGRL2	adhesion G protein-coupled receptor L2	1.38087

118.	ENSG00000235823	OLMALINC	oligodendrocyte maturation-associated long intergenic non-coding RNA	0.489124
119.	ENSG00000145832	SLC25A48	solute carrier family 25 member 48	2.62358
120.	ENSG00000213468	FIRRE	firre intergenic repeating RNA element	0.60146
121.	ENSG00000237732	LOC440934	uncharacterized LOC440934	1.06641
122.	ENSG00000236850	BMS1P20	"BMS1, ribosome biogenesis factor pseudogene 20"	0.42462
123.	ENSG00000198121	LPAR1	lysophosphatidic acid receptor 1	1.78063
124.	ENSG00000117600	PLPPR4	phospholipid phosphatase related 4	2.03628
125.	ENSG00000168904	LRRC28	leucine rich repeat containing 28	0.44925
126.	ENSG00000066557	LRRC40	leucine rich repeat containing 40	0.368294
127.	ENSG00000106853	PTGR1	prostaglandin reductase 1	0.548995
128.	ENSG00000049323	LTBP1	latent transforming growth factor beta binding protein 1	0.591944
129.	ENSG00000178802	MPI	mannose phosphate isomerase	0.488671
130.	ENSG00000116586	LAMTOR2	"late endosomal/lysosomal adaptor, MAPK and MTOR activator 2"	0.365329
131.	ENSG00000166974	MAPRE2	microtubule associated protein RP/EB family member 2	1.40219
132.	ENSG00000076003	MCM6	minichromosome maintenance complex component 6	0.531703
133.	ENSG00000065833	ME1	malic enzyme 1	0.423041
134.	ENSG00000175581	MRPL48	mitochondrial ribosomal protein L48	0.562058
135.	ENSG00000048544	MRPS10	mitochondrial ribosomal protein S10	0.366277
136.	ENSG00000164953	TMEM67	transmembrane protein 67	0.890988
137.	ENSG00000147166	ITGB1BP2	integrin subunit beta 1 binding protein 2	1.7052
138.	ENSG00000126858	RHOT1	ras homolog family member T1	0.621903
139.	ENSG00000078177	N4BP2	NEDD4 binding protein 2	0.775605
140.	ENSG00000228224	NACAP1	nascent polypeptide associated complex alpha subunit pseudogene 1	0.852377
141.	ENSG00000125814	NAPB	NSF attachment protein beta	0.41552
142.	ENSG00000110583	NAA40	"N(alpha)-acetyltransferase 40, NatD catalytic subunit"	0.93559
143.	ENSG00000196290	NIF3L1	NGG1 interacting factor 3 like 1	0.477036
144.	ENSG00000176171	BNIP3	BCL2 interacting protein 3	0.400854
145.	ENSG00000113389	NPR3	natriuretic peptide receptor 3	0.731253
146.	ENSG00000184117	NIPSNAP1	nipsnap homolog 1 (C. elegans)	0.419627
147.	ENSG00000084628	NKAIN1	Na+/K+ transporting ATPase interacting 1	0.930873
148.	ENSG00000218336	TENM3	teneurin transmembrane protein 3	0.946142
149.	ENSG00000122884	P4HA1	prolyl 4-hydroxylase subunit alpha 1	0.670883
150.	ENSG00000180228	PRKRA	protein activator of interferon induced protein kinase	0.415149
151.	ENSG00000141127	PRPSAP2	phosphoribosyl pyrophosphate synthetase associated protein 2	0.413774
152.	ENSG00000177839	PCDHB9	protocadherin beta 9	0.795703
153.	ENSG00000205268	PDE7A	phosphodiesterase 7A	0.626122
154.	ENSG00000170962	PDGFD	platelet derived growth factor D	1.08647
155.	ENSG00000100227	POLDIP3	DNA polymerase delta interacting protein 3	0.621359
156.	ENSG00000198721	ECI2	enoyl-CoA delta isomerase 2	0.724378
157.	ENSG00000173868	PHOSPHO1	phosphoethanolamine/phosphocholine phosphatase	1.0788
158.	ENSG00000169756	LIMS1	LIM zinc finger domain containing 1	0.507993
159.	ENSG00000005249	PRKAR2B	protein kinase cAMP-dependent typeII regulatory subunit β	0.96804
160.	ENSG00000169621	PROKR1	prokineticin receptor 1	0.666282
161.	ENSG00000106086	PLEKHA8	pleckstrin homology domain containing A8	0.54894
162.	ENSG00000014138	POLA2	"DNA polymerase alpha 2, accessory subunit"	0.465248
163.	ENSG00000144231	POLR2D	RNA polymerase II subunit D	0.50258
164.	ENSG00000185238	PRMT3	protein arginine methyltransferase 3	0.399367
165.	ENSG00000166033	HTRA1	HtrA serine peptidase 1	0.448859
166.	ENSG00000121766	ZCCHC17	zinc finger CCHC-type containing 17	0.745644
167.	ENSG00000138430	OLA1	Obg like ATPase 1	0.454699
168.	ENSG00000139304	PTPRQ	"protein tyrosine phosphatase, receptor type Q"	1.30696
169.	ENSG00000091127	PUS7	pseudouridylate synthase 7 (putative)	1.05676
170.	ENSG00000059573	ALDH18A1	aldehyde dehydrogenase 18 family member A1	0.531767
171.	ENSG00000004399	PLXND1	plexin D1	0.785074
172.	ENSG00000143801	PSEN2	presenilin 2	0.577816
173.	ENSG00000089050	RBBP9	"RB binding protein 9, serine hydrolase"	0.62783
174.	ENSG00000213516	RBMXL1	"RNA binding motif protein, X-linked like 1"	0.83167
175.	ENSG00000162444	RBP7	retinol binding protein 7	0.731566
176.	ENSG00000122707	RECK	reversion inducing cysteine rich protein with kazal motifs	0.634226
177.	ENSG00000203668	CHML	"CHM like, Rab escort protein 2"	0.51309
178.	ENSG00000111404	RERGL	RERG like	2.21964
179.	ENSG00000165731	RET	ret proto-oncogene	0.50531

180.	ENSG00000121481	RNF2	ring finger protein 2	0.509205
181.	ENSG00000180530	NRIP1	nuclear receptor interacting protein 1	0.37917
182.	ENSG00000110315	RNF141	ring finger protein 141	0.670646
183.	ENSG00000198242	RPL23A	ribosomal protein L23a	0.381132
184.	ENSG00000089009	RPL6	ribosomal protein L6	0.636679
185.	ENSG00000146223	RPL7L1	ribosomal protein L7 like 1	0.477004
186.	ENSG00000139998	RAB15	"RAB15, member RAS oncogene family"	1.00517
187.	ENSG00000133318	RTN3	reticulon 3	0.404803
188.	ENSG00000140943	MBTPS1	"membrane bound transcription factor peptidase, site 1"	0.791293
189.	ENSG00000092108	SCFD1	sec1 family domain containing 1	0.462588
190.	ENSG00000102098	SCML2	sex comb on midleg-like 2 (Drosophila)	0.614317
191.	ENSG00000143653	SCCPDH	saccharopine dehydrogenase (putative)	0.383584
192.	ENSG00000086475	SEPHS1	selenophosphate synthetase 1	0.581941
193.	ENSG00000196136	SERPINA3	serpin family A member 3	0.834504
194.	ENSG00000176974	SHMT1	serine hydroxymethyltransferase 1	0.464031
195.	ENSG00000146414	SHPRH	SNF2 histone linker PHD RING helicase	0.631553
196.	ENSG00000072858	SIDT1	SID1 transmembrane family member 1	0.514638
197.	ENSG00000179542	SLITRK4	SLIT and NTRK like family member 4	0.584921
198.	ENSG00000139324	TMTC3	transmembrane and tetratricopeptide repeat containing 3	0.659666
199.	ENSG00000188176	SMTNL2	smoothelin like 2	1.49332
200.	ENSG00000132639	SNAP25	synaptosome associated protein 25	2.16937
201.	ENSG00000129673	AANAT	aralkylamine N-acetyltransferase	2.09567
202.	ENSG00000112335	SNX3	sorting nexin 3	0.378761
203.	ENSG00000145375	SPATA5	spermatogenesis associated 5	0.491729
204.	ENSG00000149136	SSRP1	structure specific recognition protein 1	0.392846
205.	ENSG00000110066	KMT5B	lysine methyltransferase 5B	0.482419
206.	ENSG00000159164	SV2A	synaptic vesicle glycoprotein 2A	0.398681
207.	ENSG00000006747	SCIN	scinderin	0.478395
208.	ENSG00000150961	SEC24D	"SEC24 homolog D, COPII coat complex component"	0.852999
209.	ENSG00000167680	SEMA6B	semaphorin 6B	0.508275
210.	ENSG00000198879	SFMBT2	Scm-like with four mbt domains 2	0.390137
211.	ENSG00000187164	SHTN1	shootin 1	0.496706
212.	ENSG00000150753	CCT5	chaperonin containing TCP1 subunit 5	0.621055
213.	ENSG00000204852	TCTN1	tectonic family member 1	0.814604
214.	ENSG00000083544	TDRD3	tudor domain containing 3	0.599608
215.	ENSG00000187735	TCEA1	transcription elongation factor A1	0.363363
216.	ENSG00000118707	TGIF2	TGFB induced factor homeobox 2	0.91099
217.	ENSG00000111602	TIMELESS	timeless circadian clock	0.468897
218.	ENSG00000100234	TIMP3	TIMP metallopeptidase inhibitor 3	0.884252
219.	ENSG00000185650	ZFP36L1	ZFP36 ring finger protein like 1	0.363495
220.	ENSG00000164841	TMEM74	transmembrane protein 74	0.659316
221.	ENSG00000168234	TTC39C	tetratricopeptide repeat domain 39C	0.645904
222.	ENSG00000114999	TTL	tubulin tyrosine ligase	0.436904
223.	ENSG00000253352	TUG1	taurine up-regulated 1 (non-protein coding)	0.663468
224.	ENSG00000102241	HTATSF1	HIV-1 Tat specific factor 1	0.438483
225.	ENSG00000140534	TICRR	TOPBP1 interacting checkpoint and replication regulator	0.49207
226.	ENSG00000152086	TUBA3E	tubulin alpha 3e	2.34108
227.	ENSG00000123416	TUBA1B	tubulin alpha 1b	0.396279
228.	ENSG00000074935	TUBE1	tubulin epsilon 1	0.587981
229.	ENSG00000117143	UAP1	UDP-N-acetylglucosamine pyrophosphorylase 1	0.455078
230.	ENSG00000078967	UBE2D4	ubiquitin conjugating enzyme E2 D4 (putative)	0.778811
231.	ENSG00000165816	VWA2	von Willebrand factor A domain containing 2	0.928517
232.	ENSG00000132970	WASF3	WAS protein family member 3	0.629683
233.	ENSG00000065183	WDR3	WD repeat domain 3	0.500013
234.	ENSG00000176105	YES1	"YES proto-oncogene 1, Src family tyrosine kinase"	0.431171
235.	ENSG00000257267	ZNF271P	"zinc finger protein 271, pseudogene"	0.497983
236.	ENSG00000130844	ZNF331	zinc finger protein 331	0.516318
237.	ENSG00000160094	ZNF362	zinc finger protein 362	0.911363
238.	ENSG00000142556	ZNF614	zinc finger protein 614	0.740139
239.	ENSG00000186777	ZNF732	zinc finger protein 732	0.491996
240.	ENSG00000091428	RAPGEF4	Rap guanine nucleotide exchange factor 4	1.03583
241.	ENSG00000138660	AP1AR	adaptor related protein complex 1 associated regulatory protein	1.03233
242.	ENSG00000256806	C17orf100	chromosome 17 open reading frame 100	1.62273
243.	ENSG00000207652	MIR621	microRNA 621	1.4975

Supplementary Table 3B: Common miR-29b-1 and miR-29a targets in LCC9 cells

				LCC9 Pre-miR-29b-1 vs Anti-miR-29a	LCC9 Pre-miR-29a vs Anti-miR-29a
	Input IDs	**Gene Symbol**	**Gene Name**	**$\log_2$ (fold change)**	**$\log_2$ (fold change)**
1.	ENSG00000108953	YWHAE	tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein epsilon	0.487217	0.457738
2.	ENSG00000223414	LINC00473	long intergenic non-protein coding RNA 473	4.3032	5.28493
3.	ENSG00000172243	CLEC7A	C-type lectin domain family 7 member A	2.31239	4.17419
4.	ENSG00000152661	GJA1	gap junction protein alpha 1	4.11427	3.86025
5.	ENSG00000168306	ACOX2	acyl-CoA oxidase 2	4.65734	3.66441
6.	ENSG00000187678	SPRY4	sprouty RTK signaling antagonist 4	2.72265	3.40137
7.	ENSG00000198937	CCDC167	coiled-coil domain containing 167	3.39142	3.38646
8.	ENSG00000113140	SPARC	secreted protein acidic and cysteine rich	2.76873	3.35492
9.	ENSG00000150779	TIMM8B	translocase of inner mitochondrial membrane 8 homolog B	2.80661	3.09556
10.	ENSG00000143546	S100A8	S100 calcium binding protein A8	1.92461	3.08523
11.	ENSG00000175832	ETV4	ETS variant 4	2.98963	2.98716
12.	ENSG00000128271	ADORA2A	adenosine A2a receptor	2.30518	2.9572
13.	ENSG00000145979	TBC1D7	TBC1 domain family member 7	2.64112	2.93259
14.	ENSG00000144891	AGTR1	angiotensin II receptor type 1	2.79834	2.8424
15.	ENSG00000064205	WISP2	WNT1 inducible signaling pathway protein 2	2.80975	2.83438
16.	ENSG00000169181	GSG1L	GSG1 like	3.08116	2.83152
17.	ENSG00000163485	ADORA1	adenosine A1 receptor	2.51826	2.81189
18.	ENSG00000160050	CCDC28B	coiled-coil domain containing 28B	2.65578	2.80182
19.	ENSG00000134901	KDELC1	KDEL motif containing 1	3.01117	2.79997
20.	ENSG00000071575	TRIB2	tribbles pseudokinase 2	2.8007	2.78841
21.	ENSG00000174453	VWC2L	von Willebrand factor C domain containing protein 2-like	3.02552	2.7854
22.	ENSG00000123560	PLP1	proteolipid protein 1	1.78971	2.78286
23.	ENSG00000198890	PRMT6	protein arginine methyltransferase 6	2.51833	2.72602
24.	ENSG00000126010	GRPR	gastrin releasing peptide receptor	2.54854	2.69536
25.	ENSG00000116774	OLFML3	olfactomedin like 3	2.60869	2.68797
26.	ENSG00000244405	ETV5	ETS variant 5	1.71214	2.63838
27.	ENSG00000162892	IL24	interleukin 24	2.76179	2.61736
28.	ENSG00000064995	TAF11	TATA-box binding protein associated factor 11	2.53393	2.61299
29.	ENSG00000164120	HPGD	hydroxyprostaglandin dehydrogenase 15-(NAD)	2.94784	2.59741
30.	ENSG00000105671	DDX49	DEAD-box helicase 49	2.34706	2.59104
31.	ENSG00000163220	S100A9	S100 calcium binding protein A9	1.53666	2.52338
32.	ENSG00000164761	TNFRSF11B	TNF receptor superfamily member 11b	2.27648	2.51838
33.	ENSG00000179051	RCC2	regulator of chromosome condensation 2	2.40005	2.4671
34.	ENSG00000132821	VSTM2L	V-set and transmembrane domain containing 2 like	2.51467	2.41676
35.	ENSG00000105967	TFEC	transcription factor EC	2.11704	2.40168
36.	ENSG00000142224	IL19	interleukin 19	3.06232	2.39884
37.	ENSG00000104147	OIP5	Opa interacting protein 5	2.11953	2.39693
38.	ENSG00000092208	GEMIN2	gem nuclear organelle associated protein 2	2.09195	2.368
39.	ENSG00000136783	NIPSNAP3A	nipsnap homolog 3A	1.98433	2.36503
40.	ENSG00000138326	RPS24	ribosomal protein S24	2.25259	2.36119
41.	ENSG00000198856	OSTC	oligosaccharyltransferase complex non-catalytic subunit	2.19415	2.35898
42.	ENSG00000139372	TDG	thymine DNA glycosylase	2.25669	2.35879
43.	ENSG00000163347	CLDN1	claudin 1	1.59109	2.35224
44.	ENSG00000166106	ADAMTS15	ADAM metallopeptidase with thrombospondin type 1 motif 15	2.63156	2.34575
45.	ENSG00000256870	SLC5A8	solute carrier family 5 member 8	2.78152	2.31415
46.	ENSG00000183036	PCP4	Purkinje cell protein 4	2.79053	2.29124
47.	ENSG00000260231	JHDM1D-AS1	JHDM1D antisense RNA 1 (head to head)	1.91105	2.28899
48.	ENSG00000173950	XXYLT1	xyloside xylosyltransferase 1	2.16137	2.27884
49.	ENSG00000179388	EGR3	early growth response 3	2.35585	2.26571
50.	ENSG00000132004	FBXW9	F-box and WD repeat domain containing 9	1.83408	2.26133
51.	ENSG00000123364	HOXC13	homeobox C13	2.13121	2.22351

52.	ENSG00000158164	TMSB15A	thymosin beta 15a	2.53916	2.21981
53.	ENSG00000169248	CXCL11	C-X-C motif chemokine ligand 11	2.02203	2.21208
54.	ENSG00000242265	PEG10	paternally expressed 10	2.10984	2.21207
55.	ENSG00000137441	FGFBP2	fibroblast growth factor binding protein 2	2.90166	2.19779
56.	ENSG00000135046	ANXA1	annexin A1	2.13207	2.17304
57.	ENSG00000170855	TRIAP1	TP53 regulated inhibitor of apoptosis 1	2.00172	2.1629
58.	ENSG00000168938	PPIC	peptidylprolyl isomerase C	2.04242	2.15937
59.	ENSG00000135346	CGA	"glycoprotein hormones, alpha polypeptide"	1.43795	2.15628
60.	ENSG00000108984	MAP2K6	mitogen-activated protein kinase kinase 6	2.61089	2.15353
61.	ENSG00000006625	GGCT	gamma-glutamylcyclotransferase	2.08826	2.14783
62.	ENSG00000146425	DYNLT1	dynein light chain Tctex-type 1	1.94914	2.14702
63.	ENSG00000101057	MYBL2	MYB proto-oncogene like 2	2.03609	2.14457
64.	ENSG00000179010	MRFAP1	Morf4 family associated protein 1	2.03319	2.14254
65.	ENSG00000108578	BLMH	bleomycin hydrolase	2.51864	2.13864
66.	ENSG00000139055	ERP27	endoplasmic reticulum protein 27	1.63098	2.08328
67.	ENSG00000075290	WNT8B	Wnt family member 8B	1.5311	2.08131
68.	ENSG00000226950	DANCR	differentiation antagonizing non-protein coding RNA	1.67735	2.07894
69.	ENSG00000124702	KLHDC3	kelch domain containing 3	1.94245	2.07298
70.	ENSG00000149257	SERPINH1	serpin family H member 1	1.97041	2.06858
71.	ENSG00000121005	CRISPLD1	cysteine rich secretory protein LCCL domain containing 1	2.05979	2.05316
72.	ENSG00000108511	HOXB6	homeobox B6	1.8322	2.04239
73.	ENSG00000106484	MEST	mesoderm specific transcript	2.28148	2.02826
74.	ENSG00000198729	PPP1R14C	protein phosphatase 1 regulatory inhibitor subunit 14C	2.03073	2.02062
75.	ENSG00000170899	GSTA4	glutathione S-transferase alpha 4	1.77556	2.01732
76.	ENSG00000153012	LGI2	leucine rich repeat LGI family member 2	2.18862	2.00029
77.	ENSG00000140905	GCSH	glycine cleavage system protein H	2.03522	1.98461
78.	ENSG00000168256	NKIRAS2	NFKB inhibitor interacting Ras like 2	1.79244	1.98048
79.	ENSG00000233101	HOXB-AS3	HOXB cluster antisense RNA 3	2.07946	1.9725
80.	ENSG00000157404	KIT	KIT proto-oncogene receptor tyrosine kinase	2.10612	1.97156
81.	ENSG00000144451	SPAG16	sperm associated antigen 16	2.78745	1.96532
82.	ENSG00000164362	TERT	telomerase reverse transcriptase	1.89687	1.94267
83.	ENSG00000144857	BOC	"BOC cell adhesion associated, oncogene regulated"	2.16198	1.93153
84.	ENSG00000120875	DUSP4	dual specificity phosphatase 4	2.05306	1.92245
85.	ENSG00000170465	KRT6C	keratin 6C	1.27008	1.92117
86.	ENSG00000119929	CUTC	cutC copper transporter	1.76035	1.9119
87.	ENSG00000178585	CTNNBIP1	catenin beta interacting protein 1	1.85451	1.90993
88.	ENSG00000181788	SIAH2	siah E3 ubiquitin protein ligase 2	1.85018	1.90909
89.	ENSG00000078725	BRINP1	BMP/retinoic acid inducible neural specific 1	1.72664	1.90507
90.	ENSG00000243317	C7orf73	chromosome 7 open reading frame 73	1.89354	1.90098
91.	ENSG00000146409	SLC18B1	solute carrier family 18 member B1	1.68871	1.89729
92.	ENSG00000035141	FAM136A	family with sequence similarity 136 member A	1.77743	1.89115
93.	ENSG00000145632	PLK2	polo like kinase 2	2.01513	1.87612
94.	ENSG00000174721	FGFBP3	fibroblast growth factor binding protein 3	1.23721	1.87457
95.	ENSG00000066583	ISOC1	isochorismatase domain containing 1	1.88871	1.87293
96.	ENSG00000165806	CASP7	caspase 7	1.81119	1.87049
97.	ENSG00000169282	KCNAB1	potassium voltage-gated channel subfamily A member regulatory beta subunit 1	2.691	1.84939
98.	ENSG00000167536	DHRS13	dehydrogenase/reductase 13	1.78083	1.83441
99.	ENSG00000135930	EIF4E2	eukaryotic translation initiation factor 4E family member 2	1.81313	1.83072
100.	ENSG00000114646	CSPG5	chondroitin sulfate proteoglycan 5	1.77322	1.8202
101.	ENSG00000131153	GINS2	GINS complex subunit 2	1.68133	1.7959
102.	ENSG00000137965	IFI44	interferon induced protein 44	1.07807	1.79376
103.	ENSG00000155330	C16orf87	chromosome 16 open reading frame 87	1.76765	1.78206
104.	ENSG00000118418	HMGN3	high mobility group nucleosomal binding domain 3	1.75435	1.77512
105.	ENSG00000114744	COMMD2	COMM domain containing 2	1.81109	1.76506
106.	ENSG00000102683	SGCG	sarcoglycan gamma	1.58645	1.76154
107.	ENSG00000247556	OIP5-AS1	OIP5 antisense RNA 1	1.90865	1.75325
108.	ENSG00000134258	VTCN1	V-set domain containing T cell activation inhibitor 1	1.77544	1.75288
109.	ENSG00000174827	PDZK1	PDZ domain containing 1	2.32078	1.75265
110.	ENSG00000103495	MAZ	MYC associated zinc finger protein	1.56603	1.75118
111.	ENSG00000204103	MAFB	MAF bZIP transcription factor B	1.68057	1.74892
112.	ENSG00000112149	CD83	CD83 molecule	1.92141	1.74713
113.	ENSG00000140600	SH3GL3	"SH3 domain containing GRB2 like 3, endophilin A3"	1.68462	1.73615
114.	ENSG00000165061	ZMAT4	zinc finger matrin-type 4	1.53596	1.73342

115.	ENSG00000123219	CENPK	centromere protein K	1.76657	1.73323
116.	ENSG00000186480	INSIG1	insulin induced gene 1	1.83312	1.73253
117.	ENSG00000133466	C1QTNF6	C1q and tumor necrosis factor related protein 6	1.65012	1.72005
118.	ENSG00000071909	MYO3B	myosin IIIB	1.78755	1.71407
119.	ENSG00000112394	SLC16A10	solute carrier family 16 member 10	1.92999	1.71366
120.	ENSG00000172331	BPGM	bisphosphoglycerate mutase	1.74992	1.71232
121.	ENSG00000216490	IFI30	"IFI30, lysosomal thiol reductase"	1.18563	1.69327
122.	ENSG00000163444	TMEM183A	transmembrane protein 183A	1.61754	1.69108
123.	ENSG00000143633	C1orf131	chromosome 1 open reading frame 131	1.49237	1.68842
124.	ENSG00000148053	NTRK2	neurotrophic receptor tyrosine kinase 2	2.31639	1.68192
125.	ENSG00000088305	DNMT3B	DNA methyltransferase 3 beta	1.75426	1.6786
126.	ENSG00000115380	EFEMP1	EGF containing fibulin like extracellular matrix protein 1	1.53166	1.67697
127.	ENSG00000126709	IFI6	interferon alpha inducible protein 6	0.854428	1.67039
128.	ENSG00000188643	S100A16	S100 calcium binding protein A16	1.68258	1.66285
129.	ENSG00000141627	DYM	dymeclin	1.72405	1.65591
130.	ENSG00000235123	DSCAM-AS1	DSCAM antisense RNA 1	1.79876	1.65099
131.	ENSG00000066926	FECH	ferrochelatase	1.68044	1.65016
132.	ENSG00000188613	NANOS1	nanos C2HC-type zinc finger 1	1.56703	1.64991
133.	ENSG00000164619	BMPER	BMP binding endothelial regulator	1.90746	1.64764
134.	ENSG00000184515	BEX5	brain expressed X-linked 5	1.2185	1.64046
135.	ENSG00000162704	ARPC5	actin related protein 2/3 complex subunit 5	1.505	1.64043
136.	ENSG00000197696	NMB	neuromedin B	1.57817	1.63764
137.	ENSG00000113583	C5orf15	chromosome 5 open reading frame 15	1.65814	1.63619
138.	ENSG00000177971	IMP3	"IMP3, U3 small nucleolar ribonucleoprotein"	1.2763	1.63331
139.	ENSG00000107833	NPM3	nucleophosmin/nucleoplasmin 3	1.59262	1.6237
140.	ENSG00000168913	ENHO	energy homeostasis associated	1.61978	1.62355
141.	ENSG00000108423	TUBD1	tubulin delta 1	1.66967	1.62302
142.	ENSG00000124333	VAMP7	vesicle associated membrane protein 7	1.74104	1.60978
143.	ENSG00000162599	NFIA	nuclear factor I A	1.93518	1.60973
144.	ENSG00000186470	BTN3A2	butyrophilin subfamily 3 member A2	1.66846	1.60858
145.	ENSG00000123570	RAB9B	"RAB9B, member RAS oncogene family"	1.39674	1.60651
146.	ENSG00000198797	BRINP2	BMP/retinoic acid inducible neural specific 2	2.03546	1.60345
147.	ENSG00000141696	P3H4	prolyl 3-hydroxylase family member 4 (non-enzymatic)	1.43784	1.60295
148.	ENSG00000117148	ACTL8	actin like 8	1.37881	1.60098
149.	ENSG00000149547	EI24	"EI24, autophagy associated transmembrane protein"	1.58026	1.59393
150.	ENSG00000149596	JPH2	junctophilin 2	1.83951	1.59197
151.	ENSG00000223658	C1GALT1C1L	C1GALT1-specific chaperone 1 like	1.17377	1.59184
152.	ENSG00000165996	HACD1	3-hydroxyacyl-CoA dehydratase 1	1.31717	1.5829
153.	ENSG00000152766	ANKRD22	ankyrin repeat domain 22	1.83286	1.5803
154.	ENSG00000180329	CCDC43	coiled-coil domain containing 43	1.47159	1.5781
155.	ENSG00000246223	LINC01550	long intergenic non-protein coding RNA 1550	1.32543	1.57637
156.	ENSG00000100362	PVALB	parvalbumin	1.21037	1.57428
157.	ENSG00000144401	METTL21A	methyltransferase like 21A	1.81833	1.57057
158.	ENSG00000157593	SLC35B2	solute carrier family 35 member B2	1.49914	1.5692
159.	ENSG00000113838	TBCCD1	TBCC domain containing 1	1.68387	1.5637
160.	ENSG00000152284	TCF7L1	transcription factor 7 like 1	1.48257	1.55383
161.	ENSG00000122035	RASL11A	RAS like family 11 member A	1.18544	1.55333
162.	ENSG00000236603	RANP1	"RAN, member RAS oncogene family pseudogene 1"	0.818454	1.5527
163.	ENSG00000136982	DSCC1	DNA replication and sister chromatid cohesion 1	1.65166	1.54324
164.	ENSG00000134748	PRPF38A	pre-mRNA processing factor 38A	1.47559	1.5399
165.	ENSG00000117122	MFAP2	microfibrillar associated protein 2	1.55689	1.53872
166.	ENSG00000162642	C1orf52	chromosome 1 open reading frame 52	1.30657	1.53613
167.	ENSG00000115252	PDE1A	phosphodiesterase 1A	1.68231	1.53396
168.	ENSG00000107562	CXCL12	C-X-C motif chemokine ligand 12	1.71022	1.52676
169.	ENSG00000087111	PIGS	phosphatidylinositol glycan anchor biosynthesis class S	1.71025	1.52542
170.	ENSG00000164932	CTHRC1	collagen triple helix repeat containing 1	1.78111	1.52537
171.	ENSG00000103942	HOMER2	homer scaffolding protein 2	1.61365	1.51969
172.	ENSG00000157502	MUM1L1	MUM1 like 1	1.46894	1.51818
173.	ENSG00000154274	C4orf19	chromosome 4 open reading frame 19	1.57704	1.5167
174.	ENSG00000171503	ETFDH	electron transfer flavoprotein dehydrogenase	1.6454	1.51574
175.	ENSG00000104679	R3HCC1	R3H domain and coiled-coil containing 1	1.47594	1.51118
176.	ENSG00000181274	FRAT2	frequently rearranged in advanced T-cell lymphomas 2	1.26584	1.50653
177.	ENSG00000148229	POLE3	"DNA polymerase epsilon 3, accessory subunit"	1.31072	1.50374

178.	ENSG00000030110	BAK1	BCL2 antagonist/killer 1	1.22959	1.49069
179.	ENSG00000127124	HIVEP3	human immunodeficiency virus type I enhancer binding protein 3	1.71264	1.48377
180.	ENSG00000141540	TTYH2	tweety family member 2	1.39606	1.47698
181.	ENSG00000196839	ADA	adenosine deaminase	1.37348	1.47158
182.	ENSG00000149600	COMMD7	COMM domain containing 7	1.39645	1.46911
183.	ENSG00000185745	IFIT1	interferon induced protein with tetratricopeptide repeats 1	0.683847	1.46504
184.	ENSG00000171119	NRTN	neurturin	1.42941	1.46177
185.	ENSG00000170775	GPR37	G protein-coupled receptor 37	1.6004	1.4605
186.	ENSG00000168874	ATOH8	atonal bHLH transcription factor 8	1.53391	1.45938
187.	ENSG00000180834	MAP6D1	MAP6 domain containing 1	1.64809	1.45758
188.	ENSG00000168350	DEGS2	"delta 4-desaturase, sphingolipid 2"	1.16509	1.45397
189.	ENSG00000156299	TIAM1	T-cell lymphoma invasion and metastasis 1	1.78994	1.45061
190.	ENSG00000157600	TMEM164	transmembrane protein 164	1.45174	1.44885
191.	ENSG00000135218	CD36	CD36 molecule	1.5895	1.44303
192.	ENSG00000204950	LRRC10B	leucine rich repeat containing 10B	1.33852	1.43715
193.	ENSG00000004864	SLC25A13	solute carrier family 25 member 13	1.29903	1.43565
194.	ENSG00000240849	TMEM189	transmembrane protein 189	1.4711	1.43429
195.	ENSG00000135114	OASL	2'-5'-oligoadenylate synthetase like	0.68925	1.43106
196.	ENSG00000186184	POLR1D	RNA polymerase I subunit D	1.21672	1.4292
197.	ENSG00000130024	PHF10	PHD finger protein 10	1.47714	1.42481
198.	ENSG00000186832	KRT16	keratin 16	1.41614	1.42172
199.	ENSG00000135374	ELF5	E74 like ETS transcription factor 5	1.54622	1.41993
200.	ENSG00000214063	TSPAN4	tetraspanin 4	1.20445	1.41946
201.	ENSG00000157303	SUSD3	sushi domain containing 3	1.38012	1.41753
202.	ENSG00000060138	YBX3	Y-box binding protein 3	1.38701	1.41547
203.	ENSG00000110330	BIRC2	baculoviral IAP repeat containing 2	1.50289	1.41292
204.	ENSG00000175928	LRRN1	leucine rich repeat neuronal 1	1.58509	1.41155
205.	ENSG00000076604	TRAF4	TNF receptor associated factor 4	1.40716	1.41039
206.	ENSG00000168569	TMEM223	transmembrane protein 223	1.13466	1.40979
207.	ENSG00000159763	PIP	prolactin induced protein	1.58833	1.40631
208.	ENSG00000166803	KIAA0101	KIAA0101	1.25341	1.39906
209.	ENSG00000212747	FAM127C	family with sequence similarity 127 member C	1.25769	1.39421
210.	ENSG00000162639	HENMT1	HEN1 methyltransferase homolog 1	1.27558	1.38603
211.	ENSG00000009844	VTA1	vesicle trafficking 1	1.32726	1.38368
212.	ENSG00000168246	UBTD2	ubiquitin domain containing 2	1.45232	1.38079
213.	ENSG00000139173	TMEM117	transmembrane protein 117	1.22016	1.36977
214.	ENSG00000149043	SYT8	synaptotagmin 8	1.65318	1.36842
215.	ENSG00000132383	RPA1	replication protein A1	1.3934	1.36769
216.	ENSG00000042753	AP2S1	adaptor related protein complex 2 sigma 1 subunit	1.22989	1.36345
217.	ENSG00000117411	B4GALT2	"beta-1,4-galactosyltransferase 2"	1.18107	1.36107
218.	ENSG00000187601	MAGEH1	MAGE family member H1	1.16952	1.36045
219.	ENSG00000141985	SH3GL1	"SH3 domain containing GRB2 like 1, endophilin A2"	1.20402	1.35972
220.	ENSG00000175730	BAK1P1	BCL2 antagonist/killer 1 pseudogene 1	1.33959	1.35957
221.	ENSG00000128309	MPST	mercaptopyruvate sulfurtransferase	0.954081	1.3583
222.	ENSG00000156113	KCNMA1	potassium calcium-activated channel subfamily M alpha 1	1.55427	1.35738
223.	ENSG00000170819	BFSP2	beaded filament structural protein 2	1.60905	1.3469
224.	ENSG00000172663	TMEM134	transmembrane protein 134	0.907853	1.34654
225.	ENSG00000165629	ATP5C1	"ATP synthase, H+ transporting, mitochondrial F1 complex, gamma polypeptide 1"	1.43753	1.34628
226.	ENSG00000145425	RPS3A	ribosomal protein S3A	1.35179	1.34338
227.	ENSG00000213753	CENPBD1P1	CENPB DNA-binding domains containing 1 pseudogene 1	1.15072	1.34084
228.	ENSG00000134986	NREP	neuronal regeneration related protein	1.5593	1.33906
229.	ENSG00000137959	IFI44L	interferon induced protein 44 like	0.595391	1.33428
230.	ENSG00000138336	TET1	tet methylcytosine dioxygenase 1	1.61365	1.33383
231.	ENSG00000176396	EID2	EP300 interacting inhibitor of differentiation 2	1.02888	1.32895
232.	ENSG00000162441	LZIC	leucine zipper and CTNNBIP1 domain containing	1.51983	1.32526
233.	ENSG00000123562	MORF4L2	mortality factor 4 like 2	1.31419	1.32475
234.	ENSG00000171612	SLC25A33	solute carrier family 25 member 33	1.28595	1.32461
235.	ENSG00000196620	UGT2B15	UDP glucuronosyltransferase family 2 member B15	1.18061	1.32403
236.	ENSG00000109321	AREG	amphiregulin	1.42032	1.32116
237.	ENSG00000174599	TRAM1L1	translocation associated membrane protein 1-like 1	1.03518	1.32007
238.	ENSG00000144677	CTDSPL	CTD small phosphatase like	1.29415	1.31864
239.	ENSG00000239900	ADSL	adenylosuccinate lyase	1.28924	1.31677

240.	ENSG00000175130	MARCKSL1	MARCKS like 1	1.18066	1.31506
241.	ENSG00000180992	MRPL14	mitochondrial ribosomal protein L14	1.09525	1.31287
242.	ENSG00000113648	H2AFY	H2A histone family member Y	1.35164	1.31266
243.	ENSG00000255302	EID1	EP300 interacting inhibitor of differentiation 1	1.13643	1.31191
244.	ENSG00000188681	TEKT4P2	tektin 4 pseudogene 2	1.25626	1.31105
245.	ENSG00000180573	HIST1H2AC	histone cluster 1 H2A family member c	1.2603	1.30951
246.	ENSG00000083807	SLC27A5	solute carrier family 27 member 5	1.0881	1.3092
247.	ENSG00000183688	RFLNB	refilin B	1.58933	1.30077
248.	ENSG00000253719	ATXN7L3B	ataxin 7 like 3B	1.23747	1.29717
249.	ENSG00000205643	CDPF1	cysteine rich DPF motif domain containing 1	0.989699	1.29684
250.	ENSG00000145808	ADAMTS19	ADAM metallopeptidase with thrombospondin type 1 motif 19	1.47001	1.29029
251.	ENSG00000131238	PPT1	palmitoyl-protein thioesterase 1	1.33288	1.28796
252.	ENSG00000037280	FLT4	fms related tyrosine kinase 4	0.967415	1.2875
253.	ENSG00000105549	THEG	theg spermatid protein	1.36115	1.28725
254.	ENSG00000184678	HIST2H2BE	histone cluster 2 H2B family member e	1.19281	1.28682
255.	ENSG00000163156	TNFAIP8L2-SCNM1	TNFAIP8L2-SCNM1 readthrough	1.15396	1.28294
256.	ENSG00000172201	ID4	"inhibitor of DNA binding 4, HLH protein"	1.1042	1.28042
257.	ENSG00000136261	BZW2	basic leucine zipper and W2 domains 2	1.33163	1.28027
258.	ENSG00000171476	HOPX	HOP homeobox	1.87771	1.27803
259.	ENSG00000163006	CCDC138	coiled-coil domain containing 138	1.54328	1.27542
260.	ENSG00000256073	URB1-AS1	URB1 antisense RNA 1 (head to head)	0.768621	1.27432
261.	ENSG00000185885	IFITM1	interferon induced transmembrane protein 1	0.866949	1.27411
262.	ENSG00000149646	CNBD2	cyclic nucleotide binding domain containing 2	0.837055	1.27329
263.	ENSG00000197763	TXNRD3NB	thioredoxin reductase 3 neighbor	1.05308	1.27236
264.	ENSG00000160183	TMPRSS3	"transmembrane protease, serine 3"	1.50993	1.27099
265.	ENSG00000113761	ZNF346	zinc finger protein 346	1.50192	1.26861
266.	ENSG00000100211	CBY1	"chibby family member 1, beta catenin antagonist"	1.33359	1.26603
267.	ENSG00000237984	PTENP1	phosphatase and tensin homolog pseudogene 1	1.06433	1.26423
268.	ENSG00000198054	DSCR8	Down syndrome critical region 8	1.86764	1.26283
269.	ENSG00000168303	MPLKIP	M-phase specific PLK1 interacting protein	0.939126	1.25982
270.	ENSG00000136295	TTYH3	tweety family member 3	1.29448	1.25873
271.	ENSG00000172428	COPS9	COP9 signalosome subunit 9	1.02218	1.25621
272.	ENSG00000137364	TPMT	thiopurine S-methyltransferase	1.40831	1.2533
273.	ENSG00000196739	COL27A1	collagen type XXVII alpha 1 chain	1.67382	1.25171
274.	ENSG00000165724	ZMYND19	zinc finger MYND-type containing 19	1.05418	1.24949
275.	ENSG00000167930	FAM234A	family with sequence similarity 234 member A	1.20283	1.24764
276.	ENSG00000111181	SLC6A12	solute carrier family 6 member 12	1.42094	1.24514
277.	ENSG00000176401	EID2B	EP300 interacting inhibitor of differentiation 2B	0.663137	1.24476
278.	ENSG00000168405	CMAHP	"cytidine monophospho-N-acetylneuraminic acid hydroxylase, pseudogene"	0.825125	1.24412
279.	ENSG00000139970	RTN1	reticulon 1	1.33667	1.24382
280.	ENSG00000186162	CIDECP	cell death-inducing DFFA-like effector c pseudogene	1.01528	1.24263
281.	ENSG00000176022	B3GALT6	"beta-1,3-galactosyltransferase 6"	0.891879	1.24243
282.	ENSG00000121022	COPS5	COP9 signalosome subunit 5	1.20623	1.24081
283.	ENSG00000164172	MOCS2	molybdenum cofactor synthesis 2	1.286	1.24044
284.	ENSG00000166450	PRTG	protogenin	1.31376	1.23996
285.	ENSG00000160180	TFF3	trefoil factor 3	1.06078	1.23842
286.	ENSG00000115657	ABCB6	ATP binding cassette subfamily B member 6 (Langereis blood group)	1.20686	1.2379
287.	ENSG00000134809	TIMM10	translocase of inner mitochondrial membrane 10 homolog (yeast)	1.08019	1.23627
288.	ENSG00000155380	SLC16A1	solute carrier family 16 member 1	1.27052	1.23591
289.	ENSG00000205363	C15orf59	chromosome 15 open reading frame 59	1.07989	1.23498
290.	ENSG00000213741	RPS29	ribosomal protein S29	1.07896	1.23262
291.	ENSG00000134758	RNF138	ring finger protein 138	0.993903	1.2314
292.	ENSG00000064835	POU1F1	POU class 1 homeobox 1	1.10366	1.22851
293.	ENSG00000184232	OAF	out at first homolog	0.614108	1.2268
294.	ENSG00000164111	ANXA5	annexin A5	1.17391	1.22543
295.	ENSG00000160588	MPZL3	myelin protein zero like 3	1.30983	1.22454
296.	ENSG00000166794	PPIB	peptidylprolyl isomerase B	1.11594	1.2242
297.	ENSG00000262904	TMPOP2	thymopoietin pseudogene 2	0.815511	1.2229
298.	ENSG00000165512	ZNF22	zinc finger protein 22	1.10956	1.22216
299.	ENSG00000101098	RIMS4	regulating synaptic membrane exocytosis 4	1.25577	1.2212
300.	ENSG00000150893	FREM2	FRAS1 related extracellular matrix protein 2	1.6484	1.22025
301.	ENSG00000137558	PI15	peptidase inhibitor 15	1.38949	1.21943

302.	ENSG00000111653	ING4	inhibitor of growth family member 4	1.19538	1.21837
303.	ENSG00000185787	MORF4L1	mortality factor 4 like 1	1.23656	1.21828
304.	ENSG00000224287	MSL3P1	male-specific lethal 3 homolog (Drosophila) pseudogene 1	1.08888	1.21766
305.	ENSG00000250722	SEPP1	"selenoprotein P, plasma, 1"	1.09129	1.21632
306.	ENSG00000148300	REXO4	"REX4 homolog, 3'-5' exonuclease"	0.991587	1.21563
307.	ENSG00000172867	KRT2	keratin 2	1.2364	1.21345
308.	ENSG00000204228	HSD17B8	hydroxysteroid 17-beta dehydrogenase 8	1.0486	1.21188
309.	ENSG00000100814	CCNB1IP1	cyclin B1 interacting protein 1	1.22499	1.20591
310.	ENSG00000171631	P2RY6	pyrimidinergic receptor P2Y6	1.07541	1.20488
311.	ENSG00000196636	SDHAF3	succinate dehydrogenase complex assembly factor 3	1.03412	1.20257
312.	ENSG00000102172	SMS	spermine synthase	1.1773	1.20089
313.	ENSG00000154553	PDLIM3	PDZ and LIM domain 3	1.21686	1.19913
314.	ENSG00000102743	SLC25A15	solute carrier family 25 member 15	1.27744	1.19857
315.	ENSG00000122068	FYTTD1	forty-two-three domain containing 1	1.3472	1.19733
316.	ENSG00000167767	KRT80	keratin 80	1.24017	1.19701
317.	ENSG00000091592	NLRP1	NLR family pyrin domain containing 1	1.09248	1.19686
318.	ENSG00000102543	CDADC1	cytidine and dCMP deaminase domain containing 1	0.972441	1.19253
319.	ENSG00000185475	TMEM179B	transmembrane protein 179B	1.13071	1.1919
320.	ENSG00000166073	GPR176	G protein-coupled receptor 176	0.911931	1.19186
321.	ENSG00000186603	HPDL	4-hydroxyphenylpyruvate dioxygenase like	0.801218	1.19059
322.	ENSG00000104980	TIMM44	translocase of inner mitochondrial membrane 44	0.990688	1.19053
323.	ENSG00000178896	EXOSC4	exosome component 4	0.624955	1.19043
324.	ENSG00000104341	LAPTM4B	lysosomal protein transmembrane 4 beta	1.26545	1.18734
325.	ENSG00000155329	ZCCHC10	zinc finger CCHC-type containing 10	0.96443	1.18733
326.	ENSG00000164291	ARSK	arylsulfatase family member K	1.09553	1.18466
327.	ENSG00000040275	SPDL1	spindle apparatus coiled-coil protein 1	1.36245	1.18421
328.	ENSG00000041357	PSMA4	proteasome subunit alpha 4	1.20228	1.18312
329.	ENSG00000184486	POU3F2	POU class 3 homeobox 2	1.23518	1.18252
330.	ENSG00000010319	SEMA3G	semaphorin 3G	1.08938	1.18135
331.	ENSG00000131373	HACL1	2-hydroxyacyl-CoA lyase 1	1.08995	1.17999
332.	ENSG00000185504	FAAP100	Fanconi anemia core complex associated protein 100	0.924334	1.1769
333.	ENSG00000244187	TMEM141	transmembrane protein 141	1.08181	1.17586
334.	ENSG00000171984	C20orf196	chromosome 20 open reading frame 196	0.846608	1.17566
335.	ENSG00000120697	ALG5	"ALG5, dolichyl-phosphate beta-glucosyltransferase"	0.974665	1.17464
336.	ENSG00000110871	COQ5	"coenzyme Q5, methyltransferase"	1.12072	1.17251
337.	ENSG00000180611	MB21D2	Mab-21 domain containing 2	1.01576	1.17096
338.	ENSG00000101255	TRIB3	tribbles pseudokinase 3	1.04783	1.16733
339.	ENSG00000131475	VPS25	vacuolar protein sorting 25 homolog	1.09281	1.16585
340.	ENSG00000169908	TM4SF1	transmembrane 4 L six family member 1	0.892293	1.16473
341.	ENSG00000134864	GGACT	gamma-glutamylamine cyclotransferase	0.730741	1.16279
342.	ENSG00000101546	RBFA	ribosome binding factor A (putative)	1.08745	1.15657
343.	ENSG00000128294	TPST2	tyrosylprotein sulfotransferase 2	1.27295	1.15574
344.	ENSG00000186767	SPIN4	spindlin family member 4	1.20897	1.15524
345.	ENSG00000169218	RSPO1	R-spondin 1	1.00213	1.14493
346.	ENSG00000160446	ZDHHC12	zinc finger DHHC-type containing 12	0.720658	1.1442
347.	ENSG00000188763	FZD9	frizzled class receptor 9	0.881945	1.14293
348.	ENSG00000066697	MSANTD3	Myb/SANT DNA binding domain containing 3	1.03394	1.14267
349.	ENSG00000168785	TSPAN5	tetraspanin 5	1.45388	1.14094
350.	ENSG00000182575	NXPH3	neurexophilin 3	1.14279	1.13923
351.	ENSG00000144867	SRPRB	SRP receptor beta subunit	1.135	1.13818
352.	ENSG00000162891	IL20	interleukin 20	1.37049	1.13747
353.	ENSG00000164128	NPY1R	neuropeptide Y receptor Y1	1.33529	1.13624
354.	ENSG00000169976	SF3B5	splicing factor 3b subunit 5	0.996388	1.13546
355.	ENSG00000150687	PRSS23	"protease, serine 23"	1.31424	1.13168
356.	ENSG00000173141	MRPL57	mitochondrial ribosomal protein L57	0.811779	1.13103
357.	ENSG00000110442	COMMD9	COMM domain containing 9	1.13099	1.13093
358.	ENSG00000101850	GPR143	G protein-coupled receptor 143	0.864325	1.13005
359.	ENSG00000182117	NOP10	NOP10 ribonucleoprotein	1.02759	1.12941
360.	ENSG00000077274	CAPN6	calpain 6	1.02668	1.12836
361.	ENSG00000188820	FAM26F	family with sequence similarity 26 member F	0.969095	1.12822
362.	ENSG00000124813	RUNX2	runt related transcription factor 2	1.40906	1.12666
363.	ENSG00000142619	PADI3	peptidyl arginine deiminase 3	1.29671	1.12462
364.	ENSG00000196741	LINC01560	long intergenic non-protein coding RNA 1560	0.9892	1.12458
365.	ENSG00000103257	SLC7A5	solute carrier family 7 member 5	1.31711	1.12174
366.	ENSG00000110435	PDHX	pyruvate dehydrogenase complex component X	1.11496	1.1193

367.	ENSG00000121753	ADGRB2	adhesion G protein-coupled receptor B2	0.874388	1.11731
368.	ENSG00000065268	WDR18	WD repeat domain 18	0.938405	1.11267
369.	ENSG00000168002	POLR2G	RNA polymerase II subunit G	1.0195	1.11076
370.	ENSG00000148824	MTG1	mitochondrial ribosome associated GTPase 1	0.930824	1.10945
371.	ENSG00000143013	LMO4	LIM domain only 4	1.21488	1.10918
372.	ENSG00000243646	IL10RB	interleukin 10 receptor subunit beta	1.09275	1.10894
373.	ENSG00000184588	PDE4B	phosphodiesterase 4B	1.30251	1.10839
374.	ENSG00000103415	HMOX2	heme oxygenase 2	0.981092	1.10676
375.	ENSG00000165389	SPTSSA	serine palmitoyltransferase small subunit A	1.13176	1.10577
376.	ENSG00000139144	PIK3C2G	phosphatidylinositol-4-phosphate 3-kinase catalytic subunit type 2 gamma	1.32998	1.10551
377.	ENSG00000145545	SRD5A1	steroid 5 alpha-reductase 1	0.903325	1.10497
378.	ENSG00000204344	STK19	serine/threonine kinase 19	1.04042	1.10347
379.	ENSG00000162384	C1orf123	chromosome 1 open reading frame 123	0.966238	1.10235
380.	ENSG00000103855	CD276	CD276 molecule	1.24127	1.1014
381.	ENSG00000035687	ADSS	adenylosuccinate synthase	0.989145	1.09993
382.	ENSG00000185090	MANEAL	mannosidase endo-alpha like	1.09	1.09727
383.	ENSG00000087842	PIR	pirin	1.18405	1.09699
384.	ENSG00000169372	CRADD	CASP2 and RIPK1 domain containing adaptor with death domain	0.94901	1.09059
385.	ENSG00000133627	ACTR3B	ARP3 actin related protein 3 homolog B	1.03853	1.08886
386.	ENSG00000137992	DBT	dihydrolipoamide branched chain transacylase E2	1.19273	1.08744
387.	ENSG00000109452	INPP4B	inositol polyphosphate-4-phosphatase type II B	1.41143	1.08739
388.	ENSG00000108010	GLRX3	glutaredoxin 3	0.917546	1.0863
389.	ENSG00000169884	WNT10B	Wnt family member 10B	0.553471	1.08361
390.	ENSG00000122873	CISD1	CDGSH iron sulfur domain 1	1.01027	1.0821
391.	ENSG00000230844	ZNF674-AS1	ZNF674 antisense RNA 1 (head to head)	0.734379	1.08159
392.	ENSG00000246705	H2AFJ	H2A histone family member J	0.688296	1.08134
393.	ENSG00000176108	CHMP6	charged multivesicular body protein 6	0.715407	1.0806
394.	ENSG00000115596	WNT6	Wnt family member 6	0.563029	1.08002
395.	ENSG00000204576	PRR3	proline rich 3	1.05653	1.07873
396.	ENSG00000184220	CMSS1	cms1 ribosomal small subunit homolog (yeast)	1.11261	1.07853
397.	ENSG00000040731	CDH10	cadherin 10	1.37135	1.077
398.	ENSG00000196776	CD47	CD47 molecule	1.08686	1.07416
399.	ENSG00000188042	ARL4C	ADP ribosylation factor like GTPase 4C	1.11503	1.06863
400.	ENSG00000166123	GPT2	glutamic--pyruvic transaminase 2	1.20088	1.06805
401.	ENSG00000119326	CTNNAL1	catenin alpha like 1	1.10965	1.06564
402.	ENSG00000138670	RASGEF1B	RasGEF domain family member 1B	0.863543	1.06333
403.	ENSG00000168495	POLR3D	RNA polymerase III subunit D	0.922376	1.05985
404.	ENSG00000175137	SH3BP5L	SH3 binding domain protein 5 like	1.04061	1.05831
405.	ENSG00000094804	CDC6	cell division cycle 6	0.995412	1.05737
406.	ENSG00000171428	NAT1	N-acetyltransferase 1	0.828996	1.0541
407.	ENSG00000167552	TUBA1A	tubulin alpha 1a	1.22901	1.05345
408.	ENSG00000143845	ETNK2	ethanolamine kinase 2	1.11182	1.05306
409.	ENSG00000174109	C16orf91	chromosome 16 open reading frame 91	0.529916	1.05276
410.	ENSG00000135828	RNASEL	ribonuclease L	1.11074	1.05212
411.	ENSG00000110987	BCL7A	BCL tumor suppressor 7A	0.971165	1.052
412.	ENSG00000185615	PDIA2	protein disulfide isomerase family A member 2	0.84232	1.0513
413.	ENSG00000171135	JAGN1	jagunal homolog 1	0.901859	1.05076
414.	ENSG00000107968	MAP3K8	mitogen-activated protein kinase kinase kinase 8	0.80049	1.05051
415.	ENSG00000173894	CBX2	chromobox 2	1.05339	1.05031
416.	ENSG00000160182	TFF1	trefoil factor 1	1.12383	1.05027
417.	ENSG00000158715	SLC45A3	solute carrier family 45 member 3	0.928566	1.04996
418.	ENSG00000143162	CREG1	cellular repressor of E1A stimulated genes 1	1.06377	1.04923
419.	ENSG00000117461	PIK3R3	phosphoinositide-3-kinase regulatory subunit 3	1.14694	1.04752
420.	ENSG00000185015	CA13	carbonic anhydrase 13	1.36253	1.04568
421.	ENSG00000158769	F11R	F11 receptor	1.09778	1.04492
422.	ENSG00000167695	FAM57A	family with sequence similarity 57 member A	1.08004	1.04424
423.	ENSG00000145882	PCYOX1L	prenylcysteine oxidase 1 like	1.0197	1.04292
424.	ENSG00000133142	TCEAL4	transcription elongation factor A like 4	0.865075	1.04156
425.	ENSG00000163053	SLC16A14	solute carrier family 16 member 14	0.890857	1.04069
426.	ENSG00000124006	OBSL1	obscurin like 1	0.990759	1.04061
427.	ENSG00000151917	BEND6	BEN domain containing 6	1.01679	1.03956
428.	ENSG00000169682	SPNS1	sphingolipid transporter 1 (putative)	0.993692	1.03893
429.	ENSG00000131043	AAR2	AAR2 splicing factor homolog	0.927601	1.03828
430.	ENSG00000177614	PGBD5	piggyBac transposable element derived 5	0.874885	1.03782

431.	ENSG00000165732	DDX21	DEAD-box helicase 21	1.0968	1.03752
432.	ENSG00000172171	TEFM	"transcription elongation factor, mitochondrial"	0.886352	1.03729
433.	ENSG00000117479	SLC19A2	solute carrier family 19 member 2	0.994844	1.03721
434.	ENSG00000270170	NCBP2-AS2	NCBP2 antisense RNA 2 (head to head)	0.585973	1.03664
435.	ENSG00000197894	ADH5	"alcohol dehydrogenase 5 (class III), chi polypeptide"	1.00464	1.03491
436.	ENSG00000187231	SESTD1	SEC14 and spectrin domain containing 1	1.24413	1.03235
437.	ENSG00000135148	TRAFD1	TRAF-type zinc finger domain containing 1	1.11782	1.02991
438.	ENSG00000153485	TMEM251	transmembrane protein 251	0.873496	1.02926
439.	ENSG00000113356	POLR3G	RNA polymerase III subunit G	0.810646	1.02777
440.	ENSG00000136527	TRA2B	transformer 2 beta homolog (Drosophila)	0.93612	1.02773
441.	ENSG00000177383	MAGEF1	MAGE family member F1	0.775277	1.0272
442.	ENSG00000158042	MRPL17	mitochondrial ribosomal protein L17	0.790089	1.02674
443.	ENSG00000113209	PCDHB5	protocadherin beta 5	1.21352	1.02547
444.	ENSG00000168101	NUDT16L1	nudix hydrolase 16 like 1	0.742033	1.02527
445.	ENSG00000158050	DUSP2	dual specificity phosphatase 2	0.861033	1.02365
446.	ENSG00000167272	POP5	"POP5 homolog, ribonuclease P/MRP subunit"	0.785138	1.02197
447.	ENSG00000043039	BARX2	BARX homeobox 2	1.10383	1.02157
448.	ENSG00000131015	ULBP2	UL16 binding protein 2	1.14969	1.02138
449.	ENSG00000167747	C19orf48	chromosome 19 open reading frame 48	0.550821	1.02046
450.	ENSG00000140280	LYSMD2	LysM domain containing 2	0.879903	1.02031
451.	ENSG00000143179	UCK2	uridine-cytidine kinase 2	0.9374	1.01923
452.	ENSG00000175768	TOMM5	translocase of outer mitochondrial membrane 5	0.924343	1.01822
453.	ENSG00000151611	MMAA	methylmalonic aciduria (cobalamin deficiency) cblA type	0.736563	1.01764
454.	ENSG00000116761	CTH	cystathionine gamma-lyase	1.37027	1.01686
455.	ENSG00000181634	TNFSF15	tumor necrosis factor superfamily member 15	0.836726	1.01551
456.	ENSG00000221926	TRIM16	tripartite motif containing 16	0.993213	1.01247
457.	ENSG00000154429	CCSAP	"centriole, cilia and spindle associated protein"	1.0959	1.01218
458.	ENSG00000163041	H3F3A	H3 histone family member 3A	0.858372	1.01209
459.	ENSG00000267368	UPK3BL	uroplakin 3B-like	0.806669	1.01034
460.	ENSG00000163931	TKT	transketolase	0.929334	1.00705
461.	ENSG00000132429	POPDC3	popeye domain containing 3	0.787233	1.0069
462.	ENSG00000178096	BOLA1	bolA family member 1	0.570531	1.00556
463.	ENSG00000151575	TEX9	testis expressed 9	0.870901	1.00428
464.	ENSG00000174013	FBXO45	F-box protein 45	1.04396	1.00334
465.	ENSG00000139211	AMIGO2	adhesion molecule with Ig like domain 2	1.01909	1.00302
466.	ENSG00000159640	ACE	angiotensin I converting enzyme	1.21031	1.00259
467.	ENSG00000154518	ATP5G3	"ATP synthase, H+ transporting, mitochondrial Fo complex subunit C3 (subunit 9)"	0.885476	1.00146
468.	ENSG00000008083	JARID2	jumonji and AT-rich interaction domain containing 2	1.09834	0.998283
469.	ENSG00000156374	PCGF6	polycomb group ring finger 6	0.935854	0.998118
470.	ENSG00000167780	SOAT2	sterol O-acyltransferase 2	0.946383	0.996519
471.	ENSG00000092841	MYL6	myosin light chain 6	0.876249	0.994649
472.	ENSG00000113924	HGD	"homogentisate 1,2-dioxygenase"	1.31709	0.994539
473.	ENSG00000232388	LINC00493	long intergenic non-protein coding RNA 493	0.794676	0.993629
474.	ENSG00000198055	GRK6	G protein-coupled receptor kinase 6	0.718213	0.990066
475.	ENSG00000136143	SUCLA2	succinate-CoA ligase ADP-forming beta subunit	1.17971	0.989095
476.	ENSG00000134240	HMGCS2	3-hydroxy-3-methylglutaryl-CoA synthase 2	1.89403	0.988791
477.	ENSG00000023902	PLEKHO1	pleckstrin homology domain containing O1	0.955779	0.986967
478.	ENSG00000143061	IGSF3	immunoglobulin superfamily member 3	1.06424	0.986889
479.	ENSG00000239672	NME1	NME/NM23 nucleoside diphosphate kinase 1	0.856472	0.982628
480.	ENSG00000130332	LSM7	"LSM7 homolog, U6 small nuclear RNA and mRNA degradation associated"	0.610844	0.982496
481.	ENSG00000171863	RPS7	ribosomal protein S7	0.976177	0.982406
482.	ENSG00000112320	SOBP	sine oculis binding protein homolog	1.12312	0.97963
483.	ENSG00000133874	RNF122	ring finger protein 122	1.14128	0.979431
484.	ENSG00000030066	NUP160	nucleoporin 160	1.02944	0.977176
485.	ENSG00000174749	C4orf32	chromosome 4 open reading frame 32	0.895463	0.976444
486.	ENSG00000163710	PCOLCE2	procollagen C-endopeptidase enhancer 2	0.623997	0.976315
487.	ENSG00000138166	DUSP5	dual specificity phosphatase 5	1.16304	0.974547
488.	ENSG00000007392	LUC7L	LUC7 like	0.729032	0.973398
489.	ENSG00000147533	GOLGA7	golgin A7	1.14222	0.971833
490.	ENSG00000108826	MRPL27	mitochondrial ribosomal protein L27	0.756929	0.97082
491.	ENSG00000125977	EIF2S2	eukaryotic translation initiation factor 2 subunit beta	0.929427	0.970642
492.	ENSG00000188636	LDOC1L	leucine zipper down-regulated in cancer 1 like	1.00147	0.970258
493.	ENSG00000189007	ADAT2	"adenosine deaminase, tRNA specific 2"	0.875681	0.969717

494.	ENSG00000143947	RPS27A	ribosomal protein S27a	0.982195	0.969381
495.	ENSG00000023697	DERA	deoxyribose-phosphate aldolase	0.991452	0.967232
496.	ENSG00000168291	PDHB	pyruvate dehydrogenase (lipoamide) beta	1.02254	0.966478
497.	ENSG00000267100	ILF3-AS1	ILF3 antisense RNA 1 (head to head)	0.605486	0.965656
498.	ENSG00000127337	YEATS4	YEATS domain containing 4	0.743376	0.965598
499.	ENSG00000162244	RPL29	ribosomal protein L29	0.678791	0.965449
500.	ENSG00000163584	RPL22L1	ribosomal protein L22 like 1	0.864808	0.965201
501.	ENSG00000100395	L3MBTL2	L3MBTL2 polycomb repressive complex 1 subunit	0.91279	0.965081
502.	ENSG00000169826	CSGALNACT2	chondroitin sulfate N-acetylgalactosaminyltransferase 2	1.09471	0.964817
503.	ENSG00000163933	RFT1	RFT1 homolog	1.00573	0.963011
504.	ENSG00000006459	KDM7A	lysine demethylase 7A	1.0876	0.962187
505.	ENSG00000073536	NLE1	notchless homolog 1	0.739256	0.961983
506.	ENSG00000145604	SKP2	"S-phase kinase-associated protein 2, E3 ubiquitin protein ligase"	0.987079	0.961049
507.	ENSG00000156103	MMP16	matrix metallopeptidase 16	1.33017	0.960805
508.	ENSG00000131849	ZNF132	zinc finger protein 132	0.974712	0.960395
509.	ENSG00000079257	LXN	latexin	0.957785	0.959065
510.	ENSG00000183648	NDUFB1	NADH:ubiquinone oxidoreductase subunit B1	0.794603	0.958529
511.	ENSG00000107020	PLGRKT	plasminogen receptor with a C-terminal lysine	1.03486	0.956894
512.	ENSG00000111361	EIF2B1	eukaryotic translation initiation factor 2B subunit alpha	0.842259	0.955928
513.	ENSG00000135250	SRPK2	SRSF protein kinase 2	0.962142	0.955164
514.	ENSG00000134419	RPS15A	ribosomal protein S15a	0.97588	0.954983
515.	ENSG00000205542	TMSB4X	"thymosin beta 4, X-linked"	0.828414	0.954921
516.	ENSG00000166557	TMED3	transmembrane p24 trafficking protein 3	0.862257	0.952594
517.	ENSG00000170027	YWHAG	tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein gamma	0.868706	0.950922
518.	ENSG00000156398	SFXN2	sideroflexin 2	0.977583	0.949226
519.	ENSG00000259803	SLC22A31	solute carrier family 22 member 31	0.856728	0.948328
520.	ENSG00000166226	CCT2	chaperonin containing TCP1 subunit 2	0.955846	0.94792
521.	ENSG00000132768	DPH2	DPH2 homolog	0.873147	0.947896
522.	ENSG00000107938	EDRF1	erythroid differentiation regulatory factor 1	0.87891	0.947828
523.	ENSG00000168672	FAM84B	family with sequence similarity 84 member B	0.978182	0.9469
524.	ENSG00000133111	RFXAP	regulatory factor X associated protein	1.06703	0.94652
525.	ENSG00000142864	SERBP1	SERPINE1 mRNA binding protein 1	0.99881	0.945595
526.	ENSG00000183665	TRMT12	tRNA methyltransferase 12 homolog	0.867535	0.94512
527.	ENSG00000142632	ARHGEF19	Rho guanine nucleotide exchange factor 19	0.840479	0.944296
528.	ENSG00000023734	STRAP	serine/threonine kinase receptor associated protein	0.923435	0.944209
529.	ENSG00000111341	MGP	matrix Gla protein	0.989572	0.94395
530.	ENSG00000063241	ISOC2	isochorismatase domain containing 2	0.578063	0.943153
531.	ENSG00000214194	LINC00998	long intergenic non-protein coding RNA 998	0.915797	0.942618
532.	ENSG00000154639	CXADR	coxsackie virus and adenovirus receptor	1.04079	0.942615
533.	ENSG00000155254	MARVELD1	MARVEL domain containing 1	0.787191	0.941691
534.	ENSG00000143977	SNRPG	small nuclear ribonucleoprotein polypeptide G	0.722707	0.941404
535.	ENSG00000093009	CDC45	cell division cycle 45	0.95113	0.941068
536.	ENSG00000123131	PRDX4	peroxiredoxin 4	0.874995	0.937589
537.	ENSG00000163479	SSR2	signal sequence receptor subunit 2	0.883125	0.937574
538.	ENSG00000170779	CDCA4	cell division cycle associated 4	0.679391	0.937433
539.	ENSG00000184675	AMER1	APC membrane recruitment protein 1	0.999996	0.936081
540.	ENSG00000221990	EXOC3-AS1	EXOC3 antisense RNA 1	0.65992	0.935699
541.	ENSG00000066468	FGFR2	fibroblast growth factor receptor 2	0.947844	0.935403
542.	ENSG00000131873	CHSY1	chondroitin sulfate synthase 1	1.12941	0.935212
543.	ENSG00000171574	ZNF584	zinc finger protein 584	0.928914	0.934971
544.	ENSG00000136319	TTC5	tetratricopeptide repeat domain 5	0.895979	0.934807
545.	ENSG00000006576	PHTF2	putative homeodomain transcription factor 2	0.995553	0.932872
546.	ENSG00000120341	SEC16B	"SEC16 homolog B, endoplasmic reticulum export factor"	1.14986	0.932813
547.	ENSG00000005022	SLC25A5	solute carrier family 25 member 5	0.874204	0.931417
548.	ENSG00000187605	TET3	tet methylcytosine dioxygenase 3	0.964832	0.931351
549.	ENSG00000140450	ARRDC4	arrestin domain containing 4	0.676729	0.931238
550.	ENSG00000090520	DNAJB11	DnaJ heat shock protein family (Hsp40) member B11	0.904611	0.930958
551.	ENSG00000162377	COA7	cytochrome c oxidase assembly factor 7 (putative)	0.72858	0.930403
552.	ENSG00000242372	EIF6	eukaryotic translation initiation factor 6	0.77994	0.930112
553.	ENSG00000188010	MORN2	MORN repeat containing 2	1.01867	0.929174
554.	ENSG00000107014	RLN2	relaxin 2	0.992626	0.927344
555.	ENSG00000124588	NQO2	NAD(P)H quinone dehydrogenase 2	0.893087	0.924738

556.	ENSG00000100604	CHGA	chromogranin A	0.921886	0.924259
557.	ENSG00000131844	MCCC2	methylcrotonoyl-CoA carboxylase 2	0.928812	0.924177
558.	ENSG00000196449	YRDC	yrdC N6-threonylcarbamoyltransferase domain containing	0.756552	0.92334
559.	ENSG00000166896	ATP23	ATP23 metallopeptidase and ATP synthase assembly factor homolog	0.957749	0.922681
560.	ENSG00000108448	TRIM16L	tripartite motif containing 16-like	0.910647	0.922332
561.	ENSG00000100028	SNRPD3	small nuclear ribonucleoprotein D3 polypeptide	0.859864	0.921748
562.	ENSG00000152229	PSTPIP2	proline-serine-threonine phosphatase interacting protein 2	0.853152	0.921707
563.	ENSG00000204315	FKBPL	FK506 binding protein like	0.676845	0.921371
564.	ENSG00000176055	MBLAC2	metallo-beta-lactamase domain containing 2	0.798222	0.920713
565.	ENSG00000116221	MRPL37	mitochondrial ribosomal protein L37	0.844301	0.91952
566.	ENSG00000105058	FAM32A	family with sequence similarity 32 member A	0.887943	0.919503
567.	ENSG00000232654	FAM136BP	"family with sequence similarity 136 member B, pseudogene"	1.19572	0.919494
568.	ENSG00000071054	MAP4K4	mitogen-activated protein kinase kinase kinase kinase 4	1.24666	0.919106
569.	ENSG00000165688	PMPCA	"peptidase, mitochondrial processing alpha subunit"	0.741118	0.917951
570.	ENSG00000180817	PPA1	pyrophosphatase (inorganic) 1	0.889133	0.91749
571.	ENSG00000225470	JPX	"JPX transcript, XIST activator (non-protein coding)"	0.797853	0.917472
572.	ENSG00000109775	UFSP2	UFM1 specific peptidase 2	0.918514	0.915898
573.	ENSG00000172551	MUCL1	mucin like 1	1.29882	0.915705
574.	ENSG00000167118	URM1	ubiquitin related modifier 1	0.777266	0.915202
575.	ENSG00000131469	RPL27	ribosomal protein L27	0.818785	0.914966
576.	ENSG00000124370	MCEE	methylmalonyl-CoA epimerase	0.841898	0.914268
577.	ENSG00000172819	RARG	retinoic acid receptor gamma	0.99176	0.914053
578.	ENSG00000115204	MPV17	"MPV17, mitochondrial inner membrane protein"	0.799041	0.913382
579.	ENSG00000227345	PARG	poly(ADP-ribose) glycohydrolase	0.88996	0.913123
580.	ENSG00000087301	TXNDC16	thioredoxin domain containing 16	1.2185	0.912998
581.	ENSG00000070785	EIF2B3	eukaryotic translation initiation factor 2B subunit gamma	0.854297	0.912875
582.	ENSG00000205670	SMIM11A	small integral membrane protein 11A	0.844039	0.910736
583.	ENSG00000163466	ARPC2	actin related protein 2/3 complex subunit 2	0.827089	0.909638
584.	ENSG00000198133	TMEM229B	transmembrane protein 229B	0.964364	0.908993
585.	ENSG00000167645	YIF1B	"Yip1 interacting factor homolog B, membrane trafficking protein"	0.721536	0.907742
586.	ENSG00000033867	SLC4A7	solute carrier family 4 member 7	0.972962	0.90704
587.	ENSG00000108352	RAPGEFL1	Rap guanine nucleotide exchange factor like 1	1.07791	0.906922
588.	ENSG00000004059	ARF5	ADP ribosylation factor 5	0.739554	0.905469
589.	ENSG00000166171	DPCD	deleted in primary ciliary dyskinesia homolog (mouse)	0.96135	0.905369
590.	ENSG00000178053	MLF1	myeloid leukemia factor 1	1.03219	0.903088
591.	ENSG00000082482	KCNK2	potassium two pore domain channel subfamily K member 2	1.34367	0.902705
592.	ENSG00000162636	FAM102B	family with sequence similarity 102 member B	1.13096	0.902373
593.	ENSG00000164627	KIF6	kinesin family member 6	0.904727	0.902278
594.	ENSG00000180185	FAHD1	fumarylacetoacetate hydrolase domain containing 1	0.636851	0.901924
595.	ENSG00000183765	CHEK2	checkpoint kinase 2	0.827479	0.90164
596.	ENSG00000182518	FAM104B	family with sequence similarity 104 member B	0.817937	0.900684
597.	ENSG00000070501	POLB	DNA polymerase beta	0.679722	0.900578
598.	ENSG00000178773	CPNE7	copine 7	0.884544	0.900155
599.	ENSG00000136997	MYC	v-myc avian myelocytomatosis viral oncogene homolog	0.888765	0.900107
600.	ENSG00000166402	TUB	tubby bipartite transcription factor	1.14111	0.899701
601.	ENSG00000113916	BCL6	B-cell CLL/lymphoma 6	1.04653	0.899591
602.	ENSG00000094880	CDC23	cell division cycle 23	0.89469	0.898371
603.	ENSG00000197261	C6orf141	chromosome 6 open reading frame 141	0.756503	0.897626
604.	ENSG00000009950	MLXIPL	MLX interacting protein like	0.650685	0.897178
605.	ENSG00000110042	DTX4	deltex E3 ubiquitin ligase 4	1.46128	0.89692
606.	ENSG00000112039	FANCE	Fanconi anemia complementation group E	0.788509	0.896597
607.	ENSG00000115486	GGCX	gamma-glutamyl carboxylase	0.84325	0.896333
608.	ENSG00000183741	CBX6	chromobox 6	0.744626	0.895712
609.	ENSG00000137692	DCUN1D5	defective in cullin neddylation 1 domain containing 5	0.895144	0.894684
610.	ENSG00000103550	KNOP1	lysine rich nucleolar protein 1	0.996013	0.893312
611.	ENSG00000100116	GCAT	glycine C-acetyltransferase	0.816279	0.888683
612.	ENSG00000149573	MPZL2	myelin protein zero like 2	0.733585	0.887167
613.	ENSG00000134202	GSTM3	glutathione S-transferase mu 3	0.95424	0.886405
614.	ENSG00000165795	NDRG2	NDRG family member 2	1.06254	0.885938

615.	ENSG00000125743	SNRPD2	small nuclear ribonucleoprotein D2 polypeptide	0.748278	0.885684
616.	ENSG00000187889	C1orf168	chromosome 1 open reading frame 168	1.05566	0.884423
617.	ENSG00000163923	RPL39L	ribosomal protein L39 like	0.71943	0.884334
618.	ENSG00000178449	COX14	"COX14, cytochrome c oxidase assembly factor"	0.697269	0.884169
619.	ENSG00000158882	TOMM40L	translocase of outer mitochondrial membrane 40 like	0.675673	0.883447
620.	ENSG00000168505	GBX2	gastrulation brain homeobox 2	0.911229	0.883168
621.	ENSG00000170191	NANP	N-acetylneuraminic acid phosphatase	0.857126	0.883009
622.	ENSG00000126767	ELK1	"ELK1, ETS transcription factor"	0.774281	0.883002
623.	ENSG00000182195	LDOC1	leucine zipper down-regulated in cancer 1	0.909283	0.882885
624.	ENSG00000117385	P3H1	prolyl 3-hydroxylase 1	1.17836	0.882606
625.	ENSG00000160221	C21orf33	chromosome 21 open reading frame 33	0.576514	0.882266
626.	ENSG00000103187	COTL1	coactosin like F-actin binding protein 1	0.904161	0.881233
627.	ENSG00000139726	DENR	density regulated re-initiation and release factor	0.927438	0.880601
628.	ENSG00000105227	PRX	periaxin	1.08466	0.880227
629.	ENSG00000075618	FSCN1	fascin actin-bundling protein 1	0.883641	0.88007
630.	ENSG00000171858	RPS21	ribosomal protein S21	0.612498	0.878411
631.	ENSG00000235655	H3F3AP4	"H3 histone, family 3A, pseudogene 4"	0.994267	0.877585
632.	ENSG00000157111	TMEM171	transmembrane protein 171	0.878415	0.876701
633.	ENSG00000128228	SDF2L1	stromal cell derived factor 2 like 1	0.554218	0.876166
634.	ENSG00000117407	ARTN	artemin	0.779861	0.876064
635.	ENSG00000128708	HAT1	histone acetyltransferase 1	0.915354	0.875117
636.	ENSG00000100483	VCPKMT	valosin containing protein lysine methyltransferase	0.605394	0.87448
637.	ENSG00000143155	TIPRL	TOR signaling pathway regulator	0.811212	0.873609
638.	ENSG00000243479	MNX1-AS1	MNX1 antisense RNA 1 (head to head)	0.688844	0.870034
639.	ENSG00000148925	BTBD10	BTB domain containing 10	0.947219	0.868464
640.	ENSG00000107949	BCCIP	BRCA2 and CDKN1A interacting protein	0.802714	0.867996
641.	ENSG00000112164	GLP1R	glucagon like peptide 1 receptor	0.964153	0.86756
642.	ENSG00000164039	BDH2	"3-hydroxybutyrate dehydrogenase, type 2"	0.843871	0.866672
643.	ENSG00000119705	SLIRP	SRA stem-loop interacting RNA binding protein	0.769817	0.866559
644.	ENSG00000215386	MIR99AHG	mir-99a-let-7c cluster host gene	0.706262	0.866057
645.	ENSG00000132780	NASP	nuclear autoantigenic sperm protein	0.889616	0.865998
646.	ENSG00000140395	WDR61	WD repeat domain 61	0.783432	0.865257
647.	ENSG00000130066	SAT1	spermidine/spermine N1-acetyltransferase 1	0.701296	0.864274
648.	ENSG00000104756	KCTD9	potassium channel tetramerization domain containing 9	0.999242	0.863835
649.	ENSG00000108219	TSPAN14	tetraspanin 14	0.869488	0.86275
650.	ENSG00000131876	SNRPA1	small nuclear ribonucleoprotein polypeptide A'	0.885467	0.861662
651.	ENSG00000141622	RNF165	ring finger protein 165	1.06013	0.861514
652.	ENSG00000175061	LRRC75A-AS1	LRRC75A antisense RNA 1	0.730571	0.859008
653.	ENSG00000109475	RPL34	ribosomal protein L34	0.791899	0.858151
654.	ENSG00000164983	TMEM65	transmembrane protein 65	1.01325	0.856892
655.	ENSG00000102996	MMP15	matrix metallopeptidase 15	0.898084	0.856742
656.	ENSG00000253626	EIF5AL1	eukaryotic translation initiation factor 5A-like 1	0.937528	0.856409
657.	ENSG00000125901	MRPS26	mitochondrial ribosomal protein S26	0.590285	0.855188
658.	ENSG00000171953	ATPAF2	ATP synthase mitochondrial F1 complex assembly factor 2	0.668871	0.853675
659.	ENSG00000108561	C1QBP	complement C1q binding protein	0.842575	0.853417
660.	ENSG00000092036	HAUS4	HAUS augmin like complex subunit 4	0.81204	0.852708
661.	ENSG00000143486	EIF2D	eukaryotic translation initiation factor 2D	0.89687	0.852116
662.	ENSG00000120322	PCDHB8	protocadherin beta 8	1.12031	0.851423
663.	ENSG00000106628	POLD2	"DNA polymerase delta 2, accessory subunit"	0.947729	0.850791
664.	ENSG00000100600	LGMN	legumain	0.997135	0.849279
665.	ENSG00000139547	RDH16	retinol dehydrogenase 16 (all-trans)	0.549674	0.848992
666.	ENSG00000173638	SLC19A1	solute carrier family 19 member 1	0.711999	0.848981
667.	ENSG00000166961	MS4A15	membrane spanning 4-domains A15	1.42859	0.848195
668.	ENSG00000127152	BCL11B	B-cell CLL/lymphoma 11B	0.889491	0.847944
669.	ENSG00000214113	LYRM4	LYR motif containing 4	0.816561	0.847357
670.	ENSG00000169740	ZNF32	zinc finger protein 32	0.790834	0.846533
671.	ENSG00000153574	RPIA	ribose 5-phosphate isomerase A	0.794538	0.845553
672.	ENSG00000222041	LINC00152	long intergenic non-protein coding RNA 152	0.642621	0.845507
673.	ENSG00000088832	FKBP1A	FK506 binding protein 1A	0.791857	0.845083
674.	ENSG00000075336	TIMM21	translocase of inner mitochondrial membrane 21	0.679132	0.844579
675.	ENSG00000174672	BRSK2	BR serine/threonine kinase 2	1.05141	0.844313
676.	ENSG00000111911	HINT3	histidine triad nucleotide binding protein 3	0.862346	0.844222
677.	ENSG00000150433	TMEM218	transmembrane protein 218	0.819994	0.843916

678.	ENSG00000197563	PIGN	phosphatidylinositol glycan anchor biosynthesis class N	1.27463	0.843688
679.	ENSG00000148803	FUOM	fucose mutarotase	0.512164	0.843375
680.	ENSG00000126953	TIMM8A	translocase of inner mitochondrial membrane 8 homolog A (yeast)	0.716225	0.843205
681.	ENSG00000088035	ALG6	"ALG6, alpha-1,3-glucosyltransferase"	0.725901	0.842662
682.	ENSG00000229117	RPL41	ribosomal protein L41	0.863473	0.842525
683.	ENSG00000145912	NHP2	NHP2 ribonucleoprotein	0.656477	0.842416
684.	ENSG00000087510	TFAP2C	transcription factor AP-2 gamma	0.827	0.84
685.	ENSG00000152939	MARVELD2	MARVEL domain containing 2	0.848956	0.83838
686.	ENSG00000106603	COA1	cytochrome c oxidase assembly factor 1 homolog	0.866394	0.834569
687.	ENSG00000122406	RPL5	ribosomal protein L5	0.876493	0.834361
688.	ENSG00000241127	YAE1D1	Yae1 domain containing 1	0.528961	0.833542
689.	ENSG00000165916	PSMC3	"proteasome 26S subunit, ATPase 3"	0.867627	0.83266
690.	ENSG00000131174	COX7B	cytochrome c oxidase subunit 7B	0.743747	0.832255
691.	ENSG00000134882	UBAC2	UBA domain containing 2	0.761043	0.832168
692.	ENSG00000114054	PCCB	propionyl-CoA carboxylase beta subunit	0.879864	0.830985
693.	ENSG00000137834	SMAD6	SMAD family member 6	0.666859	0.829978
694.	ENSG00000157827	FMNL2	formin like 2	0.941409	0.829786
695.	ENSG00000136636	KCTD3	potassium channel tetramerization domain containing 3	0.882766	0.829573
696.	ENSG00000204308	RNF5	ring finger protein 5	0.74448	0.82896
697.	ENSG00000170836	PPM1D	"protein phosphatase, Mg2+/Mn2+ dependent 1D"	0.805558	0.828481
698.	ENSG00000189046	ALKBH2	"alkB homolog 2, alpha-ketoglutarate dependent dioxygenase"	0.534917	0.826004
699.	ENSG00000116833	NR5A2	nuclear receptor subfamily 5 group A member 2	1.21764	0.825542
700.	ENSG00000183010	PYCR1	pyrroline-5-carboxylate reductase 1	0.667415	0.824556
701.	ENSG00000261437	LOC100288748	uncharacterized LOC100288748	0.514374	0.824425
702.	ENSG00000250588	IQCJ-SCHIP1	IQCJ-SCHIP1 readthrough	1.07634	0.824338
703.	ENSG00000164967	RPP25L	ribonuclease P/MRP subunit p25 like	0.589825	0.823949
704.	ENSG00000073464	CLCN4	chloride voltage-gated channel 4	1.05748	0.823801
705.	ENSG00000169902	TPST1	tyrosylprotein sulfotransferase 1	0.973886	0.823435
706.	ENSG00000181350	LRRC75A	leucine rich repeat containing 75A	0.828751	0.822573
707.	ENSG00000135549	PKIB	"protein kinase (cAMP-dependent, catalytic) inhibitor beta"	0.923158	0.820975
708.	ENSG00000169021	UQCRFS1	"ubiquinol-cytochrome c reductase, Rieske iron-sulfur polypeptide 1"	0.673997	0.820654
709.	ENSG00000138035	PNPT1	polyribonucleotide nucleotidyltransferase 1	0.771053	0.820103
710.	ENSG00000099284	H2AFY2	H2A histone family member Y2	0.758477	0.819214
711.	ENSG00000105552	BCAT2	branched chain amino acid transaminase 2	0.627225	0.819078
712.	ENSG00000003436	TFPI	tissue factor pathway inhibitor	0.685574	0.818259
713.	ENSG00000111850	SMIM8	small integral membrane protein 8	0.664991	0.817361
714.	ENSG00000139428	MMAB	methylmalonic aciduria (cobalamin deficiency) cblB type	0.698355	0.816792
715.	ENSG00000165028	NIPSNAP3B	nipsnap homolog 3B	0.977539	0.816229
716.	ENSG00000176124	DLEU1	deleted in lymphocytic leukemia 1	1.11632	0.816194
717.	ENSG00000072954	TMEM38A	transmembrane protein 38A	0.820518	0.816127
718.	ENSG00000203875	SNHG5	small nucleolar RNA host gene 5	0.587049	0.815636
719.	ENSG00000173467	AGR3	"anterior gradient 3, protein disulphide isomerase family member"	0.59845	0.815454
720.	ENSG00000164163	ABCE1	ATP binding cassette subfamily E member 1	0.876384	0.815314
721.	ENSG00000137038	TMEM261	transmembrane protein 261	0.671823	0.814308
722.	ENSG00000155508	CNOT8	CCR4-NOT transcription complex subunit 8	0.78093	0.812067
723.	ENSG00000164096	C4orf3	chromosome 4 open reading frame 3	0.665988	0.811939
724.	ENSG00000026950	BTN3A1	butyrophilin subfamily 3 member A1	0.701139	0.811308
725.	ENSG00000155876	RRAGA	Ras related GTP binding A	0.713067	0.811297
726.	ENSG00000171421	MRPL36	mitochondrial ribosomal protein L36	0.541391	0.810266
727.	ENSG00000164751	PEX2	peroxisomal biogenesis factor 2	0.769444	0.809132
728.	ENSG00000071462	WBSCR22	Williams-Beuren syndrome chromosome region 22	0.693725	0.809007
729.	ENSG00000112667	DNPH1	2'-deoxynucleoside 5'-phosphate N-hydrolase 1	0.415004	0.808615
730.	ENSG00000120093	HOXB3	homeobox B3	0.917468	0.808306
731.	ENSG00000134759	ELP2	elongator acetyltransferase complex subunit 2	0.751258	0.807974
732.	ENSG00000150093	ITGB1	integrin subunit beta 1	0.987881	0.80671
733.	ENSG00000168389	MFSD2A	major facilitator superfamily domain containing 2A	1.167	0.806571
734.	ENSG00000145220	LYAR	Ly1 antibody reactive	0.775255	0.806391
735.	ENSG00000104064	GABPB1	GA binding protein transcription factor beta subunit 1	0.78914	0.806187

736.	ENSG00000134375	TIMM17A	translocase of inner mitochondrial membrane 17 homolog A (yeast)	0.741463	0.806169
737.	ENSG00000169020	ATP5I	"ATP synthase, H+ transporting, mitochondrial Fo complex subunit E"	0.572728	0.805795
738.	ENSG00000128694	OSGEPL1	O-sialoglycoprotein endopeptidase like 1	0.946834	0.805438
739.	ENSG00000113621	TXNDC15	thioredoxin domain containing 15	0.674132	0.804971
740.	ENSG00000172345	STARD5	StAR related lipid transfer domain containing 5	0.757691	0.804855
741.	ENSG00000151729	SLC25A4	solute carrier family 25 member 4	0.688413	0.804581
742.	ENSG00000114391	RPL24	ribosomal protein L24	0.775667	0.80338
743.	ENSG00000185627	PSMD13	"proteasome 26S subunit, non-ATPase 13"	0.720864	0.803083
744.	ENSG00000168769	TET2	tet methylcytosine dioxygenase 2	0.974007	0.8011
745.	ENSG00000165264	NDUFB6	NADH:ubiquinone oxidoreductase subunit B6	0.611903	0.800763
746.	ENSG00000124641	MED20	mediator complex subunit 20	0.783132	0.800067
747.	ENSG00000167693	NXN	nucleoredoxin	0.717945	0.799884
748.	ENSG00000140740	UQCRC2	ubiquinol-cytochrome c reductase core protein II	0.756596	0.79963
749.	ENSG00000146950	SHROOM2	shroom family member 2	0.930158	0.799281
750.	ENSG00000170260	ZNF212	zinc finger protein 212	0.573246	0.799225
751.	ENSG00000184182	UBE2F	ubiquitin conjugating enzyme E2 F (putative)	0.847813	0.799021
752.	ENSG00000254999	BRK1	"BRICK1, SCAR/WAVE actin nucleating complex subunit"	0.750387	0.79901
753.	ENSG00000189120	SP6	Sp6 transcription factor	0.627875	0.798127
754.	ENSG00000163682	RPL9	ribosomal protein L9	0.790399	0.797841
755.	ENSG00000181392	SYNE4	spectrin repeat containing nuclear envelope family member 4	0.83352	0.797764
756.	ENSG00000237190	CDKN2AIPNL	CDKN2A interacting protein N-terminal like	0.749947	0.797643
757.	ENSG00000129195	FAM64A	family with sequence similarity 64 member A	0.685687	0.797623
758.	ENSG00000238227	C9orf69	chromosome 9 open reading frame 69	0.476335	0.79721
759.	ENSG00000108830	RND2	Rho family GTPase 2	0.528641	0.797044
760.	ENSG00000198042	MAK16	MAK16 homolog	0.777235	0.79678
761.	ENSG00000132661	NXT1	nuclear transport factor 2 like export factor 1	0.594323	0.796174
762.	ENSG00000262814	MRPL12	mitochondrial ribosomal protein L12	0.508657	0.795649
763.	ENSG00000088356	PDRG1	p53 and DNA damage regulated 1	0.59653	0.79471
764.	ENSG00000243147	MRPL33	mitochondrial ribosomal protein L33	0.747995	0.79456
765.	ENSG00000198918	RPL39	ribosomal protein L39	0.790025	0.793589
766.	ENSG00000156384	SFR1	SWI5 dependent homologous recombination repair protein 1	0.733793	0.792653
767.	ENSG00000184402	SS18L1	"SS18L1, nBAF chromatin remodeling complex subunit"	0.699734	0.792439
768.	ENSG00000112290	WASF1	WAS protein family member 1	1.0033	0.791938
769.	ENSG00000013561	RNF14	ring finger protein 14	0.744299	0.790873
770.	ENSG00000138138	ATAD1	"ATPase family, AAA domain containing 1"	0.789302	0.790079
771.	ENSG00000069956	MAPK6	mitogen-activated protein kinase 6	0.93147	0.789119
772.	ENSG00000106153	CHCHD2	coiled-coil-helix-coiled-coil-helix domain containing 2	0.673485	0.788832
773.	ENSG00000104131	EIF3J	eukaryotic translation initiation factor 3 subunit J	0.920679	0.788568
774.	ENSG00000173660	UQCRH	ubiquinol-cytochrome c reductase hinge protein	0.730635	0.787734
775.	ENSG00000023892	DEF6	"DEF6, guanine nucleotide exchange factor"	0.674619	0.787547
776.	ENSG00000136897	MRPL50	mitochondrial ribosomal protein L50	0.727963	0.787498
777.	ENSG00000166347	CYB5A	cytochrome b5 type A	0.776375	0.787099
778.	ENSG00000179431	FJX1	four jointed box 1	0.673003	0.786922
779.	ENSG00000173436	MINOS1	mitochondrial inner membrane organizing system 1	0.553804	0.786255
780.	ENSG00000135469	COQ10A	coenzyme Q10A	0.61573	0.786051
781.	ENSG00000223802	GDF1	growth differentiation factor 1	0.939212	0.785672
782.	ENSG00000113387	SUB1	"SUB1 homolog, transcriptional regulator"	0.789299	0.78565
783.	ENSG00000160703	NLRX1	NLR family member X1	0.861659	0.784992
784.	ENSG00000118690	ARMC2	armadillo repeat containing 2	0.696103	0.782873
785.	ENSG00000027001	MIPEP	mitochondrial intermediate peptidase	0.710182	0.782334
786.	ENSG00000214114	MYCBP	MYC binding protein	0.834701	0.780983
787.	ENSG00000175279	APITD1	"apoptosis-inducing, TAF9-like domain 1"	0.815897	0.780221
788.	ENSG00000180777	ANKRD30B	ankyrin repeat domain 30B	0.863248	0.779758
789.	ENSG00000163138	PACRGL	PARK2 coregulated like	0.71929	0.778749
790.	ENSG00000076248	UNG	uracil DNA glycosylase	0.816379	0.778265
791.	ENSG00000170846	LOC93622	Morf4 family associated protein 1 like 1 pseudogene	0.617748	0.775301
792.	ENSG00000267296	CEBPA-AS1	CEBPA antisense RNA 1 (head to head)	0.653322	0.775162
793.	ENSG00000125991	ERGIC3	ERGIC and golgi 3	0.703577	0.774335
794.	ENSG00000124614	RPS10	ribosomal protein S10	0.69203	0.772701
795.	ENSG00000185432	METTL7A	methyltransferase like 7A	0.867371	0.772139

796.	ENSG00000143622	RIT1	Ras like without CAAX 1	0.743862	0.771635
797.	ENSG00000114686	MRPL3	mitochondrial ribosomal protein L3	0.752811	0.771381
798.	ENSG00000137168	PPIL1	peptidylprolyl isomerase like 1	0.72316	0.771098
799.	ENSG00000114650	SCAP	SREBF chaperone	0.857089	0.770539
800.	ENSG00000120158	RCL1	RNA terminal phosphate cyclase like 1	0.58902	0.770248
801.	ENSG00000133818	RRAS2	related RAS viral (r-ras) oncogene homolog 2	0.839157	0.770152
802.	ENSG00000156253	RWDD2B	RWD domain containing 2B	0.760684	0.77008
803.	ENSG00000168116	KIAA1586	KIAA1586	0.802731	0.769537
804.	ENSG00000101003	GINS1	GINS complex subunit 1	0.825391	0.768927
805.	ENSG00000177508	IRX3	iroquois homeobox 3	0.704955	0.768635
806.	ENSG00000143621	ILF2	interleukin enhancer binding factor 2	0.778354	0.768432
807.	ENSG00000125843	AP5S1	adaptor related protein complex 5 sigma 1 subunit	0.456215	0.768152
808.	ENSG00000079739	PGM1	phosphoglucomutase 1	0.901442	0.766433
809.	ENSG00000106367	AP1S1	adaptor related protein complex 1 sigma 1 subunit	0.712681	0.766289
810.	ENSG00000142937	RPS8	ribosomal protein S8	0.798614	0.76595
811.	ENSG00000166902	MRPL16	mitochondrial ribosomal protein L16	0.6387	0.765245
812.	ENSG00000112972	HMGCS1	3-hydroxy-3-methylglutaryl-CoA synthase 1	0.995823	0.765179
813.	ENSG00000183527	PSMG1	proteasome assembly chaperone 1	0.681266	0.765086
814.	ENSG00000164687	FABP5	fatty acid binding protein 5	0.582434	0.764601
815.	ENSG00000002549	LAP3	leucine aminopeptidase 3	0.654389	0.76435
816.	ENSG00000155660	PDIA4	protein disulfide isomerase family A member 4	0.832177	0.763579
817.	ENSG00000114812	VIPR1	vasoactive intestinal peptide receptor 1	0.945101	0.763107
818.	ENSG00000132507	EIF5A	eukaryotic translation initiation factor 5A	0.682438	0.762379
819.	ENSG00000154930	ACSS1	acyl-CoA synthetase short-chain family member 1	0.732909	0.762267
820.	ENSG00000073282	TP63	tumor protein p63	1.17284	0.761436
821.	ENSG00000169139	UBE2V2	ubiquitin conjugating enzyme E2 V2	0.847768	0.761367
822.	ENSG00000189403	HMGB1	high mobility group box 1	0.862235	0.760277
823.	ENSG00000165506	DNAAF2	dynein axonemal assembly factor 2	0.627346	0.76001
824.	ENSG00000071994	PDCD2	programmed cell death 2	0.709717	0.75917
825.	ENSG00000143319	ISG20L2	interferon stimulated exonuclease gene 20 like 2	0.800567	0.759151
826.	ENSG00000138587	MNS1	meiosis specific nuclear structural 1	0.840035	0.758889
827.	ENSG00000175093	SPSB4	splA/ryanodine receptor domain and SOCS box containing 4	1.17641	0.758689
828.	ENSG00000265688	MAFG-AS1	MAFG antisense RNA 1 (head to head)	0.488091	0.758365
829.	ENSG00000139620	KANSL2	KAT8 regulatory NSL complex subunit 2	0.647085	0.758256
830.	ENSG00000137210	TMEM14B	transmembrane protein 14B	0.746991	0.758224
831.	ENSG00000181924	COA4	cytochrome c oxidase assembly factor 4 homolog	0.567114	0.757669
832.	ENSG00000146963	LUC7L2	"LUC7 like 2, pre-mRNA splicing factor"	0.803454	0.757396
833.	ENSG00000170425	ADORA2B	adenosine A2b receptor	0.715716	0.757347
834.	ENSG00000116353	MECR	mitochondrial trans-2-enoyl-CoA reductase	0.629844	0.756609
835.	ENSG00000159792	PSKH1	protein serine kinase H1	0.564947	0.756137
836.	ENSG00000090971	NAT14	N-acetyltransferase 14 (putative)	0.436621	0.755597
837.	ENSG00000182899	RPL35A	ribosomal protein L35a	0.687875	0.754828
838.	ENSG00000196782	MAML3	mastermind like transcriptional coactivator 3	1.17245	0.753546
839.	ENSG00000102390	PBDC1	polysaccharide biosynthesis domain containing 1	0.702885	0.752183
840.	ENSG00000198876	DCAF12	DDB1 and CUL4 associated factor 12	0.792873	0.751584
841.	ENSG00000035499	DEPDC1B	DEP domain containing 1B	0.948026	0.751444
842.	ENSG00000137154	RPS6	ribosomal protein S6	0.80126	0.751089
843.	ENSG00000109534	GAR1	GAR1 ribonucleoprotein	0.712978	0.750716
844.	ENSG00000105948	TTC26	tetratricopeptide repeat domain 26	0.645484	0.750698
845.	ENSG00000198755	RPL10A	ribosomal protein L10a	0.714578	0.750405
846.	ENSG00000091140	DLD	dihydrolipoamide dehydrogenase	0.797122	0.750107
847.	ENSG00000140416	TPM1	tropomyosin 1 (alpha)	0.801783	0.748702
848.	ENSG00000071553	ATP6AP1	ATPase H+ transporting accessory protein 1	0.725615	0.747385
849.	ENSG00000106588	PSMA2	proteasome subunit alpha 2	0.711013	0.747366
850.	ENSG00000104915	STX10	syntaxin 10	0.682659	0.746872
851.	ENSG00000105173	CCNE1	cyclin E1	0.708192	0.746412
852.	ENSG00000214706	IFRD2	interferon related developmental regulator 2	0.559552	0.745983
853.	ENSG00000164182	NDUFAF2	NADH:ubiquinone oxidoreductase complex assembly factor 2	0.783876	0.745836
854.	ENSG00000164305	CASP3	caspase 3	0.729553	0.745127
855.	ENSG00000149273	RPS3	ribosomal protein S3	0.756681	0.745014
856.	ENSG00000172500	FIBP	FGF1 intracellular binding protein	0.762325	0.744858
857.	ENSG00000144120	TMEM177	transmembrane protein 177	0.455281	0.744802
858.	ENSG00000161267	BDH1	"3-hydroxybutyrate dehydrogenase, type 1"	0.715878	0.744706
859.	ENSG00000213782	DDX47	DEAD-box helicase 47	0.765994	0.743859

860.	ENSG00000164978	NUDT2	nudix hydrolase 2	0.587172	0.742747
861.	ENSG00000215021	PHB2	prohibitin 2	0.658567	0.742473
862.	ENSG00000130414	NDUFA10	NADH:ubiquinone oxidoreductase subunit A10	0.587629	0.742002
863.	ENSG00000163738	MTHFD2L	methylenetetrahydrofolate dehydrogenase (NADP+ dependent) 2-like	0.589263	0.741144
864.	ENSG00000047634	SCML1	sex comb on midleg-like 1 (Drosophila)	0.763639	0.740902
865.	ENSG00000129071	MBD4	"methyl-CpG binding domain 4, DNA glycosylase"	0.679262	0.740153
866.	ENSG00000174173	TRMT10C	"tRNA methyltransferase 10C, mitochondrial RNase P subunit"	0.656297	0.739582
867.	ENSG00000083845	RPS5	ribosomal protein S5	0.563525	0.738254
868.	ENSG00000165997	ARL5B	ADP ribosylation factor like GTPase 5B	0.799245	0.737761
869.	ENSG00000122026	RPL21	ribosomal protein L21	0.755891	0.73765
870.	ENSG00000070831	CDC42	cell division cycle 42	0.724433	0.737603
871.	ENSG00000152795	HNRNPDL	heterogeneous nuclear ribonucleoprotein D like	0.624528	0.737366
872.	ENSG00000182512	GLRX5	glutaredoxin 5	0.741695	0.736694
873.	ENSG00000056736	IL17RB	interleukin 17 receptor B	0.884077	0.736462
874.	ENSG00000105607	GCDH	glutaryl-CoA dehydrogenase	0.848594	0.735966
875.	ENSG00000059378	PARP12	poly(ADP-ribose) polymerase family member 12	0.41123	0.735736
876.	ENSG00000232112	TMA7	translation machinery associated 7 homolog	0.568972	0.735707
877.	ENSG00000164405	UQCRQ	ubiquinol-cytochrome c reductase complex III subunit VII	0.655835	0.735397
878.	ENSG00000110955	ATP5B	"ATP synthase, H+ transporting, mitochondrial F1 complex, beta polypeptide"	0.738957	0.734603
879.	ENSG00000105677	TMEM147	transmembrane protein 147	0.659977	0.73448
880.	ENSG00000136930	PSMB7	proteasome subunit beta 7	0.703839	0.733512
881.	ENSG00000183605	SFXN4	sideroflexin 4	0.706769	0.733447
882.	ENSG00000135587	SMPD2	sphingomyelin phosphodiesterase 2	0.898892	0.733124
883.	ENSG00000133678	TMEM254	transmembrane protein 254	0.725767	0.733062
884.	ENSG00000123600	METTL8	methyltransferase like 8	0.803202	0.731764
885.	ENSG00000231500	RPS18	ribosomal protein S18	0.638633	0.730978
886.	ENSG00000152782	PANK1	pantothenate kinase 1	0.797274	0.730937
887.	ENSG00000146535	GNA12	G protein subunit alpha 12	0.878071	0.730274
888.	ENSG00000181817	LSM10	"LSM10, U7 small nuclear RNA associated"	0.568817	0.730227
889.	ENSG00000109911	ELP4	elongator acetyltransferase complex subunit 4	0.670908	0.728065
890.	ENSG00000169738	DCXR	dicarbonyl and L-xylulose reductase	0.639569	0.72724
891.	ENSG00000100865	CINP	cyclin dependent kinase 2 interacting protein	0.658014	0.726846
892.	ENSG00000147155	EBP	emopamil binding protein (sterol isomerase)	0.72739	0.726358
893.	ENSG00000087053	MTMR2	myotubularin related protein 2	0.910336	0.726056
894.	ENSG00000161980	POLR3K	RNA polymerase III subunit K	0.601195	0.724844
895.	ENSG00000206503	HLA-A	"major histocompatibility complex, class I, A"	0.642678	0.723941
896.	ENSG00000198142	SOWAHC	sosondowah ankyrin repeat domain family member C	0.757397	0.721909
897.	ENSG00000141384	TAF4B	TATA-box binding protein associated factor 4b	0.927441	0.721482
898.	ENSG00000196976	LAGE3	L antigen family member 3	0.51342	0.72033
899.	ENSG00000137563	GGH	gamma-glutamyl hydrolase	0.863208	0.719927
900.	ENSG00000140718	FTO	fat mass and obesity associated	0.807692	0.719746
901.	ENSG00000224877	NDUFAF8	NADH:ubiquinone oxidoreductase complex assembly factor 8	0.438455	0.719152
902.	ENSG00000132341	RAN	"RAN, member RAS oncogene family"	0.649795	0.716611
903.	ENSG00000070761	CFAP20	cilia and flagella associated protein 20	0.673339	0.71513
904.	ENSG00000185989	RASA3	RAS p21 protein activator 3	0.752342	0.715053
905.	ENSG00000154642	C21orf91	chromosome 21 open reading frame 91	0.691422	0.713411
906.	ENSG00000167283	ATP5L	"ATP synthase, H+ transporting, mitochondrial Fo complex subunit G"	0.641905	0.713396
907.	ENSG00000197345	MRPL21	mitochondrial ribosomal protein L21	0.620408	0.711494
908.	ENSG00000108651	UTP6	"UTP6, small subunit processome component"	0.626186	0.711473
909.	ENSG00000171954	CYP4F22	cytochrome P450 family 4 subfamily F member 22	0.607833	0.711376
910.	ENSG00000197728	RPS26	ribosomal protein S26	0.600671	0.710175
911.	ENSG00000122783	C7orf49	chromosome 7 open reading frame 49	0.651726	0.709833
912.	ENSG00000116285	ERRFI1	ERBB receptor feedback inhibitor 1	0.525362	0.709608
913.	ENSG00000075413	MARK3	microtubule affinity regulating kinase 3	0.541086	0.708198
914.	ENSG00000159228	CBR1	carbonyl reductase 1	0.60378	0.707936
915.	ENSG00000123179	EBPL	emopamil binding protein like	0.759841	0.707649
916.	ENSG00000136770	DNAJC1	DnaJ heat shock protein family (Hsp40) member C1	0.628416	0.707132
917.	ENSG00000051596	THOC3	THO complex 3	0.747607	0.706681
918.	ENSG00000092094	OSGEP	O-sialoglycoprotein endopeptidase	0.590015	0.706425
919.	ENSG00000127334	DYRK2	dual specificity tyrosine phosphorylation regulated kinase 2	0.937423	0.706077

920.	ENSG00000217555	CKLF	chemokine like factor	0.618983	0.705915
921.	ENSG00000178537	SLC25A20	solute carrier family 25 member 20	0.55318	0.705508
922.	ENSG00000132591	ERAL1	Era like 12S mitochondrial rRNA chaperone 1	0.638027	0.704868
923.	ENSG00000167862	MRPL58	mitochondrial ribosomal protein L58	0.589747	0.704769
924.	ENSG00000125484	GTF3C4	general transcription factor IIIC subunit 4	0.760099	0.704617
925.	ENSG00000116922	C1orf109	chromosome 1 open reading frame 109	0.578077	0.703725
926.	ENSG00000111832	RWDD1	RWD domain containing 1	0.790947	0.703144
927.	ENSG00000187713	TMEM203	transmembrane protein 203	0.536841	0.70267
928.	ENSG00000144354	CDCA7	cell division cycle associated 7	0.780818	0.700558
929.	ENSG00000107223	EDF1	endothelial differentiation related factor 1	0.499046	0.698612
930.	ENSG00000154217	PITPNC1	"phosphatidylinositol transfer protein, cytoplasmic 1"	0.752945	0.698521
931.	ENSG00000137267	TUBB2A	tubulin beta 2A class IIa	0.556047	0.69846
932.	ENSG00000175322	ZNF519	zinc finger protein 519	0.57224	0.698319
933.	ENSG00000047621	C12orf4	chromosome 12 open reading frame 4	0.589379	0.697994
934.	ENSG00000055211	GINM1	glycoprotein integral membrane 1	0.775513	0.697549
935.	ENSG00000066379	ZNRD1	zinc ribbon domain containing 1	0.479523	0.696981
936.	ENSG00000080189	SLC35C2	solute carrier family 35 member C2	0.614949	0.696564
937.	ENSG00000179862	CITED4	Cbp/p300 interacting transactivator with Glu/Asp rich carboxy-terminal domain 4	0.482466	0.696028
938.	ENSG00000076067	RBMS2	RNA binding motif single stranded interacting protein 2	0.988779	0.695869
939.	ENSG00000088451	TGDS	"TDP-glucose 4,6-dehydratase"	0.708024	0.695662
940.	ENSG00000182307	C8orf33	chromosome 8 open reading frame 33	0.660074	0.695409
941.	ENSG00000166441	RPL27A	ribosomal protein L27a	0.602351	0.694477
942.	ENSG00000186132	C2orf76	chromosome 2 open reading frame 76	0.748832	0.69391
943.	ENSG00000004779	NDUFAB1	NADH:ubiquinone oxidoreductase subunit AB1	0.596311	0.692596
944.	ENSG00000112977	DAP	death associated protein	0.676437	0.692041
945.	ENSG00000168028	RPSA	ribosomal protein SA	0.728888	0.69114
946.	ENSG00000078070	MCCC1	methylcrotonoyl-CoA carboxylase 1	0.606684	0.691066
947.	ENSG00000169684	CHRNA5	cholinergic receptor nicotinic alpha 5 subunit	0.704088	0.690746
948.	ENSG00000142541	RPL13A	ribosomal protein L13a	0.565281	0.690617
949.	ENSG00000117691	NENF	neudesin neurotrophic factor	0.63689	0.689993
950.	ENSG00000231584	FAHD2CP	"fumarylacetoacetate hydrolase domain containing 2C, pseudogene"	0.698245	0.689497
951.	ENSG00000109919	MTCH2	mitochondrial carrier 2	0.643666	0.688932
952.	ENSG00000012660	ELOVL5	ELOVL fatty acid elongase 5	0.835545	0.688405
953.	ENSG00000164976	KIAA1161	KIAA1161	0.655048	0.688324
954.	ENSG00000164442	CITED2	Cbp/p300 interacting transactivator with Glu/Asp rich carboxy-terminal domain 2	0.558277	0.687849
955.	ENSG00000137513	NARS2	"asparaginyl-tRNA synthetase 2, mitochondrial (putative)"	0.792649	0.687521
956.	ENSG00000163818	LZTFL1	leucine zipper transcription factor like 1	0.597137	0.686555
957.	ENSG00000187193	MT1X	metallothionein 1X	0.426134	0.685788
958.	ENSG00000076513	ANKRD13A	ankyrin repeat domain 13A	0.696859	0.685671
959.	ENSG00000176903	PNMA1	paraneoplastic Ma antigen 1	0.569994	0.68552
960.	ENSG00000100804	PSMB5	proteasome subunit beta 5	0.647283	0.685028
961.	ENSG00000132467	UTP3	"UTP3, small subunit processome component homolog (S. cerevisiae)"	0.539582	0.683986
962.	ENSG00000166710	B2M	beta-2-microglobulin	0.660654	0.683885
963.	ENSG00000172115	CYCS	"cytochrome c, somatic"	0.634708	0.683778
964.	ENSG00000163249	CCNYL1	cyclin Y like 1	0.891729	0.683649
965.	ENSG00000164109	MAD2L1	MAD2 mitotic arrest deficient-like 1 (yeast)	0.684397	0.683566
966.	ENSG00000074201	CLNS1A	chloride nucleotide-sensitive channel 1A	0.581412	0.683439
967.	ENSG00000077549	CAPZB	capping actin protein of muscle Z-line beta subunit	0.666538	0.682933
968.	ENSG00000163382	NAXE	NAD(P)HX epimerase	0.699496	0.682152
969.	ENSG00000148335	NTMT1	N-terminal Xaa-Pro-Lys N-methyltransferase 1	0.366753	0.68196
970.	ENSG00000136942	RPL35	ribosomal protein L35	0.587071	0.681671
971.	ENSG00000162961	DPY30	"dpy-30, histone methyltransferase complex regulatory subunit"	0.745031	0.681298
972.	ENSG00000152455	SUV39H2	suppressor of variegation 3-9 homolog 2	0.68922	0.680572
973.	ENSG00000116273	PHF13	PHD finger protein 13	0.548822	0.679934
974.	ENSG00000117697	NSL1	"NSL1, MIS12 kinetochore complex component"	0.575272	0.679574
975.	ENSG00000204392	LSM2	"LSM2 homolog, U6 small nuclear RNA and mRNA degradation associated"	0.576788	0.679191
976.	ENSG00000138764	CCNG2	cyclin G2	0.662931	0.679027
977.	ENSG00000186468	RPS23	ribosomal protein S23	0.644234	0.677774
978.	ENSG00000114850	SSR3	signal sequence receptor subunit 3	0.712814	0.67759

979.	ENSG00000145990	GFOD1	glucose-fructose oxidoreductase domain containing 1	0.655897	0.677425
980.	ENSG00000111669	TPI1	triosephosphate isomerase 1	0.662608	0.676696
981.	ENSG00000162894	FCMR	Fc fragment of IgM receptor	0.62598	0.67407
982.	ENSG00000174547	MRPL11	mitochondrial ribosomal protein L11	0.561701	0.673595
983.	ENSG00000177519	RPRM	"reprimo, TP53 dependent G2 arrest mediator candidate"	0.725484	0.672673
984.	ENSG00000145386	CCNA2	cyclin A2	0.683344	0.672626
985.	ENSG00000198680	TUSC1	tumor suppressor candidate 1	0.434468	0.671859
986.	ENSG00000139832	RAB20	"RAB20, member RAS oncogene family"	0.54106	0.671545
987.	ENSG00000138442	WDR12	WD repeat domain 12	0.631358	0.671058
988.	ENSG00000187049	TMEM216	transmembrane protein 216	0.578493	0.670693
989.	ENSG00000137393	RNF144B	ring finger protein 144B	0.536437	0.670161
990.	ENSG00000150456	EEF1AKMT1	eukaryotic translation elongation factor 1 alpha lysine methyltransferase 1	0.694379	0.670003
991.	ENSG00000075223	SEMA3C	semaphorin 3C	0.907207	0.669273
992.	ENSG00000160783	PMF1	polyamine modulated factor 1	0.49455	0.668554
993.	ENSG00000103121	CMC2	C-X9-C motif containing 2	0.595229	0.668355
994.	ENSG00000077152	UBE2T	ubiquitin conjugating enzyme E2 T	0.641735	0.668278
995.	ENSG00000109255	NMU	neuromedin U	1.0744	0.667768
996.	ENSG00000088766	CRLS1	cardiolipin synthase 1	0.531102	0.667133
997.	ENSG00000256269	HMBS	hydroxymethylbilane synthase	0.562652	0.666744
998.	ENSG00000111845	PAK1IP1	PAK1 interacting protein 1	0.562759	0.666736
999.	ENSG00000158427	TMSB15B	thymosin beta 15B	0.668357	0.666676
1000.	ENSG00000100462	PRMT5	protein arginine methyltransferase 5	0.737209	0.665835
1001.	ENSG00000062582	MRPS24	mitochondrial ribosomal protein S24	0.555455	0.665775
1002.	ENSG00000114942	EEF1B2	eukaryotic translation elongation factor 1 beta 2	0.68232	0.665074
1003.	ENSG00000095203	EPB41L4B	erythrocyte membrane protein band 4.1 like 4B	0.73561	0.664133
1004.	ENSG00000171735	CAMTA1	calmodulin binding transcription activator 1	0.642045	0.662908
1005.	ENSG00000164587	RPS14	ribosomal protein S14	0.610268	0.66288
1006.	ENSG00000198807	PAX9	paired box 9	0.58445	0.662648
1007.	ENSG00000173207	CKS1B	CDC28 protein kinase regulatory subunit 1B	0.59821	0.662221
1008.	ENSG00000132275	RRP8	"ribosomal RNA processing 8, methyltransferase, homolog (yeast)"	0.501806	0.66187
1009.	ENSG00000213339	QTRT1	queuine tRNA-ribosyltransferase catalytic subunit 1	0.471824	0.661715
1010.	ENSG00000272047	GTF2H5	general transcription factor IIH subunit 5	0.482877	0.661587
1011.	ENSG00000108443	RPS6KB1	ribosomal protein S6 kinase B1	0.690924	0.661297
1012.	ENSG00000167526	RPL13	ribosomal protein L13	0.48154	0.660912
1013.	ENSG00000116685	KIAA2013	KIAA2013	0.458529	0.66025
1014.	ENSG00000164008	C1orf50	chromosome 1 open reading frame 50	0.506735	0.660153
1015.	ENSG00000176422	SPRYD4	SPRY domain containing 4	0.498969	0.658557
1016.	ENSG00000125691	RPL23	ribosomal protein L23	0.713014	0.658251
1017.	ENSG00000178913	TAF7	TATA-box binding protein associated factor 7	0.495937	0.658128
1018.	ENSG00000135617	PRADC1	protease associated domain containing 1	0.539953	0.658061
1019.	ENSG00000188372	ZP3	zona pellucida glycoprotein 3	0.598498	0.657539
1020.	ENSG00000165502	RPL36AL	ribosomal protein L36a like	0.544335	0.657496
1021.	ENSG00000117139	KDM5B	lysine demethylase 5B	0.845657	0.65676
1022.	ENSG00000137274	BPHL	biphenyl hydrolase like	0.722898	0.655604
1023.	ENSG00000065328	MCM10	minichromosome maintenance 10 replication initiation factor	0.658391	0.655249
1024.	ENSG00000182004	SNRPE	small nuclear ribonucleoprotein polypeptide E	0.579614	0.655083
1025.	ENSG00000114491	UMPS	uridine monophosphate synthetase	0.618575	0.654156
1026.	ENSG00000118181	RPS25	ribosomal protein S25	0.679746	0.654124
1027.	ENSG00000100811	YY1	YY1 transcription factor	0.656623	0.652961
1028.	ENSG00000139289	PHLDA1	pleckstrin homology like domain family A member 1	0.52809	0.652852
1029.	ENSG00000104549	SQLE	squalene epoxidase	0.859419	0.65273
1030.	ENSG00000114125	RNF7	ring finger protein 7	0.475151	0.652396
1031.	ENSG00000174444	RPL4	ribosomal protein L4	0.727798	0.651767
1032.	ENSG00000114023	FAM162A	family with sequence similarity 162 member A	0.512759	0.651472
1033.	ENSG00000205581	HMGN1	high mobility group nucleosome binding domain 1	0.671758	0.650796
1034.	ENSG00000134533	RERG	RAS like estrogen regulated growth inhibitor	0.739758	0.650693
1035.	ENSG00000107882	SUFU	SUFU negative regulator of hedgehog signaling	0.632929	0.650479
1036.	ENSG00000164258	NDUFS4	NADH:ubiquinone oxidoreductase subunit S4	0.599484	0.649652
1037.	ENSG00000133247	KMT5C	lysine methyltransferase 5C	0.564812	0.649637
1038.	ENSG00000170089	LOC728554	THO complex 3 pseudogene	0.691449	0.649272
1039.	ENSG00000155438	NIFK	nucleolar protein interacting with the FHA domain of MKI67	0.614676	0.649105
1040.	ENSG00000186998	EMID1	EMI domain containing 1	0.485272	0.647797

1041.	ENSG00000089157	RPLP0	ribosomal protein lateral stalk subunit P0	0.690141	0.646959
1042.	ENSG00000105193	RPS16	ribosomal protein S16	0.595941	0.646833
1043.	ENSG00000092068	SLC7A8	solute carrier family 7 member 8	0.772529	0.646335
1044.	ENSG00000198034	RPS4X	"ribosomal protein S4, X-linked"	0.617263	0.645454
1045.	ENSG00000109016	DHRS7B	dehydrogenase/reductase 7B	0.519399	0.643293
1046.	ENSG00000184076	UQCR10	"ubiquinol-cytochrome c reductase, complex III subunit X"	0.440544	0.643124
1047.	ENSG00000169093	ASMTL	acetylserotonin O-methyltransferase-like	0.627943	0.643094
1048.	ENSG00000162594	IL23R	interleukin 23 receptor	0.901047	0.643077
1049.	ENSG00000214253	FIS1	"fission, mitochondrial 1"	0.477	0.64285
1050.	ENSG00000121691	CAT	catalase	0.739667	0.642768
1051.	ENSG00000172965	MIR4435-2HG	MIR4435-2 host gene	0.680475	0.642404
1052.	ENSG00000152102	FAM168B	family with sequence similarity 168 member B	0.732542	0.642111
1053.	ENSG00000171204	TMEM126B	transmembrane protein 126B	0.727283	0.641183
1054.	ENSG00000088986	DYNLL1	dynein light chain LC8-type 1	0.629238	0.640647
1055.	ENSG00000266967	AARSD1	alanyl-tRNA synthetase domain containing 1	0.659615	0.639813
1056.	ENSG00000223797	ENTPD3-AS1	ENTPD3 antisense RNA 1	0.509316	0.639276
1057.	ENSG00000147654	EBAG9	"estrogen receptor binding site associated, antigen, 9"	0.596474	0.638776
1058.	ENSG00000109270	LAMTOR3	"late endosomal/lysosomal adaptor, MAPK and MTOR activator 3"	0.519875	0.638155
1059.	ENSG00000143207	RFWD2	ring finger and WD repeat domain 2	0.768969	0.637484
1060.	ENSG00000180739	S1PR5	sphingosine-1-phosphate receptor 5	0.544561	0.637201
1061.	ENSG00000173409	ARV1	"ARV1 homolog, fatty acid homeostasis modulator"	0.443626	0.636535
1062.	ENSG00000168393	DTYMK	deoxythymidylate kinase	0.550339	0.636515
1063.	ENSG00000179941	BBS10	Bardet-Biedl syndrome 10	0.549438	0.635606
1064.	ENSG00000198805	PNP	purine nucleoside phosphorylase	0.562185	0.634676
1065.	ENSG00000186205	MARC1	mitochondrial amidoxime reducing component 1	0.739496	0.634046
1066.	ENSG00000100316	RPL3	ribosomal protein L3	0.643843	0.633513
1067.	ENSG00000148677	ANKRD1	ankyrin repeat domain 1	0.498224	0.633051
1068.	ENSG00000165283	STOML2	stomatin like 2	0.620558	0.633006
1069.	ENSG00000213281	NRAS	neuroblastoma RAS viral oncogene homolog	0.650742	0.632976
1070.	ENSG00000117395	EBNA1BP2	EBNA1 binding protein 2	0.637167	0.63253
1071.	ENSG00000175970	UNC119B	unc-119 lipid binding chaperone B	0.57547	0.632513
1072.	ENSG00000146242	TPBG	trophoblast glycoprotein	0.510288	0.632264
1073.	ENSG00000198130	HIBCH	3-hydroxyisobutyryl-CoA hydrolase	0.842222	0.631806
1074.	ENSG00000138385	SSB	Sjogren syndrome antigen B	0.68798	0.631619
1075.	ENSG00000175334	BANF1	barrier to autointegration factor 1	0.576179	0.631429
1076.	ENSG00000116898	MRPS15	mitochondrial ribosomal protein S15	0.589601	0.631072
1077.	ENSG00000183291	SEP15	15 kDa selenoprotein	0.612944	0.630963
1078.	ENSG00000145982	FARS2	"phenylalanyl-tRNA synthetase 2, mitochondrial"	0.604479	0.630769
1079.	ENSG00000113368	LMNB1	lamin B1	0.627999	0.630477
1080.	ENSG00000169288	MRPL1	mitochondrial ribosomal protein L1	0.613311	0.6288
1081.	ENSG00000198324	FAM109A	family with sequence similarity 109 member A	0.510703	0.628693
1082.	ENSG00000128581	IFT22	intraflagellar transport 22	0.595712	0.628508
1083.	ENSG00000111906	HDDC2	HD domain containing 2	0.704719	0.628219
1084.	ENSG00000136830	FAM129B	family with sequence similarity 129 member B	0.567133	0.628176
1085.	ENSG00000000003	TSPAN6	tetraspanin 6	0.6999	0.627904
1086.	ENSG00000104408	EIF3E	eukaryotic translation initiation factor 3 subunit E	0.693977	0.627349
1087.	ENSG00000125356	NDUFA1	NADH:ubiquinone oxidoreductase subunit A1	0.481754	0.626363
1088.	ENSG00000241343	RPL36A	ribosomal protein L36a	0.665105	0.625905
1089.	ENSG00000101361	NOP56	NOP56 ribonucleoprotein	0.588583	0.625073
1090.	ENSG00000100528	CNIH1	cornichon family AMPA receptor auxiliary protein 1	0.527042	0.625035
1091.	ENSG00000106610	STAG3L4	stromal antigen 3-like 4 (pseudogene)	0.59115	0.623864
1092.	ENSG00000165948	IFI27L1	interferon alpha inducible protein 27 like 1	0.498304	0.623056
1093.	ENSG00000053371	AKR7A2	aldo-keto reductase family 7 member A2	0.590043	0.622283
1094.	ENSG00000188313	PLSCR1	phospholipid scramblase 1	0.400567	0.622252
1095.	ENSG00000187189	TSPYL4	TSPY like 4	0.461534	0.620688
1096.	ENSG00000120662	MTRF1	mitochondrial translational release factor 1	0.447792	0.619521
1097.	ENSG00000119335	SET	SET nuclear proto-oncogene	0.742598	0.618882
1098.	ENSG00000169567	HINT1	histidine triad nucleotide binding protein 1	0.531404	0.618637
1099.	ENSG00000147684	NDUFB9	NADH:ubiquinone oxidoreductase subunit B9	0.555857	0.618531
1100.	ENSG00000143333	RGS16	regulator of G-protein signaling 16	0.542244	0.617958
1101.	ENSG00000143420	ENSA	endosulfine alpha	0.669224	0.617762
1102.	ENSG00000101193	GID8	GID complex subunit 8 homolog	0.555707	0.617716
1103.	ENSG00000172315	TP53RK	TP53 regulating kinase	0.565331	0.617696

1104.	ENSG00000174371	EXO1	exonuclease 1	0.586883	0.616257
1105.	ENSG00000079459	FDFT1	farnesyl-diphosphate farnesyltransferase 1	0.83121	0.616238
1106.	ENSG00000170889	RPS9	ribosomal protein S9	0.494933	0.615055
1107.	ENSG00000254093	PINX1	"PIN2/TERF1 interacting, telomerase inhibitor 1"	0.563699	0.614464
1108.	ENSG00000069998	CECR5	"cat eye syndrome chromosome region, candidate 5"	0.4713	0.614461
1109.	ENSG00000161057	PSMC2	"proteasome 26S subunit, ATPase 2"	0.556815	0.614312
1110.	ENSG00000130713	EXOSC2	exosome component 2	0.584958	0.614102
1111.	ENSG00000152402	GUCY1A2	guanylate cyclase 1 soluble subunit alpha 2	0.645431	0.613243
1112.	ENSG00000109084	TMEM97	transmembrane protein 97	0.833185	0.612911
1113.	ENSG00000155755	TMEM237	transmembrane protein 237	0.646639	0.612708
1114.	ENSG00000126088	UROD	uroporphyrinogen decarboxylase	0.562775	0.612601
1115.	ENSG00000166598	HSP90B1	heat shock protein 90 beta family member 1	0.780005	0.61235
1116.	ENSG00000196683	TOMM7	translocase of outer mitochondrial membrane 7	0.557692	0.611233
1117.	ENSG00000166415	WDR72	WD repeat domain 72	0.705664	0.610389
1118.	ENSG00000176890	TYMS	thymidylate synthetase	0.594336	0.609152
1119.	ENSG00000116815	CD58	CD58 molecule	0.574278	0.608606
1120.	ENSG00000118939	UCHL3	ubiquitin C-terminal hydrolase L3	0.62191	0.608182
1121.	ENSG00000011260	UTP18	"UTP18, small subunit processome component"	0.537868	0.60794
1122.	ENSG00000214954	LRRC69	leucine rich repeat containing 69	0.555951	0.606239
1123.	ENSG00000170142	UBE2E1	ubiquitin conjugating enzyme E2 E1	0.619358	0.605514
1124.	ENSG00000116459	ATP5F1	"ATP synthase, H+ transporting, mitochondrial Fo complex subunit B1"	0.570357	0.604812
1125.	ENSG00000142676	RPL11	ribosomal protein L11	0.642594	0.604273
1126.	ENSG00000124172	ATP5E	"ATP synthase, H+ transporting, mitochondrial F1 complex, epsilon subunit"	0.553854	0.60387
1127.	ENSG00000122034	GTF3A	general transcription factor IIIA	0.639956	0.603777
1128.	ENSG00000161981	SNRNP25	small nuclear ribonucleoprotein U11/U12 subunit 25	0.656031	0.603566
1129.	ENSG00000160049	DFFA	DNA fragmentation factor subunit alpha	0.675709	0.602846
1130.	ENSG00000159873	CCDC117	coiled-coil domain containing 117	0.801064	0.602464
1131.	ENSG00000143315	PIGM	phosphatidylinositol glycan anchor biosynthesis class M	0.537811	0.601687
1132.	ENSG00000169439	SDC2	syndecan 2	0.629612	0.601104
1133.	ENSG00000004455	AK2	adenylate kinase 2	0.58514	0.599814
1134.	ENSG00000163002	NUP35	nucleoporin 35	0.649279	0.599748
1135.	ENSG00000008283	CYB561	cytochrome b561	0.490292	0.599664
1136.	ENSG00000136933	RABEPK	Rab9 effector protein with kelch motifs	0.550754	0.599569
1137.	ENSG00000116030	SUMO1	small ubiquitin-like modifier 1	0.650273	0.599114
1138.	ENSG00000100982	PCIF1	PDX1 C-terminal inhibiting factor 1	0.398303	0.598229
1139.	ENSG00000230989	HSBP1	heat shock factor binding protein 1	0.545827	0.597753
1140.	ENSG00000185842	DNAH14	dynein axonemal heavy chain 14	0.576577	0.597049
1141.	ENSG00000115216	NRBP1	nuclear receptor binding protein 1	0.590665	0.596604
1142.	ENSG00000139197	PEX5	peroxisomal biogenesis factor 5	0.622786	0.595623
1143.	ENSG00000135070	ISCA1	iron-sulfur cluster assembly 1	0.603147	0.595407
1144.	ENSG00000172380	GNG12	G protein subunit gamma 12	0.792578	0.595368
1145.	ENSG00000114446	IFT57	intraflagellar transport 57	0.619088	0.594426
1146.	ENSG00000203760	CENPW	centromere protein W	0.460512	0.594347
1147.	ENSG00000178307	TMEM11	transmembrane protein 11	0.395127	0.594322
1148.	ENSG00000104979	C19orf53	chromosome 19 open reading frame 53	0.508361	0.593913
1149.	ENSG00000117448	AKR1A1	aldo-keto reductase family 1 member A1	0.690468	0.593904
1150.	ENSG00000187607	ZNF286A	zinc finger protein 286A	0.765241	0.59238
1151.	ENSG00000189043	NDUFA4	"NDUFA4, mitochondrial complex associated"	0.620783	0.591739
1152.	ENSG00000197958	RPL12	ribosomal protein L12	0.609403	0.591557
1153.	ENSG00000198015	MRPL42	mitochondrial ribosomal protein L42	0.558932	0.591286
1154.	ENSG00000173085	COQ2	"coenzyme Q2, polyprenyltransferase"	0.51358	0.591104
1155.	ENSG00000186416	NKRF	NFKB repressing factor	0.562578	0.591047
1156.	ENSG00000111843	TMEM14C	transmembrane protein 14C	0.620905	0.590898
1157.	ENSG00000156411	C14orf2	chromosome 14 open reading frame 2	0.523541	0.590597
1158.	ENSG00000115875	SRSF7	serine and arginine rich splicing factor 7	0.558072	0.589317
1159.	ENSG00000172586	CHCHD1	coiled-coil-helix-coiled-coil-helix domain containing 1	0.506416	0.588876
1160.	ENSG00000118579	MED28	mediator complex subunit 28	0.537528	0.58869
1161.	ENSG00000151743	AMN1	antagonist of mitotic exit network 1 homolog	0.683819	0.588496
1162.	ENSG00000117906	RCN2	reticulocalbin 2	0.698454	0.588073
1163.	ENSG00000132646	PCNA	proliferating cell nuclear antigen	0.420561	0.587194
1164.	ENSG00000100632	ERH	enhancer of rudimentary homolog (Drosophila)	0.573351	0.58719
1165.	ENSG00000175193	PARL	presenilin associated rhomboid like	0.535057	0.586764
1166.	ENSG00000145293	ENOPH1	enolase-phosphatase 1	0.606649	0.586319

1167.	ENSG00000156110	ADK	adenosine kinase	0.60946	0.586069
1168.	ENSG00000197756	RPL37A	ribosomal protein L37a	0.534367	0.585879
1169.	ENSG00000156471	PTDSS1	phosphatidylserine synthase 1	0.677304	0.585521
1170.	ENSG00000186625	KATNA1	katanin catalytic subunit A1	0.442418	0.585361
1171.	ENSG00000143033	MTF2	metal response element binding transcription factor 2	0.620632	0.58535
1172.	ENSG00000163634	THOC7	THO complex 7	0.662423	0.585282
1173.	ENSG00000113269	RNF130	ring finger protein 130	0.700167	0.585128
1174.	ENSG00000168288	MMADHC	"methylmalonic aciduria and homocystinuria, cblD type"	0.552518	0.585056
1175.	ENSG00000183978	COA3	cytochrome c oxidase assembly factor 3	0.454443	0.58493
1176.	ENSG00000106355	LSM5	"LSM5 homolog, U6 small nuclear RNA and mRNA degradation associated"	0.556302	0.584585
1177.	ENSG00000256525	POLG2	"DNA polymerase gamma 2, accessory subunit"	0.496162	0.584555
1178.	ENSG00000050405	LIMA1	LIM domain and actin binding 1	0.590325	0.584341
1179.	ENSG00000166562	SEC11C	"SEC11 homolog C, signal peptidase complex subunit"	0.493302	0.583424
1180.	ENSG00000179918	SEPHS2	selenophosphate synthetase 2	0.470174	0.583339
1181.	ENSG00000168653	NDUFS5	NADH:ubiquinone oxidoreductase subunit S5	0.447218	0.58327
1182.	ENSG00000078668	VDAC3	voltage dependent anion channel 3	0.599311	0.583252
1183.	ENSG00000141401	IMPA2	inositol monophosphatase 2	0.564067	0.582915
1184.	ENSG00000156469	MTERF3	mitochondrial transcription termination factor 3	0.452698	0.582238
1185.	ENSG00000106993	CDC37L1	cell division cycle 37 like 1	0.652822	0.581541
1186.	ENSG00000133872	SARAF	store-operated calcium entry associated regulatory factor	0.651737	0.581324
1187.	ENSG00000254858	MPV17L2	MPV17 mitochondrial inner membrane protein like 2	0.55069	0.580507
1188.	ENSG00000131269	ABCB7	ATP binding cassette subfamily B member 7	0.688644	0.580453
1189.	ENSG00000110063	DCPS	"decapping enzyme, scavenger"	0.545144	0.580398
1190.	ENSG00000265681	RPL17	ribosomal protein L17	0.608482	0.579599
1191.	ENSG00000065911	MTHFD2	"methylenetetrahydrofolate dehydrogenase (NADP+ dependent) 2, methenyltetrahydrofolate cyclohydrolase"	0.67394	0.578727
1192.	ENSG00000113211	PCDHB6	protocadherin beta 6	0.547292	0.578213
1193.	ENSG00000149923	PPP4C	protein phosphatase 4 catalytic subunit	0.389742	0.577441
1194.	ENSG00000115350	POLE4	"DNA polymerase epsilon 4, accessory subunit"	0.373808	0.576856
1195.	ENSG00000179958	DCTPP1	dCTP pyrophosphatase 1	0.486552	0.575999
1196.	ENSG00000169570	DTWD2	DTW domain containing 2	0.732857	0.575587
1197.	ENSG00000172062	SMN1	"survival of motor neuron 1, telomeric"	0.581755	0.575289
1198.	ENSG00000239779	WBP1	WW domain binding protein 1	0.580605	0.575147
1199.	ENSG00000006831	ADIPOR2	adiponectin receptor 2	0.690701	0.574571
1200.	ENSG00000144713	RPL32	ribosomal protein L32	0.541315	0.574202
1201.	ENSG00000106268	NUDT1	nudix hydrolase 1	0.488716	0.574153
1202.	ENSG00000068383	INPP5A	inositol polyphosphate-5-phosphatase A	0.67894	0.574134
1203.	ENSG00000178035	IMPDH2	inosine monophosphate dehydrogenase 2	0.480604	0.573689
1204.	ENSG00000249264	EEF1A1P9	eukaryotic translation elongation factor 1 alpha 1 pseudogene 9	0.580221	0.572346
1205.	ENSG00000176273	SLC35G1	solute carrier family 35 member G1	0.497059	0.57222
1206.	ENSG00000067064	IDI1	isopentenyl-diphosphate delta isomerase 1	0.710248	0.57221
1207.	ENSG00000167085	PHB	prohibitin	0.558869	0.571996
1208.	ENSG00000198860	TSEN15	tRNA splicing endonuclease subunit 15	0.543937	0.571189
1209.	ENSG00000148334	PTGES2	prostaglandin E synthase 2	0.415851	0.570339
1210.	ENSG00000187626	ZKSCAN4	zinc finger with KRAB and SCAN domains 4	0.541057	0.569274
1211.	ENSG00000101182	PSMA7	proteasome subunit alpha 7	0.611977	0.569242
1212.	ENSG00000183283	DAZAP2	DAZ associated protein 2	0.572756	0.569066
1213.	ENSG00000091483	FH	fumarate hydratase	0.517003	0.568854
1214.	ENSG00000011052	NME1-NME2	NME1-NME2 readthrough	0.537902	0.568051
1215.	ENSG00000113460	BRIX1	"BRX1, biogenesis of ribosomes"	0.518963	0.56702
1216.	ENSG00000160298	C21orf58	chromosome 21 open reading frame 58	0.574076	0.566849
1217.	ENSG00000112306	RPS12	ribosomal protein S12	0.585658	0.565778
1218.	ENSG00000100764	PSMC1	"proteasome 26S subunit, ATPase 1"	0.568718	0.565683
1219.	ENSG00000136943	CTSV	cathepsin V	0.653027	0.565642
1220.	ENSG00000130935	NOL11	nucleolar protein 11	0.584325	0.564753
1221.	ENSG00000132423	COQ3	"coenzyme Q3, methyltransferase"	0.454187	0.564536
1222.	ENSG00000242616	GNG10	G protein subunit gamma 10	0.677874	0.564374
1223.	ENSG00000101444	AHCY	adenosylhomocysteinase	0.494678	0.563421
1224.	ENSG00000164904	ALDH7A1	aldehyde dehydrogenase 7 family member A1	0.711066	0.563229
1225.	ENSG00000162433	AK4	adenylate kinase 4	0.59315	0.563226
1226.	ENSG00000139343	SNRPF	small nuclear ribonucleoprotein polypeptide F	0.378183	0.562532
1227.	ENSG00000133119	RFC3	replication factor C subunit 3	0.585816	0.562186

1228.	ENSG00000113811	SELK	selenoprotein K	0.506295	0.561729
1229.	ENSG00000116120	FARSB	phenylalanyl-tRNA synthetase beta subunit	0.589758	0.56169
1230.	ENSG00000117592	PRDX6	peroxiredoxin 6	0.644178	0.561437
1231.	ENSG00000102967	DHODH	dihydroorotate dehydrogenase (quinone)	0.584332	0.561185
1232.	ENSG00000171960	PPIH	peptidylprolyl isomerase H	0.40786	0.56116
1233.	ENSG00000128039	SRD5A3	steroid 5 alpha-reductase 3	0.53407	0.56115
1234.	ENSG00000132950	ZMYM5	zinc finger MYM-type containing 5	0.458967	0.56089
1235.	ENSG00000110700	RPS13	ribosomal protein S13	0.506	0.560536
1236.	ENSG00000141101	NOB1	NIN1/PSMD8 binding protein 1 homolog	0.454083	0.560442
1237.	ENSG00000161970	RPL26	ribosomal protein L26	0.635677	0.560063
1238.	ENSG00000198830	HMGN2	high mobility group nucleosomal binding domain 2	0.431841	0.559308
1239.	ENSG00000169714	CNBP	CCHC-type zinc finger nucleic acid binding protein	0.47528	0.558615
1240.	ENSG00000138641	HERC3	HECT and RLD domain containing E3 ubiquitin protein ligase 3	0.458215	0.557969
1241.	ENSG00000198176	TFDP1	transcription factor Dp-1	0.598627	0.557178
1242.	ENSG00000188529	SRSF10	serine and arginine rich splicing factor 10	0.581423	0.557139
1243.	ENSG00000169174	PCSK9	proprotein convertase subtilisin/kexin type 9	0.536665	0.556471
1244.	ENSG00000158470	B4GALT5	"beta-1,4-galactosyltransferase 5"	0.648518	0.556421
1245.	ENSG00000147400	CETN2	centrin 2	0.67484	0.556184
1246.	ENSG00000141543	EIF4A3	eukaryotic translation initiation factor 4A3	0.444924	0.555671
1247.	ENSG00000104884	ERCC2	"ERCC excision repair 2, TFIIH core complex helicase subunit"	0.760713	0.555621
1248.	ENSG00000108298	RPL19	ribosomal protein L19	0.501585	0.555254
1249.	ENSG00000071082	RPL31	ribosomal protein L31	0.500837	0.553839
1250.	ENSG00000103035	PSMD7	"proteasome 26S subunit, non-ATPase 7"	0.485609	0.55362
1251.	ENSG00000100216	TOMM22	translocase of outer mitochondrial membrane 22	0.494304	0.551779
1252.	ENSG00000114520	SNX4	sorting nexin 4	0.537189	0.550717
1253.	ENSG00000100372	SLC25A17	solute carrier family 25 member 17	0.567036	0.550626
1254.	ENSG00000152147	GEMIN6	gem nuclear organelle associated protein 6	0.527315	0.549781
1255.	ENSG00000004142	POLDIP2	DNA polymerase delta interacting protein 2	0.545445	0.547899
1256.	ENSG00000143384	MCL1	BCL2 family apoptosis regulator	0.514158	0.547684
1257.	ENSG00000100442	FKBP3	FK506 binding protein 3	0.598451	0.547113
1258.	ENSG00000183207	RUVBL2	RuvB like AAA ATPase 2	0.370826	0.545808
1259.	ENSG00000126602	TRAP1	TNF receptor associated protein 1	0.620316	0.54511
1260.	ENSG00000138439	FAM117B	family with sequence similarity 117 member B	0.800434	0.544344
1261.	ENSG00000011258	MBTD1	mbt domain containing 1	0.65506	0.544341
1262.	ENSG00000119408	NEK6	NIMA related kinase 6	0.713992	0.544106
1263.	ENSG00000141429	GALNT1	polypeptide N-acetylgalactosaminyltransferase 1	0.673639	0.543714
1264.	ENSG00000174748	RPL15	ribosomal protein L15	0.477561	0.543018
1265.	ENSG00000165672	PRDX3	peroxiredoxin 3	0.627377	0.542784
1266.	ENSG00000149196	HIKESHI	"Hikeshi, heat shock protein nuclear import factor"	0.467457	0.541752
1267.	ENSG00000018699	TTC27	tetratricopeptide repeat domain 27	0.506052	0.541612
1268.	ENSG00000223768	LINC00205	long intergenic non-protein coding RNA 205	0.510607	0.541599
1269.	ENSG00000162694	EXTL2	exostosin like glycosyltransferase 2	0.709238	0.541277
1270.	ENSG00000072062	PRKACA	protein kinase cAMP-activated catalytic subunit alpha	0.628271	0.54078
1271.	ENSG00000162063	CCNF	cyclin F	0.4926	0.539965
1272.	ENSG00000135373	EHF	ETS homologous factor	0.793912	0.539603
1273.	ENSG00000151287	TEX30	testis expressed 30	0.591534	0.539069
1274.	ENSG00000120526	NUDCD1	NudC domain containing 1	0.605891	0.538786
1275.	ENSG00000139684	ESD	esterase D	0.528035	0.538701
1276.	ENSG00000151465	CDC123	cell division cycle 123	0.579892	0.537706
1277.	ENSG00000157978	LDLRAP1	low density lipoprotein receptor adaptor protein 1	0.541318	0.537152
1278.	ENSG00000140612	SEC11A	"SEC11 homolog A, signal peptidase complex subunit"	0.489579	0.537134
1279.	ENSG00000108468	CBX1	chromobox 1	0.608134	0.536891
1280.	ENSG00000164253	WDR41	WD repeat domain 41	0.607608	0.536312
1281.	ENSG00000143314	MRPL24	mitochondrial ribosomal protein L24	0.506235	0.53577
1282.	ENSG00000205981	DNAJC19	DnaJ heat shock protein family (Hsp40) member C19	0.487561	0.535434
1283.	ENSG00000142657	PGD	phosphogluconate dehydrogenase	0.551699	0.534879
1284.	ENSG00000163832	ELP6	elongator acetyltransferase complex subunit 6	0.412246	0.534597
1285.	ENSG00000166851	PLK1	polo like kinase 1	0.502805	0.534145
1286.	ENSG00000100294	MCAT	malonyl-CoA-acyl carrier protein transacylase	0.383907	0.533893
1287.	ENSG00000171202	TMEM126A	transmembrane protein 126A	0.457839	0.533496
1288.	ENSG00000008988	RPS20	ribosomal protein S20	0.495754	0.533154
1289.	ENSG00000155858	LSM11	"LSM11, U7 small nuclear RNA associated"	0.573773	0.53311
1290.	ENSG00000106803	SEC61B	Sec61 translocon beta subunit	0.380985	0.532805
1291.	ENSG00000092010	PSME1	proteasome activator subunit 1	0.489988	0.532391

1292.	ENSG00000023572	GLRX2	glutaredoxin 2	0.493896	0.530772
1293.	ENSG00000138028	CGREF1	cell growth regulator with EF-hand domain 1	0.532261	0.530638
1294.	ENSG00000108947	EFNB3	ephrin B3	0.713137	0.530624
1295.	ENSG00000164919	COX6C	cytochrome c oxidase subunit 6C	0.473092	0.529371
1296.	ENSG00000115944	COX7A2L	cytochrome c oxidase subunit 7A2 like	0.583686	0.527884
1297.	ENSG00000100504	PYGL	"phosphorylase, glycogen, liver"	0.598803	0.527726
1298.	ENSG00000091651	ORC6	origin recognition complex subunit 6	0.500223	0.527708
1299.	ENSG00000140374	ETFA	electron transfer flavoprotein alpha subunit	0.591116	0.527411
1300.	ENSG00000135624	CCT7	chaperonin containing TCP1 subunit 7	0.61167	0.525603
1301.	ENSG00000101400	SNTA1	syntrophin alpha 1	0.470681	0.524896
1302.	ENSG00000186660	ZFP91	ZFP91 zinc finger protein	0.636921	0.52485
1303.	ENSG00000102178	UBL4A	ubiquitin like 4A	0.412535	0.524187
1304.	ENSG00000164091	WDR82	WD repeat domain 82	0.498426	0.52336
1305.	ENSG00000138175	ARL3	ADP ribosylation factor like GTPase 3	0.606915	0.522059
1306.	ENSG00000224531	SMIM13	small integral membrane protein 13	0.483039	0.520542
1307.	ENSG00000082515	MRPL22	mitochondrial ribosomal protein L22	0.41355	0.520083
1308.	ENSG00000197977	ELOVL2	ELOVL fatty acid elongase 2	0.649693	0.519209
1309.	ENSG00000168795	ZBTB5	zinc finger and BTB domain containing 5	0.434602	0.518307
1310.	ENSG00000163528	CHCHD4	coiled-coil-helix-coiled-coil-helix domain containing 4	0.454512	0.51827
1311.	ENSG00000139180	NDUFA9	NADH:ubiquinone oxidoreductase subunit A9	0.482408	0.51758
1312.	ENSG00000116288	PARK7	Parkinsonism associated deglycase	0.541766	0.515431
1313.	ENSG00000183077	AFMID	arylformamidase	0.518471	0.514579
1314.	ENSG00000130560	UBAC1	UBA domain containing 1	0.517836	0.514537
1315.	ENSG00000107262	BAG1	BCL2 associated athanogene 1	0.383929	0.514251
1316.	ENSG00000156482	RPL30	ribosomal protein L30	0.483029	0.514125
1317.	ENSG00000060762	MPC1	mitochondrial pyruvate carrier 1	0.595465	0.512531
1318.	ENSG00000135446	CDK4	cyclin dependent kinase 4	0.466874	0.512105
1319.	ENSG00000171314	PGAM1	phosphoglycerate mutase 1	0.452985	0.512096
1320.	ENSG00000143742	SRP9	signal recognition particle 9	0.611286	0.511968
1321.	ENSG00000113845	TIMMDC1	translocase of inner mitochondrial membrane domain containing 1	0.470364	0.511371
1322.	ENSG00000168701	TMEM208	transmembrane protein 208	0.434963	0.511256
1323.	ENSG00000141759	TXNL4A	thioredoxin like 4A	0.436729	0.51071
1324.	ENSG00000124767	GLO1	glyoxalase I	0.596599	0.510487
1325.	ENSG00000065978	YBX1	Y-box binding protein 1	0.608175	0.510208
1326.	ENSG00000101190	TCFL5	transcription factor like 5	0.531116	0.509004
1327.	ENSG00000171490	RSL1D1	ribosomal L1 domain containing 1	0.599977	0.50853
1328.	ENSG00000176788	BASP1	brain abundant membrane attached signal protein 1	0.483084	0.508448
1329.	ENSG00000132541	RIDA	reactive intermediate imine deaminase A homolog	0.692374	0.508209
1330.	ENSG00000112699	GMDS	"GDP-mannose 4,6-dehydratase"	0.567183	0.508126
1331.	ENSG00000014641	MDH1	malate dehydrogenase 1	0.483648	0.507619
1332.	ENSG00000159377	PSMB4	proteasome subunit beta 4	0.447662	0.505157
1333.	ENSG00000197006	METTL9	methyltransferase like 9	0.619183	0.505024
1334.	ENSG00000127184	COX7C	cytochrome c oxidase subunit 7C	0.420544	0.504002
1335.	ENSG00000178741	COX5A	cytochrome c oxidase subunit 5A	0.440628	0.503475
1336.	ENSG00000115368	WDR75	WD repeat domain 75	0.497876	0.500219
1337.	ENSG00000089220	PEBP1	phosphatidylethanolamine binding protein 1	0.5634	0.499523
1338.	ENSG00000101935	AMMECR1	"Alport syndrome, mental retardation, midface hypoplasia and elliptocytosis chromosomal region gene 1"	0.486683	0.499441
1339.	ENSG00000118600	TMEM5	transmembrane protein 5	0.426584	0.498614
1340.	ENSG00000196363	WDR5	WD repeat domain 5	0.458789	0.498514
1341.	ENSG00000171155	C1GALT1C1	C1GALT1 specific chaperone 1	0.504905	0.496875
1342.	ENSG00000142534	RPS11	ribosomal protein S11	0.516476	0.496856
1343.	ENSG00000188342	GTF2F2	general transcription factor IIF subunit 2	0.413409	0.496262
1344.	ENSG00000176244	ACBD7	acyl-CoA binding domain containing 7	0.700393	0.496153
1345.	ENSG00000103502	CDIPT	CDP-diacylglycerol--inositol 3-phosphatidyltransferase	0.50783	0.492623
1346.	ENSG00000167977	KCTD5	potassium channel tetramerization domain containing 5	0.425124	0.492212
1347.	ENSG00000123349	PFDN5	prefoldin subunit 5	0.546246	0.491788
1348.	ENSG00000137106	GRHPR	glyoxylate and hydroxypyruvate reductase	0.445495	0.490305
1349.	ENSG00000158089	GALNT14	polypeptide N-acetylgalactosaminyltransferase 14	0.608762	0.488799
1350.	ENSG00000134291	TMEM106C	transmembrane protein 106C	0.585347	0.488068
1351.	ENSG00000136574	GATA4	GATA binding protein 4	0.816668	0.487858
1352.	ENSG00000145741	BTF3	basic transcription factor 3	0.506364	0.487342
1353.	ENSG00000103429	BFAR	bifunctional apoptosis regulator	0.519609	0.486401
1354.	ENSG00000160014	CALM3	calmodulin 3	0.570431	0.485807

1355.	ENSG00000127955	GNAI1	G protein subunit alpha i1	0.590945	0.485692
1356.	ENSG00000100784	RPS6KA5	ribosomal protein S6 kinase A5	0.591567	0.484197
1357.	ENSG00000148303	RPL7A	ribosomal protein L7a	0.525127	0.483312
1358.	ENSG00000100558	PLEK2	pleckstrin 2	0.612746	0.482887
1359.	ENSG00000161016	RPL8	ribosomal protein L8	0.447702	0.482796
1360.	ENSG00000115365	LANCL1	LanC like 1	0.596777	0.482519
1361.	ENSG00000133773	CCDC59	coiled-coil domain containing 59	0.410004	0.482381
1362.	ENSG00000125863	MKKS	McKusick-Kaufman syndrome	0.509373	0.481629
1363.	ENSG00000164815	ORC5	origin recognition complex subunit 5	0.451018	0.481556
1364.	ENSG00000145050	MANF	mesencephalic astrocyte derived neurotrophic factor	0.454652	0.481426
1365.	ENSG00000136158	SPRY2	sprouty RTK signaling antagonist 2	0.550961	0.481338
1366.	ENSG00000140391	TSPAN3	tetraspanin 3	0.452084	0.480864
1367.	ENSG00000128050	PAICS	phosphoribosylaminoimidazole carboxylase; phosphoribosylaminoimidazolesuccinocarboxamide synthase	0.627836	0.480478
1368.	ENSG00000170632	ARMC10	armadillo repeat containing 10	0.678404	0.480358
1369.	ENSG00000181610	MRPS23	mitochondrial ribosomal protein S23	0.403958	0.480255
1370.	ENSG00000178988	MRFAP1L1	Morf4 family associated protein 1 like 1	0.361048	0.479952
1371.	ENSG00000228409	CCT6P1	chaperonin containing TCP1 subunit 6 pseudogene 1	0.440193	0.479515
1372.	ENSG00000079785	DDX1	DEAD/H-box helicase 1	0.493408	0.479488
1373.	ENSG00000112081	SRSF3	serine and arginine rich splicing factor 3	0.459896	0.479402
1374.	ENSG00000065621	GSTO2	glutathione S-transferase omega 2	0.4087	0.479226
1375.	ENSG00000136682	CBWD2	COBW domain containing 2	0.552169	0.479109
1376.	ENSG00000026297	RNASET2	ribonuclease T2	0.439969	0.479086
1377.	ENSG00000103876	FAH	fumarylacetoacetate hydrolase	0.553601	0.478695
1378.	ENSG00000166295	ANAPC16	anaphase promoting complex subunit 16	0.486764	0.477979
1379.	ENSG00000124787	RPP40	ribonuclease P/MRP subunit p40	0.442086	0.477138
1380.	ENSG00000245694	CRNDE	colorectal neoplasia differentially expressed (non-protein coding)	0.437687	0.476426
1381.	ENSG00000180389	ATP5EP2	"ATP synthase, H+ transporting, mitochondrial F1 complex, epsilon subunit pseudogene 2"	1.06228	0.475944
1382.	ENSG00000129518	EAPP	E2F associated phosphoprotein	0.426617	0.475068
1383.	ENSG00000138777	PPA2	pyrophosphatase (inorganic) 2	0.417186	0.475001
1384.	ENSG00000055044	NOP58	NOP58 ribonucleoprotein	0.57573	0.474755
1385.	ENSG00000147604	RPL7	ribosomal protein L7	0.540895	0.474478
1386.	ENSG00000074800	ENO1	enolase 1	0.546022	0.474453
1387.	ENSG00000169230	PRELID1	PRELI domain containing 1	0.526265	0.474331
1388.	ENSG00000204628	RACK1	receptor for activated C kinase 1	0.479845	0.474264
1389.	ENSG00000159593	NAE1	NEDD8 activating enzyme E1 subunit 1	0.493453	0.473918
1390.	ENSG00000086061	DNAJA1	DnaJ heat shock protein family (Hsp40) member A1	0.475614	0.472945
1391.	ENSG00000161904	LEMD2	LEM domain containing 2	0.483313	0.472819
1392.	ENSG00000159055	MIS18A	MIS18 kinetochore protein A	0.390648	0.472706
1393.	ENSG00000119718	EIF2B2	eukaryotic translation initiation factor 2B subunit beta	0.438912	0.472013
1394.	ENSG00000198356	ASNA1	"arsA arsenite transporter, ATP-binding, homolog 1 (bacterial)"	0.380803	0.471845
1395.	ENSG00000119778	ATAD2B	"ATPase family, AAA domain containing 2B"	0.623753	0.47118
1396.	ENSG00000049541	RFC2	replication factor C subunit 2	0.554049	0.470145
1397.	ENSG00000115484	CCT4	chaperonin containing TCP1 subunit 4	0.507679	0.468577
1398.	ENSG00000169241	SLC50A1	solute carrier family 50 member 1	0.490646	0.467501
1399.	ENSG00000161960	EIF4A1	eukaryotic translation initiation factor 4A1	0.506091	0.467426
1400.	ENSG00000196154	S100A4	S100 calcium binding protein A4	0.677395	0.465981
1401.	ENSG00000172172	MRPL13	mitochondrial ribosomal protein L13	0.515309	0.464846
1402.	ENSG00000182054	IDH2	"isocitrate dehydrogenase (NADP(+)) 2, mitochondrial"	0.358842	0.464326
1403.	ENSG00000163017	ACTG2	"actin, gamma 2, smooth muscle, enteric"	0.411173	0.462855
1404.	ENSG00000147180	ZNF711	zinc finger protein 711	0.597437	0.462778
1405.	ENSG00000124535	WRNIP1	Werner helicase interacting protein 1	0.463639	0.461986
1406.	ENSG00000153989	NUS1	NUS1 dehydrodolichyl diphosphate synthase subunit	0.588642	0.461185
1407.	ENSG00000189334	S100A14	S100 calcium binding protein A14	0.526757	0.460932
1408.	ENSG00000228474	OST4	"oligosaccharyltransferase complex subunit 4, non-catalytic"	0.446121	0.460205
1409.	ENSG00000163541	SUCLG1	succinate-CoA ligase alpha subunit	0.393309	0.459611
1410.	ENSG00000090263	MRPS33	mitochondrial ribosomal protein S33	0.401031	0.459406
1411.	ENSG00000139826	ABHD13	abhydrolase domain containing 13	0.488825	0.459061
1412.	ENSG00000089053	ANAPC5	anaphase promoting complex subunit 5	0.562191	0.456977
1413.	ENSG00000073712	FERMT2	fermitin family member 2	0.511322	0.456936
1414.	ENSG00000156261	CCT8	chaperonin containing TCP1 subunit 8	0.516095	0.456799

1415.	ENSG00000112062	MAPK14	mitogen-activated protein kinase 14	0.578104	0.456541
1416.	ENSG00000124098	FAM210B	family with sequence similarity 210 member B	0.494677	0.455537
1417.	ENSG00000165775	FUNDC2	FUN14 domain containing 2	0.465033	0.455508
1418.	ENSG00000139800	ZIC5	Zic family member 5	0.519752	0.454947
1419.	ENSG00000177954	RPS27	ribosomal protein S27	0.508871	0.454789
1420.	ENSG00000008018	PSMB1	proteasome subunit beta 1	0.365698	0.454699
1421.	ENSG00000105248	CCDC94	coiled-coil domain containing 94	0.459384	0.454246
1422.	ENSG00000101391	CDK5RAP1	CDK5 regulatory subunit associated protein 1	0.421749	0.452614
1423.	ENSG00000168118	RAB4A	"RAB4A, member RAS oncogene family"	0.553993	0.451898
1424.	ENSG00000001497	LAS1L	"LAS1 like, ribosome biogenesis factor"	0.473209	0.451075
1425.	ENSG00000178952	TUFM	"Tu translation elongation factor, mitochondrial"	0.445132	0.450125
1426.	ENSG00000144746	ARL6IP5	ADP ribosylation factor like GTPase 6 interacting protein 5	0.510344	0.450079
1427.	ENSG00000168710	AHCYL1	adenosylhomocysteinase like 1	0.599927	0.449753
1428.	ENSG00000198258	UBL5	ubiquitin like 5	0.372425	0.448646
1429.	ENSG00000112592	TBP	TATA-box binding protein	0.439215	0.44549
1430.	ENSG00000174669	SLC29A2	solute carrier family 29 member 2	0.357566	0.444176
1431.	ENSG00000104723	TUSC3	tumor suppressor candidate 3	0.476439	0.443338
1432.	ENSG00000146733	PSPH	phosphoserine phosphatase	0.415752	0.442755
1433.	ENSG00000101347	SAMHD1	SAM and HD domain containing deoxynucleoside triphosphate triphosphohydrolase 1	0.422929	0.441313
1434.	ENSG00000182890	GLUD2	glutamate dehydrogenase 2	0.54971	0.439276
1435.	ENSG00000044574	HSPA5	heat shock protein family A (Hsp70) member 5	0.461655	0.437272
1436.	ENSG00000072506	HSD17B10	hydroxysteroid 17-beta dehydrogenase 10	0.404017	0.437113
1437.	ENSG00000065154	OAT	ornithine aminotransferase	0.61619	0.435381
1438.	ENSG00000165943	MOAP1	modulator of apoptosis 1	0.358154	0.435341
1439.	ENSG00000111802	TDP2	tyrosyl-DNA phosphodiesterase 2	0.488266	0.43491
1440.	ENSG00000112078	KCTD20	potassium channel tetramerization domain containing 20	0.59754	0.434534
1441.	ENSG00000127884	ECHS1	"enoyl-CoA hydratase, short chain 1"	0.423954	0.434189
1442.	ENSG00000154582	TCEB1	transcription elongation factor B subunit 1	0.384157	0.433829
1443.	ENSG00000133112	TPT1	"tumor protein, translationally-controlled 1"	0.512395	0.431892
1444.	ENSG00000196262	PPIA	peptidylprolyl isomerase A	0.404212	0.429638
1445.	ENSG00000179399	GPC5	glypican 5	0.529826	0.4271
1446.	ENSG00000188211	NCR3LG1	natural killer cell cytotoxicity receptor 3 ligand 1	0.504336	0.427074
1447.	ENSG00000139990	DCAF5	DDB1 and CUL4 associated factor 5	0.49886	0.426772
1448.	ENSG00000131778	CHD1L	chromodomain helicase DNA binding protein 1 like	0.459906	0.425305
1449.	ENSG00000104047	DTWD1	DTW domain containing 1	0.501435	0.424841
1450.	ENSG00000132963	POMP	proteasome maturation protein	0.398388	0.424103
1451.	ENSG00000129562	DAD1	defender against cell death 1	0.483024	0.423811
1452.	ENSG00000092199	HNRNPC	heterogeneous nuclear ribonucleoprotein C (C1/C2)	0.47602	0.42311
1453.	ENSG00000117118	SDHB	succinate dehydrogenase complex iron sulfur subunit B	0.436855	0.422219
1454.	ENSG00000143870	PDIA6	protein disulfide isomerase family A member 6	0.540674	0.422012
1455.	ENSG00000146433	TMEM181	transmembrane protein 181	0.528742	0.421469
1456.	ENSG00000197771	MCMBP	minichromosome maintenance complex binding protein	0.539588	0.420955
1457.	ENSG00000108384	RAD51C	RAD51 paralog C	0.445142	0.420747
1458.	ENSG00000120696	KBTBD7	kelch repeat and BTB domain containing 7	0.400185	0.420395
1459.	ENSG00000148834	GSTO1	glutathione S-transferase omega 1	0.382099	0.419248
1460.	ENSG00000173145	NOC3L	NOC3 like DNA replication regulator	0.463655	0.418221
1461.	ENSG00000154978	VOPP1	"vesicular, overexpressed in cancer, prosurvival protein 1"	0.46844	0.41793
1462.	ENSG00000175691	ZNF77	zinc finger protein 77	0.396748	0.416536
1463.	ENSG00000128463	EMC4	ER membrane protein complex subunit 4	0.519872	0.416206
1464.	ENSG00000164930	FZD6	frizzled class receptor 6	0.513988	0.416162
1465.	ENSG00000129103	SUMF2	sulfatase modifying factor 2	0.425012	0.415504
1466.	ENSG00000058804	NDC1	NDC1 transmembrane nucleoporin	0.581386	0.415238
1467.	ENSG00000152234	ATP5A1	"ATP synthase, H+ transporting, mitochondrial F1 complex, alpha subunit 1, cardiac muscle"	0.424851	0.412725
1468.	ENSG00000182768	NGRN	"neugrin, neurite outgrowth associated"	0.449335	0.411608
1469.	ENSG00000115234	SNX17	sorting nexin 17	0.352968	0.410153
1470.	ENSG00000074219	TEAD2	TEA domain transcription factor 2	0.477682	0.408097
1471.	ENSG00000148019	CEP78	centrosomal protein 78	0.579872	0.407027
1472.	ENSG00000124570	SERPINB6	serpin family B member 6	0.400069	0.406089
1473.	ENSG00000107874	CUEDC2	CUE domain containing 2	0.421961	0.40473
1474.	ENSG00000156709	AIFM1	"apoptosis inducing factor, mitochondria associated 1"	0.517603	0.400808
1475.	ENSG00000173281	PPP1R3B	protein phosphatase 1 regulatory subunit 3B	0.433307	0.398739

1476.	ENSG00000122042	UBL3	ubiquitin like 3	0.578444	0.397981
1477.	ENSG00000135845	PIGC	phosphatidylinositol glycan anchor biosynthesis class C	0.41005	0.397585
1478.	ENSG00000131370	SH3BP5	SH3 domain binding protein 5	0.463129	0.394409
1479.	ENSG00000181751	C5orf30	chromosome 5 open reading frame 30	0.465594	0.3944
1480.	ENSG00000254772	EEF1G	eukaryotic translation elongation factor 1 gamma	0.50351	0.394335
1481.	ENSG00000141698	NT5C3B	"5'-nucleotidase, cytosolic IIIB"	0.390653	0.394116
1482.	ENSG00000140259	MFAP1	microfibrillar associated protein 1	0.40971	0.392112
1483.	ENSG00000187514	PTMA	"prothymosin, alpha"	0.472511	0.39151
1484.	ENSG00000163902	RPN1	ribophorin I	0.436504	0.390911
1485.	ENSG00000164332	UBLCP1	ubiquitin like domain containing CTD phosphatase 1	0.457536	0.390483
1486.	ENSG00000115241	PPM1G	"protein phosphatase, Mg2+/Mn2+ dependent 1G"	0.421925	0.389986
1487.	ENSG00000170185	USP38	ubiquitin specific peptidase 38	0.48234	0.389678
1488.	ENSG00000100271	TTLL1	tubulin tyrosine ligase like 1	0.686081	0.387382
1489.	ENSG00000134716	CYP2J2	cytochrome P450 family 2 subfamily J member 2	0.405508	0.386161
1490.	ENSG00000136156	ITM2B	integral membrane protein 2B	0.455403	0.385767
1491.	ENSG00000164626	KCNK5	potassium two pore domain channel subfamily K member 5	0.424791	0.385622
1492.	ENSG00000116679	IVNS1ABP	influenza virus NS1A binding protein	0.500592	0.379788
1493.	ENSG00000175785	PRIMA1	proline rich membrane anchor 1	0.382483	0.378951
1494.	ENSG00000101544	ADNP2	ADNP homeobox 2	0.389951	0.375037
1495.	ENSG00000160124	CCDC58	coiled-coil domain containing 58	0.382227	0.374341
1496.	ENSG00000196584	XRCC2	X-ray repair cross complementing 2	0.497408	0.37365
1497.	ENSG00000196659	TTC30B	tetratricopeptide repeat domain 30B	0.431373	0.372918
1498.	ENSG00000081870	HSPB11	heat shock protein family B (small) member 11	0.468481	0.371903
1499.	ENSG00000084623	EIF3I	eukaryotic translation initiation factor 3 subunit I	0.502812	0.370749
1500.	ENSG00000188021	UBQLN2	ubiquilin 2	0.454439	0.36814
1501.	ENSG00000125821	DTD1	D-tyrosyl-tRNA deacylase 1	0.439774	0.362775
1502.	ENSG00000016391	CHDH	choline dehydrogenase	0.460734	0.362754
1503.	ENSG00000137054	POLR1E	RNA polymerase I subunit E	0.416051	0.360962
1504.	ENSG00000147669	POLR2K	RNA polymerase II subunit K	0.36188	0.359019
1505.	ENSG00000163428	LRRC58	leucine rich repeat containing 58	0.529406	0.357706
1506.	ENSG00000095002	MSH2	mutS homolog 2	0.453754	0.355227
1507.	ENSG00000087302	C14orf166	chromosome 14 open reading frame 166	0.363788	0.346326
1508.	ENSG00000115128	SF3B6	splicing factor 3b subunit 6	0.369752	0.345683

Supplementary Table 3C: miR-29a unique targets in LCC9 cells

				LCC9 Pre-miR-29a vs Anti-miR-29a
	Input IDs	**Gene Symbol**	**Gene Name**	**$\log_2$(fold change)**
1.	ENSG00000089127	OAS1	2'-5'-oligoadenylate synthetase 1	1.00467
2.	ENSG00000174137	FAM53A	family with sequence similarity 53 member A	0.857463
3.	ENSG00000183513	COA5	cytochrome c oxidase assembly factor 5	0.542847
4.	ENSG00000119688	ABCD4	ATP binding cassette subfamily D member 4	0.487976
5.	ENSG00000118777	ABCG2	ATP binding cassette subfamily G member 2 (Junior blood group)	1.55682
6.	ENSG00000162482	AKR7A3	aldo-keto reductase family 7 member A3	0.843423
7.	ENSG00000137124	ALDH1B1	aldehyde dehydrogenase 1 family member B1	0.441378
8.	ENSG00000119523	ALG2	"ALG2, alpha-1,3/1,6-mannosyltransferase"	0.343699
9.	ENSG00000176248	ANAPC2	anaphase promoting complex subunit 2	0.69434
10.	ENSG00000213337	ANKRD39	ankyrin repeat domain 39	0.790548
11.	ENSG00000186106	ANKRD46	ankyrin repeat domain 46	0.550979
12.	ENSG00000214293	APTR	Alu-mediated CDKN1A/p21 transcriptional regulator (non-protein coding)	0.407018
13.	ENSG00000102030	NAA10	"N(alpha)-acetyltransferase 10, NatA catalytic subunit"	0.547257
14.	ENSG00000182196	ARL6IP4	ADP ribosylation factor like GTPase 6 interacting protein 4	0.631648
15.	ENSG00000136950	ARPC5L	actin related protein 2/3 complex subunit 5 like	0.352874
16.	ENSG00000126756	UXT	ubiquitously expressed prefoldin like chaperone	0.423882
17.	ENSG00000130768	SMPDL3B	sphingomyelin phosphodiesterase acid like 3B	0.508441
18.	ENSG00000128272	ATF4	activating transcription factor 4	0.456274
19.	ENSG00000152234	ATP5A1	"ATP synthase, H+ transporting, mitochondrial F1 complex, alpha subunit 1, cardiac muscle"	0.412725
20.	ENSG00000110955	ATP5B	"ATP synthase, H+ transporting, mitochondrial F1 complex, beta polypeptide"	0.734603
21.	ENSG00000099624	ATP5D	"ATP synthase, H+ transporting, mitochondrial F1 complex, delta subunit"	0.575794
22.	ENSG00000124172	ATP5E	"ATP synthase, H+ transporting, mitochondrial F1 complex, epsilon subunit"	0.60387
23.	ENSG00000165629	ATP5C1	"ATP synthase, H+ transporting, mitochondrial F1 complex, gamma polypeptide 1"	1.34628
24.	ENSG00000128524	ATP6V1F	ATPase H+ transporting V1 subunit F	0.541429
25.	ENSG00000130770	ATPIF1	ATPase inhibitory factor 1	0.792053
26.	ENSG00000148090	AUH	AU RNA binding methylglutaconyl-CoA hydratase	0.583462
27.	ENSG00000198563	DDX39B	DEAD-box helicase 39B	0.506986
28.	ENSG00000054116	TRAPPC3	trafficking protein particle complex 3	0.455165
29.	ENSG00000163170	BOLA3	bolA family member 3	0.453897
30.	ENSG00000130303	BST2	bone marrow stromal cell antigen 2	0.503736
31.	ENSG00000078401	EDN1	endothelin 1	0.605404
32.	ENSG00000100290	BIK	BCL2 interacting killer	0.434716
33.	ENSG00000165233	CARD19	caspase recruitment domain family member 19	0.680634
34.	ENSG00000112578	BYSL	bystin like	0.470095
35.	ENSG00000111678	C12orf57	chromosome 12 open reading frame 57	0.421145
36.	ENSG00000171224	C10orf35	chromosome 10 open reading frame 35	0.354218
37.	ENSG00000171067	C11orf24	chromosome 11 open reading frame 24	0.643369
38.	ENSG00000139438	FAM222A	family with sequence similarity 222 member A	0.560663
39.	ENSG00000151131	C12orf45	chromosome 12 open reading frame 45	0.721034
40.	ENSG00000129480	DTD2	D-tyrosyl-tRNA deacylase 2 (putative)	0.712165
41.	ENSG00000134153	EMC7	ER membrane protein complex subunit 7	0.399016
42.	ENSG00000130731	METTL26	methyltransferase like 26	0.411608
43.	ENSG00000124074	ENKD1	enkurin domain containing 1	1.20299
44.	ENSG00000182831	C16orf72	chromosome 16 open reading frame 72	0.518243
45.	ENSG00000175643	RMI2	RecQ mediated genome instability 2	0.359454
46.	ENSG00000074842	MYDGF	myeloid derived growth factor	0.462685
47.	ENSG00000197223	C1D	C1D nuclear receptor corepressor	0.440034
48.	ENSG00000057757	PITHD1	PITH domain containing 1	0.387639
49.	ENSG00000198912	C1orf174	chromosome 1 open reading frame 174	0.358429
50.	ENSG00000163866	SMIM12	small integral membrane protein 12	0.503397

51.	ENSG00000168275	COA6	cytochrome c oxidase assembly factor 6	0.436718
52.	ENSG00000203724	C1orf53	chromosome 1 open reading frame 53	0.567423
53.	ENSG00000162757	C1orf74	chromosome 1 open reading frame 74	0.715414
54.	ENSG00000116205	TCEANC2	transcription elongation factor A N-terminal and central domain containing 2	0.580425
55.	ENSG00000101220	C20orf27	chromosome 20 open reading frame 27	0.377463
56.	ENSG00000228314	CYP4F29P	"cytochrome P450 family 4 subfamily F member 29, pseudogene"	0.676683
57.	ENSG00000159079	C21orf59	chromosome 21 open reading frame 59	0.777816
58.	ENSG00000160256	FAM207A	family with sequence similarity 207 member A	0.405904
59.	ENSG00000250486	FAM218A	family with sequence similarity 218 member A	0.541897
60.	ENSG00000243449	C4orf48	chromosome 4 open reading frame 48	0.518415
61.	ENSG00000134830	C5AR2	complement component 5a receptor 2	0.41513
62.	ENSG00000151881	TMEM267	transmembrane protein 267	0.504625
63.	ENSG00000124541	RRP36	ribosomal RNA processing 36	0.454369
64.	ENSG00000204387	C6orf48	chromosome 6 open reading frame 48	0.389673
65.	ENSG00000232956	SNHG15	small nucleolar RNA host gene 15	0.773507
66.	ENSG00000146540	C7orf50	chromosome 7 open reading frame 50	0.642142
67.	ENSG00000188186	LAMTOR4	"late endosomal/lysosomal adaptor, MAPK and MTOR activator 4"	0.414919
68.	ENSG00000130193	THEM6	thioesterase superfamily member 6	0.420549
69.	ENSG00000148362	C9orf142	chromosome 9 open reading frame 142	0.387802
70.	ENSG00000163050	COQ8A	coenzyme Q8A	0.690812
71.	ENSG00000007080	CCDC124	coiled-coil domain containing 124	0.361384
72.	ENSG00000221978	CCNL2	cyclin L2	0.472603
73.	ENSG00000156345	CDK20	cyclin dependent kinase 20	0.448019
74.	ENSG00000184990	SIVA1	SIVA1 apoptosis inducing factor	0.601179
75.	ENSG00000123374	CDK2	cyclin dependent kinase 2	0.562828
76.	ENSG00000125817	CENPB	centromere protein B	0.337413
77.	ENSG00000100162	CENPM	centromere protein M	0.370338
78.	ENSG00000179604	CDC42EP4	CDC42 effector protein 4	0.416077
79.	ENSG00000166595	FAM96B	family with sequence similarity 96 member B	0.373062
80.	ENSG00000159685	CHCHD6	coiled-coil-helix-coiled-coil-helix domain containing 6	0.469047
81.	ENSG00000179271	GADD45GIP1	GADD45G interacting protein 1	0.427637
82.	ENSG00000122705	CLTA	clathrin light chain A	0.385781
83.	ENSG00000143771	CNIH4	cornichon family AMPA receptor auxiliary protein 4	0.421596
84.	ENSG00000188986	NELFB	negative elongation factor complex member B	0.363338
85.	ENSG00000135775	COG2	component of oligomeric golgi complex 2	0.403504
86.	ENSG00000170619	COMMD5	COMM domain containing 5	0.655131
87.	ENSG00000168090	COPS6	COP9 signalosome subunit 6	0.443229
88.	ENSG00000088682	COQ9	coenzyme Q9	0.821226
89.	ENSG00000131143	COX4I1	cytochrome c oxidase subunit 4I1	0.448878
90.	ENSG00000176340	COX8A	cytochrome c oxidase subunit 8A	0.517129
91.	ENSG00000112695	COX7A2	cytochrome c oxidase subunit 7A2	0.459814
92.	ENSG00000111775	COX6A1	cytochrome c oxidase subunit 6A1	0.508716
93.	ENSG00000135940	COX5B	cytochrome c oxidase subunit 5B	0.46617
94.	ENSG00000184164	CRELD2	cysteine rich with EGF like domains 2	0.52218
95.	ENSG00000233382	NKAPP1	NFKB activating protein pseudogene 1	1.42496
96.	ENSG00000179091	CYC1	cytochrome c1	0.397388
97.	ENSG00000140465	CYP1A1	cytochrome P450 family 1 subfamily A member 1	0.685945
98.	ENSG00000058404	CAMK2B	calcium/calmodulin dependent protein kinase II beta	0.714147
99.	ENSG00000004948	CALCR	calcitonin receptor	0.620437
100.	ENSG00000186222	BLOC1S4	biogenesis of lysosomal organelles complex 1 subunit 4	0.568415
101.	ENSG00000144021	CIAO1	cytosolic iron-sulfur assembly component 1	0.377027
102.	ENSG00000165215	CLDN3	claudin 3	0.476786
103.	ENSG00000181885	CLDN7	claudin 7	0.720218
104.	ENSG00000125656	CLPP	caseinolytic mitochondrial matrix peptidase proteolytic subunit	0.398841
105.	ENSG00000178531	CTXN1	cortexin 1	1.41001
106.	ENSG00000157456	CCNB2	cyclin B2	0.37596
107.	ENSG00000134480	CCNH	cyclin H	0.775269
108.	ENSG00000110104	CCDC86	coiled-coil domain containing 86	0.387673
109.	ENSG00000084072	PPIE	peptidylprolyl isomerase E	0.422785

110.	ENSG00000142871	CYR61	cysteine rich angiogenic inducer 61	0.4951
111.	ENSG00000184752	NDUFA12	NADH:ubiquinone oxidoreductase subunit A12	0.464626
112.	ENSG00000167969	ECI1	enoyl-CoA delta isomerase 1	0.525164
113.	ENSG00000137100	DCTN3	dynactin subunit 3	0.470114
114.	ENSG00000099977	DDT	D-dopachrome tautomerase	0.569309
115.	ENSG00000123136	DDX39A	DEAD-box helicase 39A	0.373273
116.	ENSG00000136271	DDX56	DEAD-box helicase 56	0.619725
117.	ENSG00000143753	DEGS1	"delta 4-desaturase, sphingolipid 1"	0.50347
118.	ENSG00000128185	DGCR6L	DiGeorge syndrome critical region gene 6-like	0.559326
119.	ENSG00000114956	DGUOK	deoxyguanosine kinase	0.398229
120.	ENSG00000104808	DHDH	dihydrodiol dehydrogenase	1.69723
121.	ENSG00000100867	DHRS2	dehydrogenase/reductase 2	0.555358
122.	ENSG00000175602	CCDC85B	coiled-coil domain containing 85B	0.992711
123.	ENSG00000203950	FAM127B	family with sequence similarity 127 member B	0.447223
124.	ENSG00000167130	DOLPP1	dolichyldiphosphatase 1	0.896244
125.	ENSG00000179085	DPM3	dolichyl-phosphate mannosyltransferase subunit 3	0.986599
126.	ENSG00000081721	DUSP12	dual specificity phosphatase 12	0.492875
127.	ENSG00000158716	DUSP23	dual specificity phosphatase 23	0.378719
128.	ENSG00000196205	EEF1A1P5	eukaryotic translation elongation factor 1 alpha 1 pseudogene 5	0.461171
129.	ENSG00000120533	ENY2	"ENY2, transcription and export complex 2 subunit"	0.63482
130.	ENSG00000224032	EPB41L4A-AS1	EPB41L4A antisense RNA 1	0.901618
131.	ENSG00000112029	FBXO5	F-box protein 5	0.374508
132.	ENSG00000144199	FAHD2B	fumarylacetoacetate hydrolase domain containing 2B	0.681793
133.	ENSG00000158234	FAIM	Fas apoptotic inhibitory molecule	0.410446
134.	ENSG00000225663	MCRIP1	MAPK regulated corepressor interacting protein 1	0.491688
135.	ENSG00000164451	FAM26D	family with sequence similarity 26 member D	1.88422
136.	ENSG00000154864	PIEZO2	piezo type mechanosensitive ion channel component 2	3.29995
137.	ENSG00000251669	FAM86EP	"family with sequence similarity 86 member E, pseudogene"	0.737164
138.	ENSG00000183161	FANCF	Fanconi anemia complementation group F	0.471178
139.	ENSG00000104870	FCGRT	Fc fragment of IgG receptor and transporter	0.776339
140.	ENSG00000156427	FGF18	fibroblast growth factor 18	0.719496
141.	ENSG00000115641	FHL2	four and a half LIM domains 2	0.445715
142.	ENSG00000160688	FLAD1	flavin adenine dinucleotide synthetase 1	0.556943
143.	ENSG00000155393	HEATR3	HEAT repeat containing 3	0.716759
144.	ENSG00000165792	METTL17	methyltransferase like 17	0.682262
145.	ENSG00000106125	FAM188B	family with sequence similarity 188 member B	0.602637
146.	ENSG00000223764	LOC100130417	uncharacterized LOC100130417	0.430213
147.	ENSG00000126391	FRMD8	FERM domain containing 8	0.585091
148.	ENSG00000186628	FSD2	fibronectin type III and SPRY domain containing 2	0.926203
149.	ENSG00000136371	MTHFS	"5,10-methenyltetrahydrofolate synthetase (5-formyltetrahydrofolate cyclo-ligase)"	0.618357
150.	ENSG00000068438	FTSJ1	FtsJ RNA methyltransferase homolog 1 (E. coli)	0.55001
151.	ENSG00000137726	FXYD6	FXYD domain containing ion transport regulator 6	0.580413
152.	ENSG00000180340	FZD2	frizzled class receptor 2	0.413671
153.	ENSG00000165060	FXN	frataxin	0.529412
154.	ENSG00000149100	EIF3M	eukaryotic translation initiation factor 3 subunit M	0.43418
155.	ENSG00000110328	GALNT18	polypeptide N-acetylgalactosaminyltransferase 18	0.394038
156.	ENSG00000174473	GALNTL6	polypeptide N-acetylgalactosaminyltransferase-like 6	0.763889
157.	ENSG00000197308	GATA3-AS1	GATA3 antisense RNA 1	0.671649
158.	ENSG00000034713	GABARAPL2	GABA type A receptor associated protein like 2	0.564498
159.	ENSG00000117228	GBP1	guanylate binding protein 1	0.784455
160.	ENSG00000120820	GLT8D2	glycosyltransferase 8 domain containing 2	1.69809
161.	ENSG00000197858	GPAA1	glycosylphosphatidylinositol anchor attachment 1	0.486139
162.	ENSG00000167468	GPX4	glutathione peroxidase 4	0.410368
163.	ENSG00000172432	GTPBP2	GTP binding protein 2	0.490921
164.	ENSG00000178605	GTPBP6	GTP binding protein 6 (putative)	0.489066
165.	ENSG00000069482	GAL	galanin and GMAP prepropeptide	0.695747
166.	ENSG00000112312	GMNN	"geminin, DNA replication inhibitor"	0.406285
167.	ENSG00000184897	H1FX	H1 histone family member X	0.388129
168.	ENSG00000213397	HAUS7	HAUS augmin like complex subunit 7	0.566935

169.	ENSG00000113070	HBEGF	heparin binding EGF like growth factor	0.895028
170.	ENSG00000164683	HEY1	hes related family bHLH transcription factor with YRPW motif 1	1.22995
171.	ENSG00000135547	HEY2	hes related family bHLH transcription factor with YRPW motif 2	0.424438
172.	ENSG00000168269	FOXI1	forkhead box I1	3.43907
173.	ENSG00000196787	HIST1H2AG	histone cluster 1 H2A family member g	0.390069
174.	ENSG00000196747	HIST1H2AI	histone cluster 1 H2A family member i	0.842689
175.	ENSG00000184260	HIST2H2AC	histone cluster 2 H2A family member c	0.939071
176.	ENSG00000181218	HIST3H2A	histone cluster 3 H2A	1.69035
177.	ENSG00000214821	HMGB1P4	high mobility group box 1 pseudogene 4	3.41823
178.	ENSG00000173917	HOXB2	homeobox B2	2.31017
179.	ENSG00000060688	SNRNP40	small nuclear ribonucleoprotein U5 subunit 40	0.487184
180.	ENSG00000133265	HSPBP1	HSPA (Hsp70) binding protein 1	0.56981
181.	ENSG00000048162	NOP16	NOP16 nucleolar protein	0.959119
182.	ENSG00000150316	CWC15	CWC15 spliceosome associated protein homolog	0.391368
183.	ENSG00000189060	H1F0	H1 histone family member 0	0.371105
184.	ENSG00000187837	HIST1H1C	histone cluster 1 H1 family member c	0.353865
185.	ENSG00000188486	H2AFX	H2A histone family member X	0.744619
186.	ENSG00000115457	IGFBP2	insulin like growth factor binding protein 2	0.597234
187.	ENSG00000125968	ID1	"inhibitor of DNA binding 1, HLH protein"	0.589337
188.	ENSG00000117318	ID3	"inhibitor of DNA binding 3, HLH protein"	0.718576
189.	ENSG00000165949	IFI27	interferon alpha inducible protein 27	1.18678
190.	ENSG00000185201	IFITM2	interferon induced transmembrane protein 2	0.714871
191.	ENSG00000142089	IFITM3	interferon induced transmembrane protein 3	0.597062
192.	ENSG00000171855	IFNB1	interferon beta 1	0.816242
193.	ENSG00000109083	IFT20	intraflagellar transport 20	1.00115
194.	ENSG00000189108	IL1RAPL2	interleukin 1 receptor accessory protein like 2	2.30333
195.	ENSG00000182393	IFNL1	interferon lambda 1	1.56572
196.	ENSG00000153391	INO80C	INO80 complex subunit C	0.530949
197.	ENSG00000169245	CXCL10	C-X-C motif chemokine ligand 10	2.51181
198.	ENSG00000160051	IQCC	IQ motif containing C	0.499756
199.	ENSG00000185507	IRF7	interferon regulatory factor 7	0.713054
200.	ENSG00000176842	IRX5	iroquois homeobox 5	0.563473
201.	ENSG00000187608	ISG15	ISG15 ubiquitin-like modifier	0.945481
202.	ENSG00000083457	ITGAE	integrin subunit alpha E	0.607598
203.	ENSG00000124249	KCNK15	potassium two pore domain channel subfamily K member 15	1.01492
204.	ENSG00000185760	KCNQ5	potassium voltage-gated channel subfamily Q member 5	1.45194
205.	ENSG00000080608	PUM3	pumilio RNA binding family member 3	0.629458
206.	ENSG00000167566	NCKAP5L	NCK associated protein 5 like	0.887664
207.	ENSG00000183655	KLHL25	kelch like family member 25	0.558841
208.	ENSG00000124743	KLHL31	kelch like family member 31	1.17539
209.	ENSG00000139187	KLRG1	killer cell lectin like receptor G1	2.02421
210.	ENSG00000157992	KRTCAP3	keratinocyte associated protein 3	0.574384
211.	ENSG00000167768	KRT1	keratin 1	1.27951
212.	ENSG00000186395	KRT10	keratin 10	0.51963
213.	ENSG00000132434	LANCL2	LanC like 2	0.746629
214.	ENSG00000106852	LHX6	LIM homeobox 6	0.774015
215.	ENSG00000224843	LINC00240	long intergenic non-protein coding RNA 240	1.60272
216.	ENSG00000203930	LINC00632	long intergenic non-protein coding RNA 632	1.50538
217.	ENSG00000175701	LINC00116	long intergenic non-protein coding RNA 116	0.452601
218.	ENSG00000221821	C6orf226	chromosome 6 open reading frame 226	0.630026
219.	ENSG00000262587	LOC554206	leucine carboxyl methyltransferase 1 pseudogene	1.35132
220.	ENSG00000223756	TSSC2	tumor suppressing subtransferable candidate 2 pseudogene	0.767636
221.	ENSG00000128011	LRFN1	leucine rich repeat and fibronectin type III domain containing 1	0.611146
222.	ENSG00000116212	LRRC42	leucine rich repeat containing 42	0.358644
223.	ENSG00000257103	LSM14A	LSM14A, mRNA processing body assembly factor	0.645035
224.	ENSG00000164167	LSM6	LSM6 homolog, U6 small nuclear RNA and mRNA degradation associated	0.417445
225.	ENSG00000073803	MAP3K13	mitogen-activated protein kinase kinase kinase 13	0.874193
226.	ENSG00000178982	EIF3K	eukaryotic translation initiation factor 3 subunit K	0.384723
227.	ENSG00000247626	MARS2	"methionyl-tRNA synthetase 2, mitochondrial"	0.42871

228.	ENSG00000168906	MAT2A	methionine adenosyltransferase 2A	0.483105
229.	ENSG00000071655	MBD3	methyl-CpG binding domain protein 3	0.865492
230.	ENSG00000106305	AIMP2	aminoacyl tRNA synthetase complex interacting multifunctional protein 2	1.51209
231.	ENSG00000076706	MCAM	melanoma cell adhesion molecule	1.18409
232.	ENSG00000037897	METTL1	methyltransferase like 1	0.906915
233.	ENSG00000087995	METTL2A	methyltransferase like 2A	0.395521
234.	ENSG00000167700	MFSD3	major facilitator superfamily domain containing 3	0.585684
235.	ENSG00000133808	MICALCL	MICAL C-terminal like	1.32669
236.	ENSG00000240972	MIF	macrophage migration inhibitory factor	0.833516
237.	ENSG00000230937	MIR205HG	MIR205 host gene	1.11661
238.	ENSG00000227195	MIR663AHG	MIR663A host gene	1.20766
239.	ENSG00000108961	RANGRF	RAN guanine nucleotide release factor	0.5459
240.	ENSG00000137547	MRPL15	mitochondrial ribosomal protein L15	0.474103
241.	ENSG00000242485	MRPL20	mitochondrial ribosomal protein L20	0.531287
242.	ENSG00000106591	MRPL32	mitochondrial ribosomal protein L32	0.858848
243.	ENSG00000130312	MRPL34	mitochondrial ribosomal protein L34	0.870551
244.	ENSG00000105364	MRPL4	mitochondrial ribosomal protein L4	0.409564
245.	ENSG00000055950	MRPL43	mitochondrial ribosomal protein L43	0.599647
246.	ENSG00000259494	MRPL46	mitochondrial ribosomal protein L46	0.762839
247.	ENSG00000183617	MRPL54	mitochondrial ribosomal protein L54	0.556519
248.	ENSG00000128626	MRPS12	mitochondrial ribosomal protein S12	0.583302
249.	ENSG00000239789	MRPS17	mitochondrial ribosomal protein S17	0.736926
250.	ENSG00000096080	MRPS18A	mitochondrial ribosomal protein S18A	0.393735
251.	ENSG00000074071	MRPS34	mitochondrial ribosomal protein S34	0.627567
252.	ENSG00000243927	MRPS6	mitochondrial ribosomal protein S6	0.739482
253.	ENSG00000183155	RABIF	RAB interacting factor	0.357549
254.	ENSG00000182551	ADI1	acireductone dioxygenase 1	0.481005
255.	ENSG00000242114	MTFP1	mitochondrial fission process 1	1.47424
256.	ENSG00000162385	MAGOH	mago homolog, exon junction complex core component	0.457134
257.	ENSG00000173171	MTX1	metaxin 1	0.663453
258.	ENSG00000182208	MOB2	MOB kinase activator 2	0.524078
259.	ENSG00000176101	SSNA1	SS nuclear autoantigen 1	0.430655
260.	ENSG00000166681	BEX3	brain expressed X-linked 3	0.43456
261.	ENSG00000147813	NAPRT	nicotinate phosphoribosyltransferase	0.653233
262.	ENSG00000174886	NDUFA11	NADH:ubiquinone oxidoreductase subunit A11	0.599199
263.	ENSG00000131495	NDUFA2	NADH:ubiquinone oxidoreductase subunit A2	0.823501
264.	ENSG00000128609	NDUFA5	NADH:ubiquinone oxidoreductase subunit A5	0.41167
265.	ENSG00000119421	NDUFA8	NADH:ubiquinone oxidoreductase subunit A8	0.45136
266.	ENSG00000147123	NDUFB11	NADH:ubiquinone oxidoreductase subunit B11	0.603894
267.	ENSG00000090266	NDUFB2	NADH:ubiquinone oxidoreductase subunit B2	0.578461
268.	ENSG00000099795	NDUFB7	NADH:ubiquinone oxidoreductase subunit B7	0.592951
269.	ENSG00000151366	NDUFC2	NADH:ubiquinone oxidoreductase subunit C2	0.539958
270.	ENSG00000145494	NDUFS6	NADH:ubiquinone oxidoreductase subunit S6	0.406572
271.	ENSG00000167792	NDUFV1	NADH:ubiquinone oxidoreductase core subunit V1	0.384126
272.	ENSG00000160949	TONSL	"tonsoku-like, DNA repair protein"	0.477561
273.	ENSG00000100138	SNU13	SNU13 homolog, small nuclear ribonucleoprotein	0.587735
274.	ENSG00000123609	NMI	N-myc and STAT interactor	0.517159
275.	ENSG00000110107	PRPF19	pre-mRNA processing factor 19	0.526223
276.	ENSG00000107672	NSMCE4A	NSE4 homolog A, SMC5-6 complex component	0.423395
277.	ENSG00000205309	NT5M	5',3'-nucleotidase, mitochondrial	0.501565
278.	ENSG00000151413	NUBPL	nucleotide binding protein like	0.558354
279.	ENSG00000083635	NUFIP1	"NUFIP1, FMR1 interacting protein 1"	0.513718
280.	ENSG00000185818	NAT8L	N-acetyltransferase 8 like	0.361264
281.	ENSG00000163938	GNL3	G protein nucleolar 3	0.741709
282.	ENSG00000154814	OXNAD1	oxidoreductase NAD binding domain containing 1	0.488446
283.	ENSG00000092010	PSME1	proteasome activator subunit 1	0.532391
284.	ENSG00000100911	PSME2	proteasome activator subunit 2	0.608229
285.	ENSG00000107951	MTPAP	mitochondrial poly(A) polymerase	0.434545
286.	ENSG00000100300	TSPO	translocator protein	0.522258
287.	ENSG00000125450	NUP85	nucleoporin 85	0.687256
288.	ENSG00000197461	PDGFA	platelet derived growth factor subunit A	0.413027
289.	ENSG00000255185	PDXDC2P	"pyridoxal dependent decarboxylase domain containing 2, pseudogene"	1.52514
290.	ENSG00000143256	PFDN2	prefoldin subunit 2	0.726832

291.	ENSG00000184207	PGP	phosphoglycolate phosphatase	0.457967
292.	ENSG00000173457	PPP1R14B	protein phosphatase 1 regulatory inhibitor subunit 14B	0.378728
293.	ENSG00000054148	PHPT1	phosphohistidine phosphatase 1	0.418984
294.	ENSG00000105559	PLEKHA4	pleckstrin homology domain containing A4	0.787814
295.	ENSG00000102934	PLLP	plasmolipin	0.437388
296.	ENSG00000114631	PODXL2	podocalyxin like 2	0.404692
297.	ENSG00000062822	POLD1	"DNA polymerase delta 1, catalytic subunit"	0.75975
298.	ENSG00000100479	POLE2	"DNA polymerase epsilon 2, accessory subunit"	0.603001
299.	ENSG00000205808	PLPP6	phospholipid phosphatase 6	0.490681
300.	ENSG00000219797	PPIAP9	peptidylprolyl isomerase A pseudogene 9	0.404168
301.	ENSG00000049769	PPP1R3F	protein phosphatase 1 regulatory subunit 3F	0.839678
302.	ENSG00000122490	PQLC1	PQ loop repeat containing 1	0.720016
303.	ENSG00000204673	AKT1S1	AKT1 substrate 1	0.445086
304.	ENSG00000123143	PKN1	protein kinase N1	0.51293
305.	ENSG00000126457	PRMT1	protein arginine methyltransferase 1	0.414225
306.	ENSG00000224940	PRRT4	proline rich transmembrane protein 4	0.60223
307.	ENSG00000205220	PSMB10	proteasome subunit beta 10	0.904058
308.	ENSG00000142507	PSMB6	proteasome subunit beta 6	0.354566
309.	ENSG00000163636	PSMD6	"proteasome 26S subunit, non-ATPase 6"	0.389134
310.	ENSG00000110801	PSMD9	"proteasome 26S subunit, non-ATPase 9"	0.380317
311.	ENSG00000157778	PSMG3	proteasome assembly chaperone 3	0.788305
312.	ENSG00000176894	PXMP2	peroxisomal membrane protein 2	1.22584
313.	ENSG00000101417	PXMP4	peroxisomal membrane protein 4	0.512692
314.	ENSG00000173599	PC	pyruvate carboxylase	1.34458
315.	ENSG00000104524	PYCRL	pyrroline-5-carboxylate reductase-like	0.68122
316.	ENSG00000099864	PALM	paralemmin	0.534304
317.	ENSG00000127445	PIN1	peptidylprolyl cis/trans isomerase, NIMA-interacting 1	0.517536
318.	ENSG00000102312	PORCN	porcupine homolog (Drosophila)	0.7285
319.	ENSG00000102109	PCSK1N	proprotein convertase subtilisin/kexin type 1 inhibitor	0.468133
320.	ENSG00000167964	RAB26	RAB26, member RAS oncogene family	0.801729
321.	ENSG00000141542	RAB40B	RAB40B, member RAS oncogene family	0.766176
322.	ENSG00000128045	RASL11B	RAS like family 11 member B	0.63957
323.	ENSG00000102317	RBM3	"RNA binding motif (RNP1, RRM) protein 3"	0.410045
324.	ENSG00000204977	TRIM13	tripartite motif containing 13	0.462184
325.	ENSG00000116741	RGS2	regulator of G-protein signaling 2	0.603821
326.	ENSG00000107201	DDX58	DEXD/H-box helicase 58	0.530166
327.	ENSG00000183421	RIPK4	receptor interacting serine/threonine kinase 4	0.396886
328.	ENSG00000269900	RMRP	RNA component of mitochondrial RNA processing endoribonuclease	1.02715
329.	ENSG00000202198	RN7SK	"RNA, 7SK small nuclear"	0.491338
330.	ENSG00000158717	RNF166	ring finger protein 166	0.601905
331.	ENSG00000117748	RPA2	replication protein A2	0.446348
332.	ENSG00000100142	POLR2F	RNA polymerase II subunit F	0.468156
333.	ENSG00000063177	RPL18	ribosomal protein L18	0.44233
334.	ENSG00000105640	RPL18A	ribosomal protein L18a	0.691689
335.	ENSG00000130255	RPL36	ribosomal protein L36	0.724443
336.	ENSG00000213553	RPLP0P6	ribosomal protein lateral stalk subunit P0 pseudogene 6	0.619279
337.	ENSG00000137818	RPLP1	ribosomal protein lateral stalk subunit P1	0.500618
338.	ENSG00000177600	RPLP2	ribosomal protein lateral stalk subunit P2	0.440122
339.	ENSG00000172336	POP7	"POP7 homolog, ribonuclease P/MRP subunit"	0.719657
340.	ENSG00000115268	RPS15	ribosomal protein S15	0.440372
341.	ENSG00000105372	RPS19	ribosomal protein S19	0.404088
342.	ENSG00000140988	RPS2	ribosomal protein S2	0.443262
343.	ENSG00000179041	RRS1	ribosome biogenesis regulator homolog	0.481912
344.	ENSG00000136444	RSAD1	radical S-adenosyl methionine domain containing 1	0.475825
345.	ENSG00000222014	RAB6C	"RAB6C, member RAS oncogene family"	0.768564
346.	ENSG00000123595	RAB9A	"RAB9A, member RAS oncogene family"	0.435617
347.	ENSG00000169750	RAC3	"ras-related C3 botulinum toxin substrate 3 (rho family, small GTP binding protein Rac3)"	0.460522
348.	ENSG00000099901	RANBP1	RAN binding protein 1	0.631193
349.	ENSG00000142552	RCN3	reticulocalbin 3	1.34694
350.	ENSG00000173156	RHOD	ras homolog family member D	0.615585
351.	ENSG00000166788	SAAL1	serum amyloid A like 1	0.448924

352.	ENSG00000168061	SAC3D1	SAC3 domain containing 1	0.824352
353.	ENSG00000205413	SAMD9	sterile alpha motif domain containing 9	0.587933
354.	ENSG00000150459	SAP18	Sin3A associated protein 18	0.407532
355.	ENSG00000105472	CLEC11A	C-type lectin domain family 11 member A	1.68108
356.	ENSG00000133028	SCO1	"SCO1, cytochrome c oxidase assembly protein"	0.387032
357.	ENSG00000121064	SCPEP1	serine carboxypeptidase 1	0.44248
358.	ENSG00000205138	SDHAF1	succinate dehydrogenase complex assembly factor 1	0.578079
359.	ENSG00000171222	SCAND1	SCAN domain containing 1	0.981319
360.	ENSG00000085415	SEH1L	SEH1 like nucleoporin	0.48006
361.	ENSG00000141295	SCRN2	secernin 2	0.474364
362.	ENSG00000161547	SRSF2	serine and arginine rich splicing factor 2	0.540135
363.	ENSG00000129946	SHC2	SHC adaptor protein 2	0.701544
364.	ENSG00000108528	SLC25A11	solute carrier family 25 member 11	0.529239
365.	ENSG00000125454	SLC25A19	solute carrier family 25 member 19	0.903744
366.	ENSG00000177542	SLC25A22	solute carrier family 25 member 22	0.81186
367.	ENSG00000155287	SLC25A28	solute carrier family 25 member 28	0.469913
368.	ENSG00000075415	SLC25A3	solute carrier family 25 member 3	0.430978
369.	ENSG00000122692	SMU1	DNA replication regulator and spliceosomal factor	0.391938
370.	ENSG00000188338	SLC38A3	solute carrier family 38 member 3	1.45116
371.	ENSG00000174365	SNHG11	small nucleolar RNA host gene 11	0.508052
372.	ENSG00000269893	SNHG8	small nucleolar RNA host gene 8	0.748491
373.	ENSG00000255198	SNHG9	small nucleolar RNA host gene 9	0.799658
374.	ENSG00000263934	SNORD3A	"small nucleolar RNA, C/D box 3A"	1.36868
375.	ENSG00000125835	SNRPB	small nuclear ribonucleoprotein polypeptides B and B1	0.614339
376.	ENSG00000028528	SNX1	sorting nexin 1	0.726085
377.	ENSG00000158792	SPATA2L	spermatogenesis associated 2 like	1.18964
378.	ENSG00000124193	SRSF6	serine and arginine rich splicing factor 6	0.382337
379.	ENSG00000106028	SSBP1	single stranded DNA binding protein 1	0.443889
380.	ENSG00000180879	SSR4	signal sequence receptor subunit 4	0.559991
381.	ENSG00000180953	ST20	suppressor of tumorigenicity 20	0.847186
382.	ENSG00000169689	STRA13	stimulated by retinoic acid 13	0.585916
383.	ENSG00000148290	SURF1	SURF1 cytochrome c oxidase assembly factor"	0.530676
384.	ENSG00000148296	SURF6	surfeit 6	0.394365
385.	ENSG00000157703	SVOPL	SVOP like	1.37631
386.	ENSG00000100321	SYNGR1	synaptogyrin 1	0.498366
387.	ENSG00000180104	EXOC3	exocyst complex component 3	0.550317
388.	ENSG00000073169	SELO	selenoprotein O	0.435145
389.	ENSG00000170892	TSEN34	tRNA splicing endonuclease subunit 34	0.365
390.	ENSG00000162878	PKDCC	"protein kinase domain containing, cytoplasmic"	0.511279
391.	ENSG00000144040	SFXN5	sideroflexin 5	1.0396
392.	ENSG00000089163	SIRT4	sirtuin 4	1.43437
393.	ENSG00000184047	DIABLO	diablo IAP-binding mitochondrial protein	0.674556
394.	ENSG00000197457	STMN3	stathmin 3	0.666294
395.	ENSG00000135111	TBX3	T-box 3	0.958524
396.	ENSG00000261787	TCF24	transcription factor 24	0.967519
397.	ENSG00000148308	GTF3C5	general transcription factor IIIC subunit 5	0.479835
398.	ENSG00000168286	THAP11	THAP domain containing 11	0.720457
399.	ENSG00000184436	THAP7	THAP domain containing 7	0.749494
400.	ENSG00000161277	THAP8	THAP domain containing 8	0.669541
401.	ENSG00000133321	RARRES3	retinoic acid receptor responder 3	0.850546
402.	ENSG00000180346	TIGD2	tigger transposable element derived 2	0.38924
403.	ENSG00000105197	TIMM50	translocase of inner mitochondrial membrane 50	0.566558
404.	ENSG00000075131	TIPIN	TIMELESS interacting protein	0.433057
405.	ENSG00000134851	TMEM165	transmembrane protein 165	0.539908
406.	ENSG00000226287	TMEM191A	transmembrane protein 191A (pseudogene)	1.01268
407.	ENSG00000188807	TMEM201	transmembrane protein 201	0.624589
408.	ENSG00000180730	SHISA2	shisa family member 2	0.457364
409.	ENSG00000178821	TMEM52	transmembrane protein 52	0.772302
410.	ENSG00000135211	TMEM60	transmembrane protein 60	0.510866
411.	ENSG00000175606	TMEM70	transmembrane protein 70	0.484836
412.	ENSG00000127774	EMC6	ER membrane protein complex subunit 6	0.852474
413.	ENSG00000187653	TMSB4XP8	"thymosin beta 4, X-linked pseudogene 8"	1.1459
414.	ENSG00000164758	MED30	mediator complex subunit 30	0.408796
415.	ENSG00000181029	TRAPPC5	trafficking protein particle complex 5	0.784778

416.	ENSG00000123297	TSFM	"Ts translation elongation factor, mitochondrial"	0.512266
417.	ENSG00000180543	TSPYL5	TSPY like 5	0.435672
418.	ENSG00000128311	TST	thiosulfate sulfurtransferase	0.563092
419.	ENSG00000104522	TSTA3	tissue specific transplantation antigen P35B	0.469903
420.	ENSG00000011295	TTC19	tetratricopeptide repeat domain 19	0.883377
421.	ENSG00000183891	TTC32	tetratricopeptide repeat domain 32	0.483994
422.	ENSG00000129235	TXNDC17	thioredoxin domain containing 17	0.462714
423.	ENSG00000156521	TYSND1	trypsin domain containing 1	0.487563
424.	ENSG00000177370	TIMM22	translocase of inner mitochondrial membrane 22 homolog	0.343774
425.	ENSG00000170315	UBB	ubiquitin B	0.431675
426.	ENSG00000160087	UBE2J2	ubiquitin conjugating enzyme E2 J2	0.371906
427.	ENSG00000156587	UBE2L6	ubiquitin conjugating enzyme E2 L6	0.405366
428.	ENSG00000115446	UNC50	unc-50 inner nuclear membrane RNA binding protein	0.381783
429.	ENSG00000127540	UQCR11	"ubiquinol-cytochrome c reductase, complex III subunit XI"	0.70226
430.	ENSG00000184979	USP18	ubiquitin specific peptidase 18	0.673708
431.	ENSG00000176125	UFSP1	UFM1 specific peptidase 1 (inactive)	0.82111
432.	ENSG00000136146	MED4	mediator complex subunit 4	0.486201
433.	ENSG00000167397	VKORC1	vitamin K epoxide reductase complex subunit 1	0.60749
434.	ENSG00000100749	VRK1	vaccinia related kinase 1	0.561483
435.	ENSG00000085449	WDFY1	WD repeat and FYVE domain containing 1	0.477846
436.	ENSG00000119333	WDR34	WD repeat domain 34	0.967734
437.	ENSG00000133316	WDR74	WD repeat domain 74	0.430277
438.	ENSG00000152763	WDR78	WD repeat domain 78	1.73907
439.	ENSG00000136936	XPA	"XPA, DNA damage recognition and repair factor"	0.635993
440.	ENSG00000103489	XYLT1	xylosyltransferase 1	0.468212
441.	ENSG00000247315	ZCCHC3	zinc finger CCHC-type containing 3	0.530817
442.	ENSG00000112473	SLC39A7	solute carrier family 39 member 7	0.427647
443.	ENSG00000197961	ZNF121	zinc finger protein 121	0.478525
444.	ENSG00000249471	ZNF324B	zinc finger protein 324B	0.824604
445.	ENSG00000131116	ZNF428	zinc finger protein 428	0.664193
446.	ENSG00000198298	ZNF485	zinc finger protein 485	0.48972
447.	ENSG00000204946	ZNF783	zinc finger family member 783	0.774064
448.	ENSG00000152475	ZNF837	zinc finger protein 837	0.399333
449.	ENSG00000166707	ZCCHC18	zinc finger CCHC-type containing 18	1.40314
450.	ENSG00000115194	SLC30A3	solute carrier family 30 member 3	1.0649
451.	ENSG00000139405	RITA1	RBPJ interacting and tubulin associated 1	0.39254

Supplementary Table 4: miR-29 targets common in MCF-7 and LCC9s

Supplementary Table 4B: Common miR-29b-1 and miR-29a targets common to both MCF-7 and LCC9 cells

			MCF-7 Pre-miR-29b-1 vs Anti-miR-29a	MCF-7 Pre-miR-29a vs Anti-miR-29a	LCC9 Pre-miR-29b-1 vs Anti-miR-29a	LCC9Pre-miR-29a vs Anti-miR-29a
	Gene Symbol	**Gene Name**	**log2(fold change)**	**log$_2$(fold change)**	**log$_2$(fold change)**	**log$_2$(fold change)**
1.	ANXA1	annexin A1	0.86142	0.786981	2.13207	2.17304
2.	ANXA5	annexin A5	0.553169	0.52333	1.17391	1.22543
3.	ARL4C	ADP ribosylation factor like GTPase 4C	0.554121	0.695993	1.11503	1.06863
4.	ARPC5	actin related protein 2/3 complex subunit 5	0.586134	0.607786	1.505	1.64043
5.	ATP5C1	"ATP synthase, H+ transporting, mitochondrial F1 complex, gamma polypeptide 1"	0.6197	0.540511	1.43753	1.34628
6.	BAK1P1	BCL2 antagonist/killer 1 pseudogene 1	0.72886	0.853615	1.33959	1.35957
7.	BPGM	bisphosphoglycerate mutase	0.744332	0.734537	1.74992	1.71232
8.	C4orf32	chromosome 4 open reading frame 32	0.716821	0.62176	0.895463	0.976444
9.	C7orf73	chromosome 7 open reading frame 73	0.803039	0.703753	1.89354	1.90098
10.	CCDC167	coiled-coil domain containing 167	0.573969	0.620072	3.39142	3.38646
11.	CD276	CD276 molecule	0.6514	0.687137	1.24127	1.1014
12.	CD36	CD36 molecule	0.991681	1.19904	1.5895	1.44303
13.	CLEC7A	C-type lectin domain family 7 member A	1.28516	1.75287	2.31239	4.17419
14.	DYNLT1	dynein light chain Tctex-type 1	0.498623	0.60201	1.94914	2.14702
15.	EFEMP1	EGF containing fibulin like extracellular matrix protein 1	0.943595	0.981479	1.53166	1.67697
16.	ELF5	E74 like ETS transcription factor 5	1.20403	1.00089	1.54622	1.41993
17.	ENO1	enolase 1	0.499112	0.49841	0.546022	0.474453
18.	EPB41L4B	erythrocyte membrane protein band 4.1 like 4B	0.59199	0.530691	0.73561	0.664133
19.	F11R	F11 receptor	0.829893	0.805344	1.09778	1.04492
20.	FAM102B	family with sequence similarity 102 member B	0.61018	0.463769	1.13096	0.902373
21.	FAM127C	family with sequence similarity 127 member C	0.511481	0.559729	1.25769	1.39421
22.	FECH	ferrochelatase	1.03486	0.802485	1.68044	1.65016
23.	FKBP1A	FK506 binding protein 1A	0.72236	0.541505	0.791857	0.845083
24.	FREM2	FRAS1 related extracellular matrix protein 2	1.2842	1.13966	1.6484	1.22025
25.	GALNT1	polypeptide N-acetylgalactosaminyltransferase 1	0.95207	0.767107	0.673639	0.543714
26.	GCSH	glycine cleavage system protein H	0.812153	0.678064	2.03522	1.98461
27.	GINM1	glycoprotein integral membrane 1	0.688129	0.599535	0.775513	0.697549
28.	GSTM3	glutathione S-transferase mu 3	0.603347	0.474469	0.95424	0.886405
29.	HOXC13	homeobox C13	0.546096	0.67975	2.13121	2.22351
30.	IGSF3	immunoglobulin superfamily member 3	0.98228	1.12764	1.06424	0.986889
31.	ISOC1	isochorismatase domain containing 1	0.720805	0.671419	1.88871	1.87293
32.	ITGB1	integrin subunit beta 1	0.816957	0.659117	0.987881	0.80671
33.	JARID2	jumonji and AT-rich interaction domain containing 2	0.474666	0.444702	1.09834	0.998283
34.	KDELC1	KDEL motif containing 1	1.0655	1.27176	3.01117	2.79997
35.	KDM5B	lysine demethylase 5B	0.98413	0.779044	0.845657	0.65676
36.	KIAA1161	KIAA1161	0.708471	0.59354	0.655048	0.688324
37.	KIT	KIT proto-oncogene receptor tyrosine kinase	1.99239	1.71144	2.10612	1.97156
38.	KLHDC3	kelch domain containing 3	0.612973	0.698181	1.94245	2.07298
39.	KRT80	keratin 80	0.387774	0.516173	1.24017	1.19701
40.	MAP2K6	mitogen-activated protein kinase kinase 6	1.35071	1.27931	2.61089	2.15353
41.	MAP4K4	mitogen-activated protein kinase kinase kinase kinase 4	0.6531	0.563603	1.24666	0.919106
42.	MBTD1	mbt domain containing 1	0.616126	0.501719	0.65506	0.544341
43.	METTL7A	methyltransferase like 7A	0.81592	0.96939	0.867371	0.772139
44.	MORF4L1	mortality factor 4 like 1	0.614757	0.563526	1.23656	1.21828
45.	MPZL3	myelin protein zero like 3	0.796882	0.842667	1.30983	1.22454
46.	MRFAP1	Morf4 family associated protein 1	0.465383	0.536648	2.03319	2.14254
47.	NANOS1	nanos C2HC-type zinc finger 1	0.858277	0.9082	1.56703	1.64991
48.	NRAS	neuroblastoma RAS viral oncogene homolog	0.552152	0.43652	0.650742	0.632976
49.	NTRK2	neurotrophic receptor tyrosine kinase 2	0.987398	1.21638	2.31639	1.68192

50.	PCP4	Purkinje cell protein 4	0.864802	0.712848	2.79053	2.29124
51.	PIK3R3	phosphoinositide-3-kinase regulatory subunit 3	0.801967	0.829185	1.14694	1.04752
52.	PPIC	peptidylprolyl isomerase C	1.21937	1.17803	2.04242	2.15937
53.	PPT1	palmitoyl-protein thioesterase 1	0.742549	0.688119	1.33288	1.28796
54.	PRMT6	protein arginine methyltransferase 6	0.576114	0.729643	2.51833	2.72602
55.	RCC2	regulator of chromosome condensation 2	0.401982	0.591432	2.40005	2.4671
56.	RCN2	reticulocalbin 2	0.531026	0.452163	0.698454	0.588073
57.	RPS24	ribosomal protein S24	0.555705	0.488549	2.25259	2.36119
58.	RPS3A	ribosomal protein S3A	0.687786	0.491714	1.35179	1.34338
59.	S100A16	S100 calcium binding protein A16	0.669323	0.682906	1.68258	1.66285
60.	SEMA3C	semaphorin 3C	0.865222	0.66281	0.907207	0.669273
61.	SESTD1	SEC14 and spectrin domain containing 1	1.10416	1.06537	1.24413	1.03235
62.	TBC1D7	TBC1 domain family member 7	0.921924	0.83745	2.64112	2.93259
63.	TDG	thymine DNA glycosylase	0.815785	0.81763	2.25669	2.35879
64.	TET1	tet methylcytosine dioxygenase 1	1.14532	1.06875	1.61365	1.33383
65.	TET3	tet methylcytosine dioxygenase 3	0.923868	1.01061	0.964832	0.931351
66.	TMEM117	transmembrane protein 117	1.76039	1.52825	1.22016	1.36977
67.	TMEM164	transmembrane protein 164	0.8879	0.803582	1.45174	1.44885
68.	TMSB4X	"thymosin beta 4, X-linked"	0.559619	0.483911	0.828414	0.954921
69.	UBTD2	ubiquitin domain containing 2	0.753085	0.627815	1.45232	1.38079
70.	VAMP7	vesicle associated membrane protein 7	0.950366	0.81555	1.74104	1.60978
71.	VOPP1	"vesicular, overexpressed in cancer, prosurvival protein 1"	0.476688	0.451507	0.46844	0.41793
72.	XXYLT1	xyloside xylosyltransferase 1	0.716947	0.799999	2.16137	2.27884

Supplementary Table 4A: Common miR-29b-1 and miR-29a targets unique MCF-7 cells

			MCF-7 Pre-miR-29b-1 vs Anti-miR-29a	**MCF-7 Pre-miR-29a vs Anti-miR-29a**
	Gene Symbol	**Gene Name**	**$\log_2$(fold change)**	**$\log_2$(fold change)**
1.	ACO1	aconitase 1	0.950629	0.626089
2.	AIM1	absent in melanoma 1	0.778095	0.658569
3.	AKR1C3	aldo-keto reductase family 1 member C3	0.885048	0.645128
4.	ANKRD50	ankyrin repeat domain 50	0.73071	0.554446
5.	ATP1A1	ATPase Na+/K+ transporting subunit alpha 1	0.64489	0.431066
6.	ATP7A	ATPase copper transporting alpha	0.798753	0.616152
7.	ATRN	attractin	0.717643	0.492748
8.	BMP5	bone morphogenetic protein 5	0.836287	0.658327
9.	CAV1	caveolin 1	1.16046	1.01584
10.	CMBL	carboxymethylenebutenolidase homolog	0.765169	0.549379
11.	CRISP3	cysteine rich secretory protein 3	1.1613	0.739149
12.	CSGALNACT1	chondroitin sulfate N-acetylgalactosaminyltransferase 1	1.41892	1.27735
13.	CYP19A1	cytochrome P450 family 19 subfamily A member 1	2.32583	2.35814
14.	DNAJC28	DnaJ heat shock protein family (Hsp40) member C28	1.06775	0.92687
15.	DSC2	desmocollin 2	1.29529	1.10679
16.	DSG2	desmoglein 2	0.743464	0.481257
17.	EPHA6	EPH receptor A6	1.03363	0.877418
18.	EPHA7	EPH receptor A7	0.879505	0.701687
19.	ERMP1	endoplasmic reticulum metallopeptidase 1	0.939574	0.679547
20.	FBP1	fructose-bisphosphatase 1	0.45042	0.490642
21.	FILIP1L	filamin A interacting protein 1 like	0.667145	0.583131
22.	HEPHL1	hephaestin like 1	1.38329	1.14249
23.	HMGCLL1	3-hydroxymethyl-3-methylglutaryl-CoA lyase like 1	1.15732	1.03274
24.	IGFBP5	insulin like growth factor binding protein 5	0.52921	0.390971
25.	KCNJ8	potassium voltage-gated channel subfamily J member 8	0.940332	0.848572
26.	KIAA1549	KIAA1549	0.770061	0.663556
27.	KLHL4	kelch like family member 4	1.07248	0.81465
28.	KLHL5	kelch like family member 5	0.756199	0.602252
29.	KRT23	keratin 23	0.859914	0.780114
30.	LTBP1	latent transforming growth factor beta binding protein 1	1.32021	0.921458
31.	MALL	"mal, T-cell differentiation protein like"	1.60014	1.58334
32.	MIB1	mindbomb E3 ubiquitin protein ligase 1	0.73351	0.521844
33.	MIR17HG	miR-17-92a-1 cluster host gene	2.37174	2.2729
34.	NAALADL2	N-acetylated alpha-linked acidic dipeptidase like 2	0.69365	0.67568
35.	NPNT	nephronectin	0.774074	0.579707
36.	PANX1	pannexin 1	0.666987	0.487432
37.	PDK3	pyruvate dehydrogenase kinase 3	0.771457	0.564068
38.	PERP	"PERP, TP53 apoptosis effector"	0.587256	0.421452
39.	PGM5	phosphoglucomutase 5	2.04583	1.71094
40.	PKP1	plakophilin 1	1.25349	1.28295
41.	PSG9	pregnancy specific beta-1-glycoprotein 9	0.84128	0.757355
42.	RTN3	reticulon 3	0.612048	0.503042
43.	S100A10	S100 calcium binding protein A10	0.574568	0.414773
44.	SCIN	scinderin	1.3387	1.19559
45.	SCUBE2	"signal peptide, CUB domain and EGF like domain containing 2"	0.935904	0.815793
46.	SEMA3D	semaphorin 3D	1.48777	1.16477
47.	SERINC5	serine incorporator 5	0.805837	0.548127
48.	SLC16A2	solute carrier family 16 member 2	1.25596	0.854277
49.	SLC24A3	solute carrier family 24 member 3	0.589257	0.4987
50.	SLITRK6	SLIT and NTRK like family member 6	0.786628	0.553729
51.	SORT1	sortilin 1	0.749978	0.522416
52.	STK38	serine/threonine kinase 38	0.455075	0.426797
53.	STON1	stonin 1	1.5401	1.4028

54.	TMEM45B	transmembrane protein 45B	0.797278	0.752252
55.	TMTC3	transmembrane and tetratricopeptide repeat containing 3	0.828496	0.643048
56.	TOP2B	topoisomerase (DNA) II beta	0.707055	0.519007
57.	TRAK2	trafficking kinesin protein 2	0.706495	0.568506
58.	UNC5C	unc-5 netrin receptor C	1.2494	1.47876
59.	VAT1L	vesicle amine transport 1 like	1.16268	1.0319
60.	WNT2B	Wnt family member 2B	1.1319	1.0473

Supplementary Table 4C: Common miR-29b-1 and miR-29a targets unique LCC9 cells

			LCC9 Pre-miR-29b-1 vs Anti-miR-29a	**LCC9 Pre-miR-29a vs Anti-miR-29a**
	Gene Symbol	**Gene Name**	**log$_2$(fold change)**	**log$_2$(fold change)**
1.	AAR2	AAR2 splicing factor homolog	0.927601	1.03828
2.	AARSD1	alanyl-tRNA synthetase domain containing 1	0.659615	0.639813
3.	ABCB6	ATP binding cassette subfamily B member 6	1.20686	1.2379
4.	ABCB7	ATP binding cassette subfamily B member 7	0.688644	0.580453
5.	ABCE1	ATP binding cassette subfamily E member 1	0.876384	0.815314
6.	ABHD13	abhydrolase domain containing 13	0.488825	0.459061
7.	ACBD7	acyl-CoA binding domain containing 7	0.700393	0.496153
8.	ACE	angiotensin I converting enzyme	1.21031	1.00259
9.	ACOX2	acyl-CoA oxidase 2	4.65734	3.66441
10.	ACSS1	acyl-CoA synthetase short-chain family member 1	0.732909	0.762267
11.	ACTG2	"actin, gamma 2, smooth muscle, enteric"	0.411173	0.462855
12.	ACTL8	actin like 8	1.37881	1.60098
13.	ACTR3B	ARP3 actin related protein 3 homolog B	1.03853	1.08886
14.	ADA	adenosine deaminase	1.37348	1.47158
15.	ADAMTS15	ADAM metallopeptidase with thrombospondin type 1 motif 15	2.63156	2.34575
16.	ADAMTS19	ADAM metallopeptidase with thrombospondin type 1 motif 19	1.47001	1.29029
17.	ADAT2	"adenosine deaminase, tRNA specific 2"	0.875681	0.969717
18.	ADGRB2	adhesion G protein-coupled receptor B2	0.874388	1.11731
19.	ADH5	"alcohol dehydrogenase 5 (class III), chi polypeptide"	1.00464	1.03491
20.	ADIPOR2	adiponectin receptor 2	0.690701	0.574571
21.	ADK	adenosine kinase	0.60946	0.586069
22.	ADNP2	ADNP homeobox 2	0.389951	0.375037
23.	ADORA1	adenosine A1 receptor	2.51826	2.81189
24.	ADORA2A	adenosine A2a receptor	2.30518	2.9572
25.	ADORA2B	adenosine A2b receptor	0.715716	0.757347
26.	ADSL	adenylosuccinate lyase	1.28924	1.31677
27.	ADSS	adenylosuccinate synthase	0.989145	1.09993
28.	AFMID	arylformamidase	0.518471	0.514579
29.	AGR3	"anterior gradient 3, protein disulphide isomerase family member"	0.59845	0.815454
30.	AGTR1	angiotensin II receptor type 1	2.79834	2.8424
31.	AHCY	adenosylhomocysteinase	0.494678	0.563421
32.	AHCYL1	adenosylhomocysteinase like 1	0.599927	0.449753
33.	AIFM1	"apoptosis inducing factor, mitochondria associated 1"	0.517603	0.400808
34.	AK2	adenylate kinase 2	0.58514	0.599814
35.	AK4	adenylate kinase 4	0.59315	0.563226
36.	AKR1A1	aldo-keto reductase family 1 member A1	0.690468	0.593904
37.	AKR7A2	aldo-keto reductase family 7 member A2	0.590043	0.622283
38.	ALDH7A1	aldehyde dehydrogenase 7 family member A1	0.711066	0.563229
39.	ALG5	"ALG5, dolichyl-phosphate beta-glucosyltransferase"	0.974665	1.17464
40.	ALG6	"ALG6, alpha-1,3-glucosyltransferase"	0.725901	0.842662
41.	ALKBH2	"alkB homolog 2, alpha-ketoglutarate dependent dioxygenase"	0.534917	0.826004
42.	AMER1	APC membrane recruitment protein 1	0.999996	0.936081
43.	AMIGO2	adhesion molecule with Ig like domain 2	1.01909	1.00302
44.	AMMECR1	"Alport syndrome, mental retardation, midface hypoplasia and elliptocytosis chromosomal region gene 1"	0.486683	0.499441
45.	AMN1	antagonist of mitotic exit network 1 homolog	0.683819	0.588496
46.	ANAPC16	anaphase promoting complex subunit 16	0.486764	0.477979
47.	ANAPC5	anaphase promoting complex subunit 5	0.562191	0.456977
48.	ANKRD1	ankyrin repeat domain 1	0.498224	0.633051
49.	ANKRD13A	ankyrin repeat domain 13A	0.696859	0.685671
50.	ANKRD22	ankyrin repeat domain 22	1.83286	1.5803
51.	ANKRD30B	ankyrin repeat domain 30B	0.863248	0.779758
52.	AP1S1	adaptor related protein complex 1 sigma 1 subunit	0.712681	0.766289
53.	AP2S1	adaptor related protein complex 2 sigma 1 subunit	1.22989	1.36345
54.	AP5S1	adaptor related protein complex 5 sigma 1 subunit	0.456215	0.768152
55.	APITD1	"apoptosis-inducing, TAF9-like domain 1"	0.815897	0.780221

56.	AREG	amphiregulin	1.42032	1.32116
57.	ARF5	ADP ribosylation factor 5	0.739554	0.905469
58.	ARHGEF19	Rho guanine nucleotide exchange factor 19	0.840479	0.944296
59.	ARL3	ADP ribosylation factor like GTPase 3	0.606915	0.522059
60.	ARL5B	ADP ribosylation factor like GTPase 5B	0.799245	0.737761
61.	ARL6IP5	ADP ribosylation factor like GTPase 6 interacting protein 5	0.510344	0.450079
62.	ARMC10	armadillo repeat containing 10	0.678404	0.480358
63.	ARMC2	armadillo repeat containing 2	0.696103	0.782873
64.	ARPC2	actin related protein 2/3 complex subunit 2	0.827089	0.909638
65.	ARRDC4	arrestin domain containing 4	0.676729	0.931238
66.	ARSK	arylsulfatase family member K	1.09553	1.18466
67.	ARTN	artemin	0.779861	0.876064
68.	ARV1	"ARV1 homolog, fatty acid homeostasis modulator"	0.443626	0.636535
69.	ASMTL	acetylserotonin O-methyltransferase-like	0.627943	0.643094
70.	ASNA1	"arsA arsenite transporter, ATP-binding, homolog 1 (bacterial)"	0.380803	0.471845
71.	ATAD1	"ATPase family, AAA domain containing 1"	0.789302	0.790079
72.	ATAD2B	"ATPase family, AAA domain containing 2B"	0.623753	0.47118
73.	ATOH8	atonal bHLH transcription factor 8	1.53391	1.45938
74.	ATP23	ATP23 metallopeptidase and ATP synthase assembly factor homolog	0.957749	0.922681
75.	ATP5A1	"ATP synthase, H+ transporting, mitochondrial F1 complex, alpha subunit 1, cardiac muscle"	0.424851	0.412725
76.	ATP5B	"ATP synthase, H+ transporting, mitochondrial F1 complex, beta polypeptide"	0.738957	0.734603
77.	ATP5E	"ATP synthase, H+ transporting, mitochondrial F1 complex, epsilon subunit"	0.553854	0.60387
78.	ATP5EP2	"ATP synthase, H+ transporting, mitochondrial F1 complex, epsilon subunit pseudogene 2"	1.06228	0.475944
79.	ATP5F1	"ATP synthase, H+ transporting, mitochondrial Fo complex subunit B1"	0.570357	0.604812
80.	ATP5G3	"ATP synthase, H+ transporting, mitochondrial Fo complex subunit C3 (subunit 9)"	0.885476	1.00146
81.	ATP5I	"ATP synthase, H+ transporting, mitochondrial Fo complex subunit E"	0.572728	0.805795
82.	ATP5L	"ATP synthase, H+ transporting, mitochondrial Fo complex subunit G"	0.641905	0.713396
83.	ATP6AP1	ATPase H+ transporting accessory protein 1	0.725615	0.747385
84.	ATPAF2	ATP synthase mitochondrial F1 complex assembly factor 2	0.668871	0.853675
85.	ATXN7L3B	ataxin 7 like 3B	1.23747	1.29717
86.	B2M	beta-2-microglobulin	0.660654	0.683885
87.	B3GALT6	"beta-1,3-galactosyltransferase 6"	0.891879	1.24243
88.	B4GALT2	"beta-1,4-galactosyltransferase 2"	1.18107	1.36107
89.	B4GALT5	"beta-1,4-galactosyltransferase 5"	0.648518	0.556421
90.	BAG1	BCL2 associated athanogene 1	0.383929	0.514251
91.	BAK1	BCL2 antagonist/killer 1	1.22959	1.49069
92.	BANF1	barrier to autointegration factor 1	0.576179	0.631429
93.	BARX2	BARX homeobox 2	1.10383	1.02157
94.	BASP1	brain abundant membrane attached signal protein 1	0.483084	0.508448
95.	BBS10	Bardet-Biedl syndrome 10	0.549438	0.635606
96.	BCAT2	branched chain amino acid transaminase 2	0.627225	0.819078
97.	BCCIP	BRCA2 and CDKN1A interacting protein	0.802714	0.867996
98.	BCL11B	B-cell CLL/lymphoma 11B	0.889491	0.847944
99.	BCL6	B-cell CLL/lymphoma 6	1.04653	0.899591
100.	BCL7A	BCL tumor suppressor 7A	0.971165	1.052
101.	BDH1	"3-hydroxybutyrate dehydrogenase, type 1"	0.715878	0.744706
102.	BDH2	"3-hydroxybutyrate dehydrogenase, type 2"	0.843871	0.866672
103.	BEND6	BEN domain containing 6	1.01679	1.03956
104.	BEX5	brain expressed X-linked 5	1.2185	1.64046
105.	BFAR	bifunctional apoptosis regulator	0.519609	0.486401
106.	BFSP2	beaded filament structural protein 2	1.60905	1.3469
107.	BIRC2	baculoviral IAP repeat containing 2	1.50289	1.41292
108.	BLMH	bleomycin hydrolase	2.51864	2.13864
109.	BMPER	BMP binding endothelial regulator	1.90746	1.64764
110.	BOC	"BOC cell adhesion associated, oncogene regulated"	2.16198	1.93153
111.	BOLA1	bolA family member 1	0.570531	1.00556
112.	BPHL	biphenyl hydrolase like	0.722898	0.655604

113.	BRINP1	BMP/retinoic acid inducible neural specific 1	1.72664	1.90507
114.	BRINP2	BMP/retinoic acid inducible neural specific 2	2.03546	1.60345
115.	BRIX1	"BRX1, biogenesis of ribosomes"	0.518963	0.56702
116.	BRK1	"BRICK1, SCAR/WAVE actin nucleating complex subunit"	0.750387	0.79901
117.	BRSK2	BR serine/threonine kinase 2	1.05141	0.844313
118.	BTBD10	BTB domain containing 10	0.947219	0.868464
119.	BTF3	basic transcription factor 3	0.506364	0.487342
120.	BTN3A1	butyrophilin subfamily 3 member A1	0.701139	0.811308
121.	BTN3A2	butyrophilin subfamily 3 member A2	1.66846	1.60858
122.	BZW2	basic leucine zipper and W2 domains 2	1.33163	1.28027
123.	C12orf4	chromosome 12 open reading frame 4	0.589379	0.697994
124.	C14orf166	chromosome 14 open reading frame 166	0.363788	0.346326
125.	C14orf2	chromosome 14 open reading frame 2	0.523541	0.590597
126.	C15orf59	chromosome 15 open reading frame 59	1.07989	1.23498
127.	C16orf87	chromosome 16 open reading frame 87	1.76765	1.78206
128.	C16orf91	chromosome 16 open reading frame 91	0.529916	1.05276
129.	C19orf48	chromosome 19 open reading frame 48	0.550821	1.02046
130.	C19orf53	chromosome 19 open reading frame 53	0.508361	0.593913
131.	C1GALT1C1	C1GALT1 specific chaperone 1	0.504905	0.496875
132.	C1GALT1C1L	C1GALT1-specific chaperone 1 like	1.17377	1.59184
133.	C1orf109	chromosome 1 open reading frame 109	0.578077	0.703725
134.	C1orf123	chromosome 1 open reading frame 123	0.966238	1.10235
135.	C1orf131	chromosome 1 open reading frame 131	1.49237	1.68842
136.	C1orf168	chromosome 1 open reading frame 168	1.05566	0.884423
137.	C1orf50	chromosome 1 open reading frame 50	0.506735	0.660153
138.	C1orf52	chromosome 1 open reading frame 52	1.30657	1.53613
139.	C1QBP	complement C1q binding protein	0.842575	0.853417
140.	C1QTNF6	C1q and tumor necrosis factor related protein 6	1.65012	1.72005
141.	C20orf196	chromosome 20 open reading frame 196	0.846608	1.17566
142.	C21orf33	chromosome 21 open reading frame 33	0.576514	0.882266
143.	C21orf58	chromosome 21 open reading frame 58	0.574076	0.566849
144.	C21orf91	chromosome 21 open reading frame 91	0.691422	0.713411
145.	C2orf76	chromosome 2 open reading frame 76	0.748832	0.69391
146.	C4orf19	chromosome 4 open reading frame 19	1.57704	1.5167
147.	C4orf3	chromosome 4 open reading frame 3	0.665988	0.811939
148.	C5orf15	chromosome 5 open reading frame 15	1.65814	1.63619
149.	C5orf30	chromosome 5 open reading frame 30	0.465594	0.3944
150.	C6orf141	chromosome 6 open reading frame 141	0.756503	0.897626
151.	C7orf49	chromosome 7 open reading frame 49	0.651726	0.709833
152.	C8orf33	chromosome 8 open reading frame 33	0.660074	0.695409
153.	C9orf69	chromosome 9 open reading frame 69	0.476335	0.79721
154.	CA13	carbonic anhydrase 13	1.36253	1.04568
155.	CALM3	calmodulin 3	0.570431	0.485807
156.	CAMTA1	calmodulin binding transcription activator 1	0.642045	0.662908
157.	CAPN6	calpain 6	1.02668	1.12836
158.	CAPZB	capping actin protein of muscle Z-line beta subunit	0.666538	0.682933
159.	CASP3	caspase 3	0.729553	0.745127
160.	CASP7	caspase 7	1.81119	1.87049
161.	CAT	catalase	0.739667	0.642768
162.	CBR1	carbonyl reductase 1	0.60378	0.707936
163.	CBWD2	COBW domain containing 2	0.552169	0.479109
164.	CBX1	chromobox 1	0.608134	0.536891
165.	CBX2	chromobox 2	1.05339	1.05031
166.	CBX6	chromobox 6	0.744626	0.895712
167.	CBY1	"chibby family member 1, beta catenin antagonist"	1.33359	1.26603
168.	CCDC117	coiled-coil domain containing 117	0.801064	0.602464
169.	CCDC138	coiled-coil domain containing 138	1.54328	1.27542
170.	CCDC28B	coiled-coil domain containing 28B	2.65578	2.80182
171.	CCDC43	coiled-coil domain containing 43	1.47159	1.5781
172.	CCDC58	coiled-coil domain containing 58	0.382227	0.374341
173.	CCDC59	coiled-coil domain containing 59	0.410004	0.482381
174.	CCDC94	coiled-coil domain containing 94	0.459384	0.454246
175.	CCNA2	cyclin A2	0.683344	0.672626
176.	CCNB1IP1	cyclin B1 interacting protein 1	1.22499	1.20591
177.	CCNE1	cyclin E1	0.708192	0.746412
178.	CCNF	cyclin F	0.4926	0.539965

179.	CCNG2	cyclin G2	0.662931	0.679027
180.	CCNYL1	cyclin Y like 1	0.891729	0.683649
181.	CCSAP	"centriole, cilia and spindle associated protein"	1.0959	1.01218
182.	CCT2	chaperonin containing TCP1 subunit 2	0.955846	0.94792
183.	CCT4	chaperonin containing TCP1 subunit 4	0.507679	0.468577
184.	CCT6P1	chaperonin containing TCP1 subunit 6 pseudogene 1	0.440193	0.479515
185.	CCT7	chaperonin containing TCP1 subunit 7	0.61167	0.525603
186.	CCT8	chaperonin containing TCP1 subunit 8	0.516095	0.456799
187.	CD47	CD47 molecule	1.08686	1.07416
188.	CD58	CD58 molecule	0.574278	0.608606
189.	CD83	CD83 molecule	1.92141	1.74713
190.	CDADC1	cytidine and dCMP deaminase domain containing 1	0.972441	1.19253
191.	CDC123	cell division cycle 123	0.579892	0.537706
192.	CDC23	cell division cycle 23	0.89469	0.898371
193.	CDC37L1	cell division cycle 37 like 1	0.652822	0.581541
194.	CDC42	cell division cycle 42	0.724433	0.737603
195.	CDC45	cell division cycle 45	0.95113	0.941068
196.	CDC6	cell division cycle 6	0.995412	1.05737
197.	CDCA4	cell division cycle associated 4	0.679391	0.937433
198.	CDCA7	cell division cycle associated 7	0.780818	0.700558
199.	CDH10	cadherin 10	1.37135	1.077
200.	CDIPT	CDP-diacylglycerol--inositol 3-phosphatidyltransferase	0.50783	0.492623
201.	CDK4	cyclin dependent kinase 4	0.466874	0.512105
202.	CDK5RAP1	CDK5 regulatory subunit associated protein 1	0.421749	0.452614
203.	CDKN2AIPNL	CDKN2A interacting protein N-terminal like	0.749947	0.797643
204.	CDPF1	cysteine rich DPF motif domain containing 1	0.989699	1.29684
205.	CEBPA-AS1	CEBPA antisense RNA 1 (head to head)	0.653322	0.775162
206.	CECR5	"cat eye syndrome chromosome region, candidate 5"	0.4713	0.614461
207.	CENPBD1P1	CENPB DNA-binding domains containing 1 pseudogene 1	1.15072	1.34084
208.	CENPK	centromere protein K	1.76657	1.73323
209.	CENPW	centromere protein W	0.460512	0.594347
210.	CEP78	centrosomal protein 78	0.579872	0.407027
211.	CETN2	centrin 2	0.67484	0.556184
212.	CFAP20	cilia and flagella associated protein 20	0.673339	0.71513
213.	CGA	"glycoprotein hormones, alpha polypeptide"	1.43795	2.15628
214.	CGREF1	cell growth regulator with EF-hand domain 1	0.532261	0.530638
215.	CHCHD1	coiled-coil-helix-coiled-coil-helix domain containing 1	0.506416	0.588876
216.	CHCHD2	coiled-coil-helix-coiled-coil-helix domain containing 2	0.673485	0.788832
217.	CHCHD4	coiled-coil-helix-coiled-coil-helix domain containing 4	0.454512	0.51827
218.	CHD1L	chromodomain helicase DNA binding protein 1 like	0.459906	0.425305
219.	CHDH	choline dehydrogenase	0.460734	0.362754
220.	CHEK2	checkpoint kinase 2	0.827479	0.90164
221.	CHGA	chromogranin A	0.921886	0.924259
222.	CHMP6	charged multivesicular body protein 6	0.715407	1.0806
223.	CHRNA5	cholinergic receptor nicotinic alpha 5 subunit	0.704088	0.690746
224.	CHSY1	chondroitin sulfate synthase 1	1.12941	0.935212
225.	CIDECP	cell death-inducing DFFA-like effector c pseudogene	1.01528	1.24263
226.	CINP	cyclin dependent kinase 2 interacting protein	0.658014	0.726846
227.	CISD1	CDGSH iron sulfur domain 1	1.01027	1.0821
228.	CITED2	Cbp/p300 interacting transactivator with Glu/Asp rich carboxy-terminal domain 2	0.558277	0.687849
229.	CITED4	Cbp/p300 interacting transactivator with Glu/Asp rich carboxy-terminal domain 4	0.482466	0.696028
230.	CKLF	chemokine like factor	0.618983	0.705915
231.	CKS1B	CDC28 protein kinase regulatory subunit 1B	0.59821	0.662221
232.	CLCN4	chloride voltage-gated channel 4	1.05748	0.823801
233.	CLDN1	claudin 1	1.59109	2.35224
234.	CLNS1A	chloride nucleotide-sensitive channel 1A	0.581412	0.683439
235.	CMAHP	"cytidine monophospho-N-acetylneuraminic acid hydroxylase, pseudogene"	0.825125	1.24412
236.	CMC2	C-X9-C motif containing 2	0.595229	0.668355
237.	CMSS1	cms1 ribosomal small subunit homolog (yeast)	1.11261	1.07853
238.	CNBD2	cyclic nucleotide binding domain containing 2	0.837055	1.27329
239.	CNBP	CCHC-type zinc finger nucleic acid binding protein	0.47528	0.558615
240.	CNIH1	cornichon family AMPA receptor auxiliary protein 1	0.527042	0.625035
241.	CNOT8	CCR4-NOT transcription complex subunit 8	0.78093	0.812067

242.	COA1	cytochrome c oxidase assembly factor 1 homolog	0.866394	0.834569
243.	COA3	cytochrome c oxidase assembly factor 3	0.454443	0.58493
244.	COA4	cytochrome c oxidase assembly factor 4 homolog	0.567114	0.757669
245.	COA7	cytochrome c oxidase assembly factor 7 (putative)	0.72858	0.930403
246.	COL27A1	collagen type XXVII alpha 1 chain	1.67382	1.25171
247.	COMMD2	COMM domain containing 2	1.81109	1.76506
248.	COMMD7	COMM domain containing 7	1.39645	1.46911
249.	COMMD9	COMM domain containing 9	1.13099	1.13093
250.	COPS5	COP9 signalosome subunit 5	1.20623	1.24081
251.	COPS9	COP9 signalosome subunit 9	1.02218	1.25621
252.	COQ10A	coenzyme Q10A	0.61573	0.786051
253.	COQ2	"coenzyme Q2, polyprenyltransferase"	0.51358	0.591104
254.	COQ3	"coenzyme Q3, methyltransferase"	0.454187	0.564536
255.	COQ5	"coenzyme Q5, methyltransferase"	1.12072	1.17251
256.	COTL1	coactosin like F-actin binding protein 1	0.904161	0.881233
257.	COX14	"COX14, cytochrome c oxidase assembly factor"	0.697269	0.884169
258.	COX5A	cytochrome c oxidase subunit 5A	0.440628	0.503475
259.	COX6C	cytochrome c oxidase subunit 6C	0.473092	0.529371
260.	COX7A2L	cytochrome c oxidase subunit 7A2 like	0.583686	0.527884
261.	COX7B	cytochrome c oxidase subunit 7B	0.743747	0.832255
262.	COX7C	cytochrome c oxidase subunit 7C	0.420544	0.504002
263.	CPNE7	copine 7	0.884544	0.900155
264.	CRADD	CASP2 and RIPK1 domain containing adaptor with death domain	0.94901	1.09059
265.	CREG1	cellular repressor of E1A stimulated genes 1	1.06377	1.04923
266.	CRISPLD1	cysteine rich secretory protein LCCL domain containing 1	2.05979	2.05316
267.	CRLS1	cardiolipin synthase 1	0.531102	0.667133
268.	CRNDE	colorectal neoplasia differentially expressed (non-protein coding)	0.437687	0.476426
269.	CSGALNACT2	chondroitin sulfate N-acetylgalactosaminyltransferase 2	1.09471	0.964817
270.	CSPG5	chondroitin sulfate proteoglycan 5	1.77322	1.8202
271.	CTDSPL	CTD small phosphatase like	1.29415	1.31864
272.	CTH	cystathionine gamma-lyase	1.37027	1.01686
273.	CTHRC1	collagen triple helix repeat containing 1	1.78111	1.52537
274.	CTNNAL1	catenin alpha like 1	1.10965	1.06564
275.	CTNNBIP1	catenin beta interacting protein 1	1.85451	1.90993
276.	CTSV	cathepsin V	0.653027	0.565642
277.	CUEDC2	CUE domain containing 2	0.421961	0.40473
278.	CUTC	cutC copper transporter	1.76035	1.9119
279.	CXADR	coxsackie virus and adenovirus receptor	1.04079	0.942615
280.	CXCL11	C-X-C motif chemokine ligand 11	2.02203	2.21208
281.	CXCL12	C-X-C motif chemokine ligand 12	1.71022	1.52676
282.	CYB561	cytochrome b561	0.490292	0.599664
283.	CYB5A	cytochrome b5 type A	0.776375	0.787099
284.	CYCS	"cytochrome c, somatic"	0.634708	0.683778
285.	CYP2J2	cytochrome P450 family 2 subfamily J member 2	0.405508	0.386161
286.	CYP4F22	cytochrome P450 family 4 subfamily F member 22	0.607833	0.711376
287.	DAD1	defender against cell death 1	0.483024	0.423811
288.	DANCR	differentiation antagonizing non-protein coding RNA	1.67735	2.07894
289.	DAP	death associated protein	0.676437	0.692041
290.	DAZAP2	DAZ associated protein 2	0.572756	0.569066
291.	DBT	dihydrolipoamide branched chain transacylase E2	1.19273	1.08744
292.	DCAF12	DDB1 and CUL4 associated factor 12	0.792873	0.751584
293.	DCAF5	DDB1 and CUL4 associated factor 5	0.49886	0.426772
294.	DCPS	"decapping enzyme, scavenger"	0.545144	0.580398
295.	DCTPP1	dCTP pyrophosphatase 1	0.486552	0.575999
296.	DCUN1D5	defective in cullin neddylation 1 domain containing 5	0.895144	0.894684
297.	DCXR	dicarbonyl and L-xylulose reductase	0.639569	0.72724
298.	DDX1	DEAD/H-box helicase 1	0.493408	0.479488
299.	DDX21	DEAD-box helicase 21	1.0968	1.03752
300.	DDX47	DEAD-box helicase 47	0.765994	0.743859
301.	DDX49	DEAD-box helicase 49	2.34706	2.59104
302.	DEF6	"DEF6, guanine nucleotide exchange factor"	0.674619	0.787547
303.	DEGS2	"delta 4-desaturase, sphingolipid 2"	1.16509	1.45397
304.	DENR	density regulated re-initiation and release factor	0.927438	0.880601
305.	DEPDC1B	DEP domain containing 1B	0.948026	0.751444

306.	DERA	deoxyribose-phosphate aldolase	0.991452	0.967232
307.	DFFA	DNA fragmentation factor subunit alpha	0.675709	0.602846
308.	DHODH	dihydroorotate dehydrogenase (quinone)	0.584332	0.561185
309.	DHRS13	dehydrogenase/reductase 13	1.78083	1.83441
310.	DHRS7B	dehydrogenase/reductase 7B	0.519399	0.643293
311.	DLD	dihydrolipoamide dehydrogenase	0.797122	0.750107
312.	DLEU1	deleted in lymphocytic leukemia 1	1.11632	0.816194
313.	DNAAF2	dynein axonemal assembly factor 2	0.627346	0.76001
314.	DNAH14	dynein axonemal heavy chain 14	0.576577	0.597049
315.	DNAJA1	DnaJ heat shock protein family (Hsp40) member A1	0.475614	0.472945
316.	DNAJB11	DnaJ heat shock protein family (Hsp40) member B11	0.904611	0.930958
317.	DNAJC1	DnaJ heat shock protein family (Hsp40) member C1	0.628416	0.707132
318.	DNAJC19	DnaJ heat shock protein family (Hsp40) member C19	0.487561	0.535434
319.	DNMT3B	DNA methyltransferase 3 beta	1.75426	1.6786
320.	DNPH1	2'-deoxynucleoside 5'-phosphate N-hydrolase 1	0.415004	0.808615
321.	DPCD	deleted in primary ciliary dyskinesia homolog (mouse)	0.96135	0.905369
322.	DPH2	DPH2 homolog	0.873147	0.947896
323.	DPY30	dpy-30, histone methyltransferase complex regulatory subunit	0.745031	0.681298
324.	DSCAM-AS1	DSCAM antisense RNA 1	1.79876	1.65099
325.	DSCC1	DNA replication and sister chromatid cohesion 1	1.65166	1.54324
326.	DSCR8	Down syndrome critical region 8	1.86764	1.26283
327.	DTD1	D-tyrosyl-tRNA deacylase 1	0.439774	0.362775
328.	DTWD1	DTW domain containing 1	0.501435	0.424841
329.	DTWD2	DTW domain containing 2	0.732857	0.575587
330.	DTX4	deltex E3 ubiquitin ligase 4	1.46128	0.89692
331.	DTYMK	deoxythymidylate kinase	0.550339	0.636515
332.	DUSP2	dual specificity phosphatase 2	0.861033	1.02365
333.	DUSP4	dual specificity phosphatase 4	2.05306	1.92245
334.	DUSP5	dual specificity phosphatase 5	1.16304	0.974547
335.	DYM	dymeclin	1.72405	1.65591
336.	DYNLL1	dynein light chain LC8-type 1	0.629238	0.640647
337.	DYRK2	dual specificity tyrosine phosphorylation regulated kinase 2	0.937423	0.706077
338.	EAPP	E2F associated phosphoprotein	0.426617	0.475068
339.	EBAG9	"estrogen receptor binding site associated, antigen, 9"	0.596474	0.638776
340.	EBNA1BP2	EBNA1 binding protein 2	0.637167	0.63253
341.	EBP	emopamil binding protein (sterol isomerase)	0.72739	0.726358
342.	EBPL	emopamil binding protein like	0.759841	0.707649
343.	ECHS1	"enoyl-CoA hydratase, short chain 1"	0.423954	0.434189
344.	EDF1	endothelial differentiation related factor 1	0.499046	0.698612
345.	EDRF1	erythroid differentiation regulatory factor 1	0.87891	0.947828
346.	EEF1A1P9	eukaryotic translation elongation factor 1 alpha1 pseudogene 9	0.580221	0.572346
347.	EEF1AKMT1	eukaryotic translation elongation factor 1 alpha lysine methyltransferase 1	0.694379	0.670003
348.	EEF1B2	eukaryotic translation elongation factor 1 beta 2	0.68232	0.665074
349.	EEF1G	eukaryotic translation elongation factor 1 gamma	0.50351	0.394335
350.	EFNB3	ephrin B3	0.713137	0.530624
351.	EGR3	early growth response 3	2.35585	2.26571
352.	EHF	ETS homologous factor	0.793912	0.539603
353.	EI24	"EI24, autophagy associated transmembrane protein"	1.58026	1.59393
354.	EID1	EP300 interacting inhibitor of differentiation 1	1.13643	1.31191
355.	EID2	EP300 interacting inhibitor of differentiation 2	1.02888	1.32895
356.	EID2B	EP300 interacting inhibitor of differentiation 2B	0.663137	1.24476
357.	EIF2B1	eukaryotic translation initiation factor 2B subunit alpha	0.842259	0.955928
358.	EIF2B2	eukaryotic translation initiation factor 2B subunit beta	0.438912	0.472013
359.	EIF2B3	eukaryotic translation initiation factor 2B subunit gamma	0.854297	0.912875
360.	EIF2D	eukaryotic translation initiation factor 2D	0.89687	0.852116
361.	EIF2S2	eukaryotic translation initiation factor 2 subunit beta	0.929427	0.970642
362.	EIF3E	eukaryotic translation initiation factor 3 subunit E	0.693977	0.627349
363.	EIF3I	eukaryotic translation initiation factor 3 subunit I	0.502812	0.370749
364.	EIF3J	eukaryotic translation initiation factor 3 subunit J	0.920679	0.788568
365.	EIF4A1	eukaryotic translation initiation factor 4A1	0.506091	0.467426
366.	EIF4A3	eukaryotic translation initiation factor 4A3	0.444924	0.555671
367.	EIF4E2	eukaryotic translation initiation factor 4E family member 2	1.81313	1.83072
368.	EIF5A	eukaryotic translation initiation factor 5A	0.682438	0.762379

369.	EIF5AL1	eukaryotic translation initiation factor 5A-like 1	0.937528	0.856409
370.	EIF6	eukaryotic translation initiation factor 6	0.77994	0.930112
371.	ELK1	"ELK1, ETS transcription factor"	0.774281	0.883002
372.	ELOVL2	ELOVL fatty acid elongase 2	0.649693	0.519209
373.	ELOVL5	ELOVL fatty acid elongase 5	0.835545	0.688405
374.	ELP2	elongator acetyltransferase complex subunit 2	0.751258	0.807974
375.	ELP4	elongator acetyltransferase complex subunit 4	0.670908	0.728065
376.	ELP6	elongator acetyltransferase complex subunit 6	0.412246	0.534597
377.	EMC4	ER membrane protein complex subunit 4	0.519872	0.416206
378.	EMID1	EMI domain containing 1	0.485272	0.647797
379.	ENHO	energy homeostasis associated	1.61978	1.62355
380.	ENOPH1	enolase-phosphatase 1	0.606649	0.586319
381.	ENSA	endosulfine alpha	0.669224	0.617762
382.	ENTPD3-AS1	ENTPD3 antisense RNA 1	0.509316	0.639276
383.	ERAL1	Era like 12S mitochondrial rRNA chaperone 1	0.638027	0.704868
384.	ERCC2	"ERCC excision repair 2, TFIIH core complex helicase subunit"	0.760713	0.555621
385.	ERGIC3	ERGIC and golgi 3	0.703577	0.774335
386.	ERH	enhancer of rudimentary homolog (Drosophila)	0.573351	0.58719
387.	ERP27	endoplasmic reticulum protein 27	1.63098	2.08328
388.	ERRFI1	ERBB receptor feedback inhibitor 1	0.525362	0.709608
389.	ESD	esterase D	0.528035	0.538701
390.	ETFA	electron transfer flavoprotein alpha subunit	0.591116	0.527411
391.	ETFDH	electron transfer flavoprotein dehydrogenase	1.6454	1.51574
392.	ETNK2	ethanolamine kinase 2	1.11182	1.05306
393.	ETV4	ETS variant 4	2.98963	2.98716
394.	ETV5	ETS variant 5	1.71214	2.63838
395.	EXO1	exonuclease 1	0.586883	0.616257
396.	EXOC3-AS1	EXOC3 antisense RNA 1	0.65992	0.935699
397.	EXOSC2	exosome component 2	0.584958	0.614102
398.	EXOSC4	exosome component 4	0.624955	1.19043
399.	EXTL2	exostosin like glycosyltransferase 2	0.709238	0.541277
400.	FAAP100	Fanconi anemia core complex associated protein 100	0.924334	1.1769
401.	FABP5	fatty acid binding protein 5	0.582434	0.764601
402.	FAH	fumarylacetoacetate hydrolase	0.553601	0.478695
403.	FAHD1	fumarylacetoacetate hydrolase domain containing 1	0.636851	0.901924
404.	FAHD2CP	"fumarylacetoacetate hydrolase domain containing 2C, pseudogene"	0.698245	0.689497
405.	FAM104B	family with sequence similarity 104 member B	0.817937	0.900684
406.	FAM109A	family with sequence similarity 109 member A	0.510703	0.628693
407.	FAM117B	family with sequence similarity 117 member B	0.800434	0.544344
408.	FAM129B	family with sequence similarity 129 member B	0.567133	0.628176
409.	FAM136A	family with sequence similarity 136 member A	1.77743	1.89115
410.	FAM136BP	"family with sequence similarity 136 member B, pseudogene"	1.19572	0.919494
411.	FAM162A	family with sequence similarity 162 member A	0.512759	0.651472
412.	FAM168B	family with sequence similarity 168 member B	0.732542	0.642111
413.	FAM210B	family with sequence similarity 210 member B	0.494677	0.455537
414.	FAM234A	family with sequence similarity 234 member A	1.20283	1.24764
415.	FAM26F	family with sequence similarity 26 member F	0.969095	1.12822
416.	FAM32A	family with sequence similarity 32 member A	0.887943	0.919503
417.	FAM57A	family with sequence similarity 57 member A	1.08004	1.04424
418.	FAM64A	family with sequence similarity 64 member A	0.685687	0.797623
419.	FAM84B	family with sequence similarity 84 member B	0.978182	0.9469
420.	FANCE	Fanconi anemia complementation group E	0.788509	0.896597
421.	FARS2	"phenylalanyl-tRNA synthetase 2, mitochondrial"	0.604479	0.630769
422.	FARSB	phenylalanyl-tRNA synthetase beta subunit	0.589758	0.56169
423.	FBXO45	F-box protein 45	1.04396	1.00334
424.	FBXW9	F-box and WD repeat domain containing 9	1.83408	2.26133
425.	FCMR	Fc fragment of IgM receptor	0.62598	0.67407
426.	FDFT1	farnesyl-diphosphate farnesyltransferase 1	0.83121	0.616238
427.	FERMT2	fermitin family member 2	0.511322	0.456936
428.	FGFBP2	fibroblast growth factor binding protein 2	2.90166	2.19779
429.	FGFBP3	fibroblast growth factor binding protein 3	1.23721	1.87457
430.	FGFR2	fibroblast growth factor receptor 2	0.947844	0.935403
431.	FH	fumarate hydratase	0.517003	0.568854

432.	FIBP	FGF1 intracellular binding protein	0.762325	0.744858
433.	FIS1	"fission, mitochondrial 1"	0.477	0.64285
434.	FJX1	four jointed box 1	0.673003	0.786922
435.	FKBP3	FK506 binding protein 3	0.598451	0.547113
436.	FKBPL	FK506 binding protein like	0.676845	0.921371
437.	FLT4	fms related tyrosine kinase 4	0.967415	1.2875
438.	FMNL2	formin like 2	0.941409	0.829786
439.	FRAT2	frequently rearranged in advanced T-cell lymphomas 2	1.26584	1.50653
440.	FSCN1	fascin actin-bundling protein 1	0.883641	0.88007
441.	FTO	fat mass and obesity associated	0.807692	0.719746
442.	FUNDC2	FUN14 domain containing 2	0.465033	0.455508
443.	FUOM	fucose mutarotase	0.512164	0.843375
444.	FYTTD1	forty-two-three domain containing 1	1.3472	1.19733
445.	FZD6	frizzled class receptor 6	0.513988	0.416162
446.	FZD9	frizzled class receptor 9	0.881945	1.14293
447.	GABPB1	GA binding protein transcription factor beta subunit 1	0.78914	0.806187
448.	GALNT14	polypeptide N-acetylgalactosaminyltransferase 14	0.608762	0.488799
449.	GAR1	GAR1 ribonucleoprotein	0.712978	0.750716
450.	GATA4	GATA binding protein 4	0.816668	0.487858
451.	GBX2	gastrulation brain homeobox 2	0.911229	0.883168
452.	GCAT	glycine C-acetyltransferase	0.816279	0.888683
453.	GCDH	glutaryl-CoA dehydrogenase	0.848594	0.735966
454.	GDF1	growth differentiation factor 1	0.939212	0.785672
455.	GEMIN2	gem nuclear organelle associated protein 2	2.09195	2.368
456.	GEMIN6	gem nuclear organelle associated protein 6	0.527315	0.549781
457.	GFOD1	glucose-fructose oxidoreductase domain containing 1	0.655897	0.677425
458.	GGACT	gamma-glutamylamine cyclotransferase	0.730741	1.16279
459.	GGCT	gamma-glutamylcyclotransferase	2.08826	2.14783
460.	GGCX	gamma-glutamyl carboxylase	0.84325	0.896333
461.	GGH	gamma-glutamyl hydrolase	0.863208	0.719927
462.	GID8	GID complex subunit 8 homolog	0.555707	0.617716
463.	GINS1	GINS complex subunit 1	0.825391	0.768927
464.	GINS2	GINS complex subunit 2	1.68133	1.7959
465.	GJA1	gap junction protein alpha 1	4.11427	3.86025
466.	GLO1	glyoxalase I	0.596599	0.510487
467.	GLP1R	glucagon like peptide 1 receptor	0.964153	0.86756
468.	GLRX2	glutaredoxin 2	0.493896	0.530772
469.	GLRX3	glutaredoxin 3	0.917546	1.0863
470.	GLRX5	glutaredoxin 5	0.741695	0.736694
471.	GLUD2	glutamate dehydrogenase 2	0.54971	0.439276
472.	GMDS	"GDP-mannose 4,6-dehydratase"	0.567183	0.508126
473.	GNA12	G protein subunit alpha 12	0.878071	0.730274
474.	GNAI1	G protein subunit alpha i1	0.590945	0.485692
475.	GNG10	G protein subunit gamma 10	0.677874	0.564374
476.	GNG12	G protein subunit gamma 12	0.792578	0.595368
477.	GOLGA7	golgin A7	1.14222	0.971833
478.	GPC5	glypican 5	0.529826	0.4271
479.	GPR143	G protein-coupled receptor 143	0.864325	1.13005
480.	GPR176	G protein-coupled receptor 176	0.911931	1.19186
481.	GPR37	G protein-coupled receptor 37	1.6004	1.4605
482.	GPT2	glutamic--pyruvic transaminase 2	1.20088	1.06805
483.	GRHPR	glyoxylate and hydroxypyruvate reductase	0.445495	0.490305
484.	GRK6	G protein-coupled receptor kinase 6	0.718213	0.990066
485.	GRPR	gastrin releasing peptide receptor	2.54854	2.69536
486.	GSG1L	GSG1 like	3.08116	2.83152
487.	GSTA4	glutathione S-transferase alpha 4	1.77556	2.01732
488.	GSTO1	glutathione S-transferase omega 1	0.382099	0.419248
489.	GSTO2	glutathione S-transferase omega 2	0.4087	0.479226
490.	GTF2F2	general transcription factor IIF subunit 2	0.413409	0.496262
491.	GTF2H5	general transcription factor IIH subunit 5	0.482877	0.661587
492.	GTF3A	general transcription factor IIIA	0.639956	0.603777
493.	GTF3C4	general transcription factor IIIC subunit 4	0.760099	0.704617
494.	GUCY1A2	guanylate cyclase 1 soluble subunit alpha 2	0.645431	0.613243
495.	H2AFJ	H2A histone family member J	0.688296	1.08134
496.	H2AFY	H2A histone family member Y	1.35164	1.31266
497.	H2AFY2	H2A histone family member Y2	0.758477	0.819214

498.	H3F3A	H3 histone family member 3A	0.858372	1.01209
499.	H3F3AP4	"H3 histone, family 3A, pseudogene 4"	0.994267	0.877585
500.	HACD1	3-hydroxyacyl-CoA dehydratase 1	1.31717	1.5829
501.	HACL1	2-hydroxyacyl-CoA lyase 1	1.08995	1.17999
502.	HAT1	histone acetyltransferase 1	0.915354	0.875117
503.	HAUS4	HAUS augmin like complex subunit 4	0.81204	0.852708
504.	HDDC2	HD domain containing 2	0.704719	0.628219
505.	HENMT1	HEN1 methyltransferase homolog 1	1.27558	1.38603
506.	HERC3	HECT and RLD domain containing E3 ubiquitin protein ligase 3	0.458215	0.557969
507.	HGD	"homogentisate 1,2-dioxygenase"	1.31709	0.994539
508.	HIBCH	3-hydroxyisobutyryl-CoA hydrolase	0.842222	0.631806
509.	HIKESHI	"Hikeshi, heat shock protein nuclear import factor"	0.467457	0.541752
510.	HINT1	histidine triad nucleotide binding protein 1	0.531404	0.618637
511.	HINT3	histidine triad nucleotide binding protein 3	0.862346	0.844222
512.	HIST1H2AC	histone cluster 1 H2A family member c	1.2603	1.30951
513.	HIST2H2BE	histone cluster 2 H2B family member e	1.19281	1.28682
514.	HIVEP3	human immunodeficiency virus type I enhancer binding protein 3	1.71264	1.48377
515.	HLA-A	"major histocompatibility complex, class I, A"	0.642678	0.723941
516.	HMBS	hydroxymethylbilane synthase	0.562652	0.666744
517.	HMGB1	high mobility group box 1	0.862235	0.760277
518.	HMGCS1	3-hydroxy-3-methylglutaryl-CoA synthase 1	0.995823	0.765179
519.	HMGCS2	3-hydroxy-3-methylglutaryl-CoA synthase 2	1.89403	0.988791
520.	HMGN1	high mobility group nucleosome binding domain 1	0.671758	0.650796
521.	HMGN2	high mobility group nucleosomal binding domain 2	0.431841	0.559308
522.	HMGN3	high mobility group nucleosomal binding domain 3	1.75435	1.77512
523.	HMOX2	heme oxygenase 2	0.981092	1.10676
524.	HNRNPC	heterogeneous nuclear ribonucleoprotein C (C1/C2)	0.47602	0.42311
525.	HNRNPDL	heterogeneous nuclear ribonucleoprotein D like	0.624528	0.737366
526.	HOMER2	homer scaffolding protein 2	1.61365	1.51969
527.	HOPX	HOP homeobox	1.87771	1.27803
528.	HOXB3	homeobox B3	0.917468	0.808306
529.	HOXB6	homeobox B6	1.8322	2.04239
530.	HOXB-AS3	HOXB cluster antisense RNA 3	2.07946	1.9725
531.	HPDL	4-hydroxyphenylpyruvate dioxygenase like	0.801218	1.19059
532.	HPGD	hydroxyprostaglandin dehydrogenase 15-(NAD)	2.94784	2.59741
533.	HSBP1	heat shock factor binding protein 1	0.545827	0.597753
534.	HSD17B10	hydroxysteroid 17-beta dehydrogenase 10	0.404017	0.437113
535.	HSD17B8	hydroxysteroid 17-beta dehydrogenase 8	1.0486	1.21188
536.	HSP90B1	heat shock protein 90 beta family member 1	0.780005	0.61235
537.	HSPA5	heat shock protein family A (Hsp70) member 5	0.461655	0.437272
538.	HSPB11	heat shock protein family B (small) member 11	0.468481	0.371903
539.	ID4	"inhibitor of DNA binding 4, HLH protein"	1.1042	1.28042
540.	IDH2	"isocitrate dehydrogenase (NADP(+)) 2, mitochondrial"	0.358842	0.464326
541.	IDI1	isopentenyl-diphosphate delta isomerase 1	0.710248	0.57221
542.	IFI27L1	interferon alpha inducible protein 27 like 1	0.498304	0.623056
543.	IFI30	"IFI30, lysosomal thiol reductase"	1.18563	1.69327
544.	IFI44	interferon induced protein 44	1.07807	1.79376
545.	IFI44L	interferon induced protein 44 like	0.595391	1.33428
546.	IFI6	interferon alpha inducible protein 6	0.854428	1.67039
547.	IFIT1	interferon induced protein with tetratricopeptide repeats 1	0.683847	1.46504
548.	IFITM1	interferon induced transmembrane protein 1	0.866949	1.27411
549.	IFRD2	interferon related developmental regulator 2	0.559552	0.745983
550.	IFT22	intraflagellar transport 22	0.595712	0.628508
551.	IFT57	intraflagellar transport 57	0.619088	0.594426
552.	IL10RB	interleukin 10 receptor subunit beta	1.09275	1.10894
553.	IL17RB	interleukin 17 receptor B	0.884077	0.736462
554.	IL19	interleukin 19	3.06232	2.39884
555.	IL20	interleukin 20	1.37049	1.13747
556.	IL23R	interleukin 23 receptor	0.901047	0.643077
557.	IL24	interleukin 24	2.76179	2.61736
558.	ILF2	interleukin enhancer binding factor 2	0.778354	0.768432
559.	ILF3-AS1	ILF3 antisense RNA 1 (head to head)	0.605486	0.965656
560.	IMP3	"IMP3, U3 small nucleolar ribonucleoprotein"	1.2763	1.63331
561.	IMPA2	inositol monophosphatase 2	0.564067	0.582915

562.	IMPDH2	inosine monophosphate dehydrogenase 2	0.480604	0.573689
563.	ING4	inhibitor of growth family member 4	1.19538	1.21837
564.	INPP4B	inositol polyphosphate-4-phosphatase type II B	1.41143	1.08739
565.	INPP5A	inositol polyphosphate-5-phosphatase A	0.67894	0.574134
566.	INSIG1	insulin induced gene 1	1.83312	1.73253
567.	IQCJ-SCHIP1	IQCJ-SCHIP1 readthrough	1.07634	0.824338
568.	IRX3	iroquois homeobox 3	0.704955	0.768635
569.	ISCA1	iron-sulfur cluster assembly 1	0.603147	0.595407
570.	ISG20L2	interferon stimulated exonuclease gene 20 like 2	0.800567	0.759151
571.	ISOC2	isochorismatase domain containing 2	0.578063	0.943153
572.	ITM2B	integral membrane protein 2B	0.455403	0.385767
573.	IVNS1ABP	influenza virus NS1A binding protein	0.500592	0.379788
574.	JAGN1	jagunal homolog 1	0.901859	1.05076
575.	JHDM1D-AS1	JHDM1D antisense RNA 1 (head to head)	1.91105	2.28899
576.	JPH2	junctophilin 2	1.83951	1.59197
577.	JPX	"JPX transcript, XIST activator (non-protein coding)"	0.797853	0.917472
578.	KANSL2	KAT8 regulatory NSL complex subunit 2	0.647085	0.758256
579.	KATNA1	katanin catalytic subunit A1	0.442418	0.585361
580.	KBTBD7	kelch repeat and BTB domain containing 7	0.400185	0.420395
581.	KCNAB1	potassium voltage-gated channel subfamily A member regulatory beta subunit 1	2.691	1.84939
582.	KCNK2	potassium two pore domain channel subfamily K member 2	1.34367	0.902705
583.	KCNK5	potassium two pore domain channel subfamily K member 5	0.424791	0.385622
584.	KCNMA1	potassium calcium-activated channel subfamily M alpha 1	1.55427	1.35738
585.	KCTD20	potassium channel tetramerization domain containing 20	0.59754	0.434534
586.	KCTD3	potassium channel tetramerization domain containing 3	0.882766	0.829573
587.	KCTD5	potassium channel tetramerization domain containing 5	0.425124	0.492212
588.	KCTD9	potassium channel tetramerization domain containing 9	0.999242	0.863835
589.	KDM7A	lysine demethylase 7A	1.0876	0.962187
590.	KIAA0101	KIAA0101	1.25341	1.39906
591.	KIAA1586	KIAA1586	0.802731	0.769537
592.	KIAA2013	KIAA2013	0.458529	0.66025
593.	KIF6	kinesin family member 6	0.904727	0.902278
594.	KMT5C	lysine methyltransferase 5C	0.564812	0.649637
595.	KNOP1	lysine rich nucleolar protein 1	0.996013	0.893312
596.	KRT16	keratin 16	1.41614	1.42172
597.	KRT2	keratin 2	1.2364	1.21345
598.	KRT6C	keratin 6C	1.27008	1.92117
599.	L3MBTL2	L3MBTL2 polycomb repressive complex 1 subunit	0.91279	0.965081
600.	LAGE3	L antigen family member 3	0.51342	0.72033
601.	LAMTOR3	"late endosomal/lysosomal adaptor, MAPK and MTOR activator 3"	0.519875	0.638155
602.	LANCL1	LanC like 1	0.596777	0.482519
603.	LAP3	leucine aminopeptidase 3	0.654389	0.76435
604.	LAPTM4B	lysosomal protein transmembrane 4 beta	1.26545	1.18734
605.	LAS1L	"LAS1 like, ribosome biogenesis factor"	0.473209	0.451075
606.	LDLRAP1	low density lipoprotein receptor adaptor protein 1	0.541318	0.537152
607.	LDOC1	leucine zipper down-regulated in cancer 1	0.909283	0.882885
608.	LDOC1L	leucine zipper down-regulated in cancer 1 like	1.00147	0.970258
609.	LEMD2	LEM domain containing 2	0.483313	0.472819
610.	LGI2	leucine rich repeat LGI family member 2	2.18862	2.00029
611.	LGMN	legumain	0.997135	0.849279
612.	LIMA1	LIM domain and actin binding 1	0.590325	0.584341
613.	LINC00152	long intergenic non-protein coding RNA 152	0.642621	0.845507
614.	LINC00205	long intergenic non-protein coding RNA 205	0.510607	0.541599
615.	LINC00473	long intergenic non-protein coding RNA 473	4.3032	5.28493
616.	LINC00493	long intergenic non-protein coding RNA 493	0.794676	0.993629
617.	LINC00998	long intergenic non-protein coding RNA 998	0.915797	0.942618
618.	LINC01550	long intergenic non-protein coding RNA 1550	1.32543	1.57637
619.	LINC01560	long intergenic non-protein coding RNA 1560	0.9892	1.12458
620.	LMNB1	lamin B1	0.627999	0.630477
621.	LMO4	LIM domain only 4	1.21488	1.10918
622.	LOC100288748	uncharacterized LOC100288748	0.514374	0.824425
623.	LOC728554	THO complex 3 pseudogene	0.691449	0.649272
624.	LOC93622	Morf4 family associated protein 1 like 1 pseudogene	0.617748	0.775301
625.	LRRC10B	leucine rich repeat containing 10B	1.33852	1.43715

626.	LRRC58	leucine rich repeat containing 58	0.529406	0.357706
627.	LRRC69	leucine rich repeat containing 69	0.555951	0.606239
628.	LRRC75A	leucine rich repeat containing 75A	0.828751	0.822573
629.	LRRC75A-AS1	LRRC75A antisense RNA 1	0.730571	0.859008
630.	LRRN1	leucine rich repeat neuronal 1	1.58509	1.41155
631.	LSM10	"LSM10, U7 small nuclear RNA associated"	0.568817	0.730227
632.	LSM11	"LSM11, U7 small nuclear RNA associated"	0.573773	0.53311
633.	LSM2	"LSM2 homolog, U6 small nuclear RNA and mRNA degradation associated"	0.576788	0.679191
634.	LSM5	"LSM5 homolog, U6 small nuclear RNA and mRNA degradation associated"	0.556302	0.584585
635.	LSM7	"LSM7 homolog, U6 small nuclear RNA and mRNA degradation associated"	0.610844	0.982496
636.	LUC7L	LUC7 like	0.729032	0.973398
637.	LUC7L2	"LUC7 like 2, pre-mRNA splicing factor"	0.803454	0.757396
638.	LXN	latexin	0.957785	0.959065
639.	LYAR	Ly1 antibody reactive	0.775255	0.806391
640.	LYRM4	LYR motif containing 4	0.816561	0.847357
641.	LYSMD2	LysM domain containing 2	0.879903	1.02031
642.	LZIC	leucine zipper and CTNNBIP1 domain containing	1.51983	1.32526
643.	LZTFL1	leucine zipper transcription factor like 1	0.597137	0.686555
644.	MAD2L1	MAD2 mitotic arrest deficient-like 1 (yeast)	0.684397	0.683566
645.	MAFB	MAF bZIP transcription factor B	1.68057	1.74892
646.	MAFG-AS1	MAFG antisense RNA 1 (head to head)	0.488091	0.758365
647.	MAGEF1	MAGE family member F1	0.775277	1.0272
648.	MAGEH1	MAGE family member H1	1.16952	1.36045
649.	MAK16	MAK16 homolog	0.777235	0.79678
650.	MAML3	mastermind like transcriptional coactivator 3	1.17245	0.753546
651.	MANEAL	mannosidase endo-alpha like	1.09	1.09727
652.	MANF	mesencephalic astrocyte derived neurotrophic factor	0.454652	0.481426
653.	MAP3K8	mitogen-activated protein kinase kinase kinase 8	0.80049	1.05051
654.	MAP6D1	MAP6 domain containing 1	1.64809	1.45758
655.	MAPK14	mitogen-activated protein kinase 14	0.578104	0.456541
656.	MAPK6	mitogen-activated protein kinase 6	0.93147	0.789119
657.	MARC1	mitochondrial amidoxime reducing component 1	0.739496	0.634046
658.	MARCKSL1	MARCKS like 1	1.18066	1.31506
659.	MARK3	microtubule affinity regulating kinase 3	0.541086	0.708198
660.	MARVELD1	MARVEL domain containing 1	0.787191	0.941691
661.	MARVELD2	MARVEL domain containing 2	0.848956	0.83838
662.	MAZ	MYC associated zinc finger protein	1.56603	1.75118
663.	MB21D2	Mab-21 domain containing 2	1.01576	1.17096
664.	MBD4	"methyl-CpG binding domain 4, DNA glycosylase"	0.679262	0.740153
665.	MBLAC2	metallo-beta-lactamase domain containing 2	0.798222	0.920713
666.	MCAT	malonyl-CoA-acyl carrier protein transacylase	0.383907	0.533893
667.	MCCC1	methylcrotonoyl-CoA carboxylase 1	0.606684	0.691066
668.	MCCC2	methylcrotonoyl-CoA carboxylase 2	0.928812	0.924177
669.	MCEE	methylmalonyl-CoA epimerase	0.841898	0.914268
670.	MCL1	BCL2 family apoptosis regulator	0.514158	0.547684
671.	MCM10	minichromosome maintenance 10 replication initiation factor	0.658391	0.655249
672.	MCMBP	minichromosome maintenance complex binding protein	0.539588	0.420955
673.	MDH1	malate dehydrogenase 1	0.483648	0.507619
674.	MECR	mitochondrial trans-2-enoyl-CoA reductase	0.629844	0.756609
675.	MED20	mediator complex subunit 20	0.783132	0.800067
676.	MED28	mediator complex subunit 28	0.537528	0.58869
677.	MEST	mesoderm specific transcript	2.28148	2.02826
678.	METTL21A	methyltransferase like 21A	1.81833	1.57057
679.	METTL8	methyltransferase like 8	0.803202	0.731764
680.	METTL9	methyltransferase like 9	0.619183	0.505024
681.	MFAP1	microfibrillar associated protein 1	0.40971	0.392112
682.	MFAP2	microfibrillar associated protein 2	1.55689	1.53872
683.	MFSD2A	major facilitator superfamily domain containing 2A	1.167	0.806571
684.	MGP	matrix Gla protein	0.989572	0.94395
685.	MINOS1	mitochondrial inner membrane organizing system 1	0.553804	0.786255
686.	MIPEP	mitochondrial intermediate peptidase	0.710182	0.782334
687.	MIR4435-2HG	MIR4435-2 host gene	0.680475	0.642404
688.	MIR99AHG	mir-99a-let-7c cluster host gene	0.706262	0.866057

689.	MIS18A	MIS18 kinetochore protein A	0.390648	0.472706
690.	MKKS	McKusick-Kaufman syndrome	0.509373	0.481629
691.	MLF1	myeloid leukemia factor 1	1.03219	0.903088
692.	MLXIPL	MLX interacting protein like	0.650685	0.897178
693.	MMAA	methylmalonic aciduria (cobalamin deficiency) cblA type	0.736563	1.01764
694.	MMAB	methylmalonic aciduria (cobalamin deficiency) cblB type	0.698355	0.816792
695.	MMADHC	"methylmalonic aciduria and homocystinuria, cblD type"	0.552518	0.585056
696.	MMP15	matrix metallopeptidase 15	0.898084	0.856742
697.	MMP16	matrix metallopeptidase 16	1.33017	0.960805
698.	MNS1	meiosis specific nuclear structural 1	0.840035	0.758889
699.	MNX1-AS1	MNX1 antisense RNA 1 (head to head)	0.688844	0.870034
700.	MOAP1	modulator of apoptosis 1	0.358154	0.435341
701.	MOCS2	molybdenum cofactor synthesis 2	1.286	1.24044
702.	MORF4L2	mortality factor 4 like 2	1.31419	1.32475
703.	MORN2	MORN repeat containing 2	1.01867	0.929174
704.	MPC1	mitochondrial pyruvate carrier 1	0.595465	0.512531
705.	MPLKIP	M-phase specific PLK1 interacting protein	0.939126	1.25982
706.	MPST	mercaptopyruvate sulfurtransferase	0.954081	1.3583
707.	MPV17	"MPV17, mitochondrial inner membrane protein"	0.799041	0.913382
708.	MPV17L2	MPV17 mitochondrial inner membrane protein like 2	0.55069	0.580507
709.	MPZL2	myelin protein zero like 2	0.733585	0.887167
710.	MRFAP1L1	Morf4 family associated protein 1 like 1	0.361048	0.479952
711.	MRPL1	mitochondrial ribosomal protein L1	0.613311	0.6288
712.	MRPL11	mitochondrial ribosomal protein L11	0.561701	0.673595
713.	MRPL12	mitochondrial ribosomal protein L12	0.508657	0.795649
714.	MRPL13	mitochondrial ribosomal protein L13	0.515309	0.464846
715.	MRPL14	mitochondrial ribosomal protein L14	1.09525	1.31287
716.	MRPL16	mitochondrial ribosomal protein L16	0.6387	0.765245
717.	MRPL17	mitochondrial ribosomal protein L17	0.790089	1.02674
718.	MRPL21	mitochondrial ribosomal protein L21	0.620408	0.711494
719.	MRPL22	mitochondrial ribosomal protein L22	0.41355	0.520083
720.	MRPL24	mitochondrial ribosomal protein L24	0.506235	0.53577
721.	MRPL27	mitochondrial ribosomal protein L27	0.756929	0.97082
722.	MRPL3	mitochondrial ribosomal protein L3	0.752811	0.771381
723.	MRPL33	mitochondrial ribosomal protein L33	0.747995	0.79456
724.	MRPL36	mitochondrial ribosomal protein L36	0.541391	0.810266
725.	MRPL37	mitochondrial ribosomal protein L37	0.844301	0.91952
726.	MRPL42	mitochondrial ribosomal protein L42	0.558932	0.591286
727.	MRPL50	mitochondrial ribosomal protein L50	0.727963	0.787498
728.	MRPL57	mitochondrial ribosomal protein L57	0.811779	1.13103
729.	MRPL58	mitochondrial ribosomal protein L58	0.589747	0.704769
730.	MRPS15	mitochondrial ribosomal protein S15	0.589601	0.631072
731.	MRPS23	mitochondrial ribosomal protein S23	0.403958	0.480255
732.	MRPS24	mitochondrial ribosomal protein S24	0.555455	0.665775
733.	MRPS26	mitochondrial ribosomal protein S26	0.590285	0.855188
734.	MRPS33	mitochondrial ribosomal protein S33	0.401031	0.459406
735.	MS4A15	membrane spanning 4-domains A15	1.42859	0.848195
736.	MSANTD3	Myb/SANT DNA binding domain containing 3	1.03394	1.14267
737.	MSH2	mutS homolog 2	0.453754	0.355227
738.	MSL3P1	male-specific lethal 3 homolog (Drosophila) pseudogene 1	1.08888	1.21766
739.	MT1X	metallothionein 1X	0.426134	0.685788
740.	MTCH2	mitochondrial carrier 2	0.643666	0.688932
741.	MTERF3	mitochondrial transcription termination factor 3	0.452698	0.582238
742.	MTF2	metal response element binding transcription factor 2	0.620632	0.58535
743.	MTG1	mitochondrial ribosome associated GTPase 1	0.930824	1.10945
744.	MTHFD2	"methylenetetrahydrofolate dehydrogenase (NADP+ dependent) 2, methenyltetrahydrofolate cyclohydrolase"	0.67394	0.578727
745.	MTHFD2L	methylenetetrahydrofolate dehydrogenase (NADP+ dependent) 2-like	0.589263	0.741144
746.	MTMR2	myotubularin related protein 2	0.910336	0.726056
747.	MTRF1	mitochondrial translational release factor 1	0.447792	0.619521
748.	MUCL1	mucin like 1	1.29882	0.915705
749.	MUM1L1	MUM1 like 1	1.46894	1.51818
750.	MYBL2	MYB proto-oncogene like 2	2.03609	2.14457
751.	MYC	v-myc avian myelocytomatosis viral oncogene homolog	0.888765	0.900107
752.	MYCBP	MYC binding protein	0.834701	0.780983

753.	MYL6	myosin light chain 6	0.876249	0.994649
754.	MYO3B	myosin IIIB	1.78755	1.71407
755.	NAE1	NEDD8 activating enzyme E1 subunit 1	0.493453	0.473918
756.	NANP	N-acetylneuraminic acid phosphatase	0.857126	0.883009
757.	NARS2	"asparaginyl-tRNA synthetase 2, mitochondrial (putative)"	0.792649	0.687521
758.	NASP	nuclear autoantigenic sperm protein	0.889616	0.865998
759.	NAT1	N-acetyltransferase 1	0.828996	1.0541
760.	NAT14	N-acetyltransferase 14 (putative)	0.436621	0.755597
761.	NAXE	NAD(P)HX epimerase	0.699496	0.682152
762.	NCBP2-AS2	NCBP2 antisense RNA 2 (head to head)	0.585973	1.03664
763.	NCR3LG1	natural killer cell cytotoxicity receptor 3 ligand 1	0.504336	0.427074
764.	NDC1	NDC1 transmembrane nucleoporin	0.581386	0.415238
765.	NDRG2	NDRG family member 2	1.06254	0.885938
766.	NDUFA1	NADH:ubiquinone oxidoreductase subunit A1	0.481754	0.626363
767.	NDUFA10	NADH:ubiquinone oxidoreductase subunit A10	0.587629	0.742002
768.	NDUFA4	"NDUFA4, mitochondrial complex associated"	0.620783	0.591739
769.	NDUFA9	NADH:ubiquinone oxidoreductase subunit A9	0.482408	0.51758
770.	NDUFAB1	NADH:ubiquinone oxidoreductase subunit AB1	0.596311	0.692596
771.	NDUFAF2	NADH:ubiquinone oxidoreductase complex assembly factor 2	0.783876	0.745836
772.	NDUFAF8	NADH:ubiquinone oxidoreductase complex assembly factor 8	0.438455	0.719152
773.	NDUFB1	NADH:ubiquinone oxidoreductase subunit B1	0.794603	0.958529
774.	NDUFB6	NADH:ubiquinone oxidoreductase subunit B6	0.611903	0.800763
775.	NDUFB9	NADH:ubiquinone oxidoreductase subunit B9	0.555857	0.618531
776.	NDUFS4	NADH:ubiquinone oxidoreductase subunit S4	0.599484	0.649652
777.	NDUFS5	NADH:ubiquinone oxidoreductase subunit S5	0.447218	0.58327
778.	NEK6	NIMA related kinase 6	0.713992	0.544106
779.	NENF	neudesin neurotrophic factor	0.63689	0.689993
780.	NFIA	nuclear factor I A	1.93518	1.60973
781.	NGRN	"neugrin, neurite outgrowth associated"	0.449335	0.411608
782.	NHP2	NHP2 ribonucleoprotein	0.656477	0.842416
783.	NIFK	nucleolar protein interacting with the FHA domain of MKI67	0.614676	0.649105
784.	NIPSNAP3A	nipsnap homolog 3A	1.98433	2.36503
785.	NIPSNAP3B	nipsnap homolog 3B	0.977539	0.816229
786.	NKIRAS2	NFKB inhibitor interacting Ras like 2	1.79244	1.98048
787.	NKRF	NFKB repressing factor	0.562578	0.591047
788.	NLE1	notchless homolog 1	0.739256	0.961983
789.	NLRP1	NLR family pyrin domain containing 1	1.09248	1.19686
790.	NLRX1	NLR family member X1	0.861659	0.784992
791.	NMB	neuromedin B	1.57817	1.63764
792.	NME1	NME/NM23 nucleoside diphosphate kinase 1	0.856472	0.982628
793.	NME1-NME2	NME1-NME2 readthrough	0.537902	0.568051
794.	NMU	neuromedin U	1.0744	0.667768
795.	NOB1	NIN1/PSMD8 binding protein 1 homolog	0.454083	0.560442
796.	NOC3L	NOC3 like DNA replication regulator	0.463655	0.418221
797.	NOL11	nucleolar protein 11	0.584325	0.564753
798.	NOP10	NOP10 ribonucleoprotein	1.02759	1.12941
799.	NOP56	NOP56 ribonucleoprotein	0.588583	0.625073
800.	NOP58	NOP58 ribonucleoprotein	0.57573	0.474755
801.	NPM3	nucleophosmin/nucleoplasmin 3	1.59262	1.6237
802.	NPY1R	neuropeptide Y receptor Y1	1.33529	1.13624
803.	NQO2	NAD(P)H quinone dehydrogenase 2	0.893087	0.924738
804.	NR5A2	nuclear receptor subfamily 5 group A member 2	1.21764	0.825542
805.	NRBP1	nuclear receptor binding protein 1	0.590665	0.596604
806.	NREP	neuronal regeneration related protein	1.5593	1.33906
807.	NRTN	neurturin	1.42941	1.46177
808.	NSL1	"NSL1, MIS12 kinetochore complex component"	0.575272	0.679574
809.	NT5C3B	"5'-nucleotidase, cytosolic IIIB"	0.390653	0.394116
810.	NTMT1	N-terminal Xaa-Pro-Lys N-methyltransferase 1	0.366753	0.68196
811.	NUDCD1	NudC domain containing 1	0.605891	0.538786
812.	NUDT1	nudix hydrolase 1	0.488716	0.574153
813.	NUDT16L1	nudix hydrolase 16 like 1	0.742033	1.02527
814.	NUDT2	nudix hydrolase 2	0.587172	0.742747
815.	NUP160	nucleoporin 160	1.02944	0.977176
816.	NUP35	nucleoporin 35	0.649279	0.599748

817.	NUS1	NUS1 dehydrodolichyl diphosphate synthase subunit	0.588642	0.461185
818.	NXN	nucleoredoxin	0.717945	0.799884
819.	NXPH3	neurexophilin 3	1.14279	1.13923
820.	NXT1	nuclear transport factor 2 like export factor 1	0.594323	0.796174
821.	OAF	out at first homolog	0.614108	1.2268
822.	OASL	2'-5'-oligoadenylate synthetase like	0.68925	1.43106
823.	OAT	ornithine aminotransferase	0.61619	0.435381
824.	OBSL1	obscurin like 1	0.990759	1.04061
825.	OIP5	Opa interacting protein 5	2.11953	2.39693
826.	OIP5-AS1	OIP5 antisense RNA 1	1.90865	1.75325
827.	OLFML3	olfactomedin like 3	2.60869	2.68797
828.	ORC5	origin recognition complex subunit 5	0.451018	0.481556
829.	ORC6	origin recognition complex subunit 6	0.500223	0.527708
830.	OSGEP	O-sialoglycoprotein endopeptidase	0.590015	0.706425
831.	OSGEPL1	O-sialoglycoprotein endopeptidase like 1	0.946834	0.805438
832.	OST4	"oligosaccharyltransferase complex subunit 4, non-catalytic"	0.446121	0.460205
833.	OSTC	oligosaccharyltransferase complex non-catalytic subunit	2.19415	2.35898
834.	P2RY6	pyrimidinergic receptor P2Y6	1.07541	1.20488
835.	P3H1	prolyl 3-hydroxylase 1	1.17836	0.882606
836.	P3H4	prolyl 3-hydroxylase family member 4 (non-enzymatic)	1.43784	1.60295
837.	PACRGL	PARK2 coregulated like	0.71929	0.778749
838.	PADI3	peptidyl arginine deiminase 3	1.29671	1.12462
839.	PAICS	phosphoribosylaminoimidazole carboxylase;	0.627836	0.480478
840.	PAK1IP1	PAK1 interacting protein 1	0.562759	0.666736
841.	PANK1	pantothenate kinase 1	0.797274	0.730937
842.	PARG	poly(ADP-ribose) glycohydrolase	0.88996	0.913123
843.	PARK7	Parkinsonism associated deglycase	0.541766	0.515431
844.	PARL	presenilin associated rhomboid like	0.535057	0.586764
845.	PARP12	poly(ADP-ribose) polymerase family member 12	0.41123	0.735736
846.	PAX9	paired box 9	0.58445	0.662648
847.	PBDC1	polysaccharide biosynthesis domain containing 1	0.702885	0.752183
848.	PCCB	propionyl-CoA carboxylase beta subunit	0.879864	0.830985
849.	PCDHB5	protocadherin beta 5	1.21352	1.02547
850.	PCDHB6	protocadherin beta 6	0.547292	0.578213
851.	PCDHB8	protocadherin beta 8	1.12031	0.851423
852.	PCGF6	polycomb group ring finger 6	0.935854	0.998118
853.	PCIF1	PDX1 C-terminal inhibiting factor 1	0.398303	0.598229
854.	PCNA	proliferating cell nuclear antigen	0.420561	0.587194
855.	PCOLCE2	procollagen C-endopeptidase enhancer 2	0.623997	0.976315
856.	PCSK9	proprotein convertase subtilisin/kexin type 9	0.536665	0.556471
857.	PCYOX1L	prenylcysteine oxidase 1 like	1.0197	1.04292
858.	PDCD2	programmed cell death 2	0.709717	0.75917
859.	PDE1A	phosphodiesterase 1A	1.68231	1.53396
860.	PDE4B	phosphodiesterase 4B	1.30251	1.10839
861.	PDHB	pyruvate dehydrogenase (lipoamide) beta	1.02254	0.966478
862.	PDHX	pyruvate dehydrogenase complex component X	1.11496	1.1193
863.	PDIA2	protein disulfide isomerase family A member 2	0.84232	1.0513
864.	PDIA4	protein disulfide isomerase family A member 4	0.832177	0.763579
865.	PDIA6	protein disulfide isomerase family A member 6	0.540674	0.422012
866.	PDLIM3	PDZ and LIM domain 3	1.21686	1.19913
867.	PDRG1	p53 and DNA damage regulated 1	0.59653	0.79471
868.	PDZK1	PDZ domain containing 1	2.32078	1.75265
869.	PEBP1	phosphatidylethanolamine binding protein 1	0.5634	0.499523
870.	PEG10	paternally expressed 10	2.10984	2.21207
871.	PEX2	peroxisomal biogenesis factor 2	0.769444	0.809132
872.	PEX5	peroxisomal biogenesis factor 5	0.622786	0.595623
873.	PFDN5	prefoldin subunit 5	0.546246	0.491788
874.	PGAM1	phosphoglycerate mutase 1	0.452985	0.512096
875.	PGBD5	piggyBac transposable element derived 5	0.874885	1.03782
876.	PGD	phosphogluconate dehydrogenase	0.551699	0.534879
877.	PGM1	phosphoglucomutase 1	0.901442	0.766433
878.	PHB	prohibitin	0.558869	0.571996
879.	PHB2	prohibitin 2	0.658567	0.742473
880.	PHF10	PHD finger protein 10	1.47714	1.42481
881.	PHF13	PHD finger protein 13	0.548822	0.679934
882.	PHLDA1	pleckstrin homology like domain family A member 1	0.52809	0.652852

883.	PHTF2	putative homeodomain transcription factor 2	0.995553	0.932872
884.	PI15	peptidase inhibitor 15	1.38949	1.21943
885.	PIGC	phosphatidylinositol glycan anchor biosynthesis class C	0.41005	0.397585
886.	PIGM	phosphatidylinositol glycan anchor biosynthesis class M	0.537811	0.601687
887.	PIGN	phosphatidylinositol glycan anchor biosynthesis class N	1.27463	0.843688
888.	PIGS	phosphatidylinositol glycan anchor biosynthesis class S	1.71025	1.52542
889.	PIK3C2G	phosphatidylinositol-4-phosphate 3-kinase catalytic subunit type 2 gamma	1.32998	1.10551
890.	PINX1	"PIN2/TERF1 interacting, telomerase inhibitor 1"	0.563699	0.614464
891.	PIP	prolactin induced protein	1.58833	1.40631
892.	PIR	pirin	1.18405	1.09699
893.	PITPNC1	"phosphatidylinositol transfer protein, cytoplasmic 1"	0.752945	0.698521
894.	PKIB	"protein kinase (cAMP-dependent, catalytic) inhibitor beta"	0.923158	0.820975
895.	PLEK2	pleckstrin 2	0.612746	0.482887
896.	PLEKHO1	pleckstrin homology domain containing O1	0.955779	0.986967
897.	PLGRKT	plasminogen receptor with a C-terminal lysine	1.03486	0.956894
898.	PLK1	polo like kinase 1	0.502805	0.534145
899.	PLK2	polo like kinase 2	2.01513	1.87612
900.	PLP1	proteolipid protein 1	1.78971	2.78286
901.	PLSCR1	phospholipid scramblase 1	0.400567	0.622252
902.	PMF1	polyamine modulated factor 1	0.49455	0.668554
903.	PMPCA	"peptidase, mitochondrial processing alpha subunit"	0.741118	0.917951
904.	PNMA1	paraneoplastic Ma antigen 1	0.569994	0.68552
905.	PNP	purine nucleoside phosphorylase	0.562185	0.634676
906.	PNPT1	polyribonucleotide nucleotidyltransferase 1	0.771053	0.820103
907.	POLB	DNA polymerase beta	0.679722	0.900578
908.	POLD2	"DNA polymerase delta 2, accessory subunit"	0.947729	0.850791
909.	POLDIP2	DNA polymerase delta interacting protein 2	0.545445	0.547899
910.	POLE3	"DNA polymerase epsilon 3, accessory subunit"	1.31072	1.50374
911.	POLE4	"DNA polymerase epsilon 4, accessory subunit"	0.373808	0.576856
912.	POLG2	"DNA polymerase gamma 2, accessory subunit"	0.496162	0.584555
913.	POLR1D	RNA polymerase I subunit D	1.21672	1.4292
914.	POLR1E	RNA polymerase I subunit E	0.416051	0.360962
915.	POLR2G	RNA polymerase II subunit G	1.0195	1.11076
916.	POLR2K	RNA polymerase II subunit K	0.36188	0.359019
917.	POLR3D	RNA polymerase III subunit D	0.922376	1.05985
918.	POLR3G	RNA polymerase III subunit G	0.810646	1.02777
919.	POLR3K	RNA polymerase III subunit K	0.601195	0.724844
920.	POMP	proteasome maturation protein	0.398388	0.424103
921.	POP5	"POP5 homolog, ribonuclease P/MRP subunit"	0.785138	1.02197
922.	POPDC3	popeye domain containing 3	0.787233	1.0069
923.	POU1F1	POU class 1 homeobox 1	1.10366	1.22851
924.	POU3F2	POU class 3 homeobox 2	1.23518	1.18252
925.	PPA1	pyrophosphatase (inorganic) 1	0.889133	0.91749
926.	PPA2	pyrophosphatase (inorganic) 2	0.417186	0.475001
927.	PPIA	peptidylprolyl isomerase A	0.404212	0.429638
928.	PPIB	peptidylprolyl isomerase B	1.11594	1.2242
929.	PPIH	peptidylprolyl isomerase H	0.40786	0.56116
930.	PPIL1	peptidylprolyl isomerase like 1	0.72316	0.771098
931.	PPM1D	"protein phosphatase, Mg2+/Mn2+ dependent 1D"	0.805558	0.828481
932.	PPM1G	"protein phosphatase, Mg2+/Mn2+ dependent 1G"	0.421925	0.389986
933.	PPP1R14C	protein phosphatase 1 regulatory inhibitor subunit 14C	2.03073	2.02062
934.	PPP1R3B	protein phosphatase 1 regulatory subunit 3B	0.433307	0.398739
935.	PPP4C	protein phosphatase 4 catalytic subunit	0.389742	0.577441
936.	PRADC1	protease associated domain containing 1	0.539953	0.658061
937.	PRDX3	peroxiredoxin 3	0.627377	0.542784
938.	PRDX4	peroxiredoxin 4	0.874995	0.937589
939.	PRDX6	peroxiredoxin 6	0.644178	0.561437
940.	PRELID1	PRELI domain containing 1	0.526265	0.474331
941.	PRIMA1	proline rich membrane anchor 1	0.382483	0.378951
942.	PRKACA	protein kinase cAMP-activated catalytic subunit alpha	0.628271	0.54078
943.	PRMT5	protein arginine methyltransferase 5	0.737209	0.665835
944.	PRPF38A	pre-mRNA processing factor 38A	1.47559	1.5399
945.	PRR3	proline rich 3	1.05653	1.07873
946.	PRSS23	"protease, serine 23"	1.31424	1.13168
947.	PRTG	protogenin	1.31376	1.23996

948.	PRX	periaxin	1.08466	0.880227
949.	PSKH1	protein serine kinase H1	0.564947	0.756137
950.	PSMA2	proteasome subunit alpha 2	0.711013	0.747366
951.	PSMA4	proteasome subunit alpha 4	1.20228	1.18312
952.	PSMA7	proteasome subunit alpha 7	0.611977	0.569242
953.	PSMB1	proteasome subunit beta 1	0.365698	0.454699
954.	PSMB4	proteasome subunit beta 4	0.447662	0.505157
955.	PSMB5	proteasome subunit beta 5	0.647283	0.685028
956.	PSMB7	proteasome subunit beta 7	0.703839	0.733512
957.	PSMC1	"proteasome 26S subunit, ATPase 1"	0.568718	0.565683
958.	PSMC2	"proteasome 26S subunit, ATPase 2"	0.556815	0.614312
959.	PSMC3	"proteasome 26S subunit, ATPase 3"	0.867627	0.83266
960.	PSMD13	"proteasome 26S subunit, non-ATPase 13"	0.720864	0.803083
961.	PSMD7	"proteasome 26S subunit, non-ATPase 7"	0.485609	0.55362
962.	PSME1	proteasome activator subunit 1	0.489988	0.532391
963.	PSMG1	proteasome assembly chaperone 1	0.681266	0.765086
964.	PSPH	phosphoserine phosphatase	0.415752	0.442755
965.	PSTPIP2	proline-serine-threonine phosphatase interacting protein 2	0.853152	0.921707
966.	PTDSS1	phosphatidylserine synthase 1	0.677304	0.585521
967.	PTENP1	phosphatase and tensin homolog pseudogene 1	1.06433	1.26423
968.	PTGES2	prostaglandin E synthase 2	0.415851	0.570339
969.	PTMA	"prothymosin, alpha"	0.472511	0.39151
970.	PVALB	parvalbumin	1.21037	1.57428
971.	PYCR1	pyrroline-5-carboxylate reductase 1	0.667415	0.824556
972.	PYGL	"phosphorylase, glycogen, liver"	0.598803	0.527726
973.	QTRT1	queuine tRNA-ribosyltransferase catalytic subunit 1	0.471824	0.661715
974.	R3HCC1	R3H domain and coiled-coil containing 1	1.47594	1.51118
975.	RAB20	"RAB20, member RAS oncogene family"	0.54106	0.671545
976.	RAB4A	"RAB4A, member RAS oncogene family"	0.553993	0.451898
977.	RAB9B	"RAB9B, member RAS oncogene family"	1.39674	1.60651
978.	RABEPK	Rab9 effector protein with kelch motifs	0.550754	0.599569
979.	RACK1	receptor for activated C kinase 1	0.479845	0.474264
980.	RAD51C	RAD51 paralog C	0.445142	0.420747
981.	RAN	"RAN, member RAS oncogene family"	0.649795	0.716611
982.	RANP1	"RAN, member RAS oncogene family pseudogene 1"	0.818454	1.5527
983.	RAPGEFL1	Rap guanine nucleotide exchange factor like 1	1.07791	0.906922
984.	RARG	retinoic acid receptor gamma	0.99176	0.914053
985.	RASA3	RAS p21 protein activator 3	0.752342	0.715053
986.	RASGEF1B	RasGEF domain family member 1B	0.863543	1.06333
987.	RASL11A	RAS like family 11 member A	1.18544	1.55333
988.	RBFA	ribosome binding factor A (putative)	1.08745	1.15657
989.	RBMS2	RNA binding motif single stranded interacting protein 2	0.988779	0.695869
990.	RCL1	RNA terminal phosphate cyclase like 1	0.58902	0.770248
991.	RDH16	retinol dehydrogenase 16 (all-trans)	0.549674	0.848992
992.	RERG	RAS like estrogen regulated growth inhibitor	0.739758	0.650693
993.	REXO4	"REX4 homolog, 3'-5' exonuclease"	0.991587	1.21563
994.	RFC2	replication factor C subunit 2	0.554049	0.470145
995.	RFC3	replication factor C subunit 3	0.585816	0.562186
996.	RFLNB	refilin B	1.58933	1.30077
997.	RFT1	RFT1 homolog	1.00573	0.963011
998.	RFWD2	ring finger and WD repeat domain 2	0.768969	0.637484
999.	RFXAP	regulatory factor X associated protein	1.06703	0.94652
1000.	RGS16	regulator of G-protein signaling 16	0.542244	0.617958
1001.	RIDA	reactive intermediate imine deaminase A homolog	0.692374	0.508209
1002.	RIMS4	regulating synaptic membrane exocytosis 4	1.25577	1.2212
1003.	RIT1	Ras like without CAAX 1	0.743862	0.771635
1004.	RLN2	relaxin 2	0.992626	0.927344
1005.	RNASEL	ribonuclease L	1.11074	1.05212
1006.	RNASET2	ribonuclease T2	0.439969	0.479086
1007.	RND2	Rho family GTPase 2	0.528641	0.797044
1008.	RNF122	ring finger protein 122	1.14128	0.979431
1009.	RNF130	ring finger protein 130	0.700167	0.585128
1010.	RNF138	ring finger protein 138	0.993903	1.2314
1011.	RNF14	ring finger protein 14	0.744299	0.790873
1012.	RNF144B	ring finger protein 144B	0.536437	0.670161
1013.	RNF165	ring finger protein 165	1.06013	0.861514

1014.	RNF5	ring finger protein 5	0.74448	0.82896
1015.	RNF7	ring finger protein 7	0.475151	0.652396
1016.	RPA1	replication protein A1	1.3934	1.36769
1017.	RPIA	ribose 5-phosphate isomerase A	0.794538	0.845553
1018.	RPL10A	ribosomal protein L10a	0.714578	0.750405
1019.	RPL11	ribosomal protein L11	0.642594	0.604273
1020.	RPL12	ribosomal protein L12	0.609403	0.591557
1021.	RPL13	ribosomal protein L13	0.48154	0.660912
1022.	RPL13A	ribosomal protein L13a	0.565281	0.690617
1023.	RPL15	ribosomal protein L15	0.477561	0.543018
1024.	RPL17	ribosomal protein L17	0.608482	0.579599
1025.	RPL19	ribosomal protein L19	0.501585	0.555254
1026.	RPL21	ribosomal protein L21	0.755891	0.73765
1027.	RPL22L1	ribosomal protein L22 like 1	0.864808	0.965201
1028.	RPL23	ribosomal protein L23	0.713014	0.658251
1029.	RPL24	ribosomal protein L24	0.775667	0.80338
1030.	RPL26	ribosomal protein L26	0.635677	0.560063
1031.	RPL27	ribosomal protein L27	0.818785	0.914966
1032.	RPL27A	ribosomal protein L27a	0.602351	0.694477
1033.	RPL29	ribosomal protein L29	0.678791	0.965449
1034.	RPL3	ribosomal protein L3	0.643843	0.633513
1035.	RPL30	ribosomal protein L30	0.483029	0.514125
1036.	RPL31	ribosomal protein L31	0.500837	0.553839
1037.	RPL32	ribosomal protein L32	0.541315	0.574202
1038.	RPL34	ribosomal protein L34	0.791899	0.858151
1039.	RPL35	ribosomal protein L35	0.587071	0.681671
1040.	RPL35A	ribosomal protein L35a	0.687875	0.754828
1041.	RPL36A	ribosomal protein L36a	0.665105	0.625905
1042.	RPL36AL	ribosomal protein L36a like	0.544335	0.657496
1043.	RPL37A	ribosomal protein L37a	0.534367	0.585879
1044.	RPL39	ribosomal protein L39	0.790025	0.793589
1045.	RPL39L	ribosomal protein L39 like	0.71943	0.884334
1046.	RPL4	ribosomal protein L4	0.727798	0.651767
1047.	RPL41	ribosomal protein L41	0.863473	0.842525
1048.	RPL5	ribosomal protein L5	0.876493	0.834361
1049.	RPL7	ribosomal protein L7	0.540895	0.474478
1050.	RPL7A	ribosomal protein L7a	0.525127	0.483312
1051.	RPL8	ribosomal protein L8	0.447702	0.482796
1052.	RPL9	ribosomal protein L9	0.790399	0.797841
1053.	RPLP0	ribosomal protein lateral stalk subunit P0	0.690141	0.646959
1054.	RPN1	ribophorin I	0.436504	0.390911
1055.	RPP25L	ribonuclease P/MRP subunit p25 like	0.589825	0.823949
1056.	RPP40	ribonuclease P/MRP subunit p40	0.442086	0.477138
1057.	RPRM	"reprimo, TP53 dependent G2 arrest mediator candidate"	0.725484	0.672673
1058.	RPS10	ribosomal protein S10	0.69203	0.772701
1059.	RPS11	ribosomal protein S11	0.516476	0.496856
1060.	RPS12	ribosomal protein S12	0.585658	0.565778
1061.	RPS13	ribosomal protein S13	0.506	0.560536
1062.	RPS14	ribosomal protein S14	0.610268	0.66288
1063.	RPS15A	ribosomal protein S15a	0.97588	0.954983
1064.	RPS16	ribosomal protein S16	0.595941	0.646833
1065.	RPS18	ribosomal protein S18	0.638633	0.730978
1066.	RPS20	ribosomal protein S20	0.495754	0.533154
1067.	RPS21	ribosomal protein S21	0.612498	0.878411
1068.	RPS23	ribosomal protein S23	0.644234	0.677774
1069.	RPS25	ribosomal protein S25	0.679746	0.654124
1070.	RPS26	ribosomal protein S26	0.600671	0.710175
1071.	RPS27	ribosomal protein S27	0.508871	0.454789
1072.	RPS27A	ribosomal protein S27a	0.982195	0.969381
1073.	RPS29	ribosomal protein S29	1.07896	1.23262
1074.	RPS3	ribosomal protein S3	0.756681	0.745014
1075.	RPS4X	"ribosomal protein S4, X-linked"	0.617263	0.645454
1076.	RPS5	ribosomal protein S5	0.563525	0.738254
1077.	RPS6	ribosomal protein S6	0.80126	0.751089
1078.	RPS6KA5	ribosomal protein S6 kinase A5	0.591567	0.484197
1079.	RPS6KB1	ribosomal protein S6 kinase B1	0.690924	0.661297

1080.	RPS7	ribosomal protein S7	0.976177	0.982406
1081.	RPS8	ribosomal protein S8	0.798614	0.76595
1082.	RPS9	ribosomal protein S9	0.494933	0.615055
1083.	RPSA	ribosomal protein SA	0.728888	0.69114
1084.	RRAGA	Ras related GTP binding A	0.713067	0.811297
1085.	RRAS2	related RAS viral (r-ras) oncogene homolog 2	0.839157	0.770152
1086.	RRP8	ribosomal RNA processing 8, methyltransferase, homolog	0.501806	0.66187
1087.	RSL1D1	ribosomal L1 domain containing 1	0.599977	0.50853
1088.	RSPO1	R-spondin 1	1.00213	1.14493
1089.	RTN1	reticulon 1	1.33667	1.24382
1090.	RUNX2	runt related transcription factor 2	1.40906	1.12666
1091.	RUVBL2	RuvB like AAA ATPase 2	0.370826	0.545808
1092.	RWDD1	RWD domain containing 1	0.790947	0.703144
1093.	RWDD2B	RWD domain containing 2B	0.760684	0.77008
1094.	S100A14	S100 calcium binding protein A14	0.526757	0.460932
1095.	S100A4	S100 calcium binding protein A4	0.677395	0.465981
1096.	S100A8	S100 calcium binding protein A8	1.92461	3.08523
1097.	S100A9	S100 calcium binding protein A9	1.53666	2.52338
1098.	S1PR5	sphingosine-1-phosphate receptor 5	0.544561	0.637201
1099.	SAMHD1	SAM and HD domain containing deoxynucleoside triphosphate triphosphohydrolase 1	0.422929	0.441313
1100.	SARAF	store-operated calcium entry associated regulatory factor	0.651737	0.581324
1101.	SAT1	spermidine/spermine N1-acetyltransferase 1	0.701296	0.864274
1102.	SCAP	SREBF chaperone	0.857089	0.770539
1103.	SCML1	sex comb on midleg-like 1 (Drosophila)	0.763639	0.740902
1104.	SDC2	syndecan 2	0.629612	0.601104
1105.	SDF2L1	stromal cell derived factor 2 like 1	0.554218	0.876166
1106.	SDHAF3	succinate dehydrogenase complex assembly factor 3	1.03412	1.20257
1107.	SDHB	succinate dehydrogenase complex iron sulfur subunit B	0.436855	0.422219
1108.	SEC11A	"SEC11 homolog A, signal peptidase complex subunit"	0.489579	0.537134
1109.	SEC11C	"SEC11 homolog C, signal peptidase complex subunit"	0.493302	0.583424
1110.	SEC16B	"SEC16 homolog B, endoplasmic reticulum export factor"	1.14986	0.932813
1111.	SEC61B	Sec61 translocon beta subunit	0.380985	0.532805
1112.	SELK	selenoprotein K	0.506295	0.561729
1113.	SEMA3G	semaphorin 3G	1.08938	1.18135
1114.	SEP15	15 kDa selenoprotein	0.612944	0.630963
1115.	SEPHS2	selenophosphate synthetase 2	0.470174	0.583339
1116.	SEPP1	"selenoprotein P, plasma, 1"	1.09129	1.21632
1117.	SERBP1	SERPINE1 mRNA binding protein 1	0.99881	0.945595
1118.	SERPINB6	serpin family B member 6	0.400069	0.406089
1119.	SERPINH1	serpin family H member 1	1.97041	2.06858
1120.	SET	SET nuclear proto-oncogene	0.742598	0.618882
1121.	SF3B5	splicing factor 3b subunit 5	0.996388	1.13546
1122.	SF3B6	splicing factor 3b subunit 6	0.369752	0.345683
1123.	SFR1	SWI5 dependent homologous recombination repair protein 1	0.733793	0.792653
1124.	SFXN2	sideroflexin 2	0.977583	0.949226
1125.	SFXN4	sideroflexin 4	0.706769	0.733447
1126.	SGCG	sarcoglycan gamma	1.58645	1.76154
1127.	SH3BP5	SH3 domain binding protein 5	0.463129	0.394409
1128.	SH3BP5L	SH3 binding domain protein 5 like	1.04061	1.05831
1129.	SH3GL1	"SH3 domain containing GRB2 like 1, endophilin A2"	1.20402	1.35972
1130.	SH3GL3	"SH3 domain containing GRB2 like 3, endophilin A3"	1.68462	1.73615
1131.	SHROOM2	shroom family member 2	0.930158	0.799281
1132.	SIAH2	siah E3 ubiquitin protein ligase 2	1.85018	1.90909
1133.	SKP2	S-phase kinase-associated protein 2, E3 ubiquitin protein ligase	0.987079	0.961049
1134.	SLC16A1	solute carrier family 16 member 1	1.27052	1.23591
1135.	SLC16A10	solute carrier family 16 member 10	1.92999	1.71366
1136.	SLC16A14	solute carrier family 16 member 14	0.890857	1.04069
1137.	SLC18B1	solute carrier family 18 member B1	1.68871	1.89729
1138.	SLC19A1	solute carrier family 19 member 1	0.711999	0.848981
1139.	SLC19A2	solute carrier family 19 member 2	0.994844	1.03721
1140.	SLC22A31	solute carrier family 22 member 31	0.856728	0.948328
1141.	SLC25A13	solute carrier family 25 member 13	1.29903	1.43565
1142.	SLC25A15	solute carrier family 25 member 15	1.27744	1.19857
1143.	SLC25A17	solute carrier family 25 member 17	0.567036	0.550626

1144.	SLC25A20	solute carrier family 25 member 20	0.55318	0.705508
1145.	SLC25A33	solute carrier family 25 member 33	1.28595	1.32461
1146.	SLC25A4	solute carrier family 25 member 4	0.688413	0.804581
1147.	SLC25A5	solute carrier family 25 member 5	0.874204	0.931417
1148.	SLC27A5	solute carrier family 27 member 5	1.0881	1.3092
1149.	SLC29A2	solute carrier family 29 member 2	0.357566	0.444176
1150.	SLC35B2	solute carrier family 35 member B2	1.49914	1.5692
1151.	SLC35C2	solute carrier family 35 member C2	0.614949	0.696564
1152.	SLC35G1	solute carrier family 35 member G1	0.497059	0.57222
1153.	SLC45A3	solute carrier family 45 member 3	0.928566	1.04996
1154.	SLC4A7	solute carrier family 4 member 7	0.972962	0.90704
1155.	SLC50A1	solute carrier family 50 member 1	0.490646	0.467501
1156.	SLC5A8	solute carrier family 5 member 8	2.78152	2.31415
1157.	SLC6A12	solute carrier family 6 member 12	1.42094	1.24514
1158.	SLC7A5	solute carrier family 7 member 5	1.31711	1.12174
1159.	SLC7A8	solute carrier family 7 member 8	0.772529	0.646335
1160.	SLIRP	SRA stem-loop interacting RNA binding protein	0.769817	0.866559
1161.	SMAD6	SMAD family member 6	0.666859	0.829978
1162.	SMIM11A	small integral membrane protein 11A	0.844039	0.910736
1163.	SMIM13	small integral membrane protein 13	0.483039	0.520542
1164.	SMIM8	small integral membrane protein 8	0.664991	0.817361
1165.	SMN1	"survival of motor neuron 1, telomeric"	0.581755	0.575289
1166.	SMPD2	sphingomyelin phosphodiesterase 2	0.898892	0.733124
1167.	SMS	spermine synthase	1.1773	1.20089
1168.	SNHG5	small nucleolar RNA host gene 5	0.587049	0.815636
1169.	SNRNP25	small nuclear ribonucleoprotein U11/U12 subunit 25	0.656031	0.603566
1170.	SNRPA1	small nuclear ribonucleoprotein polypeptide A'	0.885467	0.861662
1171.	SNRPD2	small nuclear ribonucleoprotein D2 polypeptide	0.748278	0.885684
1172.	SNRPD3	small nuclear ribonucleoprotein D3 polypeptide	0.859864	0.921748
1173.	SNRPE	small nuclear ribonucleoprotein polypeptide E	0.579614	0.655083
1174.	SNRPF	small nuclear ribonucleoprotein polypeptide F	0.378183	0.562532
1175.	SNRPG	small nuclear ribonucleoprotein polypeptide G	0.722707	0.941404
1176.	SNTA1	syntrophin alpha 1	0.470681	0.524896
1177.	SNX17	sorting nexin 17	0.352968	0.410153
1178.	SNX4	sorting nexin 4	0.537189	0.550717
1179.	SOAT2	sterol O-acyltransferase 2	0.946383	0.996519
1180.	SOBP	sine oculis binding protein homolog	1.12312	0.97963
1181.	SOWAHC	sosondowah ankyrin repeat domain family member C	0.757397	0.721909
1182.	SP6	Sp6 transcription factor	0.627875	0.798127
1183.	SPAG16	sperm associated antigen 16	2.78745	1.96532
1184.	SPARC	secreted protein acidic and cysteine rich	2.76873	3.35492
1185.	SPDL1	spindle apparatus coiled-coil protein 1	1.36245	1.18421
1186.	SPIN4	spindlin family member 4	1.20897	1.15524
1187.	SPNS1	sphingolipid transporter 1 (putative)	0.993692	1.03893
1188.	SPRY2	sprouty RTK signaling antagonist 2	0.550961	0.481338
1189.	SPRY4	sprouty RTK signaling antagonist 4	2.72265	3.40137
1190.	SPRYD4	SPRY domain containing 4	0.498969	0.658557
1191.	SPSB4	splA/ryanodine receptor domain and SOCS box containing 4	1.17641	0.758689
1192.	SPTSSA	serine palmitoyltransferase small subunit A	1.13176	1.10577
1193.	SQLE	squalene epoxidase	0.859419	0.65273
1194.	SRD5A1	steroid 5 alpha-reductase 1	0.903325	1.10497
1195.	SRD5A3	steroid 5 alpha-reductase 3	0.53407	0.56115
1196.	SRP9	signal recognition particle 9	0.611286	0.511968
1197.	SRPK2	SRSF protein kinase 2	0.962142	0.955164
1198.	SRPRB	SRP receptor beta subunit	1.135	1.13818
1199.	SRSF10	serine and arginine rich splicing factor 10	0.581423	0.557139
1200.	SRSF3	serine and arginine rich splicing factor 3	0.459896	0.479402
1201.	SRSF7	serine and arginine rich splicing factor 7	0.558072	0.589317
1202.	SS18L1	"SS18L1, nBAF chromatin remodeling complex subunit"	0.699734	0.792439
1203.	SSB	Sjogren syndrome antigen B	0.68798	0.631619
1204.	SSR2	signal sequence receptor subunit 2	0.883125	0.937574
1205.	SSR3	signal sequence receptor subunit 3	0.712814	0.67759
1206.	STAG3L4	stromal antigen 3-like 4 (pseudogene)	0.59115	0.623864
1207.	STARD5	StAR related lipid transfer domain containing 5	0.757691	0.804855
1208.	STK19	serine/threonine kinase 19	1.04042	1.10347
1209.	STOML2	stomatin like 2	0.620558	0.633006

1210.	STRAP	serine/threonine kinase receptor associated protein	0.923435	0.944209
1211.	STX10	syntaxin 10	0.682659	0.746872
1212.	SUB1	"SUB1 homolog, transcriptional regulator"	0.789299	0.78565
1213.	SUCLA2	succinate-CoA ligase ADP-forming beta subunit	1.17971	0.989095
1214.	SUCLG1	succinate-CoA ligase alpha subunit	0.393309	0.459611
1215.	SUFU	SUFU negative regulator of hedgehog signaling	0.632929	0.650479
1216.	SUMF2	sulfatase modifying factor 2	0.425012	0.415504
1217.	SUMO1	small ubiquitin-like modifier 1	0.650273	0.599114
1218.	SUSD3	sushi domain containing 3	1.38012	1.41753
1219.	SUV39H2	suppressor of variegation 3-9 homolog 2	0.68922	0.680572
1220.	SYNE4	spectrin repeat containing nuclear envelope family member 4	0.83352	0.797764
1221.	SYT8	synaptotagmin 8	1.65318	1.36842
1222.	TAF11	TATA-box binding protein associated factor 11	2.53393	2.61299
1223.	TAF4B	TATA-box binding protein associated factor 4b	0.927441	0.721482
1224.	TAF7	TATA-box binding protein associated factor 7	0.495937	0.658128
1225.	TBCCD1	TBCC domain containing 1	1.68387	1.5637
1226.	TBP	TATA-box binding protein	0.439215	0.44549
1227.	TCEAL4	transcription elongation factor A like 4	0.865075	1.04156
1228.	TCEB1	transcription elongation factor B subunit 1	0.384157	0.433829
1229.	TCF7L1	transcription factor 7 like 1	1.48257	1.55383
1230.	TCFL5	transcription factor like 5	0.531116	0.509004
1231.	TDP2	tyrosyl-DNA phosphodiesterase 2	0.488266	0.43491
1232.	TEAD2	TEA domain transcription factor 2	0.477682	0.408097
1233.	TEFM	"transcription elongation factor, mitochondrial"	0.886352	1.03729
1234.	TEKT4P2	tektin 4 pseudogene 2	1.25626	1.31105
1235.	TERT	telomerase reverse transcriptase	1.89687	1.94267
1236.	TET2	tet methylcytosine dioxygenase 2	0.974007	0.8011
1237.	TEX30	testis expressed 30	0.591534	0.539069
1238.	TEX9	testis expressed 9	0.870901	1.00428
1239.	TFAP2C	transcription factor AP-2 gamma	0.827	0.84
1240.	TFDP1	transcription factor Dp-1	0.598627	0.557178
1241.	TFEC	transcription factor EC	2.11704	2.40168
1242.	TFF1	trefoil factor 1	1.12383	1.05027
1243.	TFF3	trefoil factor 3	1.06078	1.23842
1244.	TFPI	tissue factor pathway inhibitor	0.685574	0.818259
1245.	TGDS	"TDP-glucose 4,6-dehydratase"	0.708024	0.695662
1246.	THEG	theg spermatid protein	1.36115	1.28725
1247.	THOC3	THO complex 3	0.747607	0.706681
1248.	THOC7	THO complex 7	0.662423	0.585282
1249.	TIAM1	T-cell lymphoma invasion and metastasis 1	1.78994	1.45061
1250.	TIMM10	translocase of inner mitochondrial membrane 10 homolog	1.08019	1.23627
1251.	TIMM17A	translocase of inner mitochondrial membrane 17 homolog A	0.741463	0.806169
1252.	TIMM21	translocase of inner mitochondrial membrane 21	0.679132	0.844579
1253.	TIMM44	translocase of inner mitochondrial membrane 44	0.990688	1.19053
1254.	TIMM8A	translocase of inner mitochondrial membrane 8 homolog A	0.716225	0.843205
1255.	TIMM8B	translocase of inner mitochondrial membrane 8 homolog B	2.80661	3.09556
1256.	TIMMDC1	translocase of inner mitochondrial membrane domain containing 1	0.470364	0.511371
1257.	TIPRL	TOR signaling pathway regulator	0.811212	0.873609
1258.	TKT	transketolase	0.929334	1.00705
1259.	TM4SF1	transmembrane 4 L six family member 1	0.892293	1.16473
1260.	TMA7	translation machinery associated 7 homolog	0.568972	0.735707
1261.	TMED3	transmembrane p24 trafficking protein 3	0.862257	0.952594
1262.	TMEM106C	transmembrane protein 106C	0.585347	0.488068
1263.	TMEM11	transmembrane protein 11	0.395127	0.594322
1264.	TMEM126A	transmembrane protein 126A	0.457839	0.533496
1265.	TMEM126B	transmembrane protein 126B	0.727283	0.641183
1266.	TMEM134	transmembrane protein 134	0.907853	1.34654
1267.	TMEM141	transmembrane protein 141	1.08181	1.17586
1268.	TMEM147	transmembrane protein 147	0.659977	0.73448
1269.	TMEM14B	transmembrane protein 14B	0.746991	0.758224
1270.	TMEM14C	transmembrane protein 14C	0.620905	0.590898
1271.	TMEM171	transmembrane protein 171	0.878415	0.876701
1272.	TMEM177	transmembrane protein 177	0.455281	0.744802
1273.	TMEM179B	transmembrane protein 179B	1.13071	1.1919
1274.	TMEM181	transmembrane protein 181	0.528742	0.421469

1275.	TMEM183A	transmembrane protein 183A	1.61754	1.69108
1276.	TMEM189	transmembrane protein 189	1.4711	1.43429
1277.	TMEM203	transmembrane protein 203	0.536841	0.70267
1278.	TMEM208	transmembrane protein 208	0.434963	0.511256
1279.	TMEM216	transmembrane protein 216	0.578493	0.670693
1280.	TMEM218	transmembrane protein 218	0.819994	0.843916
1281.	TMEM223	transmembrane protein 223	1.13466	1.40979
1282.	TMEM229B	transmembrane protein 229B	0.964364	0.908993
1283.	TMEM237	transmembrane protein 237	0.646639	0.612708
1284.	TMEM251	transmembrane protein 251	0.873496	1.02926
1285.	TMEM254	transmembrane protein 254	0.725767	0.733062
1286.	TMEM261	transmembrane protein 261	0.671823	0.814308
1287.	TMEM38A	transmembrane protein 38A	0.820518	0.816127
1288.	TMEM5	transmembrane protein 5	0.426584	0.498614
1289.	TMEM65	transmembrane protein 65	1.01325	0.856892
1290.	TMEM97	transmembrane protein 97	0.833185	0.612911
1291.	TMPOP2	thymopoietin pseudogene 2	0.815511	1.2229
1292.	TMPRSS3	"transmembrane protease, serine 3"	1.50993	1.27099
1293.	TMSB15A	thymosin beta 15a	2.53916	2.21981
1294.	TMSB15B	thymosin beta 15B	0.668357	0.666676
1295.	TNFAIP8L2-SCNM1	TNFAIP8L2-SCNM1 readthrough	1.15396	1.28294
1296.	TNFRSF11B	TNF receptor superfamily member 11b	2.27648	2.51838
1297.	TNFSF15	tumor necrosis factor superfamily member 15	0.836726	1.01551
1298.	TOMM22	translocase of outer mitochondrial membrane 22	0.494304	0.551779
1299.	TOMM40L	translocase of outer mitochondrial membrane 40 like	0.675673	0.883447
1300.	TOMM5	translocase of outer mitochondrial membrane 5	0.924343	1.01822
1301.	TOMM7	translocase of outer mitochondrial membrane 7	0.557692	0.611233
1302.	TP53RK	TP53 regulating kinase	0.565331	0.617696
1303.	TP63	tumor protein p63	1.17284	0.761436
1304.	TPBG	trophoblast glycoprotein	0.510288	0.632264
1305.	TPI1	triosephosphate isomerase 1	0.662608	0.676696
1306.	TPM1	tropomyosin 1 (alpha)	0.801783	0.748702
1307.	TPMT	thiopurine S-methyltransferase	1.40831	1.2533
1308.	TPST1	tyrosylprotein sulfotransferase 1	0.973886	0.823435
1309.	TPST2	tyrosylprotein sulfotransferase 2	1.27295	1.15574
1310.	TPT1	"tumor protein, translationally-controlled 1"	0.512395	0.431892
1311.	TRA2B	transformer 2 beta homolog (Drosophila)	0.93612	1.02773
1312.	TRAF4	TNF receptor associated factor 4	1.40716	1.41039
1313.	TRAFD1	TRAF-type zinc finger domain containing 1	1.11782	1.02991
1314.	TRAM1L1	translocation associated membrane protein 1-like 1	1.03518	1.32007
1315.	TRAP1	TNF receptor associated protein 1	0.620316	0.54511
1316.	TRIAP1	TP53 regulated inhibitor of apoptosis 1	2.00172	2.1629
1317.	TRIB2	tribbles pseudokinase 2	2.8007	2.78841
1318.	TRIB3	tribbles pseudokinase 3	1.04783	1.16733
1319.	TRIM16	tripartite motif containing 16	0.993213	1.01247
1320.	TRIM16L	tripartite motif containing 16-like	0.910647	0.922332
1321.	TRMT10C	"tRNA methyltransferase 10C, mitochondrial RNase P subunit"	0.656297	0.739582
1322.	TRMT12	tRNA methyltransferase 12 homolog	0.867535	0.94512
1323.	TSEN15	tRNA splicing endonuclease subunit 15	0.543937	0.571189
1324.	TSPAN14	tetraspanin 14	0.869488	0.86275
1325.	TSPAN3	tetraspanin 3	0.452084	0.480864
1326.	TSPAN4	tetraspanin 4	1.20445	1.41946
1327.	TSPAN5	tetraspanin 5	1.45388	1.14094
1328.	TSPAN6	tetraspanin 6	0.6999	0.627904
1329.	TSPYL4	TSPY like 4	0.461534	0.620688
1330.	TTC26	tetratricopeptide repeat domain 26	0.645484	0.750698
1331.	TTC27	tetratricopeptide repeat domain 27	0.506052	0.541612
1332.	TTC30B	tetratricopeptide repeat domain 30B	0.431373	0.372918
1333.	TTC5	tetratricopeptide repeat domain 5	0.895979	0.934807
1334.	TTLL1	tubulin tyrosine ligase like 1	0.686081	0.387382
1335.	TTYH2	tweety family member 2	1.39606	1.47698
1336.	TTYH3	tweety family member 3	1.29448	1.25873
1337.	TUB	tubby bipartite transcription factor	1.14111	0.899701
1338.	TUBA1A	tubulin alpha 1a	1.22901	1.05345

1339.	TUBB2A	tubulin beta 2A class IIa	0.556047	0.69846
1340.	TUBD1	tubulin delta 1	1.66967	1.62302
1341.	TUFM	"Tu translation elongation factor, mitochondrial"	0.445132	0.450125
1342.	TUSC1	tumor suppressor candidate 1	0.434468	0.671859
1343.	TUSC3	tumor suppressor candidate 3	0.476439	0.443338
1344.	TXNDC15	thioredoxin domain containing 15	0.674132	0.804971
1345.	TXNDC16	thioredoxin domain containing 16	1.2185	0.912998
1346.	TXNL4A	thioredoxin like 4A	0.436729	0.51071
1347.	TXNRD3NB	thioredoxin reductase 3 neighbor	1.05308	1.27236
1348.	TYMS	thymidylate synthetase	0.594336	0.609152
1349.	UBAC1	UBA domain containing 1	0.517836	0.514537
1350.	UBAC2	UBA domain containing 2	0.761043	0.832168
1351.	UBE2E1	ubiquitin conjugating enzyme E2 E1	0.619358	0.605514
1352.	UBE2F	ubiquitin conjugating enzyme E2 F (putative)	0.847813	0.799021
1353.	UBE2T	ubiquitin conjugating enzyme E2 T	0.641735	0.668278
1354.	UBE2V2	ubiquitin conjugating enzyme E2 V2	0.847768	0.761367
1355.	UBL3	ubiquitin like 3	0.578444	0.397981
1356.	UBL4A	ubiquitin like 4A	0.412535	0.524187
1357.	UBL5	ubiquitin like 5	0.372425	0.448646
1358.	UBLCP1	ubiquitin like domain containing CTD phosphatase 1	0.457536	0.390483
1359.	UBQLN2	ubiquilin 2	0.454439	0.36814
1360.	UCHL3	ubiquitin C-terminal hydrolase L3	0.62191	0.608182
1361.	UCK2	uridine-cytidine kinase 2	0.9374	1.01923
1362.	UFSP2	UFM1 specific peptidase 2	0.918514	0.915898
1363.	UGT2B15	UDP glucuronosyltransferase family 2 member B15	1.18061	1.32403
1364.	ULBP2	UL16 binding protein 2	1.14969	1.02138
1365.	UMPS	uridine monophosphate synthetase	0.618575	0.654156
1366.	UNC119B	unc-119 lipid binding chaperone B	0.57547	0.632513
1367.	UNG	uracil DNA glycosylase	0.816379	0.778265
1368.	UPK3BL	uroplakin 3B-like	0.806669	1.01034
1369.	UQCR10	"ubiquinol-cytochrome c reductase, complex III subunit X"	0.440544	0.643124
1370.	UQCRC2	ubiquinol-cytochrome c reductase core protein II	0.756596	0.79963
1371.	UQCRFS1	"ubiquinol-cytochrome c reductase, Rieske iron-sulfur polypeptide 1"	0.673997	0.820654
1372.	UQCRH	ubiquinol-cytochrome c reductase hinge protein	0.730635	0.787734
1373.	UQCRQ	ubiquinol-cytochrome c reductase complex III subunit VII	0.655835	0.735397
1374.	URB1-AS1	URB1 antisense RNA 1 (head to head)	0.768621	1.27432
1375.	URM1	ubiquitin related modifier 1	0.777266	0.915202
1376.	UROD	uroporphyrinogen decarboxylase	0.562775	0.612601
1377.	USP38	ubiquitin specific peptidase 38	0.48234	0.389678
1378.	UTP18	"UTP18, small subunit processome component"	0.537868	0.60794
1379.	UTP3	"UTP3, small subunit processome component homolog	0.539582	0.683986
1380.	UTP6	"UTP6, small subunit processome component"	0.626186	0.711473
1381.	VCPKMT	valosin containing protein lysine methyltransferase	0.605394	0.87448
1382.	VDAC3	voltage dependent anion channel 3	0.599311	0.583252
1383.	VIPR1	vasoactive intestinal peptide receptor 1	0.945101	0.763107
1384.	VPS25	vacuolar protein sorting 25 homolog	1.09281	1.16585
1385.	VSTM2L	V-set and transmembrane domain containing 2 like	2.51467	2.41676
1386.	VTA1	vesicle trafficking 1	1.32726	1.38368
1387.	VTCN1	V-set domain containing T cell activation inhibitor 1	1.77544	1.75288
1388.	VWC2L	von Willebrand factor C domain containing protein 2-like	3.02552	2.7854
1389.	WASF1	WAS protein family member 1	1.0033	0.791938
1390.	WBP1	WW domain binding protein 1	0.580605	0.575147
1391.	WBSCR22	Williams-Beuren syndrome chromosome region 22	0.693725	0.809007
1392.	WDR12	WD repeat domain 12	0.631358	0.671058
1393.	WDR18	WD repeat domain 18	0.938405	1.11267
1394.	WDR41	WD repeat domain 41	0.607608	0.536312
1395.	WDR5	WD repeat domain 5	0.458789	0.498514
1396.	WDR61	WD repeat domain 61	0.783432	0.865257
1397.	WDR72	WD repeat domain 72	0.705664	0.610389
1398.	WDR75	WD repeat domain 75	0.497876	0.500219
1399.	WDR82	WD repeat domain 82	0.498426	0.52336
1400.	WISP2	WNT1 inducible signaling pathway protein 2	2.80975	2.83438
1401.	WNT10B	Wnt family member 10B	0.553471	1.08361
1402.	WNT6	Wnt family member 6	0.563029	1.08002
1403.	WNT8B	Wnt family member 8B	1.5311	2.08131

1404.	WRNIP1	Werner helicase interacting protein 1	0.463639	0.461986
1405.	XRCC2	X-ray repair cross complementing 2	0.497408	0.37365
1406.	YAE1D1	Yae1 domain containing 1	0.528961	0.833542
1407.	YBX1	Y-box binding protein 1	0.608175	0.510208
1408.	YBX3	Y-box binding protein 3	1.38701	1.41547
1409.	YEATS4	YEATS domain containing 4	0.743376	0.965598
1410.	YIF1B	"Yip1 interacting factor homolog B, membrane trafficking protein"	0.721536	0.907742
1411.	YRDC	yrdC N6-threonylcarbamoyltransferase domain containing	0.756552	0.92334
1412.	YWHAE	tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein epsilon	0.487217	0.457738
1413.	YWHAG	tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein gamma	0.868706	0.950922
1414.	YY1	YY1 transcription factor	0.656623	0.652961
1415.	ZBTB5	zinc finger and BTB domain containing 5	0.434602	0.518307
1416.	ZCCHC10	zinc finger CCHC-type containing 10	0.96443	1.18733
1417.	ZDHHC12	zinc finger DHHC-type containing 12	0.720658	1.1442
1418.	ZFP91	ZFP91 zinc finger protein	0.636921	0.52485
1419.	ZIC5	Zic family member 5	0.519752	0.454947
1420.	ZKSCAN4	zinc finger with KRAB and SCAN domains 4	0.541057	0.569274
1421.	ZMAT4	zinc finger matrin-type 4	1.53596	1.73342
1422.	ZMYM5	zinc finger MYM-type containing 5	0.458967	0.56089
1423.	ZMYND19	zinc finger MYND-type containing 19	1.05418	1.24949
1424.	ZNF132	zinc finger protein 132	0.974712	0.960395
1425.	ZNF212	zinc finger protein 212	0.573246	0.799225
1426.	ZNF22	zinc finger protein 22	1.10956	1.22216
1427.	ZNF286A	zinc finger protein 286A	0.765241	0.59238
1428.	ZNF32	zinc finger protein 32	0.790834	0.846533
1429.	ZNF346	zinc finger protein 346	1.50192	1.26861
1430.	ZNF519	zinc finger protein 519	0.57224	0.698319
1431.	ZNF584	zinc finger protein 584	0.928914	0.934971
1432.	ZNF674-AS1	ZNF674 antisense RNA 1 (head to head)	0.734379	1.08159
1433.	ZNF711	zinc finger protein 711	0.597437	0.462778
1434.	ZNF77	zinc finger protein 77	0.396748	0.416536
1435.	ZNRD1	zinc ribbon domain containing 1	0.479523	0.696981
1436.	ZP3	zona pellucida glycoprotein 3	0.598498	0.657539

APPENDIX II: LICENSE AGREEMENTS

BIOSCIENTIFICA LTD. ORDER DETAILS

Jan 10, 2017

This Agreement between ("You") and BioScientifica Ltd. ("BioScientifica Ltd.") consists of your order details and the terms and conditions provided by BioScientifica Ltd. and Copyright Clearance Center.

Order Number	501222809
Order date	Jan 09, 2017
Licensed Content Publisher	BioScientifica Ltd.
Licensed Content Publication	Endocrine-Related Cancer
Licensed Content Title	Roles for miRNAs in endocrine resistance in breast cancer
Licensed Content Author	Penn Muluhngwi, Carolyn M Klinge
Licensed Content Date	Oct 1, 2015
Licensed Content Volume Number	22
Licensed Content Issue Number	5
Type of Use	Thesis/Dissertation
Requestor type	Author of requested content
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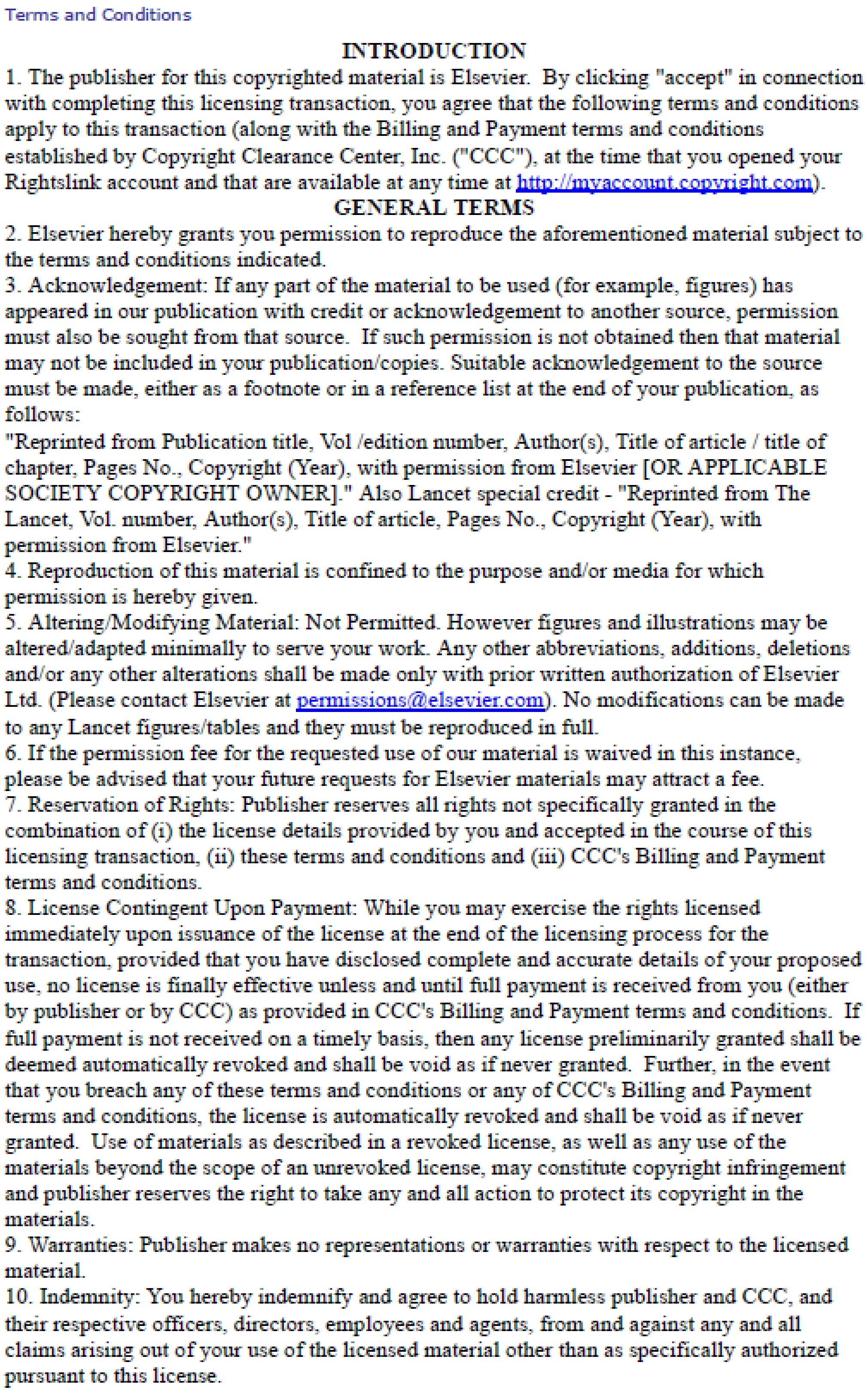

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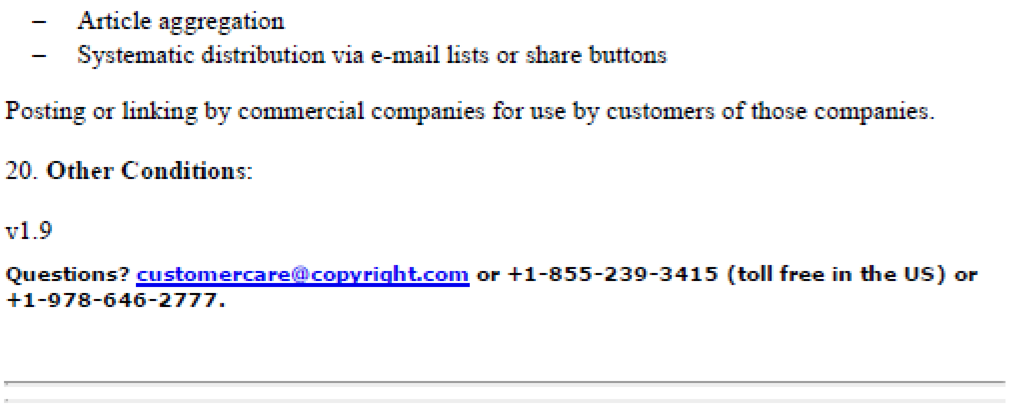

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CURRICULUM VITAE

PENN MULUHNGWI
Department of Biochemistry and Molecular Genetics
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Louisville, KY, 40292

EDUCATION

2004-2007	B.Sc., Biochemistry and Medical Laboratory Technology, University of Buea, Cameroon
2008-2010	M.Sc., Biochemistry course work, University of Buea, Cameroon
2010-2012	M.S., Biology, New Mexico Highlands University, Las Vegas, NM
2012-2015	M.S., Biochemistry and Molecular Genetics, University of Louisville School of Medicine, Louisville, KY
2012-2017	Ph.D., Department of Biochemistry and Molecular Genetics, University of Louisville School of Medicine, Louisville, KY

RESEARCH EXPERIENCE

01/20/11 - 05/11/12	M.S. Graduate research, Advisor: Sarah Corey-Rivas, Ph.D., Department of Biology, New Mexico Highlands University, Las Vegas, NM. Project title: The use of nuclear genes in defining Evolutionary Significant Units (ESUs) in the *Anaconda* genus, *Eunectes*
09/10/12 - 11/30/12	Research Rotation Student, Carolyn M. Klinge, Ph.D., Professor, Department of Biochemistry and Molecular Biology, University of Louisville, Louisville, KY
01/18/13 - 03/15/13	Research Rotation Student, Christine Schaner Tooley, Ph.D., Assistant Professor, Department of Biochemistry and Molecular Genetics, University of Louisville, Louisville, KY

04/22/13 – 07/01/17	Ph.D. Graduate Research, Advisor: Carolyn M. Klinge, Ph.D., Project title: Role of miR-29b-1 and miR-29a in endocrine-resistant breast cancer

TEACHING EXPERIENCE

08/23/10-05/11/12	Graduate teaching assistant, Department of Biology and Chemistry, New Mexico Highlands University, Las Vegas, NM Courses: Human Biology (Biol 131), Genetics (Biol 300), Biological perspectives (Biol 110)
Fall 2011	Trained one undergraduate student in the lab, New Mexico Highlands University, Las Vegas, NM
08/12/13 - 11/29/13	Graduate teaching assistant, Department of Biochemistry and Molecular Genetics, University of Louisville School of Medicine, Louisville, KY Course: Advanced techniques in Biochemistry and Molecular Biology I (Biol 613)
Summer 2014	Trained two undergraduate students in the lab, University of Louisville School of Medicine, Louisville, KY
Summer 2015	Trained a medical student in the lab, University of Louisville School of Medicine, Louisville, KY
Summer 2016	Trained a medical student and an undergraduate student in the lab, University of Louisville School of Medicine, Louisville, KY

FIELD EXPERIENCE

05/17/2010	Research foundation in tropical diseases and environment (REFOTDE), Cameroon. Collection of *Chrysops* species at Ediki, South West region, Cameroon
02/11/2011	Reptile handling/sampling techniques, Albuquerque Zoo, Albuquerque, NM

INTERNSHIPS

11/12/07 – 03/21/08	Mezam Polyclinic Hematology/Histology/Cytology Laboratory, Bamenda, North West Region, Cameroon. Human sample handling, Microscopic analysis (malaria parasite, differential cell count, and analysis of stool samples), Biochemical analysis (enzyme assays: SGOT and SGPT), erythrocyte sedimentation rate (ESR), Haemoglobin electrophoresis test, antibiotic disc screening test, Histological slide preparations

03/24/08 - 06/27/08	Institute of Agricultural Research for Development (IRAD) Ekona, South West Region, Cameroon. Plant tissue culture and pathology of the cocoyam root rot disease
06/18/12 – 08/1/12	National Center for Genome Resources (NCGR), Santa Fe, NM. Performed Next Generation Sequence analysis on RNAseq data. Analysis included differential expression, annotation, assembly and assessment of read sequences. Most analysis was done on the Unix interface and programs used include Samtool, gmap, gsnap, Tablet, Flapjack and R (DEseq and EdgeR packages)

HONORS

2011	Sigma Xi Student Research fund award for research supplies
2011	Travel award to Eastern North American Region/ International biometric conference (ENAR) Diversity workshop. Provided by ENAR
2010-2012	Graduate scholarship, New Mexico Highlands University, Las Vegas, NM
2012-2014	Integrated Program for Biomedical Science Research Fellowship (IPIBS), University of Louisville, KY
2016	Early Career Forum Travel award and complimentary registration to 100th annual meeting of the Endocrine Society (ENDO) in Boston, MA March 31-April 3, 2016
2016	Invited to present a poster at the ENDO 2016 Minority Mentoring and Poster Reception, April 2, 2016 from 7:00-9:30 PM at the Westin Boston Waterfront Hotel
2016	Second place in the Doctoral Basic-Science Graduate Student poster competition (2nd of 52 posters) at Research! Louisville, October 11, 2016 at University of Louisville, KY

PEER-REVIEWED PUBLICATIONS

1. Manavalan T.T., Teng Y., Litchfield L.M., **Muluhngwi P.**, Al-Rayyan N., Klinge, C.M. (2013) Reduced Expression of miR-200 Family Members Contributes to Antiestrogen Resistance in LY2 Human Breast Cancer Cells. *PLoS One* 8: e62334 PMID:23626803

2. **Muluhngwi, P.** and Klinge, C.M. (2015) Role of miRNAs in endocrine resistance in breast cancer. *Endocr. Rel. Cancer* 22: R279-300. PMID 26346768

3. Radde, B.N., Ivanova, M.M., Mai, H.X., Alizadeh-Rad, N., Piell, K., Van Hoose, P., Cole, M.P., **Muluhngwi, P.**, Kalbfleisch, T.S., Rouchka, E.C., Hill, B.G., Klinge, C.M. (2016) Nuclear respiratory factor-1 and bioenergetics in tamoxifen-resistant breast cancer cells, *Exp Cell Res.* 347: 222-231. PMID:27515002

4. **Muluhngwi**, P., Krishna, A., Vittitow, S.L., Napier, J.T., Richardson, M. K., Ellis, M., Mott J.L., and Klinge, C.M. (2017) Tamoxifen differentially regulates miR-29b-1 and miR-29a expression depending on endocrine-sensitivity in breast cancer cells. *Can. Lett.* 388: 230-238. PMID:27986463

5. **Muluhngwi, P.**, Richardson, M. K., Napier J., Kalbfleisch T.S., Rouchka E.C., Mott J.L., and Klinge, C.M. (2017) Regulation of miR-29b-1/a transcription and identification of target mRNAs in CHO-K1 cells. *Mol and Cell Endocrinol.* 444:38-47. PMID: 28137615

6. **Muluhngwi, P.** and Klinge, C.M. (2017) Identification of miRNAs as biomarkers for acquired endocrine resistance in breast cancer. *Mol and Cell Endocrinol.* pii: S0303-7207(17)30080-1. PMID:28163101

MANUSCRIPTS SUBMITTED

1. **Muluhngwi, P**., Alizadeh-Rad, N., Vittitow, S.L., Kalbfleisch, T.S., and Klinge, C.M. The miR-29 transcriptome in endocrine-sensitive and resistant breast cancer cells. (manuscript submitted to Nature Scientific Reports, ms # SREP-17-12926, 2017)

TECHNICAL SKILLS

Human sample handling, microscopic analysis, mammalian cell culture, transient transfection, DNA and RNA isolation, miRNA analyses, PCR and quantitative RT-PCR for mRNA and miRNA, Western blotting, ELISA, cell proliferation assays (MTT & BrdU), cell invasion and migration assays, DNA sequence analysis using Bioedit and Mega 5

PROFESSIONAL MEMBERSHIP

2010-2012	Scientific Research Society (Sigma-xi)
2015-Present	Endocrine Society
2016-Present	American Association for Cancer Research

SCIENTIFIC CONFERENCES/WORKSHOPS

2006	Buea University Biochemistry Student Association (BUBSA) seminar on Cell Language, Industrial Biochemistry, Ramification of Biochemistry and Cutting-edge discipline, University of Buea, Cameroon
2007	Symposium on Biochemistry and the Job Market, University of Buea, Cameroon
2008	Creating Awareness on Toxicology, University of Buea, Cameroon
2009	University of Buea Science Expo, University of Buea, Cameroon
2011	ENAR Diversity Workshop, Miami, Florida
2011, 2012	New Mexico Bioinformatics and Science Symposium, Santa Fe, NM
2016	100th annual meeting of the Endocrine Society
2017	Meeting of the American Association of Cancer Research, April 1-5, 2017 in Washington, DC

POSTER AND ORAL PRESENTATIONS

Abstracts of poster presentations

1. **Muluhngwi, P.**, Teng, Y., and Klinge, C.M. Upregulation of miR-29b-1 and miR-29a in endocrine-resistant breast cancer cells. (Abstract 15) 5th Biochemistry & Molecular Genetics Research Retreat, University of Louisville, August 23, 2013

2. **Muluhngwi, P.**, Teng, Y., and Klinge, C.M. Upregulation of miR-29b-1 and miR-29a in endocrine-resistant breast cancer cells. (Abstract GRM-25) Research! Louisville, University of Louisville, School of Medicine, Louisville, KY, September 24, 2013

3. **Muluhngwi, P.**, Teng, Y., and Klinge, C.M. Upregulation of miR-29b-1 and miR-29a in endocrine-resistant breast cancer cells. (Abstract 76) James Graham Brown Cancer Center 12th Annual retreat, October 25, 2013

4. Richardson, K., Ellis, M., **Muluhngwi**, **P**., and Klinge, C.M. Role of increased miR-29b-1 and miR-29a in endocrine-resistant breast cancer. SROP poster presentations, University of Louisville, School of Medicine, Louisville, KY, July 31, 2014

5. Ellis, M., Richardson, K., **Muluhngwi**, **P.**, and Klinge, C.M. Role of increased miR-29b-1 and miR-29a in endocrine-resistant breast cancer. SROP poster presentations, University of Louisville, School of Medicine, Louisville, KY, July 31, 2014

6. **Muluhngwi P.** and Klinge, C.M. Role of tamoxifen-induced miR-29b-1/a in endocrine-resistant breast cancer. (Abstract GRD-66) Research! Louisville, University of Louisville School of Medicine, Louisville, KY, September 16, 2014

7. **Muluhngwi P.** and Klinge, C.M. Role of tamoxifen-induced miR-29b-1/a in endocrine-resistant breast cancer. (Abstract 70) James Graham Brown Cancer Center 14th Annual retreat, October 17, 2014

8. Bamji, S, F.,[1], Radde, B. N.,[2], **Muluhngwi, P.,**[2] Klinge, C.M.,[2] and Corbitt, C.,[1] (Abstract 9) Neuroendocrine characterization of cell lines derived from adult female mouse hypothalamus. [1]Department of Biology, University of Louisville; [2]Department of Biochemistry & Molecular Genetics, University of Louisville School of Medicine, April 23, 2015

9. **Muluhngwi, P.**, Napier, J.T., and Klinge, C.M. Role of increased miR-29b-1 and miR-29a in endocrine-resistant breast cancer. (Abstract #4) Colloquium in Biochemistry and Molecular Genetics, Louisville, KY. August 21, 2015

10. Napier, J.T., **Muluhngwi, P.**, and Klinge, C.M. Role of increased miR-29b-1 and miR-29a in endocrine-resistant breast cancer. (Abstract MED-65) Research! Louisville, University of Louisville School of Medicine, Louisville, KY. October 27, 2015

11. **Muluhngwi, P.** and Klinge, C.M. Role of increased miR-29b-1 and miR-29a in endocrine-resistant breast cancer. (Abstract GRD-81) Research! Louisville, University of Louisville School of Medicine, Louisville, KY. October 27, 2015

12. **Muluhngwi, P.**, Napier, J. T., Klinge, C.M. Role of Increased Mir-29b-1 and Mir-29a in Endocrine-Resistant Breast Cancer. (Abstract SUN 096) Abstracts of the 100th annual meeting of the Endocrine Society, Boston, MA., April 3, 2016

13. Vittitow, S. L., Krishna, A., **Muluhngwi, P.**, and Klinge, C.M. Tamoxifen regulation of miR-29b-1 and miR-29a in endocrine sensitive *vs* resistant breast cancer cells. SROP poster presentations, University of Louisville, School of Medicine, Louisville, KY, August 3, 2016

14. Krishna, A., Vittitow, S.L., **Muluhngwi, P.**, and Klinge, C.M. Role of miR-29b-1/a in Acquired Endocrine-Resistant Breast Cancer (Abstract MED-9) Research!

Louisville, University of Louisville School of Medicine, Louisville, KY. October 11, 2016. *1st place Greater Louisville Medical Society's Women in Medical Sciences Award

15. **Muluhngwi, P.**, Krishna, A., Vittitow, S.L., Napier, J.T., and Klinge, C.M. Tamoxifen differentially regulates miR-29b-1 and miR-29a depending on endocrine-sensitivity breast cancer. (Abstract GRD-35) Research! Louisville, University of Louisville School of Medicine, Louisville, KY. October 11, 2016. *2nd of 52 Posters

16. Krishna, A., Vittitow, S.L., **Muluhngwi, P.**, and Klinge, C.M. Role of miR-29b-1/a in Acquired Endocrine-Resistant Breast Cancer (Abstract SAT 143) Abstract of the Endocrine Society annual meeting Orlando, Florida, April 1, 2017

17. **Muluhngwi, P.** and Klinge, C.M. Tamoxifen differentially regulates miR-29b-1 and miR-29a depending on endocrine-sensitivity in breast cancer. (Abstract #3428) Abstract of the AACR annual meeting, Washington, DC. April 4, 2017

Invited oral presentations

1. **Muluhngwi, P.,** Napier, J.T., and Klinge, C.M. Role of increased miR-29b-1 and miR-29a in endocrine-resistant breast cancer. (Abstract #4) 2015 Colloquium in Biochemistry and Molecular Genetics, Louisville, KY. August 21, 2015 *One of four selected for oral presentation from 25*

CAMPUS ACTIVITIES

University of Buea

2005-2006	Buea University Biochemistry Student Association (BUBSA), University of Buea, Cameroon

New Mexico Highlands University

2011	Conservation club, NMHU
Summer 2011	Student Chaperone, Laevo Sanchez reading program, New Mexico Highlands University, NM
2010-2011	NMHU Student Ambassador
2010-2011	Unicef@NMHU, Positions: Treasurer, Vice President
2010-2011	Science Club New Mexico Highlands University, NM. Position: President

2010-2011	Association of Graduate Students, New Mexico Highlands University (NMHU), NM. Positions: Secretary, President
2011	Member of the National Society of Leadership and Success NMHU, NM

University of Louisville

2012-2014	Department of Biochemistry and Molecular Genetics Student Representative to the Graduate Student Council
2014-2016	School of Interdisciplinary and Graduate Studies (SIGS) Student Ambassador, University of Louisville, KY
2016-Present	University of Louisville Hospital Emergency Room Volunteer