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Investigating the Mode of Action of a Novel N-sec-butylthiolated Beta-lactam Against *Staphylococcus aureus*

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Investigating the Mode of Action of a Novel

N-sec-butylthiolated Beta-lactam

Against *Staphylococcus aureus*

by

Katherine Rose Prosen

A thesis submitted in partial fulfillment
of the requirements for the degree of
Master of Science

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ABSTRACT

N-sec-butylthiolated β -lactam (Ns β L) is a novel beta-lactam antimicrobial with a mechanism of action proposed to inhibit 3-oxoacyl-acyl carrier protein synthase (ACP) III (FabH), resulting in the inhibition of fatty acid synthesis. It has been suggested that Ns β L inhibits FabH indirectly by inactivating coenzyme-A (CoA). CoA is an essential cofactor for numerous proteins involved in glycolysis, the citric acid cycle (TCA), and pyruvate metabolism, in addition to fatty acid biosynthesis. This study aimed to determine the effects of Ns β L on a diverse array of laboratory and clinical *Staphylococcus aureus* isolates by analyzing the mode of resistance in spontaneous and adaptive mutant Ns β L-resistant mutants. Phenotypic analysis of the mutants was performed, as well as sequence analysis of *fabH*; along with comparative proteomic analysis of intracellular proteomes. Our results indicate that Ns β L resistance is mediated by drastic changes in the cell wall, oxidative stress response, virulence regulation, and those pathways associated with CoA. It is our conclusion that Ns β L has activity towards CoA, resulting in wide-spread effects on metabolism, virulence factor production, stress response, and antimicrobial resistance.

INTRODUCTION

Staphylococcus aureus

Staphylococcus aureus is a Gram-positive coccoid bacterium that is facultatively anaerobic, non-motile, and non-sporeforming. It has a relatively small genome of 2.8 to 2.9 Mb with an approximate G+C content of 32%. *S. aureus* is part of the normal microflora of the nose, skin, gastrointestinal tract, and genitourinary tract of humans, and colonizes approximately one-third of the US population. It is an opportunistic pathogen, causing disease in immunocompromised individuals, such as children, the elderly, HIV/AIDS patients, severe burn victims, and intravenous drug users³⁷.

Besides being a human pathogen, *S. aureus* is also known to colonize and infect most other mammals, which can in turn serve as a reservoir for human inoculation. Indeed, there are a number of documented cases where companion animals have been shown to be a source of recurrent human infection. Bovine and equine infections are a concern for the agricultural industry, with infections often caused by human-associated strains⁹⁸. Alternatively, a recent report describes the case of a young, healthy girl infected with the ST398 livestock-associated strain bearing the community acquired MRSA (CA-MRSA)-associated Panton-Valentine leukocidin (PVL) toxin. This infection resulted in fatal necrotizing pneumonia, and illustrates the zoonotic potential of *S. aureus*⁹⁰.

Infections caused by *S. aureus*. *S. aureus* is able to cause disease in almost every niche of the human body. It is the major cause of skin and soft tissue infections (SSTIs) in the United States, causing 76% of all purulent SSTIs seen in hospitals between 2001 and 2003⁷⁶. SSTIs can be uncomplicated (uSSTIs) and typically involve infection of the epidermis and/or hair follicles, resulting in pimples, boils, abscesses, carbuncles, furuncles, folliculitis, tendonitis, and impetigo. Complicated SSTIs (cSSTIs) stem from uSSTIs and typically exhibit systemic symptoms; for example, *S. aureus* is also known as a ‘flesh-eating bug’ due to its ability to cause necrotizing fasciitis. *S. aureus* can also cause invasive illnesses, including septic arthritis, endocarditis, osteomyelitis, and pneumonia⁵⁴. *S. aureus* is also a leading cause of surgical wound infections⁴¹ and infections of foreign bodies, such as prosthetic joints, catheters, and pacemakers. Foreign body infections can be difficult to treat because they are often caused by biofilms forming on the indwelling device or implant¹⁰¹. The reasons for difficulty in treatment are not well elucidated, but have been attributed to reduced penetration of antibiotics into the aggregate matrix, or via the presence of persister cells, which resist antimicrobial treatment and remain after treatment to re-establish the biofilm, leading to recurrent infection. Often, the only effective treatment is to remove the implanted or indwelling device altogether⁶¹.

Virulence factors

S. aureus has an impressive array of toxins which are involved in causing illnesses that range from mild to severe. It is differentiated from other members of its family by its ability to cause disease despite the fact that 50% of the core genome is common to all

staphylococci¹⁰. Indeed, the genomes of individual strains of *S. aureus* vary by only 22%. These variable accessory regions contain mobile genetic elements (MGE) such as staphylococcal cassette chromosomes (SCC), pathogenicity islands (PI), bacteriophages (ϕ), transposons (TN), and plasmids, and often encode virulence factors, toxins, and resistance genes⁶⁴.

Adhesins, immune modulation, and evasion. A factor in the pathogenic success of *S. aureus*' stems in part from its versatile adhesion molecules. Collectively, these are known as the microbial surface components recognizing adhesive matrix molecules (MSCRAMM). The host extracellular matrix (ECM) has many components which *S. aureus* is able to target for the purpose of adhesion. Collagen, a component of cartilage, is a target for the collagen-binding adhesin (Cna), which has been implicated in osteomyelitis³³. Fibronectin-binding proteins (FnBP) allow for attachment to platelets and, subsequently, activation of clot formation, which has been associated with endocarditis³⁵. *S. aureus* also binds to fibrinogen, the precursor to fibrin, through clumping factor A (ClfA), effectively coating the bacterial cell in fibrinogen and acting as camouflage against phagocytic cells⁴². Staphylokinase (SAK) binds to plasminogen and is responsible for cleaving fibrin, allowing *S. aureus* the opportunity to move to a new site within the host¹⁵. Another factor in its success is the presence of several immunomodulatory and immune evasion proteins. Surface protein A (SpA) has anti-phagocytic activity; it binds the Fc region of immunoglobulin G (IgG), preventing opsonization and, consequently, recognition by phagocytes⁴. Another IgG-binding protein, the staphylococcal binder of immunoglobulin (Sbi), is secreted and forms

insoluble IgG complexes, reducing opportunities for opsonization. Sbi also has proteolytic activity towards complement factor 3 (C3), which is a key component of the complement system and important for the initial immune response to bacterial infection¹⁸. The combination of these surface-associated and secreted proteins affords *S. aureus* the ability to manipulate their host environment.

Cytolytic toxins. A number of staphylococcal secreted toxins have lytic activity towards different cell types present in the host. Generally, they have pore-forming activity which can lead to osmotic disregulation and cell lysis at high concentrations. Alpha-hemolysin (Hla) is strongly lytic towards rabbit erythrocytes, but also has activity towards human erythrocytes, monocytes, epithelial cells, and endothelial cells. Hla also has dermonecrotic and neurotoxic activity. Beta-hemolysin (Hlb) displays activity similar to Hla, but is less active in *S. aureus* isolates causing human disease. This is typically due to integration of a prophage within the *hlb* structural encoding gene. Delta toxin (Hld) has a mechanism different from that of either Hla or Hlb, both of which use polymers to form pores in cell membranes; instead, Hld monomers aggregate on a cell's surface until they are heavy enough to sink into the host cell, resulting in holes in the membrane and causing the release of intracellular components and cell death. Gamma-hemolysin is a bicomponent toxin with hemolytic and leukolytic activity. The level of lytic activity depends on the combination of S and F components which make up all staphylococcal bicomponent toxins. The S components of gamma-hemolysin are encoded by *hlgA* or *hlgC* and the single F component is encoded by *hlgB*. Similarly, Panton-Valentine leukocidin (PVL) is a bicomponent toxin, encoded by *lukF-PV* and *lukS-PV*, which is

significantly more leukotoxic than gamma-hemolysin^{14, 29}. The phenol soluble modulins (PSM) have been recently described and appear to have formed two major classes, α -PSMs and β -PSMs, with the former class having the most leukocytic and inflammatory activity¹⁰⁶. Both PVL and PSM- α are strongly associated with the hypervirulence of CA-MRSA infections, as detailed below. These cytolytic toxins have the overall effect of dampening the efficacy of the host immune response by destroying vital immune cells and misdirecting the immune response through the release of pro-inflammatory cytokines from lysed cells.

Staphylococcal superantigens. Superantigens are molecules which initiate a non-specific interaction between the T-cell receptor (TCR) on CD4+ T-cells and the major histocompatibility complex class II (MHC-II) on antigen presenting cells (APC). This interaction leads to a robust immune response, resulting in a cytokine storm that can lead to multi-system organ failure and death. Different isolates of *S. aureus* may carry any number of genes encoding superantigens. Toxic shock syndrome toxin 1 (TSST-1) is a bacteriophage-encoded superantigen most often linked to tampon-associated toxic shock syndrome. Scalded skin syndrome, seen almost exclusively in newborns, is caused by exfoliative toxins, which degrade desmoglein 1 and result in burn-like lesions⁷⁷. A range of staphylococcal enterotoxins (SEA – SEG) cause food poisoning, which is often self-limiting and not associated with the more serious affects caused by the other staphylococcal superantigens^{60, 77}.

Clonal variation of *S. aureus*

S. aureus has historically been considered an opportunistic pathogen, infecting primarily the elderly, the hospitalized or otherwise immunocompromised patients. However, recently, so-called CA-MRSA isolates have been causing infection in young, healthy individuals with no history of *S. aureus* infection or previous contact with the healthcare environment. CA-MRSA infections have been steadily increasing in both the community and hospital settings, while the occurrence of hospital-acquired MRSA (HA-MRSA) infections is declining^{25, 107}. CA-MRSA strains are characterized by enhanced virulence compared to the classical HA-MRSA isolates. The CA-MRSA strain USA 300 is the major cause of the alteration in epidemiology of MRSA infections in the United States, and now accounts for the majority of SSTIs presenting in emergency rooms⁵³. USA 300 is emerging as a major cause of prosthetic joint infections⁵⁶ and blood stream infections⁹⁵ in hospitals, and has been associated with necrotizing pneumonia⁵⁸ and necrotizing fasciitis⁶³. The necrotizing diseases in particular have been attributed to the presence of the PVL toxin. The association of CA-MRSA virulence with PVL remains controversial, as a number of reports have questioned whether PVL is the mediator of necrotic activity, or merely an indicator of the presence of other, as yet undefined, toxins¹⁰⁴. Diep, et. al. have suggested that PVL plays a transitory role in CA-MRSA pathogenesis, being beneficial (to the bacteria) only at the onset of infection²⁸. Furthermore, the expression of PSM-α was recently shown to be enhanced in CA-MRSA strains, and have been associated with eliciting a strong immune response in animal models of bacteremia (USA 400) and cSSTIs (USA 300), recruiting neutrophils to the site of infection, causing cell lysis leading to extensive tissue damage¹⁰⁶.

It has recently been suggested that regulation of virulence factors encoded as part of the core genome, as opposed to the acquisition of various MGEs encoding toxins or resistance genes (e.g. PVL), is the reason for the increased virulence of CA-MRSA. Li et. al. have shown that *agr*-regulated virulence factors such as HLA and PSM- α are significantly upregulated in USA 300 and USA 500 (CA-MRSA isolates) in comparison to USA 100 and USA 200 (HA-MRSA isolates); however, they also indicated that, as staphylococcal regulation is so complex, it is highly likely that this process is multifactorial⁶².

Antimicrobial therapies and resistance

S. aureus is a remarkably versatile and adaptable pathogen, in part due to its multifactorial mode of pathogenesis, but also because it has developed resistance to every therapy introduced in the last 60 years. Here, we discuss the major classes of antimicrobials used for the clinical treatment of *S. aureus* and the mechanisms of resistance it has developed to cope with challenges posed by these various therapies.

Cell-wall synthesis inhibitors. With the release of penicillin in the 1940s, previously fatal bacterial infections became treatable, heralding a new era of infection control. However, within a few short years, strains of *S. aureus* appeared that were completely resistant to this drug, and it became apparent that controlling bacterial diseases would become more complex than first perceived. Specific analysis revealed that resistance was

mediated by penicillinase, which cleaves the active β -lactam ring of this class of drugs, inactivating them entirely¹⁹.

Methicillin, a derivative of penicillin, was introduced onto the market in 1959 as one of the first semi-synthetic β -lactams, and a potential solution to penicillin-resistant strains of bacteria. The reason methicillin was considered to be so important was that its β -lactam ring is chemically buried, and is thus protected from access to β -lactamases. Unfortunately, the first reported case of resistance occurred by 1961¹⁹ and ushered in the demise of β -lactam antibiotics. Methicillin-resistance is mediated by a novel penicillin-binding protein (PBP2a), encoded by the *mecA* gene. The *mecA* gene may have been acquired from *S. sciuri* and incorporated into the staphylococcal chromosome cassette (SCC), resulting in the SCCmec mobile genetic element¹⁰⁸. There are currently eight known types of SCCmec, I – VIII¹⁹. Each type is associated with a different range and level of antimicrobial resistance. SCCmecs I – III are associated with HA-MRSA, and SCCmecs IV, V, and VI are associated with CA-MRSA^{25, 53}. In addition to methicillin/ β -lactam resistance, SCCmec can confer resistance to other antimicrobial classes, such as aminoglycosides, heavy metals, macrolides, and polyketides¹⁹.

Another commonly used class of β -lactams is the cephalosporins, which also inhibit cell-wall synthesis by a mechanism similar to the penicillins. Cephalosporins are divided into “generations” based on the time they were discovered and their spectrum of activity, with the older generations being the most limited and the newer generations being the most broadly active. They were first introduced into the clinical environment in 1962, 17 years

after their discovery in 1945⁹³. Strains resistant to methicillin are also resistant to cephalosporins, so their therapeutic use is only indicated for known methicillin-susceptible *S. aureus* (MSSA) strains¹⁹.

There are currently only a few effective antimicrobials available to treat highly resistant MRSA infections. The antibiotic most commonly used in such situations is vancomycin, a glycopeptide that has poor solubility, high toxicity, and can only be administered intravenously. Its mode of action, like β-lactams, affects bacterial cell wall synthesis, although via a slightly different mechanism. Reduced susceptibility to vancomycin in clinical isolates was first reported in 1997 in Japan, 39 years after its introduction in 1958⁴³. Since this time, so-called vancomycin-intermediate *S. aureus* (VISA) has become distributed worldwide. They are characterized by a diminished sensitivity to the drug, requiring increasing concentrations to produce positive therapeutic outcomes. Fully vancomycin resistant *S. aureus* (VRSA) was first reported in 2002 and appears to be conferred by acquisition of the *vanA* resistance gene from vancomycin-resistant Enterococci (VRE). Specifically, a study from 2003 describes a diabetes patient co-infected with methicillin-susceptible *S. aureus* (MSSA) and VRE. The patient was treated with a wide array of antibiotics, including vancomycin, and VRSA cells were isolated before the course of treatment was completed. Sulfamethoxazole-trimethoprim and metronidazole were successful in eradicating the infection, but only after the infection had disseminated to bacteremia and the patient's foot was amputated. This was the first time a clinical strain of *S. aureus* was demonstrated to carry the *vanA* gene²⁰. Another point for concern has been the appearance of heterogenous vancomycin-

intermediate strains (hVISA). These strains will appear to be susceptible to treatment by vancomycin, but a subset of the bacterial population (less than 1 in $10^{-5} - 10^{-6}$) will be resistant. The presence of hVISA is typically associated with repeated MRSA infection and exposure to vancomycin, and is often difficult to detect. Most VISA and hVISA strains do not carry *vanA*; instead, they display thickened cell walls and may have altered transcription of regulatory elements⁴⁴.

Membrane disruption. Daptomycin is one of the few novel antimicrobials that targets methicillin-resistant strains of *S. aureus*, and was approved by the FDA in 2003. It works by disrupting the charge of the cell envelope, thus weakening membrane stability. The first reported case of reduced susceptibility to daptomycin occurred in 2004 in Boston, Massachusetts⁶⁹, and resistance often occurs during a failed course of treatment for an infection previously shown to be daptomycin-susceptible^{69, 71}. The resistance mechanism, whilst not completely understood at this time, has been associated with changes in membrane fluidity and increased positive charge of the bacterial membrane^{49, 79}.

DNA synthesis inhibition. Fluoroquinolones such as ciprofloxacin, levofloxacin, and moxifloxacin inhibit bacterial DNA gyrase and topoisomerase IV. Many MRSA strains are resistant to fluoroquinolones, thus, they are infrequently used²⁷; however, many MSSA isolates are still susceptible. Even so, fluoroquinolones are known to have negative side effects, and are rarely a first-line choice for treatment. As with other therapeutics, resistance can develop during the course of treatment; as such, ciprofloxacin

is often used in combination therapy with rifampicin. Fluoroquinolone resistance is mediated by the quinolone resistance determining regions (QRDR) that are present in the genes encoding the protein targets of fluoroquinolones. Specific mutations leading to resistance have been shown to occur in *gyrAB* (DNA gyrase) and *grlAB* (topoisomerase IV), which interferes with quinolone binding whilst still allowing enzymatic function⁸⁷. The efflux pumps NorA⁵¹ and QacBIII⁷⁸ have also been shown to play a role in decreased susceptibility to these drugs.

Trimethoprim-sulfamethoxazole (TMP-SMX), a pyrimidine-sulfonamide combination drug, inhibits folic acid synthesis, an essential precursor for purines and thymine, by competitively binding dihydrofolate reductase (DHFR). TMP-SMX is typically used only for the treatment of MSSA and non-multiply resistant MRSA (nmrMRSA), as multiply-drug resistant MRSA (mdrMRSA) typically demonstrate TMP-SMX resistance^{34, 91}. Resistance is caused by point mutations in the DHFR gene, or by acquisition of a plasmid-encoded accessory DHFR. These accessory DHFRs often have very little sequence homology with other prokaryotic DHFRs, rendering them unrecognizable to TMP-SMX^{24, 47}.

Transcription inhibition. A common technique used to combat multiple-drug resistant infections is combination drug therapy. Rifampicin, a transcription inhibitor, is commonly used in combination with ciprofloxacin, vancomycin, daptomycin, or linezolid for such a purpose. Rifampicin binds to the RNA polymerase β subunit, encoded by *rpoB*, interfering with transcription of DNA to RNA. While many strains of MRSA are

resistant to rifampicin⁵, it can be effective in combination with fusidic acid or vancomycin^{50, 73}. Despite reported successes of vancomycin-rifampicin therapy, there remains a strong possibility of rifampicin resistance developing during treatment^{67, 89}.

Translation inhibition. There are a number of antimicrobial classes available that target different components of protein synthesis. Aminoglycosides (e.g. gentamycin, kanamycin, neomycin) and macrolides (e.g. erythromycin, clarithromycin, azithromycin) are classes that bind to either the 30S or 50S subunit of the ribosome and interfere with translation. These antimicrobial agents are typically used only to treat MSSA infections due to the high prevalence of resistance found in mdrMRSA isolates. Lincosamides (lincomycin and clindamycin) also bind to the 50S ribosomal subunit and inhibit translational initiation, and are also only indicated for the treatment of MSSA infections⁹¹. The streptogramin B group includes the combination therapy quinupristin/dalfopristin, which work synergistically to inhibit the elongation of polypeptides. Resistance to any member of the MLS (Macrolides, Lincosamides, and Streptogramin B) group of antibiotics often results in cross-resistance to the remaining members, and, specifically, improper use of erythromycin can induce resistance to clindamycin¹⁰⁹.

Tetracycline antibiotics of the polyketide class target the 30S subunit of ribosomes, blocking translational elongation. Strains of *S. aureus* often carry the tetracycline resistance genes *tetK* and *tetL*, encoding efflux pumps, and *tetM* and *tetO*, encoding ribosomal protection proteins, both of which confer high levels of resistance to

tetracycline antibiotics⁸⁶. A new class of protein synthesis inhibitors, the glycylcyclines, has been derived from tetracyclines, and includes tigecycline, which was approved by the FDA in 2005 to treat MRSA infections. Tigecycline blocks the A-site of the ribosome by binding to the 30S ribosomal subunit with five times greater affinity than tetracycline. The reason for this increased binding affinity is probably due to structural differences between tetracycline and tigecycline, with tigecycline forming stronger and more numerous bonds with the ribosome^{26, 84}. In 2004, an initiative was taken to establish the Tigecycline Evaluation and Surveillance Trial (TEST) whose purpose was to monitor tigecycline susceptibility and compare it to other clinically relevant drugs. As reported in 2008, there has been no change in MSSA or MRSA MICs, making tigecycline an attractive therapeutic option for otherwise untreatable infections³⁰.

Linezolid is a synthetic oxazolidinone which binds the 23s rRNA component of the 50S ribosomal subunit, and was approved in 2000 to treat multiply-drug resistant infections. Because it is completely synthetic, it was expected that there would be no reservoir for resistance. However, the first clinical isolate of linezolid-resistant MRSA was reported in 2001 in Massachusetts¹⁰², while the first clinical outbreak, consisting of 12 patients, occurred in 2008 in Madrid, Spain⁷⁵. Resistance has been associated with the presence of the *cfr* gene, which is carried on a plasmid, and confers resistance to chloramphenicol, florfenicol, and clindamycin. The mechanism of resistance involves altering the target of linezolid by introducing a mutation into the gene encoding the 23s rRNA⁷⁵. A specific resistance-inducing mutation, G2576T, in the same gene has also been reported to occur

spontaneously in 1×10^{-9} isolates. However, because *S. aureus* has multiple copies of the 23s rRNA gene, the occurrence of *in vivo* resistance is still rare⁸⁸.

Novel therapeutics

With a remarkable number of antibiotics no longer proving effective in the clinic, it appears troublesome at best to keep pace with staphylococcal drug resistance. Very few new antimicrobial classes have been developed in the past 50 years; however, there are a number of new drugs in the pipeline that display improved antimicrobial activity.

Next generation β-lactams. Two new cephalosporins with broad-spectrum, anti-MRSA activity are being investigated. The first, ceftobiprole and its prodrug ceftobiprole medocaril, are being developed by Basilea Pharmaceutica AG and Johnson & Johnson Pharmaceutical Research and Development LLC. Unlike other β-lactam antimicrobials, ceftobiprole has a very high affinity for PBP2a, the protein encoded on SCCmec which confers methicillin-resistance, and has a chemical structure more resistant to cleavage by β-lactamases. Furthermore, ceftobiprole has also shown good activity against completely vancomycin-resistant strains¹¹¹. *In vitro* experimentation has demonstrated that resistance is rare, although not impossible. To date, Phase III trials for SSTIs and pneumonias, alongside comparison to vancomycin efficacy, have been completed, with ceftobiprole showing similar cure rates and patient tolerance to vancomycin¹¹⁰. Ceftaroline and its prodrug ceftaroline fosamil act by a mechanism similar to ceftobiprole and have been compared favorably to imipenem (a carbapenem) and nitrocefin (a cephalosporin). The spontaneous mutation frequency in MSSA and MRSA is ≤ 1 in 10^{-9}

$\sim 10^{-10}$. One Phase III trial has been completed, studying the usefulness and safety of ceftaroline for the treatment of SSTIs as compared to vancomycin, and was found to be equally effective and well tolerated¹¹².

Membrane disruption. The majority of drugs available and in the pipeline today target growing bacteria, with no antimicrobials specifically targeting stationary-phase bacteria currently available. HT61 is a very early-phase, narrow-spectrum compound currently being tested by Helperby Therapeutics for its use as a topical therapeutic in humans. Its mode of action appears to be concentration-dependent membrane disruption by rapid depolarization, causing leaking of intracellular contents at low concentrations and cell wall nicking at high concentrations. *In vivo*, HT61-imbued gel completely prevented colonization of mouse skin by stationary-phase *S. aureus* cultures, as compared to mupirocin, which had no inhibitory effect. HT61 was also shown to be effective in eradicating both MSSA and MRSA in a mouse infection model using log-phase cultures, and was, again, significantly more effective than mupirocin. Interestingly, HT61 is considerably more active towards non-multiplying cells than actively growing cells, although the precise reason for this has not yet been determined. Significantly, *in vitro* experiments show that no resistance occurs in either stationary- or log-phase cultures after 50 passages at sub-MIC concentrations⁴⁵.

DNA synthesis inhibition. Iclaprim, like trimethoprim, prevents DNA synthesis by binding DHFR. Unlike TMP, it is active against those strains of MSSA, MRSA, VISA, and VRSA which are TMP resistant⁹³. *In vitro*, resistance has not been observed thus far,

and the side effects for this drug appear to be negligible, making it a very attractive therapeutic prospect. It also shows, like TMP, synergistic activity with SMX⁹⁴, and has completed Phase II trials for the treatment of SSTIs⁵⁷.

Fatty acid synthesis inhibition. Currently, triclosan is the only inhibitor of Type II fatty acid synthesis clinically available. It has more than one mode of action, but seems to function by binding to the enoyl-acyl carrier protein (FabI), and preventing initiation of fatty acid synthesis. Recently, more interest has emerged in this pathway, as it is believed to be essential to bacterial growth and is distinct from mammalian Type I fatty acid synthesis⁶. Despite the attractiveness of this pathway as a therapeutic target, there has been controversy concerning its suitability^{6, 16, 17}. Brinster, et. al. showed that *Streptococcus agalactiae*, a causative agent of neonatal meningitis, was able to survive the activity of both triclosan and cerulenin (an inhibitor of b-ketoacyl carrier protein synthetase [FabF/B]) when culture media was supplemented with long-chain fatty acids¹⁷. *S. aureus* was also demonstrated to survive cerulenin activity in the presence of both short-chain and long-chain fatty acids², but both of these claims have recently been contested by Balemans, et. al⁶. Despite this controversy, Merck & Co, Inc. is investigating the potential use of two fatty acid synthesis inhibitors, platensimycin and platencin. Platensimycin inhibits β -ketoacyl-[acyl-carrier protein (ACP)] synthase II (FabF), while platencin inhibits both FabF and β -ketoacyl-[ACP] synthase III (FabH). Both have broad-spectrum *in vitro* and *in vivo* activity against Gram-positive pathogens, including MRSA. The rate of resistance for platencin was between 2×10^{-8} and 1×10^{-9} depending on the strain tested and concentration of exposure¹⁰⁵.

| Mode of Action | Antimicrobial | Class | Date of Release | First Reported Date of Resistance | Gene/Source of Resistance | Mode of Resistance |
|--------------------------------|---------------|-----------------|-----------------|-----------------------------------|---|---|
| Cell wall synthesis inhibition | Penicillin | β-lactam | 1940s | 1940s | production of a β-lactamase | penicillinase cleaves β-lactam ring, inactivating penicillin |
| | Methicillin | β-lactam | 1959 | 1961 | acquisition of <i>mecA</i> | PBP2a |
| | Vancomycin | Glycopeptide | 1958 | 1997 | acquisition of <i>vanA</i> | altered cell wall prevents antimicrobial binding |
| Membrane disruption | Daptomycin | Lipopeptide | 2003 | 2004 | mutations in <i>mprF</i> or <i>ycgG</i> | membrane's positive charge increases, preventing drug binding |
| DNA synthesis inhibition | Ciprofloxacin | Fluoroquinolone | 1987 | 1997 | mutations in <i>gyrAB</i> or <i>grlAB</i> | structure of DNA gyrase is altered, preventing drug binding |
| Transcription inhibition | Rifampicin | Rifamycin | 1989 | 2004 | mutations in <i>rpoB</i> | structure of β-subunit of RNA polymerase is altered, reducing drug binding |
| Translation inhibition | Erythromycin | Macrolide | 1952 | 1957 | acquisition of <i>ermA</i> or <i>ermC</i> | structure of 23s rRNA is altered, reducing drug binding |
| | Gentamicin | Aminoglycoside | 1963 | 1976 | acquisition of <i>rmtC</i> | enzymatic inactivation of the drug |
| | Linezolid | Oxazolidinone | 2000 | 2001 | acquisition of <i>cfr</i> | mutation in gene encoding 23s subunit of 50S ribosome prevents drug binding |
| | Tigecycline | Glycylcycline | 2005 | Not yet detected | NA | NA |

Table 1. Overview of relevant antimicrobials and *S. aureus* resistance.

N-thiolated β-lactams. A novel β-lactam, which forms the focus of this study, has been developed, and displays a mode of action unlike any other β-lactam previously investigated. N-thiolated β lactams have shown strong activity towards MRSA, *Bacillus anthracis*, and *Micrococcus luteus*, weak activity towards *Neisseria gonorrhoeae*,

Bacteroides fragilis, and *Haemophilus influenza*, but no activity towards *Listeria monocytogenes*, *Streptococcus pyogenes*, *S. pneumoniae*, *Klebsiella pneumoniae*, *Vibrio cholerae*, *Escherichia coli*, *Salmonella typhimurium*, *Pseudomonas aeruginosa*, or *Mycobacterium smegmatis*¹⁰³. Instead of targeting cell wall synthesis, it has been suggested that Ns β L interacts with coenzyme A (CoA) by thiolating the active site cysteine residue, and similarly sulfenylating the active site cysteine of FabH¹⁰³, thus both directly and indirectly interfering with Type II fatty acid synthesis⁹². Because of the possible interaction with CoA, other pathways dependent on this intermediate may also be affected by this drug. All analogs of *N*-thiolated β lactams are unaffected by β -lactamases at every concentration tested, and activity appears to be dependent on both low intracellular concentrations of glutathione (GSH) and high concentrations of CoA, indicating that *N*-thiolated β lactams may act as a thiolating agent⁹².

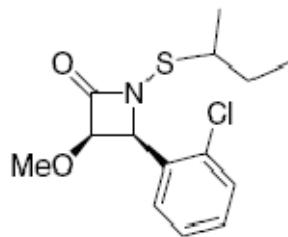


Figure 1. *N*-sec-butylthiolated β -lactam (Ns β L). This analog has the highest antimicrobial activity of all N β L analogs tested.

The activity of NsBL against a variety of laboratory and clinical *S. aureus* isolates was determined, including strains methicillin-, multidrug-, and vancomycin-resistant. Additionally, the affects of different *in vitro* conditions mimicking physiological on the activity of Ns β L were explored. In an effort to clarify the mechanism(s) of action of Ns β L, we generated mutants resistant to this drug by two different methods in three

strains. By determining the phenotypic and proteomic changes that resulted from the gain of resistance in these isolates, we hope to elucidate the primary target of Ns β L.

MATERIALS AND METHODS

Bacterial strains

Because there is a wide range of clonal variation amongst *S. aureus* strains, a variety of laboratory and clinical isolates were used in this study (Table 2).

| Strain | Source | Significant Characteristics |
|----------------------------------|------------------------|---|
| <i>S. epidermidis</i> RP62A | NARSA* | MRSE clinical isolate |
| <i>S. aureus</i> 8325-4 | Simon Foster | Defective in <i>rsbU</i> |
| <i>S. aureus</i> RN6390 | Mark Smeltzer | Derived from 8325-4 |
| <i>S. aureus</i> SH1000 | Simon Foster | Functional <i>rsbU</i> derivative of 8325-4 |
| <i>S. aureus</i> Newman | Mark Smeltzer | Laboratory strain |
| <i>S. aureus</i> COL | Lab stock | Early clinical MRSA isolate |
| <i>S. aureus</i> UAMS-1 | Mark Smeltzer | Well studied biofilm-former |
| <i>S. aureus</i> USA 100 635 | Tampa General Hospital | HA-MRSA |
| <i>S. aureus</i> USA 100 Mu50 | NARSA | VISA |
| <i>S. aureus</i> USA 200 MRSA252 | NARSA | HA-MRSA |
| <i>S. aureus</i> USA 300 Houston | Mark Smeltzer | CA-MRSA |
| <i>S. aureus</i> USA 300 LAC | Kelly Rice | CA-MRSA |
| <i>S. aureus</i> USA 300 FPR3757 | Mark Smeltzer | CA-MRSA |
| <i>S. aureus</i> USA 400 MW2 | NARSA | CA-MRSA |

Table 2. Bacterial strains used. *Network on Antimicrobial Resistance in *Staphylococcus aureus*.

Culture media

Tryptic soy broth (TSB) and brain-heart infusion broth (BHI). Tryptic soy broth (Teknova) and BHI (Bacto) were prepared according to the manufacturer's specifications. Agar was added at 15 gL⁻¹ as needed for plates. All media was autoclaved for 30 minutes at 121°C and 15 psi, unless otherwise noted.

Top Agar. Top agar was prepared by adding 0.7 g agar to 100 mL TSB and autoclaving as described.

Biofilm media (BIO). TSB was supplemented with 0.5% dextrose and 3% NaCl prior to autoclaving.

Purple broth. Purple broth was purchased from Fisher Scientific and prepared according to the manufacturer's specifications.

Chemically-defined media (CDM). Different types of chemically-defined media were prepared by combining separately prepared limiting solutions (CL# or CDM#). Refer to the appendix for the complete lists of the components of the CL and CDM solutions.

Non-Limiting CDM. Combine the following solutions:

| | |
|--------------------------|-------|
| CL1 | 50% |
| CL2 | 10% |
| CL3 | 1% |
| CL4 | 0.2% |
| CDM4 | 0.1% |
| CDM5 | 10% |
| MilliQ dH ₂ O | 28.7% |

Non-limiting CDM plates (CDM-A). Combine CL1, CL2, CL3, CDM4, and MilliQ dH₂O in the proportions described and add 15 gL⁻¹ agar, then autoclave and cool to 55°C. Add CL4 and CDM5 in the proportions described.

Amino acid-limiting CDM (AA-CDM). Combine the following solutions, then filter sterilize:

| | |
|------|--------|
| CDM1 | 0.07% |
| CDM2 | 0.02% |
| CDM3 | 0.05% |
| CDM4 | 0.001% |
| CDM5 | 0.1% |

Glucose-limiting CDM (G-CDM). Reduce the concentration of glucose in CDM5 by ten-fold and follow the recipe for amino acid-limiting CDM.

Phosphate-limiting CDM (PO₄-CDM). Reduce the concentration of Na₂HPO₄ and KH₂PO₄ in CDM1 by five-fold and follow the recipe for amino-acid limiting CDM.

Limiting CDM plates ([L]-CDMA). Combine CDM1, CDM3, CDM4, and dH₂O in the proportions described, and 15 gL⁻¹ agar, then autoclave and cool to 55°C. Add CDM2 and CDM5 in the proportions described. Do this for any type of CDM needed.

Metal ion-limiting media (ML). All glassware used for metal ion-limiting solutions was washed in 0.1M HCl overnight, rinsed thoroughly with dH₂O, and autoclaved prior to use. All solutions used in metal ion-limiting media were treated with Chelex-100 to remove trace metal ions.

Combine the following solutions:

| | |
|--------------------------|-------|
| CL1 | 50% |
| CL2 | 10% |
| CL3 | 1% |
| CL4 | 0.2% |
| MilliQ dH ₂ O | 38.8% |

Add 10gL⁻¹ Chelex-100 and stir for 4 hours. Filter sterilize, then add 0.4 mLL⁻¹ sterile 1M MgSO₄ in Chelex-treated MilliQ dH₂O.

Metal ion-limiting plates (MLA). Combine CL1, CL2, CL3, and MilliQ dH₂O in the proportions described, and add 10 gL⁻¹ agar, then autoclave and cool to 55°C. Add MgSO₄ in the proportion described. Do not treat with Chelex-100.

Milk plates. Milk plates were prepared by preparing TSA as normal, but with the addition of 2% dry skim milk and autoclaving for 10 minutes at 121°C and 15 psi. Plates were streaked from an isolated colony on a TSA plate and incubated at 37°C overnight.

Blood plates. Remel blood plates containing 5% sheep's blood were purchased from Fisher Scientific. Plates were streaked from an isolated colony on a TSA plate and incubated at 37°C overnight.

Sodium nitrate and sodium nitrite plates. Sodium nitrite plates were prepared by adding sterile 1M NaNO₂ to a final concentration of 1mM NaNO₂ or 2M NaNO₃ to a final concentration of 20mM NaNO₃ to TSA after autoclaving. Plates were streaked from an isolated colony on a TSA plate and incubated in an anaerobic GasPak chamber at 37°C overnight.

Congo red agar (CRA). Congo red agar was prepared by supplementing TSA with 5% sucrose and 0.8 gL⁻¹ congo red before autoclaving.

Maintenance and growth of bacterial cultures

Glycerol stocks. Glycerol stocks were prepared from 1 mL of overnight culture grown in 100 mL TSB in a 250 mL Erlenmeyer flask at 37°C with shaking at 250 rpm. The 1 mL aliquot was centrifuged at 13,300 x g for 10 minutes, the supernatant was discarded, and the pellet was resuspended in 1 mL TSB containing 12% glycerol. Stocks were stored at -80°C until needed, when they were streaked on TSA and incubated at 37°C overnight. Stock plates were used for a maximum of seven days before new plates were prepared.

Synchronized cultures. Two hundred-fifty mL Erlenmeyer flasks containing 100 mL TSB were inoculated with one colony from stock plates and incubated at 37°C overnight with shaking at 250 rpm. A fresh flask was inoculated with 1 mL of the overnight culture and further incubated for 3 hours. Another fresh flask was inoculated to ~OD^{600nm} 0.05 and incubated until the desired growth phase was reached. Synchronized cultures were used unless otherwise stated.

Direct plate count. Cultures were serially diluted 1:10 in sterile PBS up to a 10⁻⁷ dilution. 100 µL of the 10⁻⁶ and 10⁻⁷ dilutions were spread-plated in triplicate and incubated overnight at 37°C. Individual colonies were counted and the colony forming units per milliliter (CFU/mL) was calculated for each plate. The average was taken to give the final CFU/mL.

Determination of minimum inhibitory concentrations

Minimum inhibitory concentrations (MIC) were determined using a microbroth 96-well plate method. TSB containing the drug of interest was prepared in aliquots of at least 1 mL, then 100 µL of the antibiotic-containing TSB was added to each well of a sterile 96-well flat-bottomed plate (Greiner Bio-One). Cultures grown overnight in 10 mL TSB in a 50 mL Falcon tube were diluted 1:100 before adding 10 µL to each prepared well, resulting in a final dilution of 1:1000. At least three wells containing TSB were left uninoculated to serve as negative controls. Each MIC was performed in triplicate.

Disk diffusion assays

Pre-warmed TSA plates were overlaid with 5mL top agar inoculated with 5 μ L of overnight culture. The plates were allowed to dry before sterile Whatman paper disks imbued with the chemical stressor of interest were placed on the plates. Plates were incubated right-side up at 37°C overnight. Zones of inhibition were measured in millimeters the next day. After the first round of assays, only those stressors which resulted in a significant difference between the wild-type and mutant strains were repeated.

Fatty acid 96-well assays

Flat-bottomed 96-well plates were prepared with 200 μ L per well TSB containing 0.05% bovine serum albumin (BSA, Fisher BioReagents), 0.1% tween 80 (Fisher Scientific), or 0.01% oleic acid (Fisher Scientific). Tween 80 was prepared as a 10% solution in sterile 5% BSA. Oleic acid was prepared as a 1% solution in sterile 5% BSA. A range of antibiotic concentrations were tested from sub-MIC up to 100x MIC. Each well was inoculated with an overnight culture diluted to \sim OD_{600 nm} 0.05, and plates were incubated at 37°C overnight. Plates were examined for growth in the different media at each antibiotic concentration. To quantify, 100 μ L was removed from each well and diluted in 900 μ L diH₂O in a cuvette and the absorbance was measured at 600 nm.

Antimicrobial susceptibility of biofilms

A sterile flat-bottom 96-well plate was treated with 150 μ L human plasma per well (20% human plasma in bicarbonate/sodium bicarbonate buffer) and incubated at 4°C overnight.

The plasma was gently aspirated from each well, and each prepared well was inoculated with 150 µL culture grown overnight in 100 mL TSB-Bio in a 250 mL Erlenmeyer flask. Each culture was arbitrarily standardized to ~OD_{600 nm} 0.05. The plate was incubated at 37°C for 24 hours, then the plate was gently rinsed three times with sterile phosphate buffered saline (PBS). 150 µL TSB-Bio containing an antibiotic of interest in a range of concentrations was added to each well, and the plate was further incubated at 37°C for 24 hours. The plate was gently rinsed three times with sterile PBS and each well was fixed with 200 µL 100% ethanol. The ethanol was removed and the plate was allowed to air dry. Each well was then filled with 200 µL staining solution (41% crystal violet w/v, 12% ethanol) and allowed to stain for 2 minutes. The stain was gently aspirated, and each well was washed three times with sterile PBS. The plate was covered and allowed to air dry overnight. The stain was eluted with 100 µL of 100% ethanol for 10 minutes. The absorbance was read using a BioTek Synergy2 plate reader at 590 nm. Samples were further diluted in 100% ethanol as necessary to get a reading within range. Biofilms of interest were compared to biofilms formed by the strains *S. aureus* 8325-4 (negative control) and *S. aureus* SH1000 (positive control).

Generation of spontaneous mutants

TSA plates were supplemented with 5 µg/mL NsβL after autoclaving. 1 mL of a 10 mL overnight culture was centrifuged at full speed and all the supernatant except for 100 µL was discarded. The pellet was resuspended and spread-plated on the NsβL-TSA plates. At the same time, the CFU/mL of the inoculating culture was calculated (2.3). The plates were incubated ~36 hours at 37°C, and any colonies were counted and patched onto

Ns β L-TSA plates. The patched plates were incubated at 37°C overnight, and glycerol stocks were made from each patch.

Calculation of spontaneous mutation frequency. The spontaneous mutation frequency of each spontaneous mutant was calculated using the following equation:

$$\text{Spontaneous Mutation Frequency} = \frac{\Sigma R}{\Sigma N}$$

Where R is the number of resistant colonies obtained and N is the number of cells screened.

Generation of adaptive mutants

4 μ L of a synchronized culture was used to inoculate a 15 mL Falcon tube containing 2 mL BHI with 0.125 μ g/mL Ns β L (sub-MIC). The Falcon was incubated at 37°C for 24 h with shaking. A 4 uL aliquot was used to inoculate a new 15 mL Falcon tube containing 2 mL BHI with 0.25 μ g/mL Ns β L, which was incubated as previously. This process was repeated, doubling the Ns β L concentration until no growth was observed. A 1 mL aliquot from each day was spun down and stored in glycerol at -80°C as described.

Growth curve assays

Standard conditions. Synchronized cultures were used to inoculate 100 mL TSB or CDM in a 250 mL Erlenmeyer flask to ~OD_{600nm} 0.05. For CDM, cells were washed twice with sterile PBS before inoculation. Absorbance readings were taken once every hour for 8 hours.

Nutrient limiting conditions. Synchronized cultures were used to inoculate [L]-CDM to ~OD_{600nm} 0.05 by first measuring the absorbance then calculating the volume needed to reach the desired optical density, then washing twice with sterile PBS. Absorbance readings were taken once every hour for 8 hours.

Metal ion-limiting conditions. Isolated colonies from TSA were used to streak MLA. Isolated colonies from MLA were used to inoculate 5 mL ML in a 50 mL Falcon tube, which was incubated at 37°C for 36 – 48 hours. An Erlenmeyer flask containing 25 mL CL was inoculated to ~OD_{600 nm} 0.005 and incubated at 37°C with shaking. After 12 hours, an identical set of flasks was set up and incubated at 37°C with shaking. Twelve hours from that point is when absorbance measurements were begun, once an hour for 12 hours, resulting in a total time-point range from 12 hours to 32 hours.

Alternative sugar fermentation assay

A flat-bottomed 96-well plate was prepared with 200 µL purple broth per well. Wells were supplemented with 1% of an alternative sugar and inoculated with 5 µL overnight culture standardized to ~OD_{600 nm} 1.0. Each sugar stock was prepared at a concentration of 100 mg/mL. Alternative sugars used were dextrose, fructose, galactose, D-glucosamine, lactose, maltose, mannose, ribose, sucrose, trahalose, raffinose, and xylose. Plates were incubated at 37°C overnight, then examined for a change in color from purple to yellow. The color change indicated fermentation of the alternative carbon source. Each assay was performed in triplicate.

Autolysis assays

Triton X-100 lysis. Synchronized cultures were used to calculate the volume needed to inoculate a 10 mL solution to ~OD_{600nm} 2.0. The required volume was aliquoted and washed twice with ice cold diH₂O, then resuspended in 10 mL sterile 0.05M Tris-HCl (pH 7.6) with or without 0.05% Triton X-100. Absorbance measurements were recorded every 30 minutes for 3 hours. Each assay was performed in triplicate.

Penicillin G lysis. Synchronized cultures were used to inoculate 100 mL TSB containing 0.4 µg/mL Penicillin G in a 250 mL Erlenmeyer flask to an ~OD_{600 nm} 0.05. Absorbance measurements were recorded every 30 minutes for 5 hours. Each assay was performed in triplicate.

Gene sequencing

Solutions. All solutions used for gene sequencing were made according to the following formulas:

TE buffer

| | |
|----------|--------|
| Tris-HCl | 1 mM |
| EDTA | 0.1 mM |

Adjust pH to 7.5 and autoclave. Store at room temperature.

50x TAE buffer

Trisma base 242 g

Glacial acetic acid 57.1 mL

0.5 M Na₂EDTA, pH 8.0 100 mL

Bring up to 1L in diH₂O.

Dilute 1:10 in diH₂O before use.

DNA extraction

A 5 mL overnight culture was spun down and the pellet was resuspended in 600 µL TE buffer in a snap-cap Eppendorf tube. ~0.5 cm of 0.1mm glass beads were added, and the tube was bead beaten for six 10 second intervals. The samples were spun for 5 minutes at full speed and the supernatant was transferred to a new snap-cap Eppendorf. 200 µL 1.6% sarkosyl and 5 µL proteinase K were added, and the samples were incubated at 60°C for 60 minutes. 800 µL of phenol/chloroform was added, the samples were vortexed, and spun for 5 minutes at full speed. The upper aqueous layer was transferred to a 1.5 mL Eppendorf tube, and 500 µL 100% isopropanol and 100 µL 3M sodium acetate were added and mixed by inversion. The sample was incubated at -80°C for 30 minutes. The sample was spun at full speed for 5 minutes, the supernatant was discarded, and 500 µL 70% ethanol was added. The sample was again spun at full speed for 5 minutes and the supernatant was discarded. The pellet was air-dried at room temperature, gently resuspended in 200 µL diH₂O, then allowed to fully resuspend at 4°C overnight.

Polymerase chain reaction (PCR) conditions. Extracted DNA was prepared in PCR tubes as described and placed in a thermocycler (DNAEngine, BioRad). The following conditions were used:

Initiation: 94°C for 2 minutes

30 cycles of

- Denaturation: 94°C for 1 minute
- Annealing: 55°C for 30 seconds
- Extension: 72°C for 1 minute

Final elongation: 72°C for 7 minutes

Hold at 14°C

Primers for *fabH*

Forward primer:

5'-CCT ACC TCT GAC TTG AGT-3'

- Melting temperature: 50.1°C
- GC content: 50%
- MW: 5425.6 g/mol

Reverse primer:

5'-GAC ATC ATT ACC GAT TGG AG-3'

- Melting temperature: 50.5°C
- GC content: 45%
- MW: 6141.0 g/mol

PCR sample preparation

12.5 μ L ExTaq

2 μ L forward primer

2 μ L reverse primer

2 μ L template DNA

6.5 μ L diH₂O

Electrophoresis conditions. Gels containing 1% agarose in TAE were prepared depending on the size of the gel tank. Enough TAE buffer was added to completely cover the gel, and 5 - 10 μ L of 10 μ g/mL ethidium bromide was added to the solution. Each well was loaded with the total PCR product, and the gel was run at 110 V and 400 mA for 40 minutes. The gel was placed under ultraviolet light and photographed using the GelDoc-It System to visualize the DNA.

Gel extraction. The QIAquick gel extraction kit (Qiagen, California) was used to extract DNA from the agarose gel. Briefly, the gel was placed on a UV transilluminator and a clean scalpel was used to excise the DNA bands. The gel was placed in a microcentrifuge tube and 1 mL of Buffer QG was added. The tube was placed in a 50°C water bath and occasionally vortexed until the gel was completely dissolved. An equal volume of isopropanol was added to the solution. The solution was transferred to a QIAquick spin column in a 2 mL collection tube and spun for 1 minute. The flow through was discarded and 5 μ L Buffer QG was added, and the sample was again spun for 1 minute. The flow through was discarded, and 750 μ L Buffer PE was added to the

column, allowed to stand for 3 minutes, then spun for 1 minute. The flow through was discarded and the column was spun for 2 minutes, then the spin column was transferred to a clean 1.5 mL Eppendorf tube. 50 μ L diH₂O was added to the column, allowed to stand for 1 minute, and spun for 1 minute. Eluted DNA was stored at 4°C until needed.

Gene sequencing. PCR products extracted from gels were sent to Eurofins MWG Operon (Huntsville, Alabama) for sequencing. Samples containing 2 μ L of the appropriate primer, 8 μ L diH₂O, and 10 μ L of the DNA sample were combined in 1.5 mL Eppendorf tubes. A set for both the forward and reverse primers were each prepared in separate Eppendorf tubes. The tubes were double-sealed in parafilm, wrapped in bubble wrap, and shipped overnight via FedEx.

Sequence analysis. Sequence massager was used to obtain the complement of reverse primer sequences. Clustal W2 (European Bioinformatics Institutue, EMBL-EBI) was used to align the forward and reverse primer sequences, resulting in the whole sequenced gene. The same program was used to compare the parent and mutant sequences to determine the presence of any mutations at the genetic level.

Proteomic analysis

Solutions. All solutions used for proteomic analysis were made according to the following formulas:

Dissolution buffer

Triethylammonium bicarbonate 500 mM

Sodium dodecyl sulfate, ultrapure 0.1%

Bring up to volume in HPLC-grade diH₂O and store at 4°C in the dark.

Cytoplasmic protein extraction. A synchronized culture was used to inoculate a 1 L Erlenmeyer flask containing 400 mL TSB to ~OD_{600 nm} 0.05. The flask was incubated until the culture reached the phase of interest. The entire culture was spun down at full speed for 10 minutes. The pellet was resuspended in PBS, transferred to a 50 mL Falcon tube, and washed in PBS three times. The pellet was resuspended in 1 mL dissolution buffer, and 500 µL aliquots were transferred to screw-cap tubes, and 0.01mm glass beads were added. The tubes were subjected to vigorous bead beating using a MiniBeadbeater-16 (Biospec Products) for four 1 minute intervals. The tubes were spun at full speed in a tabletop microcentrifuge for 10 minutes, and the supernatants were combined in an Eppendorf tube. The tubes were spun again, and the supernatant was transferred to another Eppendorf tube. Extracted proteins were stored at -80°C until needed.

Concentrating proteins. The required concentration for iTRAQ analysis was 5 – 100 µg per 20 µL. Millipore concentration tubes were used to concentrate extracted proteins to the desired concentration as needed, following the manufacturer's recommendations. Protein samples were centrifuged for 30 minutes at 13,300 x g for concentration and recovered by centrifuging for 2 minutes at 2000 x g.

Protein precipitation. Concentrated proteins were precipitated by suspending overnight in a 1:10 volume of 100% trichloroacetic acid at 4°C. The resulting pellet was washed twice with ice cold 100% ethanol by centrifuging at 8500 x g for 70 minutes. The pellet was allowed to air dry then resuspended by sonication in 1 mL dissolution buffer. The samples were spun for 30 minutes at full speed, the supernatants discarded, and the pellets resuspended in 100 µL dissolution buffer. The Pierce assay was performed following manufacturer's recommendations to determine the final protein concentration.

Trypsin digest. The volume of protein sample needed to contain 100 µg of protein was calculated and aliquoted to a 1.5 mL Eppendorf tube, and 20 µL dissolution buffer and 1 µL denaturant was added. The tube was vortexed and 2 µL reducing agent was added, and the tube was vortexed again. The tube was incubated at 60°C for 1 hour and briefly centrifuged. 1 µL cysteine blocking reagent was added, vortexed to mix, and briefly centrifuged. The tube was incubated at room temperature for 10 minutes. Trypsin was provided with the iTRAQ kit and reconstituted with 25 µL MilliQ water. 10 µL was added to each protein sample, vortexed, and briefly centrifuged. The tube was incubated at 37°C for 16 hours then briefly centrifuged. The next step was begun immediately.

iTRAQ labeling. The iTRAQ reagents required for all the protein samples were allowed to reach room temperature before use, briefly centrifuged, and 70 µL ethanol was added to each tube. The reagents were vortexed, briefly centrifuged, and the contents of one vial was transferred to one protein sample. Samples were vortexed, briefly centrifuged,

and incubated at room temperature for 1 hour. All protein samples were combined into a single fresh 1.5 mL Eppendorf tube, vortexed, and briefly centrifuged.

Desalt. A MacroSpin column placed in a 2 mL Eppendorf tube was activated by adding 50 μ L acetonitrile and centrifuging at 110 \times g for 1 minute. The eluent was discarded and the column was dried with a Kim wipe. The column was equilibrated by adding 500 μ L 0.1% formic acid and centrifuged as previously. The eluent was discarded and the column was washed with 0.1% formic acid again. The labeled protein sample was added to the column and centrifuged as previously, and the eluent was discarded. The MacroSpin column was transferred to a new 2 mL Eppendorf tube, and the labeled protein sample was eluted by adding 250 μ L acetonitrile/water (90:10). The sample was spun as previously and the eluent was transferred to a 1.5 mL Eppendorf tube. Samples were dried in a speed vac for ~1 hour and resuspended in 0.1% formic acid to a final concentration of 1 μ g/ μ L. The desalted, labeled protein sample was sonicated for 10 – 15 minutes, or until completely solubilized, then stored at 4°C until needed.

Evaluation of proteins by mass spectrometry. The sonicated protein samples were transferred to cylindrical glass tubes and placed in the autosampler, which injects 5 μ L aliquots of the samples into the LTQ Orbitrap XL (ThermoFinnigan) for analysis. The program used to evaluate the labeled peptides called for two injections at 180 minutes each.

Analysis of iTRAQ data. Raw iTRAQ data was first run through Mascot. This allowed the identified fractions to be compared to a known database and compiled into a single file. The condensed files were processed by Scaffold Q+ and used to compare parent strains and mutants.

SDS-PAGE

Solutions. All solutions used for sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE) were made according to the following formulas:

SP buffer

| | |
|-------------------|-------|
| Raffinose | 30% |
| MgCl ₂ | 20 mM |

Laemmli sample buffer

| | |
|----------------------------|--------|
| diH ₂ O | 4.0 mL |
| 0.5M Tris, pH 6.8 | 1.0 mL |
| 100% glycerol | 0.8 mL |
| 10% sodium dodecyl sulfate | 1.6 mL |
| β-mercaptoethanol | 0.4 mL |
| Bromophenol blue | 0.05% |

Store at -20°C.

Coomassie blue staining solution

| | |
|----------------|-------|
| Methanol | 50% |
| Acetic acid | 10% |
| Coomassie blue | 0.25% |

Destain solution

| | |
|-------------|-----|
| Methanol | 10% |
| Acetic acid | 5% |

Separating gel

| | |
|-----------------------|---------|
| diH ₂ O | 3.35 mL |
| 1.5M Tris-HCl, pH 8.8 | 2.5 mL |
| 10% SDS | 100 µL |
| Acrylamide* | 4.0 mL |
| 10% APS | 50 µL |
| TEMED | 7 µL |

ProtoGel acrylamide was purchased from National Diagnostics. It consisted of 30% w/v acrylamide and 0.8% w/v *bis*-acrylamide.

Stacking gel

| | |
|-----------------------|---------|
| diH ₂ O | 3.05 mL |
| 0.5M Tris-HCl, pH 6.8 | 1.25 mL |
| 10% SDS | 50 µL |
| Acrylamide* | 650 µL |
| 10% APS | 25 µL |
| TEMED | 5 µL |

ProtoGel acrylamide was purchased from National Diagnostics. It consisted of 30% w/v acrylamide and 0.8% w/v *bis*-acrylamide.

10x Electrophoresis buffer

| | |
|-----------|-----------------------|
| Glycine | 144 gL ⁻¹ |
| Tris base | 30.3 gL ⁻¹ |
| SDS | 10 gL ⁻¹ |

Solution was diluted 1:10 in diH₂O before use.

Extraction of cell-wall associated proteins. The absorbance of overnight cultures were measured at OD_{600 nm}, and the volume calculated to result in an ~OD_{600nm} 50.0 in 100 mL was calculated. The calculated volume was aliquoted and spun down at full speed for 10 minutes. The supernatant was discarded, and the pellet was resuspended in 100 µL SP buffer. Twenty-five µL lysostaphin and 8µL protease inhibitor was added to the sample, and the suspension was incubated at 37°C for 20 minutes. Following incubation, the

samples were spun at full speed for 10 minutes, and the supernatants containing the proteins were collected in an Eppendorf tube to be stored at -20°C until needed for SDS-PAGE analysis. This protocol was also followed for cultures standardized to ~OD_{600 nm} 100.0 or 150.0. The addition of lysostaphin was increased accordingly. An aliquot of the protein sample was mixed with an equal volume of laemmli sample buffer and boiled for 5 minutes before loading on a gel.

Extraction of secreted proteins. Cultures grown overnight for 10 - 15 hours were standardized so that all cultures had the same arbitrary absorbance. Cultures were spun down at full speed for 10 minutes, and the supernatant containing the proteins was stored at -80°C until needed. Upon need, the samples were thawed on ice, and 1 mL was transferred to a locking-cap Eppendorf tube. 100 µL 100% trichloroacetic acid was added, and the samples were mixed by inversion and incubated on ice for 30 minutes. The samples were spun at full speed for 5 minutes and washed twice with 500 µL acetone. Each time, the pellet was broken with a pipette tip. Following the final wash, the pellet was air-dried before adding 30 µL laemmli sample buffer, then boiled for 10 minutes and cooled before loading on a gel.

Electrophoresis conditions. BioRad's Mini-Protean TETRAcell system was used to run up to four protein gels at a time. The length of time per run was increased proportionate to the number of gels being run, from ~40 minutes for one gel up to ~2 hours for four gels. The power source was set to 300 V and 30 mA.

RESULTS

Activity of Ns β L against a diverse array of laboratory and clinical strains of *S. aureus*. *S. aureus* is a clinically relevant human pathogen with a high level of clonal variation, resulting in a wide range of antimicrobial resistances. Accordingly, we screened a variety of different laboratory and clinical strains for susceptibility to Ns β L using a disk diffusion assay (**Fig. 2**). The zones of inhibition (ZOI) were found to be comparable for all strains tested, regardless of their origin or existing antimicrobial resistance. Ns β L was dissolved in dimethylsulfoxide (DMSO). DMSO was not found to have any effect on the growth of *S. aureus* in this assay (data not shown).

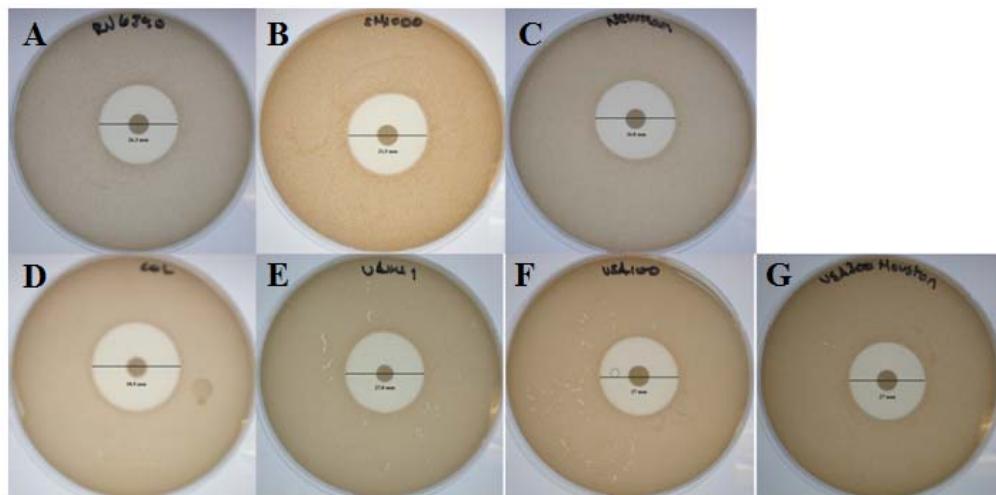


Figure 2. Disk diffusion assays using Ns β L with multiple laboratory and clinical strains of *S. aureus*. (A) RN6390; (B) SH1000; (C) Newman; (D) COL; (E) UAMS-1; (F) USA100; (G) USA 300 Houston.

In order to quantify the activity of Ns β L, the minimum inhibitory concentration (MIC) was determined for each of these strains using a 96-well plate microbroth dilution method, which allows for quick and efficient screening of multiple samples at a range of concentrations. The MIC is defined as the lowest drug concentration at which there is no visible growth, and was found to be between 0.4 μ g/mL and 1 μ g/mL for all strains tested (Fig. 3; Table 3).

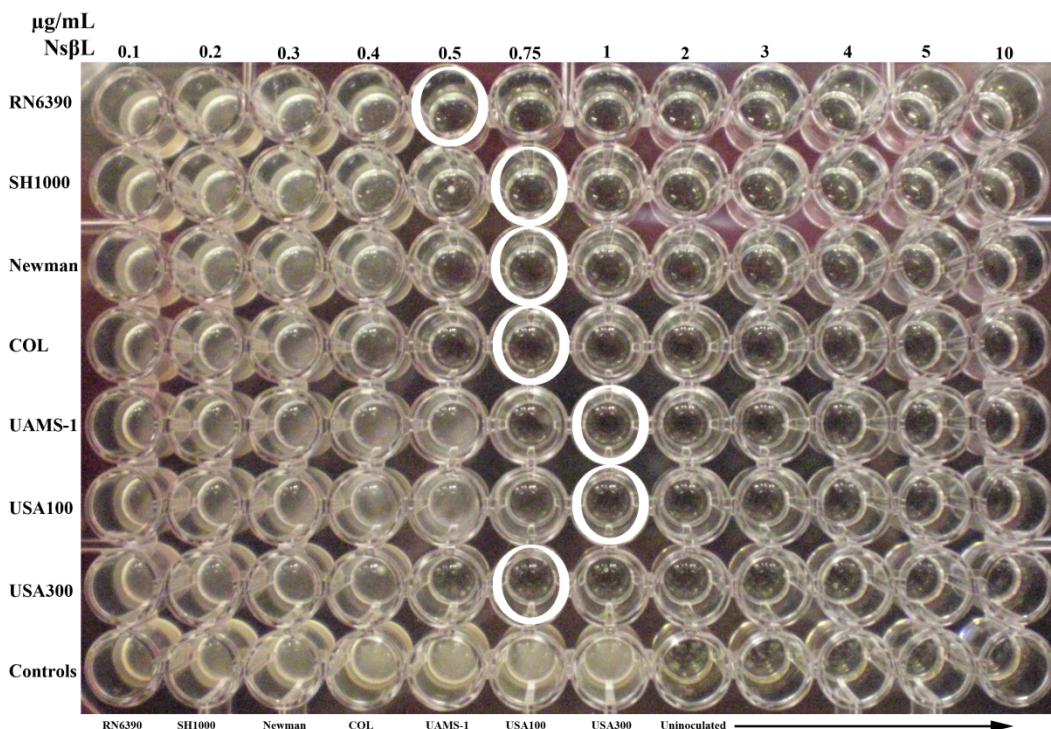


Figure 3. Microbroth dilution assay to determine MIC of Ns β L using a variety of *S. aureus* and clinical isolates. Circles indicate the lowest concentration with no visible turbidity; ie the MIC.

| Strain | MIC (μ g/mL) |
|-----------------|----------------------|
| RN6390 | 0.5 |
| SH1000 | 0.75 |
| Newman | 0.75 |
| COL | 0.75 |
| UAMS-1 | 1 |
| USA 100 635 | 1 |
| USA 300 Houston | 0.75 |

Table 3. Minimum inhibitory concentrations for laboratory and clinical *S. aureus* strains as determined using a microbroth dilution assay.

Investigation into the effects of fatty acids on the activity of Ns β L. As a result of these studies, the effect of fatty acids on the activity of Ns β L was first tested using a disk diffusion assay. There has been conflicting evidence concerning the effect of fatty acids on the growth of *S. aureus* and other Gram-positive pathogens in the presence of antimicrobials targeting fatty acid synthesis. Specifically, it has been suggested that the fatty acids can rescue growth, despite the presence of antimicrobial agents^{2, 6, 16, 17}. As previous work has indicated that Ns β L may target fatty acid synthesis⁹², 0.01% oleic acid (a long chain unsaturated fatty acid) or 0.1% Tween 80 (an oleic acid surrogate) was added to TSA to determine if there was a similar effect on Ns β L activity. As a control, Ns β L ZOIs were compared to those for vancomycin (a cell wall synthesis inhibitor). The assay was performed for *S. epidermidis* RP62A and the *S. aureus* strains SH1000, Newman, COL, USA 100 Mu50, USA 200 MRSA252, USA 300 Houston, and USA 400 MW2 (**Fig. 4**). For all strains tested, the Ns β L ZOIs were significantly and consistently reduced in the presence of Tween 80. For SH1000, COL, and USA 300 Houston, the vancomycin ZOIs were also reduced in the presence of Tween 80, but all other strains had consistent ZOIs.

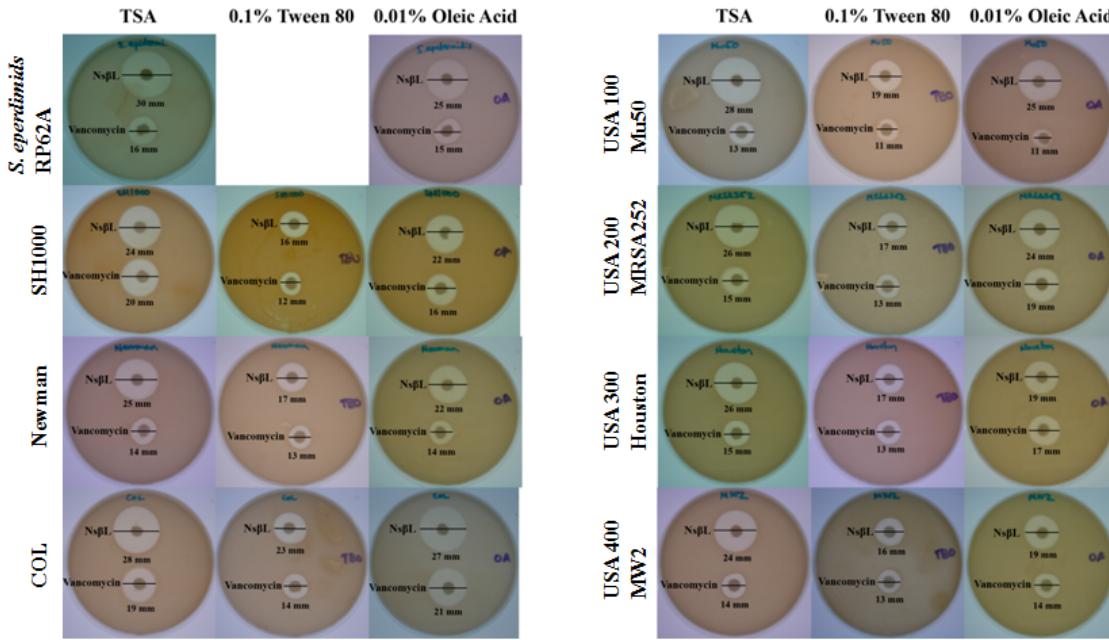


Figure 4. Disk diffusion assays comparing the effects of fatty acids on the activity of Ns β L and vancomycin against a variety of laboratory and clinical *S. aureus* isolates.

Quantification of the effects of fatty acids on antimicrobial activity was further evaluated by adding 0.1% Tween 80, 0.01% oleic acid, or 0.5% BSA to TSB and measuring the growth of *S. aureus* isolates in the presence of Ns β L, vancomycin, or triclosan (a commercially used fatty acid synthesis inhibitor). Both Tween 80 and oleic acid were dissolved in BSA, so this was included in the assay as a control. BSA, Tween 80, and oleic acid significantly reduced the MIC for vancomycin, indicating that these additives may work synergistically with vancomycin to inhibit cell wall synthesis. The MIC for triclosan was increased by Tween 80 20- to 50-fold for all strains tested; however, oleic acid did not have significant rescue activity for cultures treated with triclosan. The presence of Tween 80 allowed growth in the presence of Ns β L concentrations equal to the MIC, but not at the concentrations tested above the MIC. Cultures treated with BSA were also able to grow in the presence of Ns β L, but at a level significantly lower than the

untreated culture. These results were comparable for all strains tested, suggesting that the diverse isolates tested had similar responses to the presence of fatty acids (only USA 300 data shown: **Fig. 5**).

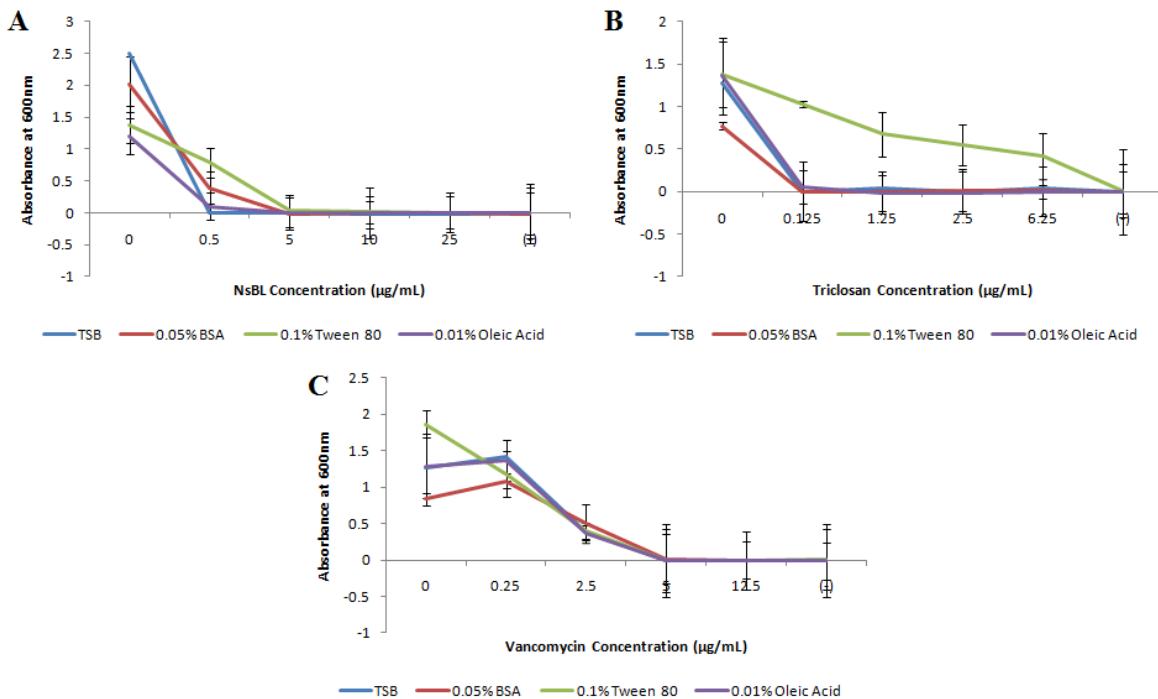


Figure 5. The effects of fatty acids on the antimicrobial activity of Ns β L towards *S. aureus* USA 300 Houston. (A) Ns β L; (B) Triclosan; (C) Vancomycin.

Comparison of the effects of Ns β L and other antibiotics on *S. aureus* biofilms. *S. aureus* biofilms are difficult to treat due to a lack of antimicrobial diffusion through the biofilm matrix and because not all of the cells are in an actively growing state⁶¹. The effects of Ns β L, triclosan, vancomycin, and tetracycline (a protein synthesis inhibitor) on UAMS-1 biofilms were analyzed using a 96-well plate method previously described by Beenken, et. al. UAMS-1 was chosen as it is a biofilm-forming strain that has previously been well characterized for this aggregate lifestyle¹¹. SH1000 was also used as a positive control, and 8325-4 as a negative control. Biofilms were allowed to establish for 24

hours before fresh media containing the relevant antimicrobial was added. Antimicrobial exposure lasted an additional 24 hours before the biofilms were stained with crystal violet for evaluation (**Fig. 6**).

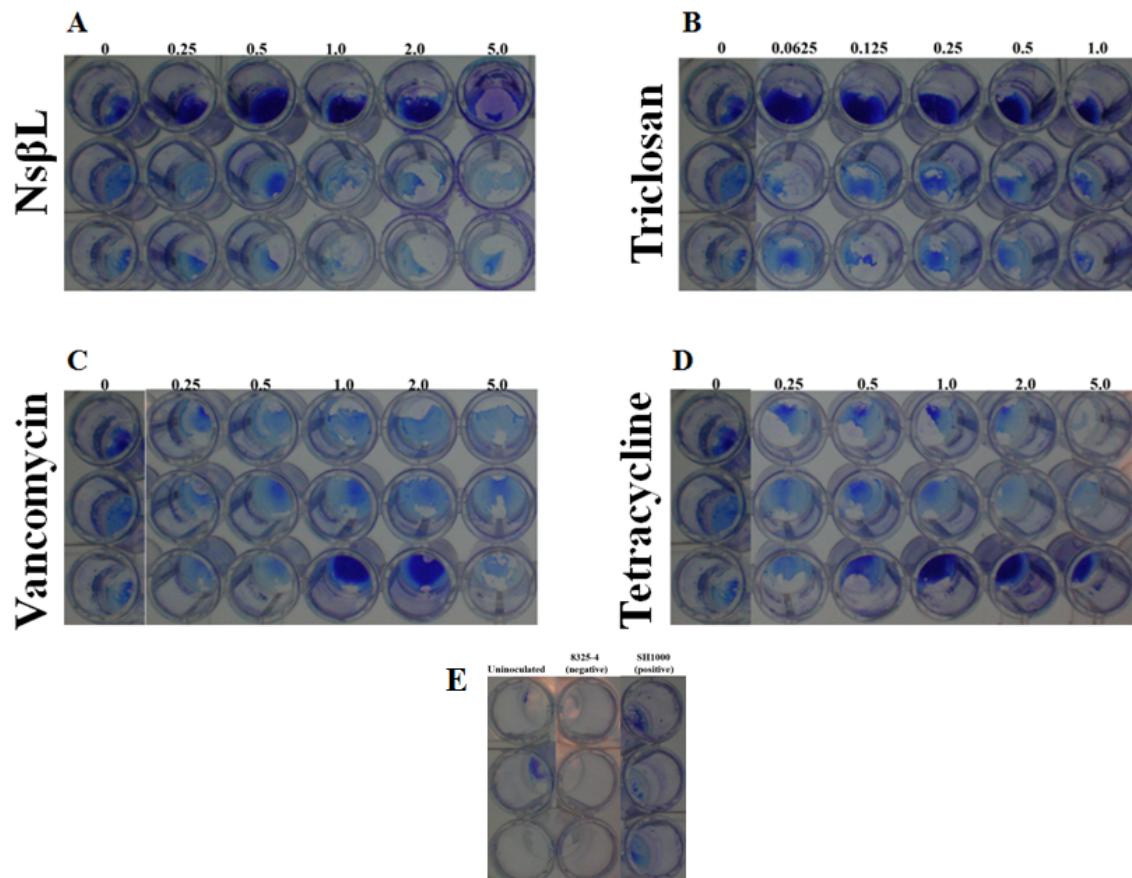


Figure 6. The effect of selected antimicrobials on *S. aureus* UAMS-1 biofilms.
Biofilms were exposed to the antimicrobials in the concentrations indicated (μ g/mL) for 24 hours before staining with crystal violet. (A) Ns β L; (B) Triclosan; (C) Vancomycin; (D) Tetracycline; (E) Untreated controls.

Quantitative analysis was performed by measuring the absorbance of eluted crystal violet at 595 nm in a BioTek Synergy2 96-well plate reader and the percent change from the untreated biofilms was calculated (**Fig. 7**). Tetracycline and Ns β L had the greatest effect on biofilm formation, reducing the absorbance at 595 nm by approximately 30% and 40%, respectively. Triclosan had only a slight effect on biofilms, reducing their

formation by 13 – 21%. Biofilms were unaffected by treatment with vancomycin, and had levels of formation comparable to or exceeding the untreated UAMS-1 control.

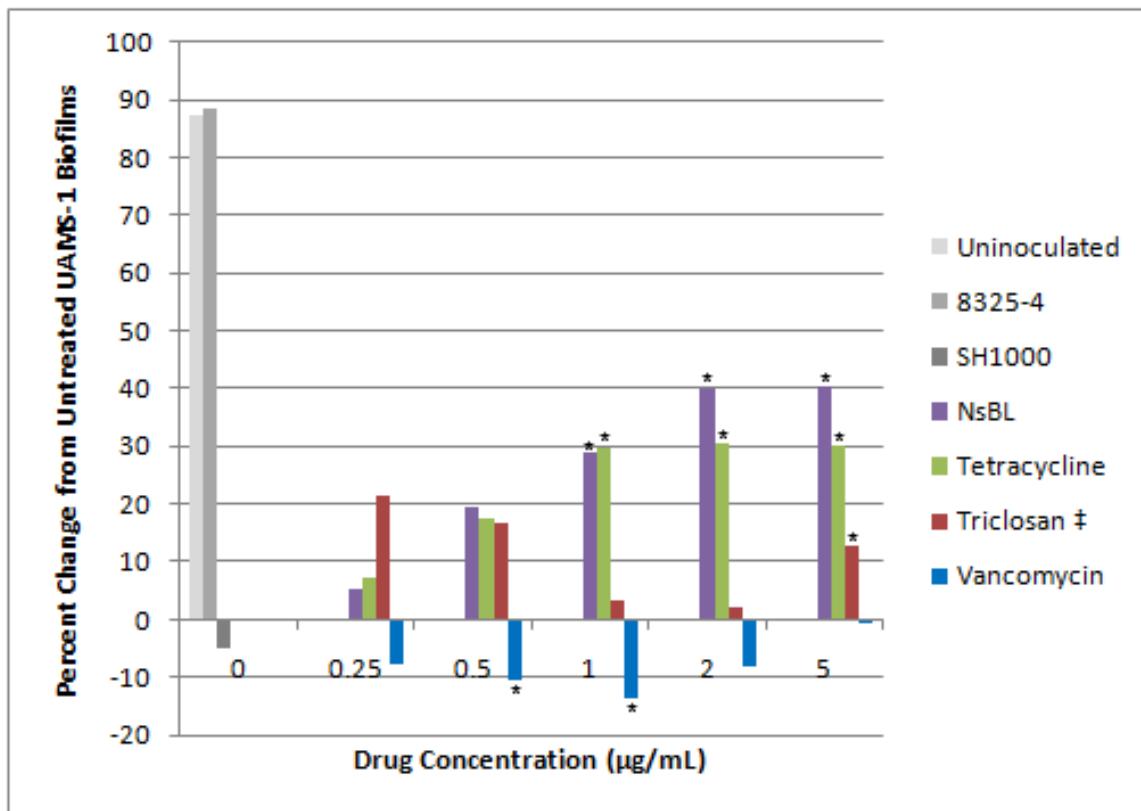


Figure 7. Quantitative analysis and comparison of antimicrobial-treated biofilms. Biofilms were stained with crystal violet as described and the absorbance of a 1:100 dilution was measured with a BioTek Synergy2 plate reader at 590 nm. The percent change as compared to the untreated UAMS-1 biofilms was calculated. * p < 0.1 using the Student's t-test comparing the antimicrobial-treated biofilms to the untreated UAMS-1 biofilms. ‡Triclosan concentrations were 0, 0.0625, 0.125, 0.25, 0.5, and 1 $\mu\text{g/mL}$.

Analysis of spontaneous mutation frequencies for Ns β L. Spontaneous mutation leading to resistance is a problem with all clinically available antimicrobials. Knowing the rate of mutation is vital in order to determine the minimum dosage required to prevent resistance. In addition, it gives a sense of the suitability of a given compound for use in treating infections. As such, TSA was supplemented with seven times the Ns β L MIC and inoculate with 3×10^9 SH1000 cells in order to determine the spontaneous mutation

frequency, calculated as the number of resistant colonies per cells screened. Four replicates were performed for this assay (**Fig. 8**), yielding a total of 98 colonies from a total inoculum of 1.38×10^{10} cells yielded a spontaneous mutation rate of 7.1×10^{-9} . The Ns β L MICs of all colonies obtained were determined by the microbroth dilution method as described, and found to be 1.5-fold to 67-fold greater than the parent strain. A total of 26 of the isolated spontaneous mutants had MICs less than 5 $\mu\text{g}/\text{mL}$. When this is taken into account, the spontaneous mutation rate becomes 5.2×10^{-9} . Two isolates, SH-11 and SH-32, were chosen to use for further experimentation because they had the highest MICs (**Table 4**).



Figure 8. Spontaneous mutagenesis of *S. aureus* SH1000 using 7X MIC of Ns β L. TSA supplemented with Ns β L was inoculated with 1×10^9 SH1000 cells and incubated at 37°C for 30 hours. Plates yielded between 11 and 49 colonies. A representative example is shown.

| Isolate | MIC $\mu\text{g}/\text{mL}$ | Isolate | MIC $\mu\text{g}/\text{mL}$ |
|---------|--------------------------------|---------|--------------------------------|
| SH-11 | 50 | SH-60 | 20 |
| SH-15 | X | SH-62 | 20 |
| SH-22 | 30 | SH-64 | 20 |
| SH-32 | 30 | SH-69 | 10 |
| SH-38 | 10 | SH-74 | 10 |
| SH-56 | 20 | SH-75 | 20 |
| SH-58 | 10 | SH-77 | X |
| SH-59 | X | SH-85 | X |

Table 4. MICs for spontaneous Ns β L SH1000 mutants. These values were determined using the microbroth dilution method, and are shown for randomly selected isolates. Ns β L concentrations tested were 0, 10, 20, 30, 40, and 50 $\mu\text{g}/\text{mL}$. X indicates no visible growth at all Ns β L concentrations. The isolates used for further experimentation in this study are highlighted.

Analysis of the effect of Ns β L on a nitrosoguanidine mutant library of *S. aureus*. We set out to determine if prior DNA mutagenesis would affect the spontaneous mutation rate of *S. aureus* to Ns β L. As such, SH1000 was treated with nitrosoguanidine (NTG), a

DNA alkylating agent, and the spontaneous mutation frequency was determined as previously described (**Fig. 9; Table 5**). Twelve colonies were isolated from the 4×10^8 NTG-treated cells plated, yielding a spontaneous mutation rate of 3×10^{-9} . However, four of the twelve NTG-treated Ns β L-resistant isolates had MICs equal to 1 $\mu\text{g/mL}$, significantly lower than the concentration used to generate them, and changes the spontaneous mutation rate to 2×10^{-8} , which is 3.85 times greater than the spontaneous mutation rate of the untreated cells.



Figure 9. Spontaneous mutagenesis of an NTG-treated SH1000 mutant library An inoculum of 4×10^8 cells yielded 12 colonies on a 5 $\mu\text{g/mL}$ Ns β L plate.

| Isolate | MIC $\mu\text{g/mL}$ | Isolate | MIC $\mu\text{g/mL}$ |
|---------|-------------------------|---------|-------------------------|
| NTG-A | 10 | NTG-G | 1 |
| NTG-B | 1 | NTG-H | 10 |
| NTG-C | 10 | NTG-I | 10 |
| NTG-D | 10 | NTG-J | 1 |
| NTG-E | 10 | NTG-K | 10 |
| NTG-F | 1 | NTG-L | 10 |

Table 5. MICs for the spontaneous NTG-treated SH1000 mutants. The MICs for library mutants were determined using the microbroth dilution method. Ns β L concentrations tested were 0, 1, 10, 15, and 20 $\mu\text{g/mL}$.

The adaptation of *S. aureus* to prolonged growth in the presence of Ns β L. In contrast to the spontaneous mutant analysis, we also set out to determine the effect of prolonged Ns β L exposure on *S. aureus* cells. Therefore, *S. aureus* strains USA 100 and USA 300 were subjected to increasingly higher concentrations of Ns β L in order to obtain highly resistant adaptive mutants. Overnight exposure began at 0.125 $\mu\text{g/mL}$ in 2 mL brain-heart infusion (BHI) broth. A 4 μL aliquot of the culture was transferred to a fresh tube

containing 2 mL BHI with double the Ns β L concentration and exposed for 24 hours. This process was repeated, making a glycerol stock of the exposed cells as previously described, and transferring a 4 μ L aliquot to fresh BHI with double the Ns β L concentration each day until no growth was obtained at 64 μ g/mL. The MICs were confirmed by the microbroth dilution method as previously described (**Table 6**).

| Strain | MIC (μ g/mL) |
|-------------------|----------------------|
| USA 100 WT | 0.75 |
| USA 100 AM | 65 |
| USA 300 WT | 0.75 |
| USA 300 AM | 55 |

Table 6. MICs of adaptive mutants (AM) and their wild-type (WT) parents.

Phenotypic characterization of the Ns β L-resistant mutants. Previous studies on the mode of action of Ns β L have indicated that this drug may target FabH, an essential component of fatty acid biosynthesis. The study also speculated that Ns β L may have an effect on coenzyme-A (CoA), which is a cofactor for a number of fatty acid synthesis, pyruvate metabolism, and the citric acid cycle (TCA) enzymes⁹². Thus far, the mode of action of Ns β L has not been fully characterized. In an effort to extrapolate the mechanism of activity of Ns β L, two of the SH1000 spontaneously generated mutants, SH-11 and SH-32, and the adaptive mutants of USA 100 and USA 300 were evaluated for phenotypic changes from their parental strains.

Growth analysis of the Ns β L-resistant mutants. Standard growth curves were performed in TSB and chemically-defined media (CDM) in order to determine if there were changes in growth of the various mutant strains (**Fig. 10**). No changes were observed for the SH-11 or SH-32 spontaneous mutants or for the USA 100 adaptive

mutant in TSB. However, the USA 300 adaptive mutant showed decreased levels of growth in TSB in comparison to its parent. In CDM, the SH-11 spontaneous mutant showed decreased growth during lag phase in comparison to both SH1000 and the SH-32 spontaneous mutant. The USA 100 adaptive mutant had increased growth levels during lag and early-exponential phase, but decreased growth during stationary phase. The USA 300 adaptive mutant had increased growth during all phases tested.

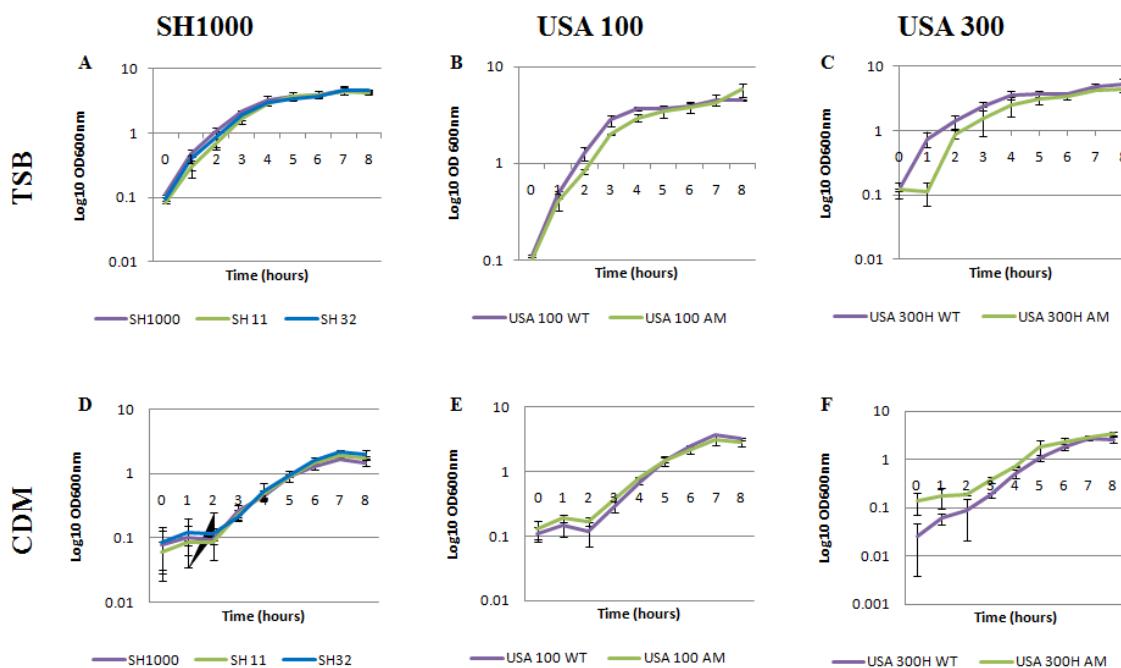


Figure 10. Growth curve analysis of the NsBL-resistant mutants in both TSB (top) and CDM (bottom). (A, D) SH1000 and its spontaneous mutants; (B, E) USA 100 and its adaptive mutants; (C, F) USA 300 Houston and its adaptive mutants. All assays were performed in triplicate.

Nutrient limiting derivatives of CDM were also used to determine if there were defects in response to nutrient starvation in the spontaneous and adaptive mutants. For amino acid-limiting CDM, no significant differences were seen for either spontaneous mutant. The USA 100 adaptive mutant showed increased growth levels in early-exponential phase, but

decreased growth in late-exponential and stationary phase. The USA 300 adaptive mutant showed decreased growth only during exponential phase (**Fig. 11**).

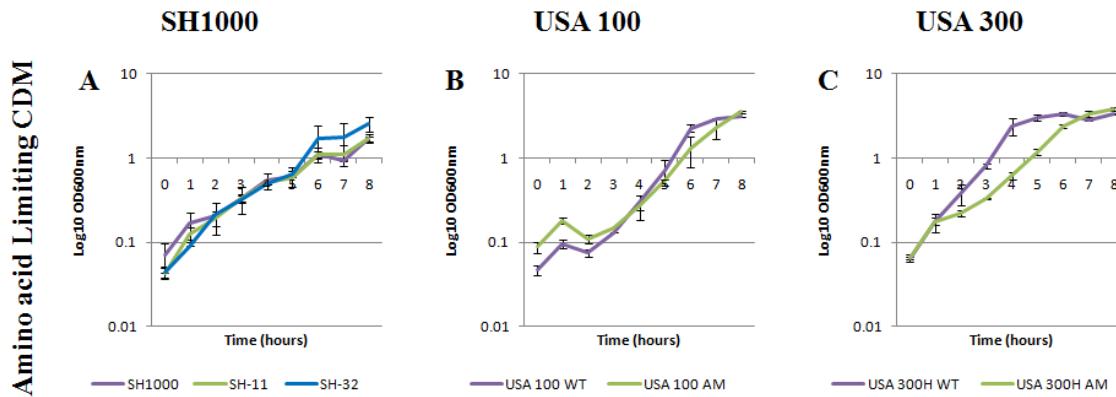


Figure 11. Amino acid-limiting growth curves of the Ns β L-resistant mutant strains.
 (A) SH1000 and its spontaneous mutants; (B) USA 100 and its adaptive mutants; (C) USA 300 Houston and its adaptive mutants. All assays were performed in triplicate.

There were no significant differences for any of the mutants when glucose was the limiting factor (data not shown).

Likewise, there were no differences for the spontaneous mutants or the USA 100 adaptive mutant when phosphate was limited. However, the USA 300 adaptive mutant showed increased growth during late lag and early-exponential phase, and decreased growth during late-exponential and stationary phase (**Fig. 12**).

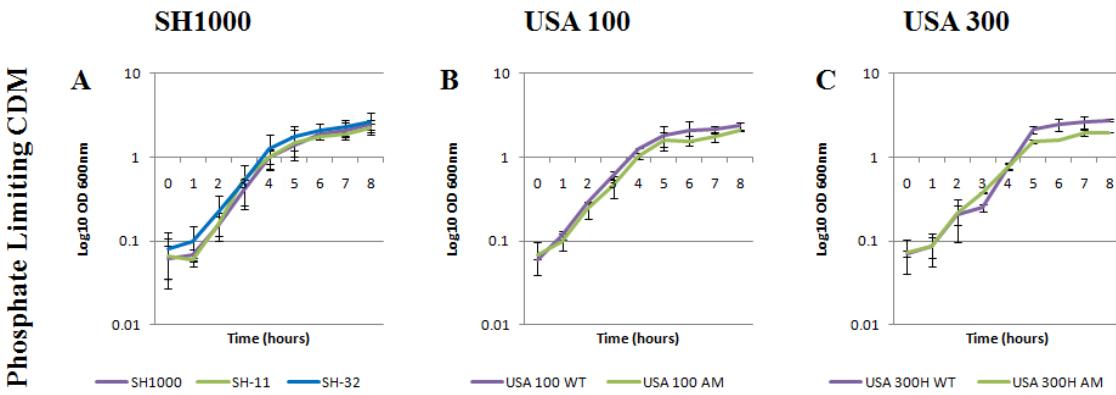


Figure 12. Phosphate-limiting growth curves of the Ns β L-resistant mutant strains.
 (A) SH1000 and its spontaneous mutants; (B) USA 100 and its adaptive mutants; (C) USA 300 Houston and its adaptive mutants. All assays were performed in triplicate.

Metal ion-limiting media was also used to analyze growth over a 36 hour period, although the first 12 hours were not assayed as *S. aureus* has a prolonged lag phase during growth under these conditions. Both spontaneous mutants had decreased levels of growth during exponential phase, with SH-32 growth more significantly reduced than SH-11. There was no change for the USA 100 adaptive mutant, while the USA 300 adaptive mutant had higher growth levels during exponential phase than its parent strain (**Fig. 13**).

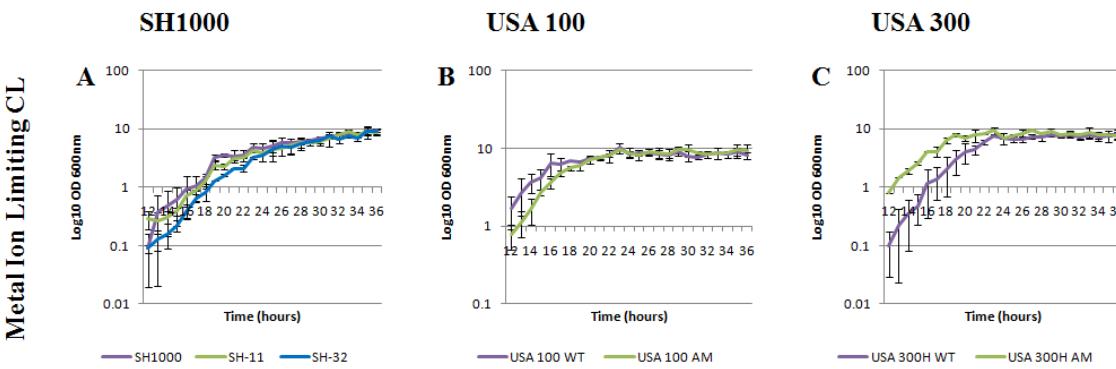


Figure 13. Metal ion-limiting growth curves for the Ns β L-resistant mutant strains.
 (A) SH1000 and its spontaneous mutants; (B) USA 100 and its adaptive mutants; (C) USA 300 Houston and its adaptive mutants. All assays were performed in triplicate.

Assessment of the proteolytic activity of the Ns β L-resistant mutant strains. *S. aureus* expresses multiple extracellular proteases as part of its virulence determinant network. To assess this activity in the Ns β L-resistant mutants, these strains were incubated both aerobically and anaerobically (Fig. 14) on plates containing 2% skim milk. SH1000 naturally has very low levels of proteolytic activity, which did not change with its Ns β L-resistant mutants (data not shown). Both the USA 100 and USA 300 adaptive mutants displayed reduced aerobic proteolytic activity compared to their parental strains. Only USA 300 retained proteolytic activity when grown in an anaerobic chamber, which was not displayed by its adaptive mutant.

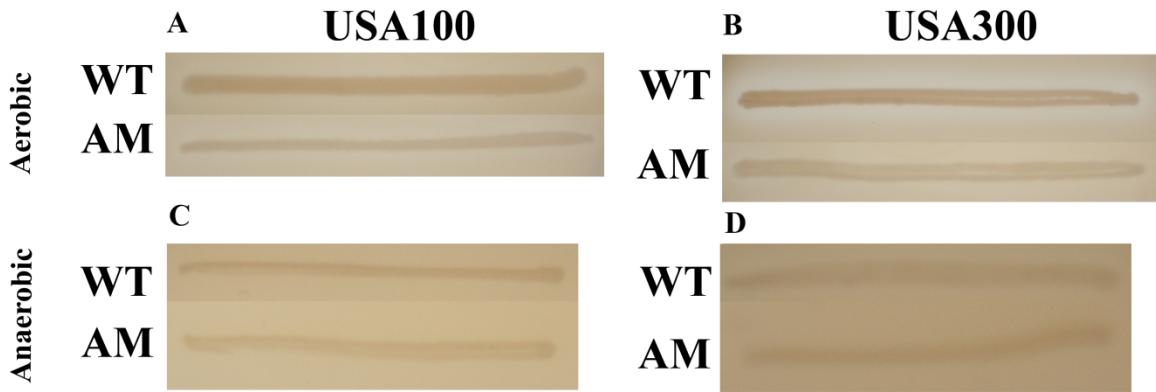


Figure 14. Changes in proteolytic activity of the Ns β L-resistant mutants under aerobic (top) and anaerobic (bottom) conditions. TSA containing 2% skim milk was inoculated with the parent strains and their respective mutants. A representative example of three experiments is shown. (A, C) USA 100 WT and its adaptive mutant; (B, D) USA 300 WT and its adaptive mutant.

Investigation of changes in the hemolytic activity of the Ns β L-resistant mutant strains. One of the major contributions to *S. aureus* disease comes from its hemolytic activity. To assay these toxins, sheep blood agar was used to compare the hemolytic activity of the parental strains with their respective mutants (Fig. 15). The SH1000 spontaneous mutants did not show any apparent change in hemolysis in comparison with the parent (data not shown), while the USA 100 adaptive mutant had reduced activity. Of

significant interest, the USA 300 adaptive mutant lost all hemolytic activity when assayed using blood agar.

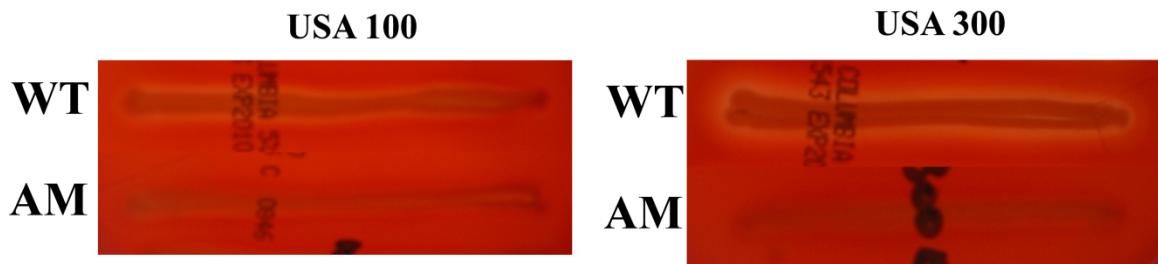


Figure 15. Alterations in hemolysis of the Ns β L-resistant mutant strains. Wild-types and their mutants were streaked in triplicate on 5% blood agar. A representative example of three experiments is shown. (A) USA 100 and its adaptive mutant; (B) USA 300 and its adaptive mutant.

Alterations in capsule production by the Ns β L-resistant mutants. *S. aureus* has the ability to produce a capsule composed of polysaccharides which aids in defense from phagocytosis, the host's primary defense against bacterial infection. To assay alterations in the production of capsule by the Ns β L-resistant mutants, congo red agar (CRA) was inoculated with the wild-types and respective mutant strains (Fig. 16). SH1000 and its spontaneous mutants displayed colony morphologies indicative of strong capsule production, i.e. rough, dry, black colonies (data not shown). Conversely, while both the USA 100 and USA 300 wild-types displayed capsule production, their adaptive mutants lost the characteristic black pigmentation altogether, indicating that they were not producing capsules.

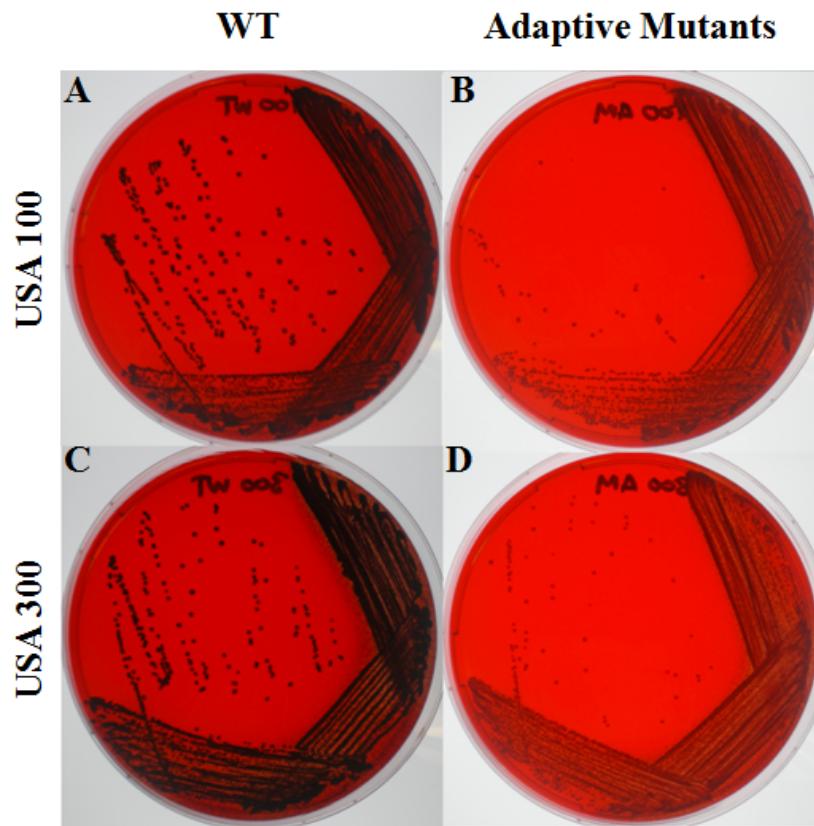
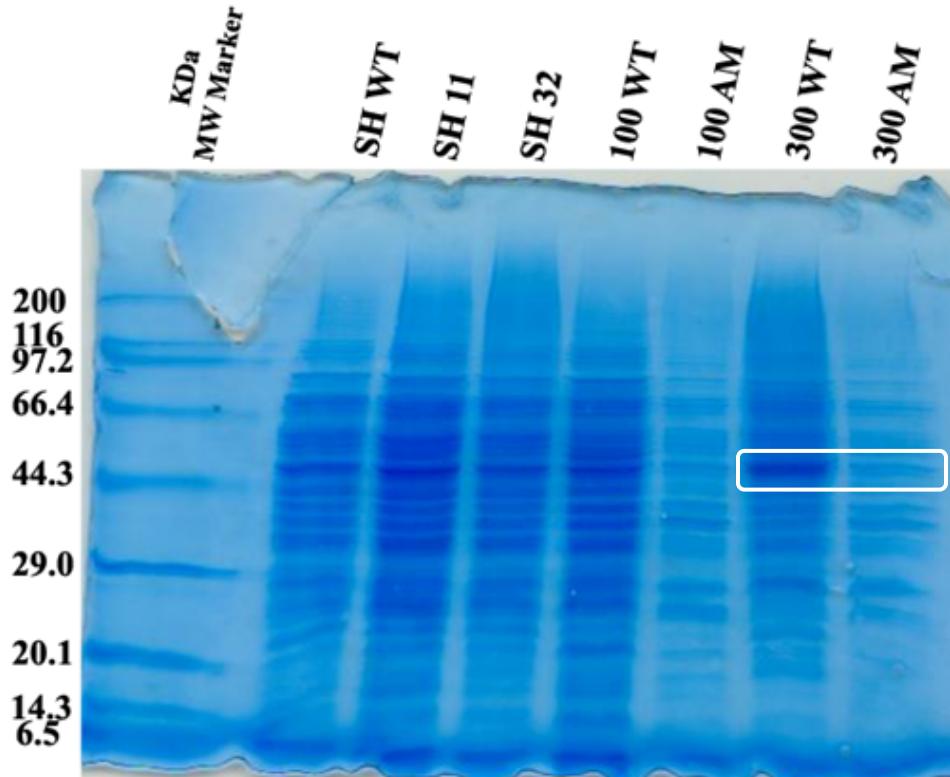


Figure 16. Alterations in capsule production by the Ns β L-resistant mutant strains. CRA was inoculated with each strain and examined for colony morphology and capsule production. (A) USA 100 wild type; (B) USA 100 adaptive mutant; (C) USA 300 wild type; (D) USA 300 adaptive mutant.

The effects of resistance to Ns β L on virulence determinant production and secretion. *S. aureus* produces a wide variety of toxins and other secreted proteins associated with virulence. In addition, MSCRAMMS and other cell-wall associated proteins are involved in invasion of the host and attachment to various surfaces. Sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE) was used to compare the production of cell-wall associated and secreted proteins produced by the parent and mutant strains. SDS-PAGE of the cell-wall associated proteins (Fig. 17) shows that SH-11 appears to produce slightly increased levels of these proteins than either the wild-type or SH-32. Both the USA 100 and USA 300 adaptive mutants produced significantly less

cell-wall associated proteins than their respective parental strains. Particularly notable is a ~45 kDa protein produced by USA 300 wild-type which is significantly diminished in its adaptive mutant.

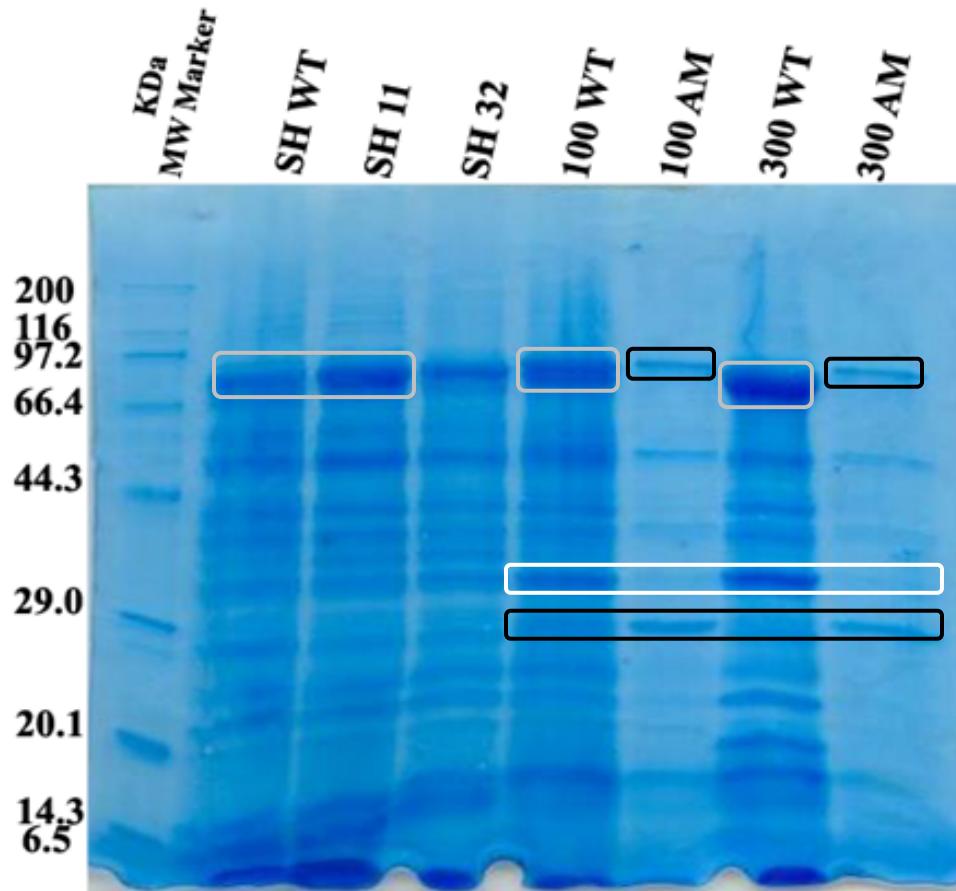


Cell-wall associated proteins

Figure 17. SDS-PAGE of cell-wall associated virulence determinants for wild-types and their Ns β L-resistant mutants. The gel shown here is representative of four experiments. The cell-wall associated proteins were extracted from a culture standardized to $OD_{600\text{nm}} = 50.0$. The white box indicates the ~45 kDa protein expressed in the USA 300 WT but not in the adaptive mutant.

SDS-PAGE of secreted proteins (Fig. 18) showed similar patterns of expression, with protein levels secreted by SH-11 slightly increased as compared to the wild-type. The increase in expression of an ~80 kDa protein was particularly apparent. The proteins secreted by both adaptive mutant strains were significantly decreased compared to their parental strains, particularly an ~80 kDa protein that was also seen over-expressed in SH-11, a ~50 kDa protein, and a ~35 kDa protein. Interestingly, the levels of two proteins

secreted by both adaptive mutant strains appeared to be less reduced than the rest, seen at ~95 kDa and ~28 kDa.



Secreted proteins

Figure 18. SDS-PAGE of secreted virulence determinants for wild-types and their Ns β L-resistant mutants. The gel shown here is representative of four experiments. The secreted proteins were extracted from a culture standardized to the same absorbance at 600nm. The gray boxes indicates the ~80 kDa protein band, the white box indicates the ~35 kDa protein band, and the black boxes indicate the ~28 kDa and ~95 kDa protein bands.

Evaluation of electron transport in the Ns β L-resistant mutants. Growth of *S. aureus* in anoxic environments requires the presence of nitrogen, which serves as a terminal electron acceptor. To assess the phenotype of the Ns β L-resistant mutants with regards to electron transport, media containing either nitrate or nitrite was inoculated with the wild-

type strains and their respective Ns β L-resistant mutants. These plates were incubated in a GasPak chamber to ensure an anaerobic environment. No significant alterations in growth were observed for any of the mutant strains tested (data not shown).

Alterations in the ability of the Ns β L-resistant mutants to ferment alternative carbon sources. Following from this, we examined the ability of the Ns β L-resistant strains to ferment a variety of carbon sources when grown under anaerobic conditions. Interestingly, *S. aureus* has the ability to use a variety of different sugars as its carbon source in the absence of glucose. As such, purple broth was used, which has a pH indicator that changes the media from purple to yellow when the media becomes acidified as the result of lactate or acetate production during fermentation. No changes in sugar fermentation were seen for dextrose, fructose, galactose, D-glucosamine, lactose, mannose, sucrose, trehalose, raffinose, or xylose. The spontaneous mutants SH-11 and SH-32 did not show any changes from their parent, while both the USA 100 and USA 300 adaptive mutants lost the ability to ferment ribose. Further to this, the USA 300 adaptive mutant was also unable to ferment maltose when compared to the parental strain (**Fig. 19**).

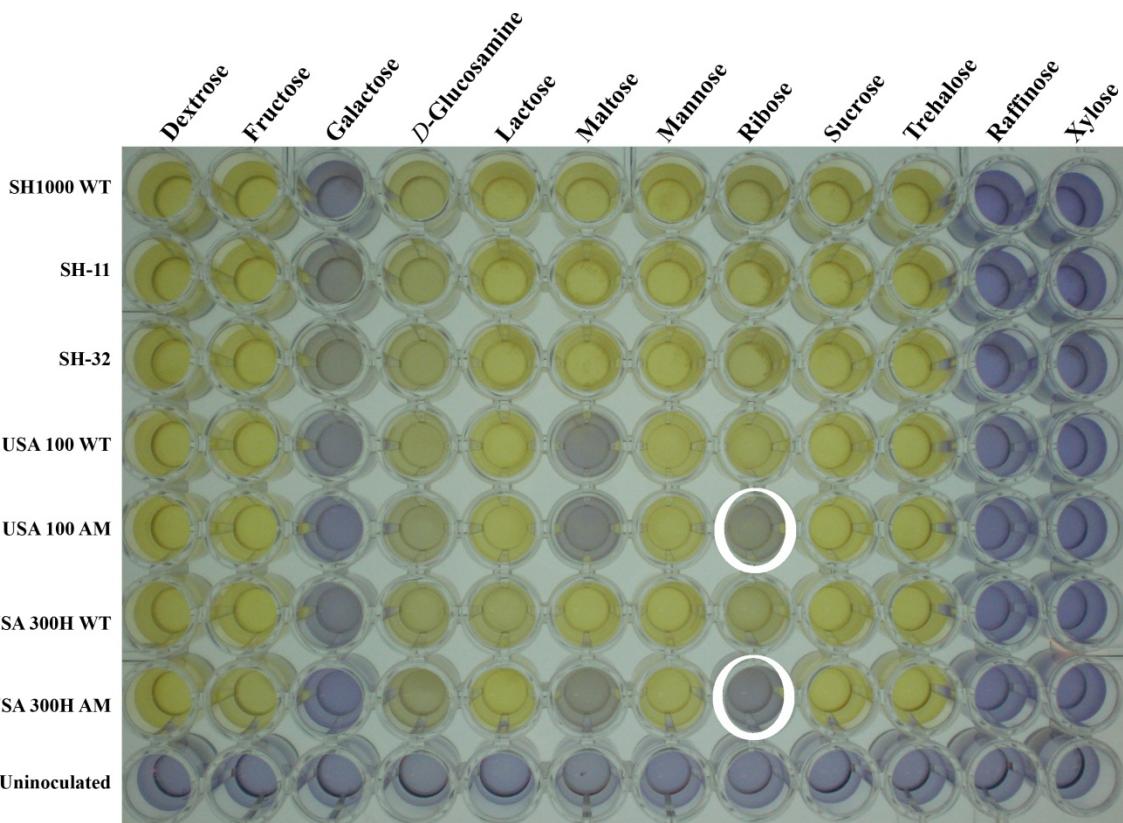


Figure 19. Microbroth dilution assay of alternative sugar fermentation by the Ns β L-resistant mutants. A 96-well plate containing purple broth supplemented with a variety of sugars (at 1%) was inoculated with parent and mutant strains and grown overnight to determine if there were any changes in the ability to ferment alternative carbon sources. The plate shown is representative of three experiments.

Alterations of the adaptive and stress resistant capacities of the Ns β L-resistant mutants. A chemical library containing diverse acids, bases, detergents, disulfides, alcohols, oxidative agents, and DNA damaging agents was used to test the spontaneous and adaptive mutants for changes in their stress resistance capabilities. This was assessed via disk diffusion assay, however, no compounds resulted in significant changes in the ZOI for any strains tested (data not shown).

Exploration of the effects of existing antibiotics on the Ns β L-resistant mutants. Disk diffusions were used to determine changes in ZOI between the parent strains and their resistant mutants for a range of antimicrobial compounds. The antimicrobials tested

included representatives of each major class, including inhibitors of DNA synthesis, RNA synthesis, protein synthesis, fatty acid synthesis, and cell wall synthesis. Only those antimicrobials that resulted in significant changes in the ZOI are shown. SH-11 and USA 100 did not show any significant changes in antimicrobial susceptibility (data not shown), while SH-32 was more resistant to mupirocin and penicillin G (**Fig. 20**; **Table 7**). Interestingly, SH-32 showed signs of heteroresistance to mupirocin, as indicated by the zone of reduced growth around the discrete ZOI.

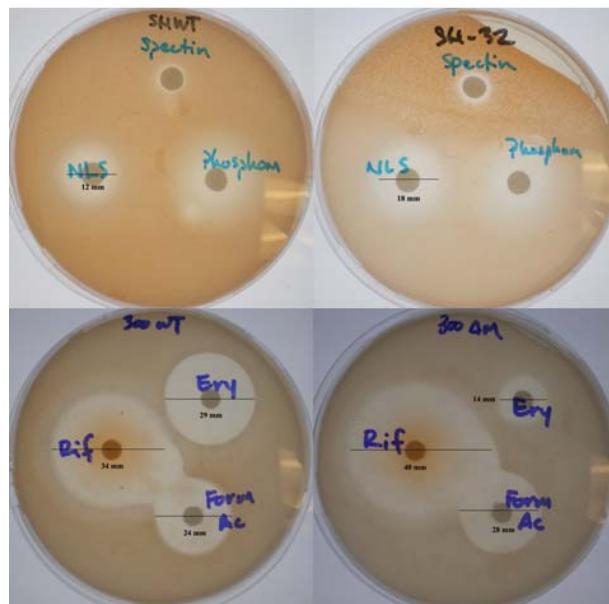


Figure 20. Disk diffusion assay of changes in antimicrobial susceptibility for the SH-32 spontaneous mutant. Mup = Mupirocin; PenG = Penicillin G; Linco = Lincomycin; Kan = Kanamycin

| Antimicrobial | Fold Change from WT |
|---------------|---------------------|
| Mupirocin | -1.77 |
| Penicillin G | -2.15 |

Table 7. Fold change for antimicrobial ZOIs of SH1000 and its SH-32 spontaneous *NsβL*-resistant mutant. Each assay was performed in triplicate.

The USA 300 adaptive mutant showed increased resistance to ampicillin, ciprofloxacin, kanamycin, and erythromycin (**Fig. 21**; **Table 8**).

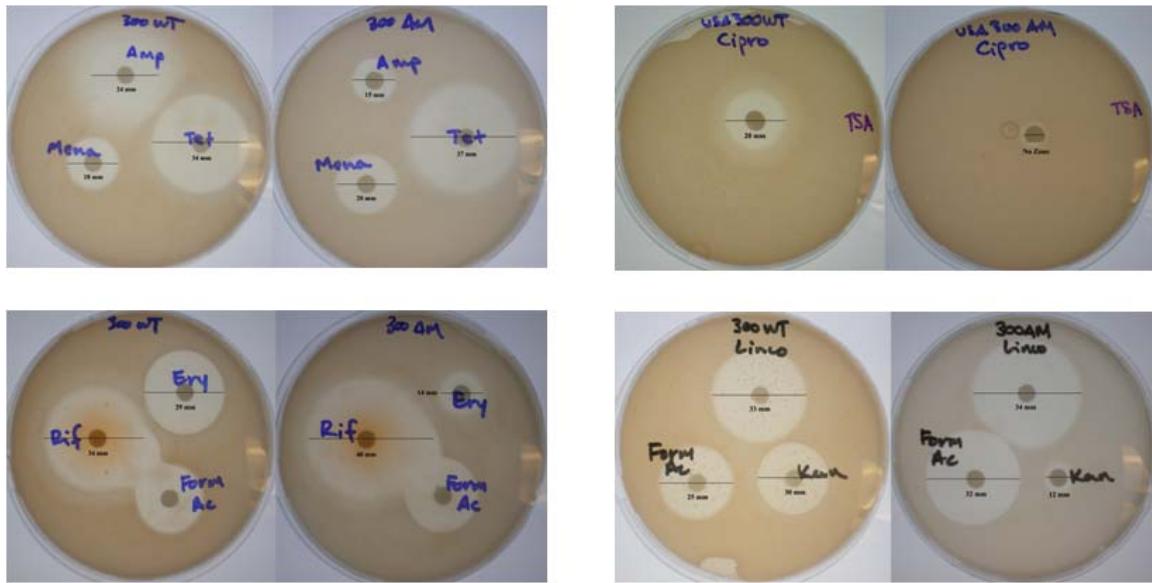


Figure 21. Disk diffusion assay of changes in antimicrobial susceptibility for the USA 300 adaptive mutant. Amp = Ampicillin; Cipro = Ciprofloxacin; Rif = Rifampicin; Ery = Erythromycin.

| Antimicrobial | Fold Change |
|---------------|--------------------|
| Ampicillin | -1.81 |
| Erythromycin | -1.91 |
| Kanamycin | -2.5 |
| Ciprofloxacin | Mutant had no zone |

Table 8. Fold change for antimicrobial ZOIs of USA 300 and its adaptive Ns β L-resistant mutant. Each assay was performed in triplicate.

Functional characterization of the stability of the cell envelope of the Ns β L-resistant mutants. The integrity of the bacterial cell envelopes for the Ns β L-resistant strains was investigated using penicillin-G and Triton X-100 lysis assays (Fig. 22). For both penicillin-G and Triton X-100, there was no apparent difference in lysis between SH1000 and its spontaneous mutants. There was also no difference in lysis when USA 100 and its adaptive mutant were treated with Triton X-100. However, the USA 100 adaptive mutant showed a reduced ability to survive prolonged exposure to penicillin-G, while the USA 300 adaptive mutant appeared to be significantly impaired at all timepoints. When

treated with Triton X-100, the USA 300 adaptive mutant showed increased lysis only towards the end of the assay.

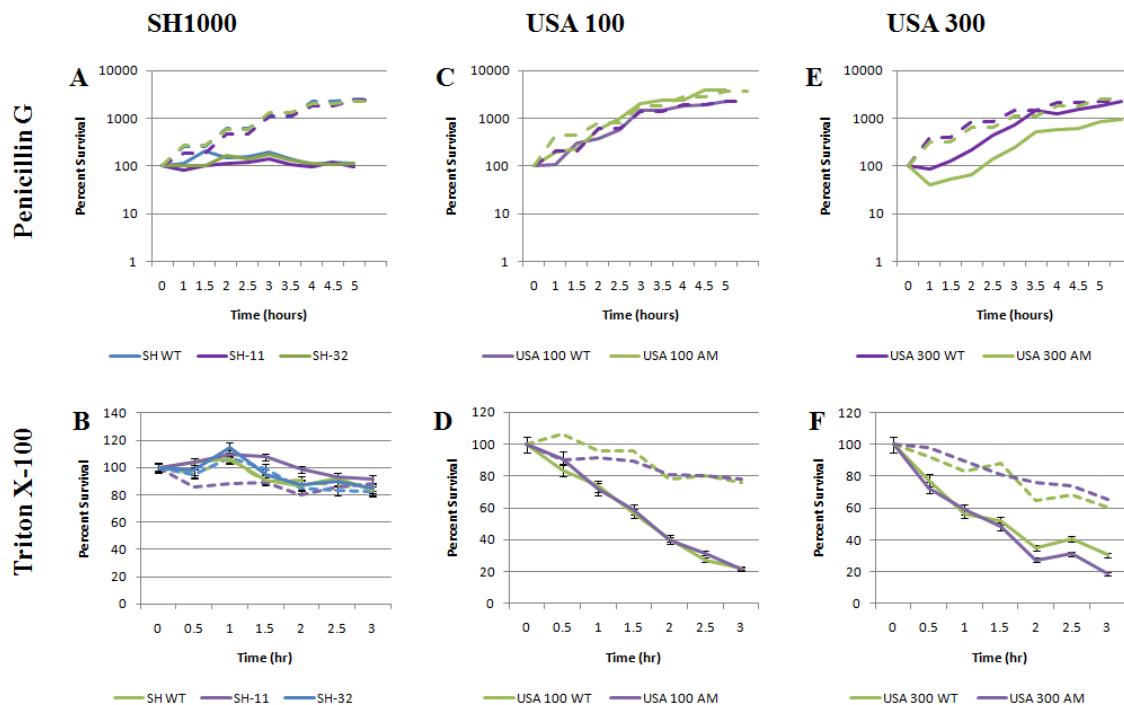


Figure 22. Assays of the stability of the cell envelope of the Ns β L-resistant mutants. Penicillin-G lysis (top) was performed over 5 hours in the presence of 0.4 μ g/mL penicillin G. Triton X-100 lysis (bottom) was performed over 3 hours in the presence of 0.5% Triton X-100. The graphs show the percent survival of each strain. All assays were performed in triplicate. The dashed lines are untreated controls. (A, B) SH1000 and its spontaneous mutants; (C, D) USA 100 and its adaptive mutant; (E, F) USA 300 Houston and its adaptive mutant.

Sequence analysis of *fabH* in the Ns β L-resistant mutants. Ns β L has previously been suggested to inhibit FabH activity⁹². One of the many ways *S. aureus* develops resistance to antibiotics is by spontaneously mutating the gene which encodes the target protein(s). Thus, genomic DNA was extracted from each of the mutant and wild-type strains and used to amplify PCR-amplify *fabH* (Fig. 23). Sequencing for each strain was attempted, but was unsuccessful, possibly due to problems at the external facility the samples were sent to, or compromised DNA samples (data not shown).

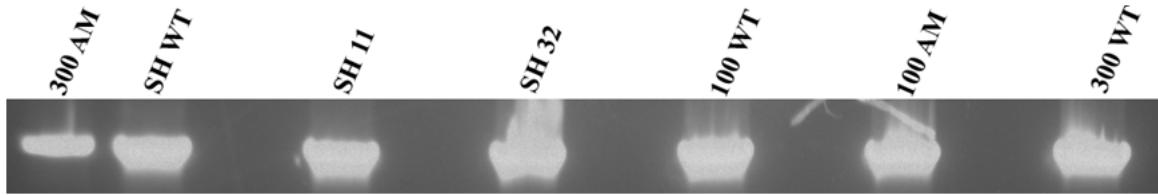


Figure 23. PCR of *fabH* genes from parental strains and their Ns β L-resistant mutants.

We were, however, able to obtain sequence data for the *fabH* gene from an additional USA 100 Ns β L-resistant mutant previously generated in our laboratory (Burda and Shaw, unpublished observation). The amino acid sequences were determined and compared, and no differences in the FabH sequences were found between the wild-type and resistant mutant (**Fig. 24**).

| | |
|----|---|
| WT | MNVGIKGFGAYAPEKIIDNAYFEQFLDTSDEWISKMTGIKERHWADDDQDTSDLAYEASV |
| SM | MNVGIKGFGAYAPEKIIDNAYFEQFLDTSDEWISKMTGIKERHWADDDQDTSDLAYEASV |
| WT | KAIADAGIQPEDIDMIIIVATATGDMFPPTVANMLQERLGTGKVASMDQLAACSGFMYSMI |
| SM | KAIADAGIQPEDIDMIIIVATATGDMFPPTVANMLQERLGTGKVASMDQLAACSGFMYSMI |
| WT | TAKQYVQSGDYHNILVVGADKLSKITDLTDRSTAVALFGDGAGAVIIGEVSEGRGIISYEM |
| SM | TAKQYVQSGDYHNILVVGADKLSKITDLTDRSTAVALFGDGAGAVIIGEVSEGRGIISYEM |
| WT | GSDGTGGKHLYLDKDTGKLKMNGREVFKFAVRIMGDASTRVEKANLTSDDIDLFIIPHQA |
| SM | GSDGTGGKHLYLDKDTGKLKMNGREVFKFAVRIMGDASTRVEKANLTSDDIDLFIIPHQA |
| WT | NIRIMESARERLGISKDKMSVSVNKGNTSAASIPLSIDQELKNGKLKDDDTIVLVGFGG |
| SM | NIRIMESARERLGISKDKMSVSVNKGNTSAASIPLSIDQELKNGKLKDDDTIVLVGFGG |
| WT | GLTWGAMT |
| SM | GLTWGAMT |

Figure 24. FabH amino acid sequence alignment of USA 100 635 wild type (WT) and its Ns β L-resistant spontaneous mutant (SM).

Proteomic analysis of the Ns β L resistant mutants. As a final and global approach to understand the mechanism of action of Ns β L, we undertook both comprehensive and quantitative proteomic analysis of the USA 100 and USA 300 adaptive strains. Differences between the intracellular proteomes of the USA 100 and USA 300 parent strains and their respective adaptive mutants were evaluated at 8 hours (post-exponential phase) and 15 hours (stationary phase) using isobaric tagging for relative and absolute quantitation (iTRAQ) mass spectrometry. For the post-exponential phase cultures, the data for each parental strain and resistant mutant was performed in duplicate, and the average fold change was calculated. At 8 hours, 85 proteins were identified from USA 100 and 66 proteins from USA 300 (see appendix for complete lists). Forty of the proteins identified from the USA 100 adaptive mutant had expression altered by 1.5-fold or greater from the parent strain, many of which were involved in nucleotide synthesis, translation, glycolysis, pyruvate metabolism, and TCA cycle (**Table 9**). However, only four proteins with a change in expression greater than 1.5-fold were identified from the USA 300 adaptive mutant, which included proteins involved in fermentation, cell wall degradation, and energy production (**Table 10**). Of all the proteins identified, 46 were found to have altered expression in both USA 100 and USA 300, including proteins involved in translation, glycolysis, pyruvate metabolism, the TCA cycle, and the oxidative stress response (**Table 11**). At 15 hours, 796 proteins were identified from USA 100 and 791 proteins from USA 300, 56 of which were found to have significantly altered expression in both strains; however, the stationary phase data is purely exploratory, as only one replicate was performed and statistical significance could not be calculated (**Table 12**). It is worth noting that a number of proteins associated with

nucleotide metabolism, transcription, DNA repair, amino acid metabolism, translation, peptidoglycan synthesis, cell division, glycolysis, the TCA cycle, and sugar transport were all significantly decreased in both the USA 100 and USA 300 adaptive mutants.

| Pathway | Late Exponential Phase Proteins Identified from USA 100 (40) | Accession Number | Fold Change from Wild-Type |
|----------------------------------|---|---------------------|----------------------------|
| Purine biosynthesis | Inosine-5'-monophosphate dehydrogenase (guaB) | P99106 IMDH_STAAN | -1.5 |
| | Phosphoribosylaminoimidazole carboxylase ATPase subunit (purK) | Q7A695 PURK_STAAN | -2.45 |
| | Phosphoribosylformylglycinamide synthase 1 (purQ) | P99166 PURQ_STAAN | -2.4 |
| Pyrimidine biosynthesis | Aspartate carbamoyltransferase (pyrB) | P65618 PYRB_STAAN | -2.65 |
| Virulence Determinant Regulation | GTP-sensing transcriptional pleiotropic repressor (codY) | P63844 CODY_STAAN | -2.2 |
| Cysteine metabolism | Cysteine synthase (cysK) | P63871 CYSK_STAAN | -2.05 |
| Nitrogen metabolism | Glutamine synthetase (glnA) | P99095 GLNA_STAAN | -1.5 |
| Electron transport | ATP synthase subunit beta (atpD) | P99112 ATPB_STAAN | -1.7 |
| Energy production | L-lactate dehydrogenase 1 (ldhA) | P65256 LDH1_STAAN | -2.55 |
| | NADH dehydrogenase-like protein SA0802 (SA0802) | Q7A6J4 Y802_STAAN | -2.5 |
| Glycolysis | Enolase (eno) | P99088 ENO_STAAN | -2.15 |
| | Glucose-6-phosphate isomerase (pgi) | P99078 G6PI_STAAN | -1.8 |
| | Pyruvate kinase (pyk) | Q7A559 KPYK_STAAN | -1.6 |
| TCA cycle | Aconitate hydratase (acnA) | P99148 ACON_STAAN | -2.6 |
| | Citrate synthase II (citZ) | Q7A561 Q7A561_STAAN | -2.55 |
| | Dihydrolipoylysine-residue succinyltransferase component of 2-oxoglutarate dehydrogenase complex (odhB) | Q7A5N4 ODO2_STAAN | -2.1 |
| | Phosphoglycerate kinase (pgk) | P99135 PGK_STAAN | -1.7 |
| | Probable malate:quinone oxidoreductase 2 (mqo2) | P99115 MQO2_STAAN | -1.55 |
| | Succinyl-CoA ligase [ADP-forming] subunit alpha (sucD) | P99070 SUCD_STAAN | -1.55 |
| Pyruvate metabolism | Dihydrolipoyle dehydrogenase (pdhD) | P99084 DLDH_STAAN | -2.25 |
| | Phosphate acetyltransferase (pta) | P99092 PTA_STAAN | -2.25 |

| | | | |
|--------------------------|---|---------------------|-------|
| | Pyruvate dehydrogenase E1 component subunit beta (pdhB) | P99063 ODPB_STAAN | -2.6 |
| Pentose-Phosphate | 6-phosphogluconate dehydrogenase, decarboxylating (gnd) | P63334 6PGD_STAAN | -2.55 |
| Iron storage | Ferritin (ftnA) | Q7A4R2 FTN_STAAN | -3 |
| Stress response | Alkaline shock protein 23 (asp23) | P99157 ASP23_STAAN | -1.55 |
| | Catalase (katA) | Q7A5T2 CATA_STAAN | -1.95 |
| | Chaperone protein (hchA) | P64313 HCHA_STAAN | -1.65 |
| | Putative uncharacterized protein (SA1528) | Q7A553 Q7A553_STAAN | -2.75 |
| | Superoxide dismutase [Mn/Fe] 1 (sodA) | P99098 SODM1_STAAN | -2.05 |
| Protein Synthesis | 30S ribosomal protein S1 (rpsA) | Q7A5J0 RS1_STAAN | -2.3 |
| | 30S ribosomal protein S10 (rpsJ) | P66334 RS10_STAAN | -2.3 |
| | 30S ribosomal protein S9 (rpsI) | P66646 RS9_STAAN | -2.1 |
| | 50S ribosomal protein L11 (rplK) | P0A0F2 RL11_STAAN | -1.75 |
| | 50S ribosomal protein L13 (rplM) | Q7A473 RL13_STAAN | -1.6 |
| | 50S ribosomal protein L18 (rplR) | Q7A467 RL18_STAAN | -1.5 |
| | Seryl-tRNA synthetase (serS) | P99178 SYS_STAAN | -1.4 |
| Unknown | SA2119 protein (SA2119) | Q7A3Z5 Q7A3Z5_STAAN | -1.6 |
| | DNA-binding protein HU (hup) | Q7A5J1 DBH_STAAN | -1.85 |

Table 9. Intracellular proteins found to have altered expression at 8 hours in the USA 100 adaptive mutant.

| Pathway | Late Exponential Phase Proteins Identified from USA 300 (4) | Accession Number | Fold Change from Wild-Type |
|------------------------------|---|--------------------|----------------------------|
| Fermentation | Alcohol dehydrogenase (adh) | Q2FJ31 ADH_STA3 | -2.3 |
| Energy production | Formate acetyltransferase (pflB) | Q2FK44 PFLB_STA3 | -2 |
| Cell wall degradation | Immunodominant staphylococcal antigen A (isaA) | Q2FDT8 ISAA_STA3 | 1.45 |
| Unknown | Putative uncharacterized protein (SAUSA300_2473) | Q2FDX1 Q2FDX1_STA3 | 2.5 |

Table 10. Intracellular proteins found to have altered expression at 8 hours in the USA 300 adaptive mutant.

| Pathway | Late Exponential Phase Proteins Identified in Common (46) | Fold Change from Wild-Type USA 100 | Fold Change from Wild-Type USA 300 |
|----------------------------|---|---------------------------------------|---------------------------------------|
| Cell division | Cell division protein ftsZ (ftsZ) | -1.15 | 0.65 |
| Cysteine metabolism | Cysteine synthase (cysK) | -2.05 | -0.75 |
| DNA replication | DNA polymerase III subunit beta (dnan) | -1.4 | 0.2 |
| Electron transport | NADH dehydrogenase-like protein | -1.7 | -0.15 |

| | | | |
|----------------------------------|--|---------------|-----------|
| | (SA0802/SAUSA300_0844) | | |
| Energy production | ATP synthase subunit alpha (atpA) | -0.8 | 0.85 |
| | ATP synthase subunit beta (atpD) | -2.5 | 0 |
| | L-lactate dehydrogenase 1 (ldhA/ldh1) | -2.55 | -0.25 |
| Folate synthesis | Serine hydroxymethyltransferase (glyA) | -0.6 | 0.65 |
| Glycolysis | Enolase (eno) | -2.15 | -0.5 |
| | Glucose-6-phosphate isomerase (pgi) | -1.8 | -0.7 |
| | Glyceraldehyde-3-phosphate dehydrogenase 1 (gapA1) | -1.35 | 0.1 |
| | Pyruvate kinase (pyk) | -1.6 | 0.15 |
| Iron storage | Ferritin (ftnA) | -3 | -0.2 |
| Nitrogen metabolism | Glutamine synthetase (glnA) | -1.5 | -0.2 |
| | NAD-specific glutamate dehydrogenase (gluD/gudB) | -1.6 | -0.6 |
| Oxidative stress response | Alkyl hydroperoxide reductase subunit C (ahpC) | -1.25 | 0.3 |
| | Alkyl hydroperoxide reductase subunit F (ahpF) | -1.55 | 0.5 |
| | Catalase (katA) | -1.65 | -0.25 |
| Pentose-Phosphate | 6-phosphogluconate dehydrogenase, decarboxylating (gnd) | -2.55 | -0.6 |
| Protein Synthesis | 30S ribosomal protein S1 (rpsA) | -1.75 | -0.35 |
| | 30S ribosomal protein S2 (rpsB) | -0.75 | 1.05 |
| | 30S ribosomal protein S5 (rpsE) | Value missing | 0.4 |
| | 30S ribosomal protein S9 (rpsI) | -2.1 | 0.15 |
| | 50S ribosomal protein L1 (rplA) | -1.35 | 0.55 |
| | 50S ribosomal protein L13 (rplM) | -1.5 | 0.55 |
| | 50S ribosomal protein L14 (rplN) | -1.05 | 0.4 |
| | 50S ribosomal protein L2 (rplB) | -1.25 | 0.25 |
| | 50S ribosomal protein L3 (rplC) | No values | 0.6 |
| | 50S ribosomal protein L6 (rplF) | No values | No values |
| | Elongation factor G (fusA) | -1.15 | 0.35 |
| | Elongation factor Tu (tuf) | -1.3 | 0.65 |
| | Glycyl-tRNA synthetase (glyQS) | -0.95 | 0.25 |
| Stress response | Alkaline shock protein 23 (asp23) | -1.55 | 0.3 |
| Purine biosynthesis | Inosine-5'-monophosphate dehydrogenase (guaB) | -1.5 | -0.4 |
| Pyruvate metabolism | Dihydrolipoyl dehydrogenase (pdhD/lpdA) | -2.25 | -0.25 |
| | D-lactate dehydrogenase (ldhD/ddh) | No values | 0.75 |
| | Pyruvate dehydrogenase E1 component subunit alpha (pdhA) | No values | 0 |
| | Pyruvate dehydrogenase E1 component subunit beta (pdhB) | -2.25 | -0.35 |
| | Formate acetyltransferase (pfkB) | Value missing | -2.3 |
| Regulation | GTP-sensing transcriptional pleiotropic repressor (codY) | -2.2 | 0.1 |
| TCA cycle | Aconitate hydratase (acnA) | -2.55 | -1.2 |
| | Phosphoglycerate kinase (pgk) | -2.6 | -0.1 |
| | Succinyl-CoA ligase [ADP-forming] subunit alpha (sucD) | -1.7 | -0.55 |

| | | | |
|----------------------|---|-------|-------|
| | Dihydrolipoyllysine-residue succinyltransferase component of 2-oxoglutarate dehydrogenase complex (<i>odhB</i>) | -1.55 | -0.45 |
| Transcription | DNA-directed RNA polymerase subunit beta (<i>rpoB</i>) | -0.8 | 0 |
| | DNA-directed RNA polymerase subunit beta' (<i>rpoC</i>) | -1.2 | 0.2 |
| Unknown | DNA-binding protein HU (<i>hup</i>) | -1.85 | 0 |

Table 11. Intracellular proteins found to have altered expression at 8 hours in both the USA 100 and USA 300 adaptive mutants.

| Pathway | Stationary Phase Proteins Identified in Common (129) | Fold Change from Wild-Type | |
|--|--|----------------------------|---------|
| | | USA 100 | USA 300 |
| Acetoin catabolism | Acetoin(diacetyl) reductase (<i>butA</i>) | -2.3 | -2.6 |
| Amino acid metabolism | Ornithine carbamoyltransferase, catabolic (<i>arcB</i>) | -2.7 | -2 |
| Arginine metabolism | Carbamate kinase 1 (<i>arcC1</i>) | -3.3 | -2.4 |
| | Carbamoyl-phosphate synthase large chain (<i>carB</i>) | -2.6 | -2.4 |
| ATP binding | Cytidylate kinase (<i>cmk</i>) | -2.2 | -2.5 |
| ATP synthesis | ATP synthase gamma chain (<i>atpG</i>) | -2.8 | -1.9 |
| | ATP synthase subunit alpha (<i>atpA</i>) | -2.4 | -2.5 |
| | ATP synthase subunit b (<i>atpF</i>) | -2.8 | -2.4 |
| | ATP synthase subunit beta (<i>atpD</i>) | -2.2 | -2.1 |
| | ATP synthase subunit delta (<i>atpH</i>) | -3.5 | -2.6 |
| Cell division | Cell division protein (<i>ftsA</i>) | -2.1 | -1.6 |
| | Septation ring formation regulator (<i>ezrA</i>) | -1.7 | -1.5 |
| | GTP-binding protein era homolog (<i>era</i>) | -1.9 | -1.6 |
| Cell redox homeostasis | Alkyl hydroperoxide reductase subunit C (<i>ahpC</i>) | -1.5 | -1.5 |
| Cell wall degredation; peptidoglycan biosynthesis; cell shape | D-alanine--D-alanine ligase (<i>ddl</i>) | -1.8 | -1.6 |
| DNA repair | ATP-dependent DNA helicase (<i>pcrA</i>) | -2.1 | -2 |
| | Protein recA (<i>recA</i>) | -1.7 | -1.7 |
| DNA replication | DNA gyrase subunit B (<i>gyrB</i>) | -1.5 | -1.7 |
| | DNA polymerase III subunit beta (<i>dnaN</i>) | -1.9 | -1.8 |
| | Ribonucleoside-diphosphate reductase (<i>nrde</i>) | -1.8 | -2.2 |
| | Single-stranded DNA-binding protein (<i>ssb</i>) | -1.6 | -1.8 |
| DNA replication; stress response | Chaperone protein (<i>dnaJ</i>) | -1.7 | -2.8 |
| Electron transport | NADH dehydrogenase-like protein SA0802 (SA0802) | -2.6 | -2 |
| | Probable quinol oxidase subunit 2 (<i>qoxA</i>) | -2.4 | -3.2 |
| Fatty acid biosynthesis | Trans-2-enoyl-ACP reductase (<i>fabI</i>) | -2.1 | -2 |
| Folic acid metabolism | Formate--tetrahydrofolate ligase (<i>fhs</i>) | -2.2 | -1.9 |
| Formate metabolism | Putative formate dehydrogenase (SA2102) | -1.6 | -1.5 |
| Glutamine metabolism | Carbamoyl-phosphate synthase small chain (<i>carA</i>) | -2.3 | -1.5 |
| Glycerol | Aerobic glycerol-3-phosphate dehydrogenase (<i>glpD</i>) | -2.2 | -1.7 |

| metabolism | | | |
|--------------------------------------|--|------|------|
| Glycolysis | 2,3-bisphosphoglycerate-dependent phosphoglycerate mutase (gpmA) | -2.3 | -2.1 |
| | Fructose-bisphosphate aldolase class 1 (fda) | -1.7 | -1.6 |
| | Glyceraldehyde-3-phosphate dehydrogenase 2 (gapA2) | -1.5 | -2.9 |
| | Pyruvate kinase (pyk) | -1.9 | -1.6 |
| | L-lactate dehydrogenase 1 (ldhA) | -3 | -1.6 |
| | L-lactate dehydrogenase 2 (ldhB) | -2.7 | -2.5 |
| Histidine metabolism | Urocanate hydratase (hutU) | -2.1 | -1.8 |
| Lipoate biosynthesis | Lipoyl synthase (lipA) | -2 | -3.1 |
| Metabolism | Putative dipeptidase SA1572 (SA1572) | -1.9 | -1.5 |
| | Pyridoxal biosynthesis lyase (pdxS) | -1.8 | -2.9 |
| Peptidoglycan biosynthesis | Aminoacyltransferase femB (femB) | -2.1 | -3.1 |
| | D-alanine--D-alanine ligase (ddl) | -1.8 | -1.6 |
| | Penicillin binding protein 2 prime (mecA) | -2.1 | -2.1 |
| | UDP-N-acetyl muramoyl-tripeptide--D-alanyl-D-alanine ligase (murF) | -1.5 | -1.7 |
| MSCRAMMs | Elastin-binding protein (ebpS) | -1.7 | -2 |
| | Extracellular matrix protein-binding protein (emp) | -2 | -1.8 |
| Nucleoside transport | Pyrimidine nucleoside transport protein (nupC) | -2 | -2.2 |
| Nucleotide biosynthesis | Ribose-phosphate pyrophosphokinase (prs) | -2.8 | -1.9 |
| Organic acid metabolism | Acetate kinase (ackA) | -1.9 | -1.6 |
| Phospholipid biosynthesis | Glycerol-3-phosphate dehydrogenase [NAD(P)+] (gpsA) | -2.3 | -2.1 |
| Porphyrin biosynthesis | Glutamate-1-semialdehyde 2,1-aminomutase 1 (hemL1) | -2.9 | -1.9 |
| | Glutamate-1-semialdehyde 2,1-aminomutase 2 (hemL2) | -1.8 | -3.3 |
| Proline biosynthesis | 1-pyrroline-5-carboxylate dehydrogenase (rocA) | -2.1 | -1.7 |
| | Ornithine aminotransferase 2 (rocD2) | -2.9 | -1.7 |
| | Pyrroline-5-carboxylate reductase (proC) | -1.6 | -1.7 |
| Protein folding | ATP-dependent Clp protease ATP-binding subunit (clpX) | -2.2 | -1.7 |
| | Putative peptidyl-prolyl cis-trans isomerase (SA0815) | -1.5 | -1.7 |
| Protein transport | Protein translocase subunit secA 1 (secA1) | -2.4 | -2.3 |
| | Protein-export membrane protein (secF) | -2.5 | -2.8 |
| Purine biosynthesis | Adenylosuccinate synthetase (purA) | -1.6 | -1.7 |
| | Amidophosphoribosyltransferase (purF) | -2.3 | -2.5 |
| | Bifunctional purine biosynthesis protein purH (purH) | -2.9 | -2.3 |
| | Phosphoribosylamine-glycine ligase (purD) | -3.1 | -2.9 |
| | Phosphoribosylaminoimidazole carboxylase ATPase subunit (purK) | -2.9 | -2.4 |
| | Phosphoribosylaminoimidazole-succinocarboxamide synthase (purC) | -3.5 | -2.7 |
| | Phosphoribosylformylglycinamidine synthase 1 (purQ) | -2.6 | -3.1 |
| | Phosphoribosylformylglycinamidine synthase 2 (purL) | -3 | -3.4 |
| Purine ribonucleoside salvage | Hypoxanthine-guanine phosphoribosyltransferase (hpt) | -1.8 | -1.9 |
| | Xanthine phosphoribosyltransferase (xpt) | -2.1 | -2.1 |
| Pyrimidine | Pyrimidine-nucleoside phosphorylase (pdp) | -2.9 | -1.5 |

| | | | |
|---------------------------------|--|------|------|
| metabolism | Uracil phosphoribosyltransferase (upp) | -1.5 | -3.4 |
| | Uridine kinase (udk) | -2.1 | -3.2 |
| Pyruvate biosynthesis | Pyruvate dehydrogenase E1 component subunit beta (pdhB) | -1.8 | -1.5 |
| RNA degradation | Ribonuclease J 2 (SA1118) | -1.8 | -2.7 |
| Stress response | 10 kDa chaperonin (groS) | -1.6 | -1.5 |
| | ATP-dependent protease ATPase subunit (hslU) | -2 | -3.2 |
| | GTPase obg (obg) | -2.6 | -2 |
| Stringent response | GTP pyrophosphokinase (relA) | -2.4 | -1.6 |
| Sugar metabolism | Acetyl-CoA synthetase (acsA) | -1.9 | -1.7 |
| Sugar transport | PTS system EIIBC component (SA0186) | -1.8 | -1.5 |
| | PTS system glucose-specific EIICBA component (ptsG) | -3 | -3.6 |
| | PTS system glucoside-specific EIICBA component (glcB) | -3.2 | -1.6 |
| TCA cycle | Citrate synthase II (citZ) | -2 | -1.6 |
| | Isocitrate dehydrogenase [NADP] (icd) | -1.9 | -1.9 |
| | Succinate dehydrogenase flavoprotein subunit (sdhA) | -2.2 | -1.8 |
| | Succinate dehydrogenase iron-sulfur protein subunit (sdhB) | -1.9 | -2 |
| | Succinyl-CoA ligase [ADP-forming] subunit alpha (sucD) | -1.8 | -1.6 |
| | Succinyl-CoA ligase [ADP-forming] subunit beta (sucC) | -1.5 | -1.5 |
| Transcription | DNA-directed RNA polymerase subunit beta (rpoB) | -1.6 | -1.5 |
| | DNA-directed RNA polymerase subunit beta' (rpoC) | -2 | -1.5 |
| | Probable DNA-directed RNA polymerase subunit delta (rpoE) | -1.9 | -1.6 |
| Transcription regulation | Serine-protein kinase (rsbW) | -2.2 | -2.3 |
| | Bifunctional protein (pyrR) | -3.2 | -2.4 |
| Translation | Asparaginyl-tRNA synthetase (asnS) | -2.5 | -1.9 |
| | Elongation factor Tu (tuf) | -1.8 | -1.5 |
| | Methionyl-tRNA formyltransferase (fmt) | -1.9 | -2.3 |
| | Prolyl-tRNA synthetase (proS) | -1.9 | -1.7 |
| | Seryl-tRNA synthetase (serS) | -3.3 | -1.5 |
| | Threonyl-tRNA synthetase (thrS) | -2.2 | -1.5 |
| | Translation initiation factor IF-2 (infB) | -2.1 | -1.9 |
| | 30S ribosomal protein S11 (rpsK) | -2.1 | -1.8 |
| | 30S ribosomal protein S12 (rpsL) | -1.9 | -1.7 |
| | 30S ribosomal protein S13 (rpsM) | -1.9 | -1.6 |
| | 30S ribosomal protein S14 type Z (rpsZ) | -2 | -1.8 |
| | 30S ribosomal protein S3 (rpsC) | -1.5 | -2.1 |
| | 30S ribosomal protein S4 (rpsD) | -1.5 | -1.6 |
| | 30S ribosomal protein S5 (rpsE) | -2.1 | -1.5 |
| | 30S ribosomal protein S6 (rpsF) | -1.8 | -1.6 |
| | 50S ribosomal protein L1 (rplA) | -2.2 | -2 |
| | 50S ribosomal protein L10 (rplJ) | -1.7 | -1.6 |
| | 50S ribosomal protein L13 (rplM) | -2.3 | -1.6 |
| | 50S ribosomal protein L14 (rplN) | -2.6 | -1.6 |
| | 50S ribosomal protein L19 (rplS) | -2.4 | -1.8 |
| | 50S ribosomal protein L2 (rplB) | -1.9 | -1.7 |
| | 50S ribosomal protein L20 (rplT) | -2.8 | -2.1 |
| | 50S ribosomal protein L3 (rplC) | -1.5 | -1.9 |
| | 50S ribosomal protein L4 (rplD) | -2.2 | -1.9 |

| | | | |
|--------------------------|--|------|------|
| | 50S ribosomal protein L5 (rplE) | -2.7 | -2.5 |
| tRNA modification | (Dimethylallyl)adenosine tRNA methylthiotransferase (miaB) | -1.5 | -1.5 |
| | tRNA modification GTPase (mnmE) | -1.7 | -2.2 |
| Virulence | Conserved virulence factor B (cvfB) | -1.5 | -1.7 |
| Unknown | DegV domain-containing protein (SA1258) | -2.3 | -1.9 |
| | GTP-binding protein (engA) | -2.5 | -1.8 |
| | PhoH protein (phoH) | -1.9 | -1.5 |
| | Putative phosphotransferase (SA1392) | -2 | -1.9 |
| | Uncharacterized lipoprotein (SA2158) | -3 | -1.5 |
| | UPF0051 protein (SA0778) | -1.9 | -1.8 |
| | UPF0133 protein (SA0437) | -1.5 | -1.5 |
| | UPF0365 protein SA1402 (SA1402) | -1.7 | -2 |
| | UPF0477 protein (SA0873) | -1.9 | -1.9 |
| | UPF0478 protein SA1560 (SA1560) | -1.9 | -2 |

Table 12. Intracellular proteins found to have altered expression at 15 hours in both the USA 100 and USA 300 adaptive mutants.

DISCUSSION

Antimicrobial resistance has been an escalating problem since the advent of clinical antimicrobial use. Every new antibiotic that has been released, including completely synthetic antimicrobials, has rapidly encountered resistance in one form or another^{19, 43, 69, 75, 102}. The cost of developing antibiotics is high, especially considering their short lifespan; and is not considered lucrative by pharmaceutical companies. For this reason, the number of new therapies has dwindled, while the number of effective therapeutics continues to decrease. The research presented here investigates the mode of action of a novel β -lactam antimicrobial, with potent activity against MRSA by analyzing laboratory-generated resistant mutants.

A number of diverse laboratory and clinical *S. aureus* isolates were used in this study because the characteristics of pathogenesis and antimicrobial susceptibility can differ widely depending on the strain. Importantly, the Ns β L MIC was found to be comparable across all strains tested, so the mode of action of this drug does not appear to be affected by existing, intrinsic resistance factors. Previous studies have suggested that Ns β L may target 3-oxoacyl-acyl carrier protein synthase (ACP) III (FabH) either directly or indirectly⁹², so we set forth to determine if the addition of fatty acids to the culture media would have an effect on the Ns β L MICs.

The results of our fatty acid assays with Ns β L indicate that fatty acid biosynthesis may not be the sole or primary target of this drug. This is apparent when the effects of fatty acids on Ns β L activity are compared to their effects on triclosan and vancomycin activity. The MIC of vancomycin, a cell wall synthesis inhibitor, was reduced by Tween 80. The effect of Tween 80 on the MIC of Ns β L was, however, not significant. The MIC of triclosan, an inhibitor of enoyl-ACP reductase (FabI), which catalyzes the final step of fatty acid synthesis, was significantly affected by the presence of Tween 80, being increased by at least 20-fold for all strains tested, from 0.125 μ g/mL to $\geq 6.25 \mu$ g/mL. It is noteworthy that this drastic increase in MIC does not agree with that published by Balemans, et. al⁶. They saw that the MIC of triclosan increased from 0.125 μ g/mL to 2 μ g/mL in the presence of the same concentration of Tween 80 as used in our study, and attributed this to the plasma binding properties of triclosan. They also showed that other known fatty acid synthesis inhibitors behaved similarly⁶. However, Altenbernd showed that cerulenin, an inhibitor of 3-oxoacyl-ACP synthase I/II (FabB/F), which catalyzes the second condensation step of fatty acid synthesis, lost efficacy in the presence of both saturated and unsaturated fatty acids². This was confirmed by Brinster, et. al, who used *Streptococcus agalactiae* as their initial model¹⁷, and *S. aureus* in response to the criticism from Balemans, et. al.¹⁶, which is again confirmed by our work. Because Ns β L does not follow the rescue pattern established by triclosan and other fatty acid synthesis inhibitors, an enzyme of the fatty acid synthesis pathway may not be its primary target.

Biofilm-mediated infections often lead to chronic illness due to persistence, and difficulty in treating biofilm-mediated conditions. Currently, a prophylactic view towards

preventing colonization is taken, but there are many limitations, particularly considering only catheter-associated biofilms are targeted by this method. Our study compared the effects of vancomycin, triclosan, and tetracycline to Ns β L on biofilms and found that the ability of Ns β L to kill established biofilms exceeded that of the other antimicrobials tested, as measured by percent reduction. There are a number of factors that affect the activity of an antimicrobial on the target biofilm, such as the rate of diffusion of the drug through the biofilm⁶¹ and the ability of the drug to kill stationary phase bacteria⁷⁴. Ns β L reduced biofilm formation by 43%, which was the greatest observed decrease. Tetracycline was shown in one *in vitro* experiment to completely reduce metabolic activity in an *S. aureus* biofilm³⁶ and to have high levels of killing of *S. epidermidis* biofilms⁷⁴; we showed here that tetracycline was effective at reducing biofilms by 29%. Both vancomycin and triclosan were ineffective at killing biofilms, which has been demonstrated previously in *S. aureus*³², *S. epidermidis*⁷⁴, and *Salmonella typhimurium*⁹⁹ to be due to restricted diffusion through the biofilm. The biofilm-killing activity of Ns β L may be due to high levels of diffusion through the biofilm matrix, an enhanced ability to kill stationary phase cells, or a combination of both of these factors.

It is important, when dealing with antimicrobial agents, to have a sense of the rate at which clinical isolates spontaneously become resistant to the drug. This is particularly important when determining the dose to administer to patients. The spontaneous mutation rate for SH1000, a non-resistant laboratory strain, was 5.2×10^{-9} at 7x the Ns β L MIC. Interestingly, resistance occurred more frequently at 2×10^{-8} when a nitrosoguanidine (NTG) mutant library of SH1000 was exposed to the same Ns β L

concentration. With that said, these latter isolates had Ns β L MICs no greater than 10 $\mu\text{g}/\text{mL}$, whereas the spontaneous, untreated SH1000 mutants had Ns β L MICs as high as 50 $\mu\text{g}/\text{mL}$. The spontaneous mutation rate of Ns β L was found to be comparable to a number of clinically relevant antimicrobials having a wide range of modes of action (**Table 13**). Rifampicin, for example, is used only as a combination therapy due to its high rate of spontaneous mutagenesis resulting in resistance⁷². Ns β L had a spontaneous mutation rate 19- to 20-fold lower than rifampicin, indicating that it could conceivably be used in single therapy.

| Antimicrobial | Spontaneous Mutation Rate at 8x MIC | References |
|---|---|------------|
| Ceftobiprole | $0.9 \times 10^{-10} - 5.3 \times 10^{-10}$ | 13 |
| Ciprofloxacin | 3.2×10^{-10} | 85 |
| Daptomycin | $0.8 \times 10^{-10} - 9.1 \times 10^{-11}$ | 13, 55 |
| Levofloxacin | 6.4×10^{-10} | 85 |
| Linezolid | $1.3 \times 10^{-9} - 8.7 \times 10^{-10}$ | 13 |
| Minocycline | $6.7 \times 10^{-9} - 9.5 \times 10^{-10}$ | 13 |
| Mupirocin | $1.5 \times 10^{-8} - 9.5 \times 10^{-10}$ | 13 |
| Ns β L (SH1000) [†] | 5.2×10^{-9} | This study |
| Ns β L (MNNG-treated SH1000) [†] | 2×10^{-8} | This study |
| Quinupristin/Dalfopristin | $3.3 \times 10^{-9} - 8.7 \times 10^{-10}$ | 13 |
| Rifampicin [‡] | $10^{-7} - 10^{-8}$ | 72 |
| Teicoplanin | $1.6 \times 10^{-8} - 7.1 \times 10^{-11}$ | 55 |
| Telavancin | $1 \times 10^{-11} - 5 \times 10^{-11}$ | 55 |

Table 13. Spontaneous mutation rates for various antimicrobials. The single-step spontaneous mutation rates for various clinically relevant antimicrobials are reported in the literature and compiled here for comparison to Ns β L. [†] Ns β L spontaneous mutagenesis was performed at 7x MIC. [‡] Rifampicin spontaneous mutagenesis was performed at 10x MIC.

The spontaneous and adaptive mutants generated were characterized in order to provide insight into their mechanism(s) of resistance to Ns β L. The rationale for this is that we may be able to extrapolate the mode of action of Ns β L, by examining the phenotypic changes of the mutants. Based on previous analysis of the drug⁹², we would expect to see

changes in those processes involving coenzyme-A (CoA), such as glycolysis, the citric acid cycle (TCA), pyruvate metabolism, and, particularly, fatty acid biosynthesis. Because changes in these pathways would have widespread consequences, we used a global approach to determine phenotypic changes in the Ns β L-resistant mutants.

The production of virulence factors by *S. aureus* is a complex and highly regulated process involving multiple regulatory systems which control growth phase-dependent virulence factor production⁸¹. No changes were found in virulence factor production for either of the SH1000 spontaneous mutants as determined by growth on blood or milk plates. Conversely, it is interesting to note that SDS-PAGE analysis of SH-11 appears to show an increase in production of cell-wall associated and secreted proteins. This may simply be an incongruity in the SDS-PAGE, rather than a true phenotypic change, or it may be that SH-11 is producing other virulence factors that were not tested for. On the other hand, virulence determinant production in both the USA 100 and USA 300 adaptive mutants was dramatically reduced, as shown by a reduction or loss of proteolytic activity, hemolysis, capsule production, and cell-wall and secreted protein production. The genes encoding proteases, hemolysins, exotoxins, and capsular polysaccharides are all positively regulated by the central virulence regulator, *agr* (accessory gene regulator)⁸¹, indicating that both the USA 100 and USA 300 adaptive mutants may have developed *agr* mutations. Because staphylococcal virulence regulation is so convoluted, there may be additional changes in the adaptive mutants that resulted in the observed phenotype, such as repression of, or changes in, the staphylococcal accessory regulator A (SarA), an activator of *agr*¹². It is also possible that there is repression of, or changes in, SaeRS,

which increases transcription of hemolysins and capsule genes⁶⁸. Finally, there may be an increase in transcription of the repressor of toxin (Rot), which inhibits transcription of multiple protease and hemolysin genes⁴⁸. Interestingly, deletion of *sarA* was shown to result in increased susceptibility to ciprofloxacin, rifampicin, and vancomycin⁸³ and deletion of *sarA* and *agr* together resulted in increased susceptibility to oxacillin, cefoxitin, and imipenem³⁸. To date, changes in *sarA* or *agr* have not been associated with increased antimicrobial resistance. These and other issues will be addressed in more detail in the proteomics section.

Amino acid limitation leads to activation of the stringent response in *S. aureus*, mediated by the synthesis of polyphosphorylated guanosine nucleotides ((p)ppGpp) by *rsh* (RelA/SpoT homolog)⁴⁰. (p)ppGpp induces overexpression of genes involved in amino acid synthesis and repression of ribosomal and tRNA genes, allowing the bacteria to survive under less than optimal conditions. Mutants defective in *rsh* were found to be more susceptible to mupirocin, and not changed in susceptibility to vancomycin and ciprofloxacin^{22, 40}. A clinical isolate with a persistently active stringent response was also found to have no changes in susceptibility to vancomycin, teicoplanin, gentamycin, linezolid, daptomycin, tigecycline, rifampicin, or ciprofloxacin³⁹. While neither spontaneous mutant showed changes in growth under amino acid limiting conditions, both adaptive mutants showed changes. The USA 100 adaptive mutant had increased growth levels during lag and early-exponential phase, but decreased levels of growth during late- and post-exponential phase. The USA 300 adaptive mutant had significantly reduced levels of growth during exponential phase as compared to its parent. While

glucose limitation is also known to induce the stringent response⁴⁰, none of the strains tested showed changes in growth in glucose limiting media. It has also been suggested that a fully functioning TCA cycle is necessary for effective amino acid catabolism⁹⁶, which will be further discussed in the proteomics section. We know from growth curves in tryptic soy broth (TSB) that both adaptive mutants have reduced growth levels during exponential phase, a possible indicator of defects in energy production. Furthermore, SarA, proposed above to be repressed, is known to positively regulate expression of amino acid transport and metabolism proteins³¹; thus, if the adaptive mutants have defects in regulation by SarA, they will have reduced viability under amino acid limiting conditions. Taken together, along with the increased resistance of SH-32 and the USA 300 adaptive mutant to a number of antimicrobials (discussed later), this may indicate that the adaptive mutants are defective in transport of extracellular amino acids, rather than in their overall response to nutrient limitation as regulated by (p)ppGpp or SarA. Such a deficiency in amino acid utilization may lead to weaker peptidoglycan cross-links, resulting in changes in susceptibility to cell wall-active antimicrobials and autolytic activity⁹⁷, possibly implying that NsβL has an effect on the integrity of the cell wall.

Reduced survivability in response to phosphate limitation has been attributed to a number of factors. Lithgow et. al. have described the role of cysteine synthase⁶⁵ and FtsH⁶⁶ in recovery from amino acid- and phosphate limiting-conditions as due to defects in protein synthesis during starvation. Cysteine synthase is responsible for *S. aureus*' resistance to tellurite, oxidative stress, and disulfides, and is proposed to be important as part of the thiol redox balance in *S. aureus*⁶⁵, while FtsH has chaperone-like activities and mediates

resistance to methyl viologen and tellurite⁶⁶. This is of particular interest concerning NsβL, as Revell, et. al. have proposed that this drug may alter the thiol redox balance by reducing CoA, which would prevent it performing its role in this buffer system⁹². The USA 300 adaptive mutant showed reduced growth levels in amino acid- and phosphate-limiting conditions, and the USA 100 adaptive mutant had reduced growth levels during late exponential and stationary phase in amino acid-limiting conditions, suggesting that cysteine synthase and/or FtsH activity may have been reduced as a result of gaining resistance to NsβL.

The loss of the ability to ferment ribose, as seen with both the USA 100 and USA 300 adaptive mutants, has been associated with an increase in fitness under nutrient limiting conditions in *Escherichia coli*²¹. This may indicate that gaining resistance to NsβL results in insufficient metabolism or utilization of nutrients, and that the loss of ribose fermentation ameliorates this defect.

The NsβL-resistant mutants were subjected to metal ion-limiting conditions by growing them in CL medium, which contains only magnesium as a metal ion source. The spontaneous mutant SH-32 was shown to have decreased fitness during exponential phase under these conditions. The binding and uptake of magnesium from the environment has been shown to be related to the composition of teichoic acids in the bacterial cell wall. Specifically, increased D-alanine content of teichoic acids in *Bacillus subtilis*, *Lactobacillus buchneri*, and *S. aureus* resulted in a reduced ability to bind magnesium ions^{3, 59, 80}. Additionally, changes in the D-alanine content of the cell walls

has been associated with increased resistance to β -lactam antimicrobials^{80, 82}, which is further addressed below.

The oxidative stress response in *S. aureus* is highly regulated and dependent on the availability of iron, manganese (Mn^{2+}) and zinc. Uptake of Mn^{2+} is regulated by MntR, which induces expression of superoxide dismutase (SodA and SodM)⁵². Recently, it has been shown that SH1000 defective in *sarA* had increased superoxide dismutase activity in an Mn^{2+} -independent manner⁷. Based on the increased levels of exponential phase growth in the USA 300 adaptive mutant, and the obvious lack of Mn^{2+} ions, it may be that its oxidative stress response is increased due to defects in regulation by SarA. As mentioned previously, SarA deficiencies have been linked to increased susceptibility to a number of antimicrobials^{38, 83}. Additionally, ciprofloxacin and chloramphenicol have been known to induce the oxidative stress response of *S. aureus*, resulting in increased production of superoxide dismutase^{1, 9}. This is particularly relevant, as the USA 300 adaptive mutant showed a complete loss of susceptibility to ciprofloxacin, and indicates that Ns β L may induce a similar response in this strain.

Changes in the integrity of the cell wall can lead to increased autolysis and susceptibility to cell wall-synthesis inhibiting antimicrobials. While the spontaneous mutants did not exhibit changes in autolysis, SH-32 became 2-fold more resistant to penicillin G than its parent. The mechanism of penicillin G involves inhibiting the cross-linking of peptidoglycan, causing osmotic stress and cell lysis. As previously mentioned, penicillin G resistance can be correlated to increased D-alanine content of the cell wall⁸². It is

interesting to note that no changes in autolysis were observed in this strain, which is often associated with cell wall synthesis-inhibitor resistance. SH-32 also gained heteroresistance to mupirocin, which has primarily been associated with the inhibition of isoleucine-tRNA synthetase, but also with inhibiting cell wall synthesis⁴⁶. This heteroresistance may be similar to that seen with heteroresistance to vancomycin, where only a small subset of the bacterial population is resistant⁴⁴, indicating that the mutation induced by resistance to NsβL does not confer complete protection from mupirocin in SH-32.

While the USA 100 adaptive mutant did not show any changes in antimicrobial susceptibility, the USA 300 adaptive mutant gained resistance to kanamycin, ampicillin, erythromycin, and ciprofloxacin. A study using *S. aureus* strain COL showed that prolonged exposure to oxacillin resulted in increased resistance to erythromycin, kanamycin, and ciprofloxacin, among others, due to increased efflux pump activity⁷⁰. Considering that this efflux pump activity arose in COL after a similar antimicrobial treatment as used in our study, and that they both had similar antimicrobial resistance profiles, it is possible that the increased resistance of the USA 300 adaptive mutant to NsβL may be due to efflux of these antimicrobials out of the cells.

As mentioned before, previous studies have suggested that NsβL may target FabH, the initial enzyme involved in fatty acid biosynthesis⁹². With this in mind, the *fabH* gene of a USA 100 spontaneous mutant was sequenced, but found to have no differences from its parent, implying that altering FabH did not induce a benefit leading to NsβL-resistance.

Consequently, the sequenced gene was compared to *fabH* of the COL strain and found to have differences in three distinct amino acids, L40V, D151E, and I276L. Additionally, the USA 100 FabH sequence was found to have the same amino acid differences when compared to Newman, USA 300 Houston, and USA 400 MW2, but was identical to USA 100 Mu50 and USA 200 MRSA252. Comparison of the predicted secondary structures of the amino acid sequences of COL and USA 100 635 using QuickPhyre analysis did not reveal any structural differences in FabH; thus, the structure of FabH likely does not have an effect on the response of these strains to Ns β L (see appendix for results).

Comparative proteomic analysis of the USA 100 and USA 300 wild-type strains, and their respective adaptive mutants was performed at 8 hours (post-exponential phase) in duplicate and a pilot run at 15 hours (stationary phase) in order to further elucidate the mechanism(s) by which these isolates gained resistance to Ns β L. A change in protein expression of 1.5-fold or more was considered to be significant.

During post-exponential phase, the USA 100 adaptive mutant was found to have reduced expression of numerous proteins involved in nucleotide synthesis, glycolysis, pyruvate metabolism, the TCA cycle, amino acid synthesis, protein synthesis, and stress responses. A specific protein from the TCA cycle, aconitate hydratase, was reduced by 2.6 fold. Aconitate hydratase has been shown by Somerville, et. al. to be required for amino acid catabolism, specifically for synthesis of arginine, leucine, proline, and histidine⁹⁶, and this mutant had reduced growth levels under amino acid-limiting conditions. This protein was also expressed 2.2-fold less during stationary phase. Interestingly, cysteine synthase

(CysK) expression was reduced by 2.05-fold during post-exponential and 1.9-fold during stationary phase. In addition to being involved in the synthesis of cysteine, CysK has also been associated with stress response to H₂O₂, acidic pH, tellurite, diamide (Fig. 25), and limited amino acids and phosphate⁶⁵. Revell, et. al. have proposed that NsβL may act as a sulfenylating agent towards CoA, leading to its inactivation⁹², similar to the thiol-oxidizing activity of diamide. Specific proteins affected during post-exponential phase that utilize CoA in one form or another are citrate synthase II (2.5-fold reduction), the 2-oxoglutarate dehydrogenase complex (2.1-fold reduction), and phosphate acetyltransferase (2.25-fold reduction). During stationary phase, the expression of multiple proteins with acetyl-CoA as their final product were significantly reduced, including alcohol-acetaldehyde dehydrogenase (1.7-fold reduction), acetyl-CoA synthetase (1.9-fold reduction), formic acetyltransferase (2.4-fold reduction), and pyruvate dehydrogenase (3-fold reduction). Notably, while acetyl-CoA is required for initiation of fatty acid synthesis by FabH, no changes in expression of this enzyme were detected at any time point tested. However, AccA, FabF, FabI, and FabZ were all found to have expression reduced between 1.8- and 2.2-fold during stationary phase.

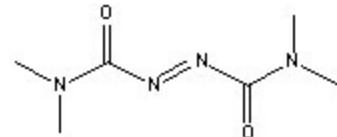


Figure 25. Diamide.

Analysis of the USA 300 adaptive mutant at 8 hours resulted in only four proteins with a significant change from the parent; however, analysis at 15 hours resulted in 11 proteins upregulated and 260 downregulated proteins changed by 1.5-fold or more. Proteins involved in glycolysis, the TCA cycle, and pyruvate metabolism were found to be decreased during stationary phase, but, unexpectedly, proteins involved in fatty acid

synthesis were not identified as significantly altered. Unlike the USA 100 adaptive mutant or other timepoints tested, the USA 300 adaptive mutant showed a number of proteins overexpressed during stationary phase. Both forms of superoxide dismutase (SodA and SodM) were upregulated 1.6- and 2.2-fold, respectively, possibly due to deficiencies in regulation by SarA, as discussed previously. Most interesting in this mutant were the changes in its global regulators. CodY and σ^B were detected, but not significantly changed, while Agr (3.8 fold reduction), SarR (2.6-fold reduction), and SaeS (2.2-fold reduction) were all significantly reduced. These regulators were previously discussed in reference to the marked decrease in virulence factors detected in this mutant strain. SarR is a repressor of SarA⁸¹, expression of which was found to be increased by only 0.6-fold, which may mean that there is another factor involved in regulation of *agr*. The repressor of *sarR* (*rsr*) was recently described as reducing transcription of both *sarR* and *agr*¹⁰⁰. This supports the hypothesis that *agr* was downregulated in this mutant, and that SarA was not playing a significant role in virulence factor determination or antimicrobial susceptibility.

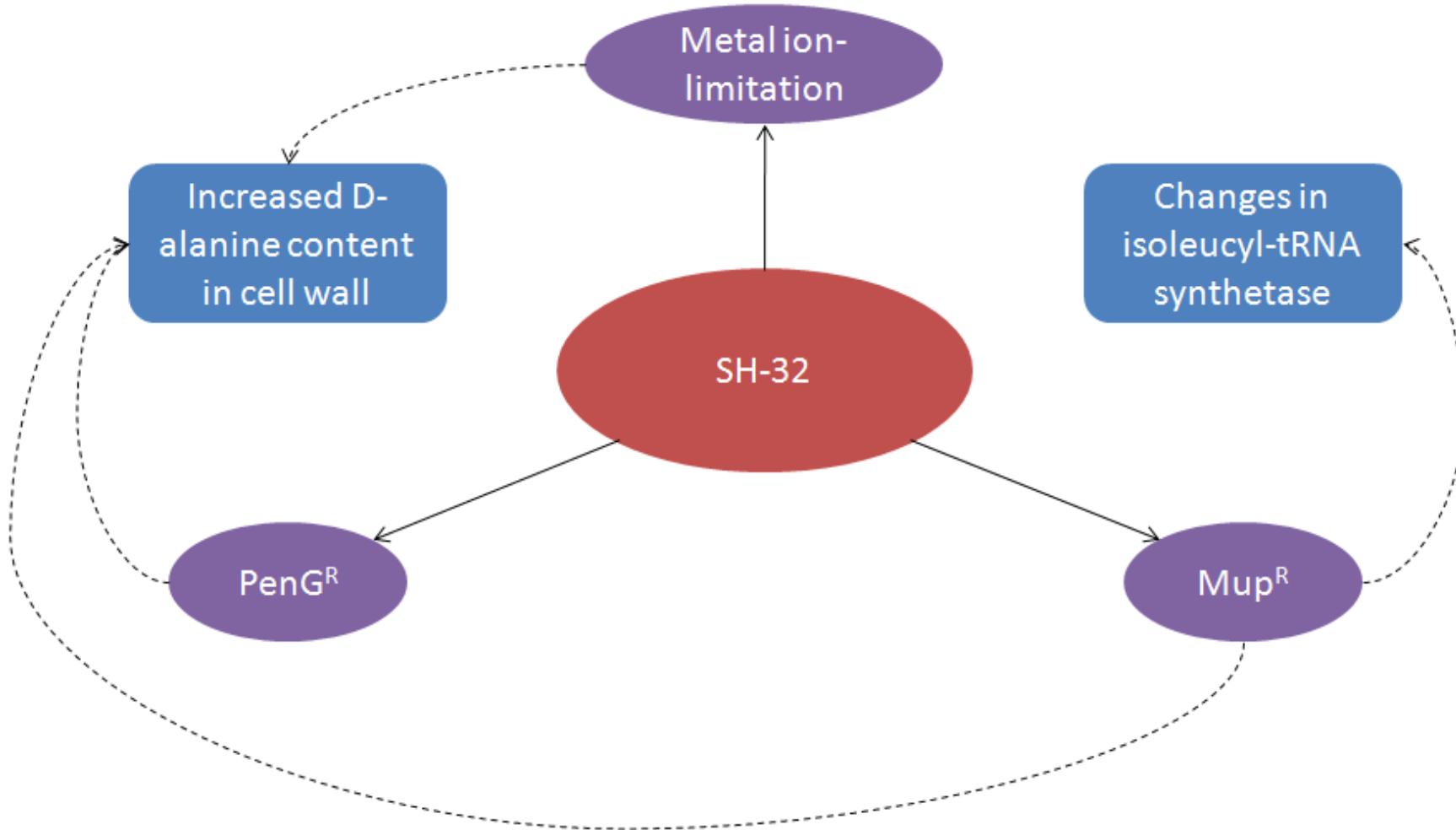


Figure 26. Phenotypic changes observed in SH-32 spontaneous mutant and proposed mechanisms of those changes. Purple indicates the observed phenotypic change. Arrows with dotted lines pointing to blue indicates the proposed mechanism.

While few changes were observed in the spontaneous mutants used in this study, a key point can be gleaned from analysis of SH-32. Based on the increased resistance to penicillin G and the decreased growth in metal ion limiting conditions, resistance to Ns β L may have induced changes in the D-alanine content of the cell wall. It is possible that this is the mechanism by which heteroresistance to mupirocin was caused, and that the primary target, isoleucyl-tRNA synthetase, was not affected by resistance to Ns β L.

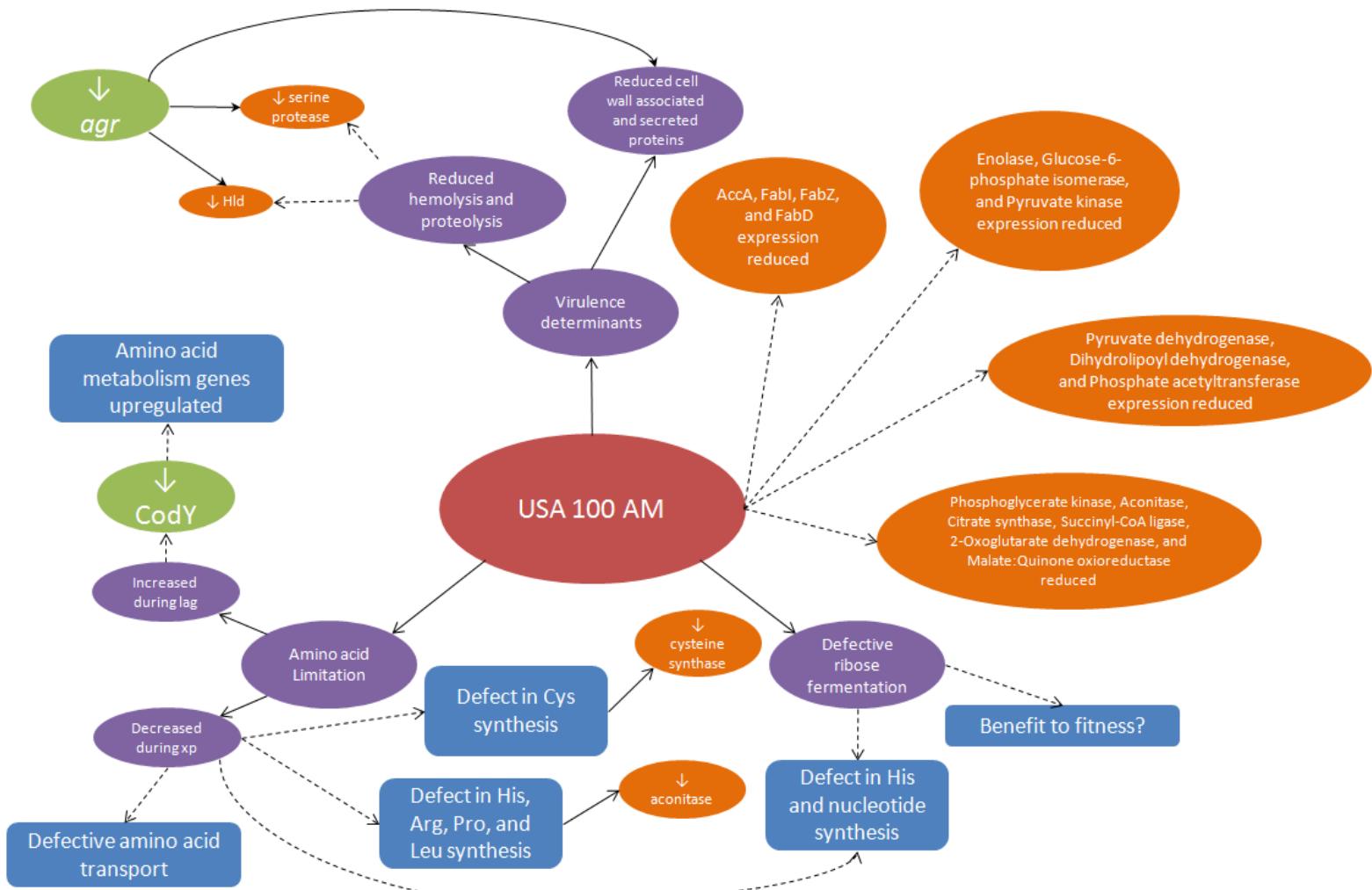


Figure 27. Phenotypic changes observed in USA 100 adaptive mutant (AM) and proposed mechanisms of those changes. Purple indicates the observed phenotypic change. Arrows with dotted lines pointing to blue indicates the proposed mechanism. Both green and orange indicate proteins observed by proteomic analysis.

Analysis of the comparative proteomics results for the USA 100 adaptive mutant was most insightful and indicates that those pathways reliant on CoA were significantly downregulated. While expression of FabH was not specifically reduced, the majority of proteins involved in fatty acid synthesis were found to be significantly reduced, as were glycolysis, pyruvate metabolism, and TCA cycle enzymes. This supports the conclusions made in previous studies that Ns β L has an effect on CoA⁹².

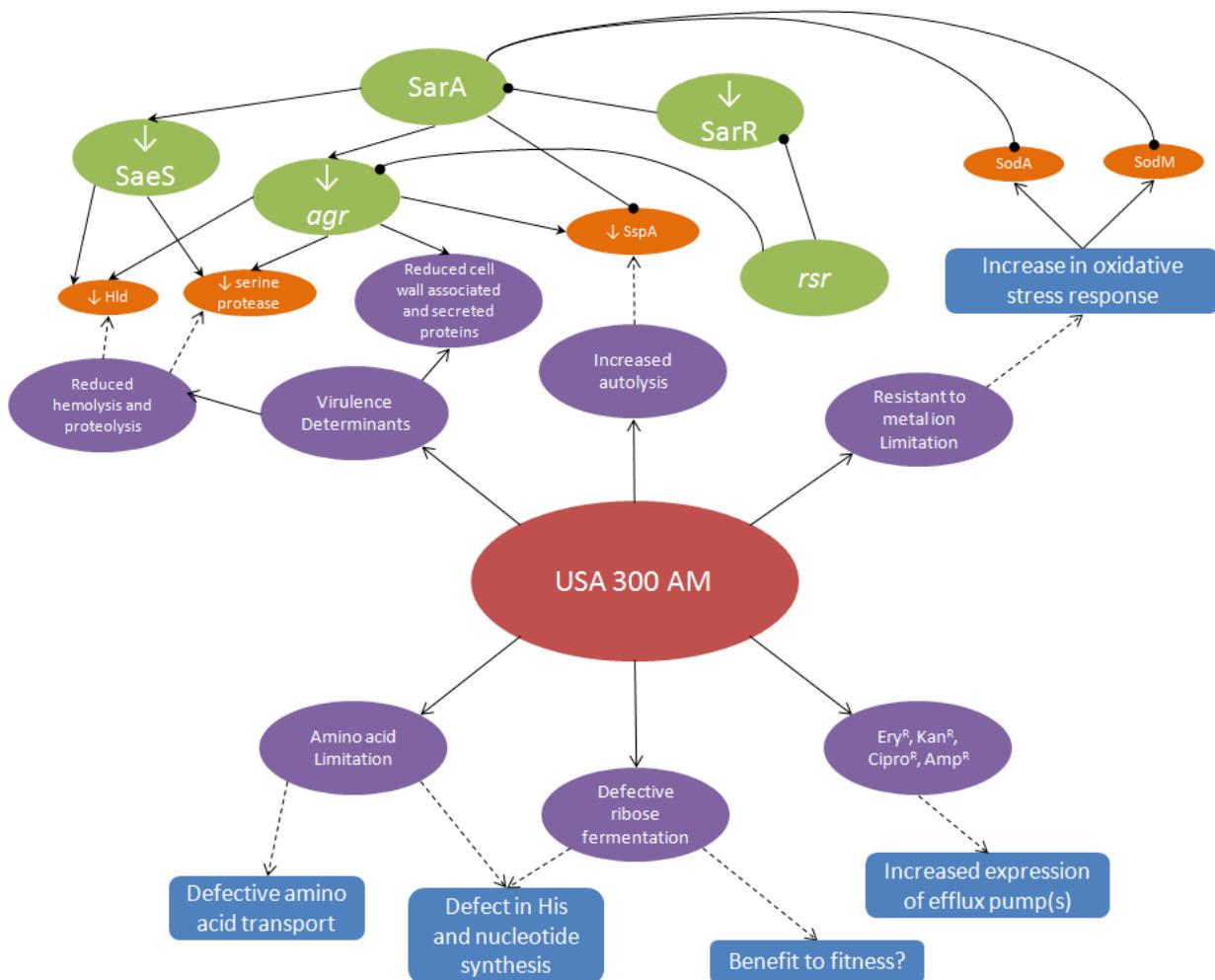


Figure 28. Phenotypic changes observed in USA 300 adaptive mutant and proposed mechanisms of those changes. Purple indicates the observed phenotypic change. Arrows with dotted lines pointing to blue indicates the proposed mechanism. Both green and orange indicate proteins observed by proteomic analysis. Green indicates regulators known to affect the indicated phenotype. Both green and orange indicate proteins observed by proteomic analysis, except for SarA and rsr. Lines with a blunt end indicate downregulation of that protein or gene.

The USA 300 adaptive mutant appears to have developed a number of alterations in its regulatory pathways. SarR expression was found to be reduced, while SarA expression was unaltered. Agr expression was also reduced, resulting in abridged expression of various virulence factors. Loss of *agr* and SarA activity has been shown to cause increased susceptibility to antimicrobials^{38, 83}; however, the USA 300 adaptive mutant displayed increased antimicrobial resistance in the disk diffusion assays. These regulatory changes may be secondary to the expression of a multi-drug efflux pump⁷⁰, conferring resistance to kanamycin, ampicillin, erythromycin, ciprofloxacin, and, ultimately, NsβL.

FUTURE DIRECTIONS

There are a number of experiments that could be performed to clarify the precise mechanisms of resistance exhibited by the spontaneous and adaptive mutants. First and foremost, further analysis of the intracellular proteome would allow for statistically significant data. SH-11 and SH-32 could also be evaluated by the same process, particularly as phenotypic analysis did not show dramatic changes. It would also be beneficial to perform whole-genome sequencing of the Ns β L-resistant mutants, to further pinpoint genetic changes leading to resistance. This would be further confirmed by introducing similar changes into a clean wild-type strain and observing if there were the expected changes in resistance to Ns β L. A straightforward experiment that could be performed is measurement of the efflux activity of the USA 300 adaptive mutant towards Ns β L, which would confirm if this was its primary mode of resistance, as hypothesized. Complementation of any clean *S. aureus* strain with a coaABCDE overexpression vector could help determine if Ns β L actually targets CoA by monitoring growth for changes in the Ns β L MIC as compared to the wild-type strain.

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APPENDICES

Appendix A. Chemically-defined media.

| | | | |
|------------------------|-----------------------|------------------------|-----------------------|
| L-glutamic acid | 4.44 gL ⁻¹ | L-histidine | 0.88 gL ⁻¹ |
| L-aspartic acid | 4.44 gL ⁻¹ | L-valine | 0.88 gL ⁻¹ |
| L-proline | 4.44 gL ⁻¹ | L-arginine | 0.66 gL ⁻¹ |
| Glycine | 4.44 gL ⁻¹ | L-cysteine | 0.44 gL ⁻¹ |
| L-threonine | 4.44 gL ⁻¹ | L-phenylalanine | 0.38 gL ⁻¹ |
| L-serine | 4.44 gL ⁻¹ | L-tyrosine | 0.34 gL ⁻¹ |
| L-alanine | 4.44 gL ⁻¹ | L-methionine | 0.34 gL ⁻¹ |
| L-lysine HCl | 1.12 gL ⁻¹ | L-tryptophan | 0.12 gL ⁻¹ |
| L-isoleucine | 1.12 gL ⁻¹ | | |

Table A1. CL1. Autoclave and store at -20°C.

| | |
|--------------------------------------|---------------------|
| Na₂HPO₄ | 70 gL ⁻¹ |
| KH₂PO₄ | 30 gL ⁻¹ |

Table A2. CL2. Autoclave and store at 4°C.

| | |
|------------------------|--------------------|
| Adenine sulfate | 2 gL ⁻¹ |
| Guanine HCl | 2 gL ⁻¹ |

Table A3. CL3. Make up in 0.1M HCl. Autoclave and store at 4°C.

| | | | |
|---------------------------|----------------------|-----------------------|-----------------------|
| Pyridoxal | 0.4 gL ⁻¹ | Nicotinic acid | 0.2 gL ⁻¹ |
| Pyridoxamine HCl | 0.4 gL ⁻¹ | Thiamine HCl | 0.2 gL ⁻¹ |
| D-pantothenic acid | 0.2 gL ⁻¹ | Biotin | 0.01 gL ⁻¹ |
| Riboflavin | 0.2 gL ⁻¹ | | |

Table A4. CL4. Add 10g Chelex-100 and stir for 4 hours before filter sterilizing. Store at 4°C.

| | | | |
|------------------------|------------------------|--------------------------------------|------------------------|
| L-aspartic acid | 2.14 gL ⁻¹ | L-methionine | 1.43 gL ⁻¹ |
| L-alanine | 1.43 gL ⁻¹ | L-phenylalanine | 1.43 gL ⁻¹ |
| L-arginine | 1.43 gL ⁻¹ | L-proline | 2.14 gL ⁻¹ |
| L-cysteine | 0.714 gL ⁻¹ | L-serine | 1.43 gL ⁻¹ |
| Glycine | 1.43 gL ⁻¹ | L-threonine | 2.14 gL ⁻¹ |
| L-glutamic acid | 2.14 gL ⁻¹ | L-tryptophan | 1.43 gL ⁻¹ |
| L-histidine | 1.43 gL ⁻¹ | L-tyrosine | 1.43 gL ⁻¹ |
| L-isoleucine | 2.14 gL ⁻¹ | L-valine | 2.14 gL ⁻¹ |
| L-lysine HCl | 1.43 gL ⁻¹ | Na₂HPO₄ | 50 gL ⁻¹ |
| L-leucine | 2.14 gL ⁻¹ | KH₂PO₄ | 21.43 gL ⁻¹ |

Table A5. CDM1. Autoclave and store at -20°C.

| | | | |
|--------------------------|-------------------------|-----------------------|------------------------|
| Biotin | 0.001 gL^{-1} | Riboflavin | 0.02 gL^{-1} |
| D-pantthenic acid | 0.02 gL^{-1} | Nicotinic acid | 0.02 gL^{-1} |
| Pyridoxal | 0.04 gL^{-1} | Thiamine HCl | 0.02 gL^{-1} |
| Pyridoxamine HCl | 0.04 gL^{-1} | | |

Table A6. CDM2. Filter sterilize and store at 4°C.

| | |
|-----------------|-----------------------|
| Adenine sulfate | 0.4 gL^{-1} |
| Guanine HCl | 0.4 gL^{-1} |

Table A7. CDM3. Make up in 0.1M HCl. Autoclave and store at 4°C.

| | |
|--|----------------------|
| CaCl₂·6H₂O | 10 gL^{-1} |
| MnSO₄ | 5 gL^{-1} |
| FeNH₄(SO₄)₂·12H₂O | 6 gL^{-1} |

Table A8. CDM4. Make up in 0.1M HCl. Autoclave and store at room temperature.

| | |
|---|-----------------------|
| Glucose | 100 gL^{-1} |
| MgSO₄·7H₂O | 5g |

Table A9. CDM 5. Autoclave and store at room temperature.

Appendix B. Complete proteomics data.

| # | Identified Proteins (85) | Accession Number | Fold Change from WT | | Average Fold Change |
|----|--|---------------------|---------------------|---------------|---------------------|
| 37 | SA0295 protein OS=Staphylococcus aureus (strain N315) GN=SA0295 PE=4 SV=1 | Q7A7Q2 Q7A7Q2_STAAN | -4.2 | Value Missing | -4.2 |
| 40 | Ferritin OS=Staphylococcus aureus (strain N315) GN=ftnA PE=1 SV=1 | Q7A4R2 FTN_STAAN | -2.9 | -3.1 | -3 |
| 64 | Chaperone protein hchA OS=Staphylococcus aureus (strain N315) GN=hchA PE=1 SV=1 | P64313 HCHA_STAAN | -2.9 | -2.6 | -2.75 |
| 65 | Aspartate carbamoyltransferase OS=Staphylococcus aureus (strain N315) GN=pyrB PE=1 SV=1 | P65618 PYRB_STAAN | -2.5 | -2.8 | -2.65 |
| 47 | Phosphate acetyltransferase OS=Staphylococcus aureus (strain N315) GN=pta PE=1 SV=1 | P99092 PTA_STAAN | -2.7 | -2.5 | -2.6 |
| 73 | Phosphoglycerate kinase OS=Staphylococcus aureus (strain N315) GN=pgk PE=1 SV=1 | P99135 PGK_STAAN | -2.6 | -2.6 | -2.6 |
| 8 | L-lactate dehydrogenase 1 OS=Staphylococcus aureus (strain N315) GN=ldhA PE=1 SV=1 | P65256 LDH1_STAAN | -2.5 | -2.6 | -2.55 |
| 20 | Aconitate hydratase OS=Staphylococcus aureus (strain N315) GN=acnA PE=1 SV=1 | P99148 ACON_STAAN | -2.7 | -2.4 | -2.55 |
| 29 | 6-phosphogluconate dehydrogenase, decarboxylating OS=Staphylococcus aureus (strain N315) GN=gnd PE=1 SV=1 | P63334 6PGD_STAAN | -2.6 | -2.5 | -2.55 |
| 23 | ATP synthase subunit beta OS=Staphylococcus aureus (strain N315) GN=atpD PE=1 SV=1 | P99112 ATPB_STAAN | -2.6 | -2.4 | -2.5 |
| 32 | Phosphoribosylformylglycinamide synthase 1 OS=Staphylococcus aureus (strain N315) GN=purQ PE=1 SV=1 | P99166 PURQ_STAAN | -2.3 | -2.6 | -2.45 |
| 79 | Phosphoribosylaminoimidazole carboxylase ATPase subunit OS=Staphylococcus aureus (strain N315) GN=purK PE=1 SV=1 | Q7A695 PURK_STAAN | -2.3 | -2.5 | -2.4 |
| 52 | 50S ribosomal protein L18 OS=Staphylococcus aureus (strain N315) GN=rplR PE=1 SV=1 | Q7A467 RL18_STAAN | -2.3 | -2.3 | -2.3 |
| 74 | Seryl-tRNA synthetase OS=Staphylococcus aureus (strain N315) GN=serS PE=1 SV=1 | P99178 SYS_STAAN | -2.3 | -2.3 | -2.3 |
| 4 | Dihydrolipoyl dehydrogenase OS=Staphylococcus aureus (strain N315) GN=pdhD PE=1 SV=1 | P99084 DLDH_STAAN | -2.2 | -2.3 | -2.25 |
| 5 | Pyruvate dehydrogenase E1 component subunit beta OS=Staphylococcus aureus (strain N315) GN=pdhB PE=1 SV=1 | P99063 ODPB_STAAN | -2.1 | -2.4 | -2.25 |
| 61 | GTP-sensing transcriptional pleiotropic repressor codY OS=Staphylococcus aureus (strain N315) GN=codY PE=1 SV=1 | P63844 CODY_STAAN | -2.2 | -2.2 | -2.2 |
| 15 | Enolase OS=Staphylococcus aureus (strain N315) GN=eno PE=1 SV=1 | P99088 ENO_STAAN | -2 | -2.3 | -2.15 |
| 25 | 30S ribosomal protein S9 OS=Staphylococcus aureus (strain N315) GN=rpsI PE=1 SV=1 | P66646 RS9_STAAN | -2 | -2.2 | -2.1 |

| | | | | | |
|----|---|---------------------|------|------|--------------|
| 76 | Citrate synthase II OS=Staphylococcus aureus (strain N315) GN=citZ PE=1 SV=1 | Q7A561 Q7A561_STAAN | -2.2 | -2 | -2.1 |
| 62 | Cysteine synthase OS=Staphylococcus aureus (strain N315) GN=cysK PE=1 SV=1 | P63871 CYSK_STAAN | -2.1 | -2 | -2.05 |
| 75 | Putative uncharacterized protein SA1528 OS=Staphylococcus aureus (strain N315) GN=SA1528 PE=4 SV=1 | Q7A553 Q7A553_STAAN | -2.1 | -2 | -2.05 |
| 70 | Superoxide dismutase [Mn/Fe] 1 OS=Staphylococcus aureus (strain N315) GN=sodA PE=1 SV=1 | P99098 SODM1_STAAN | -1.8 | -2.1 | -1.95 |
| 45 | DNA-binding protein HU OS=Staphylococcus aureus (strain N315) GN=hup PE=1 SV=1 | Q7A5J1 DBH_STAAN | -1.8 | -1.9 | -1.85 |
| 24 | Glucose-6-phosphate isomerase OS=Staphylococcus aureus (strain N315) GN=pgi PE=1 SV=1 | P99078 G6PI_STAAN | -1.7 | -1.9 | -1.8 |
| 28 | 30S ribosomal protein S1 OS=Staphylococcus aureus (strain N315) GN=rpsA PE=1 SV=1 | Q7A5J0 RS1_STAAN | -1.7 | -1.8 | -1.75 |
| 18 | Succinyl-CoA ligase [ADP-forming] subunit alpha OS=Staphylococcus aureus (strain N315) GN=sucD PE=1 SV=1 | P99070 SUCD_STAAN | -1.8 | -1.6 | -1.7 |
| 82 | NADH dehydrogenase-like protein SA0802 OS=Staphylococcus aureus (strain N315) GN=SA0802 PE=1 SV=1 | Q7A6J4 Y802_STAAN | -1.7 | -1.7 | -1.7 |
| 17 | Catalase OS=Staphylococcus aureus (strain N315) GN=katA PE=1 SV=2 | Q7A5T2 CATA_STAAN | -1.4 | -1.9 | -1.65 |
| 35 | Pyruvate kinase OS=Staphylococcus aureus (strain N315) GN=pyk PE=1 SV=1 | Q7A559 KPYK_STAAN | -1.6 | -1.6 | -1.6 |
| 43 | SA2119 protein OS=Staphylococcus aureus (strain N315) GN=SA2119 PE=1 SV=1 | Q7A3Z5 Q7A3Z5_STAAN | -1.6 | -1.6 | -1.6 |
| 66 | 30S ribosomal protein S10 OS=Staphylococcus aureus (strain N315) GN=rpsJ PE=1 SV=1 | P66334 RS10_STAAN | -1.5 | -1.7 | -1.6 |
| 81 | NAD-specific glutamate dehydrogenase OS=Staphylococcus aureus (strain N315) GN=gluD PE=1 SV=1 | Q7A6H8 DHE2_STAAN | -1.8 | -1.4 | -1.6 |
| 6 | Probable malate:quinone oxidoreductase 2 OS=Staphylococcus aureus (strain N315) GN=mqo2 PE=1 SV=1 | P99115 MQO2_STAAN | -1.6 | -1.5 | -1.55 |
| 9 | Alkaline shock protein 23 OS=Staphylococcus aureus (strain N315) GN=asp23 PE=1 SV=1 | P99157 ASP23_STAAN | -1.5 | -1.6 | -1.55 |
| 57 | Dihydrolipooyllysine-residue succinyltransferase component of 2-oxoglutarate dehydrogenase complex OS=Staphylococcus aureus (strain N315) GN=odhB PE=1 SV=1 | Q7A5N4 ODO2_STAAN | -1.6 | -1.5 | -1.55 |
| 50 | Alkyl hydroperoxide reductase subunit F OS=Staphylococcus aureus (strain N315) GN=ahpF PE=1 SV=1 | P99118 AHPF_STAAN | -1.7 | -1.4 | -1.55 |
| 10 | Inosine-5'-monophosphate dehydrogenase OS=Staphylococcus aureus (strain N315) GN=guAB PE=1 SV=1 | P99106 IMDH_STAAN | -1.5 | -1.5 | -1.5 |
| 19 | Glutamine synthetase OS=Staphylococcus aureus (strain N315) GN=glnA PE=1 SV=1 | P99095 GLNA_STAAN | -1.5 | -1.5 | -1.5 |
| 21 | 50S ribosomal protein L13 OS=Staphylococcus aureus (strain N315) GN=rplM PE=1 SV=1 | Q7A473 RL13_STAAN | -1.4 | -1.6 | -1.5 |

| | | | | | |
|----|---|-----------------------------------|------|------|--------------|
| 34 | Q7A3N7 RANDOM_Q7A3N7_STAAN-R | Q7A3N7 RANDOM_Q7A3N7_STAAN-R (+2) | -1.4 | -1.4 | -1.4 |
| 48 | DNA polymerase III subunit beta OS=Staphylococcus aureus (strain N315) GN=dnaN PE=1 SV=1 | P99103 DPO3B_STAAN | -1.4 | -1.4 | -1.4 |
| 58 | NADPH-dependent oxidoreductase OS=Staphylococcus aureus (strain N315) GN=nfrA PE=3 SV=1 | Q7A7J0 RANDOM_NFRA_STAAN-R | -1.4 | -1.4 | -1.4 |
| 59 | 50S ribosomal protein L11 OS=Staphylococcus aureus (strain N315) GN=rplK PE=1 SV=2 | P0A0F2 RL11_STAAN | -1.3 | -1.5 | -1.4 |
| 2 | Glyceraldehyde-3-phosphate dehydrogenase 1 OS=Staphylococcus aureus (strain N315) GN=gapA1 PE=1 SV=1 | P99136 G3P1_STAAN | -1.4 | -1.3 | -1.35 |
| 13 | 50S ribosomal protein L1 OS=Staphylococcus aureus (strain N315) GN=rplA PE=1 SV=1 | Q99W68 RL1_STAAN | -1.3 | -1.4 | -1.35 |
| 1 | Elongation factor Tu OS=Staphylococcus aureus (strain N315) GN=tuf PE=1 SV=1 | P99152 EFTU_STAAN | -1.3 | -1.3 | -1.3 |
| 22 | 50S ribosomal protein L22 OS=Staphylococcus aureus (strain N315) GN=rplV PE=1 SV=1 | Q7A460 RL22_STAAN | -1.4 | -1.2 | -1.3 |
| 53 | Adenylosuccinate lyase OS=Staphylococcus aureus (strain N315) GN=purB PE=1 SV=1 | Q7A4Q3 PUR8_STAAN | -1.2 | -1.4 | -1.3 |
| 7 | Alkyl hydroperoxide reductase subunit C OS=Staphylococcus aureus (strain N315) GN=ahpC PE=1 SV=1 | P99074 AHPC_STAAN | -1.3 | -1.2 | -1.25 |
| 11 | 50S ribosomal protein L2 OS=Staphylococcus aureus (strain N315) GN=rplB PE=1 SV=1 | P60432 RL2_STAAN | -1.2 | -1.3 | -1.25 |
| 69 | D-alanine aminotransferase OS=Staphylococcus aureus (strain N315) GN=dat PE=1 SV=1 | P99090 DAAA_STAAN | -1.3 | -1.2 | -1.25 |
| 42 | DNA-directed RNA polymerase subunit beta' OS=Staphylococcus aureus (strain N315) GN=rpoC PE=1 SV=1 | P60285 RPOC_STAAN | -1.3 | -1.1 | -1.2 |
| 77 | SA1224 protein OS=Staphylococcus aureus (strain N315) GN=SA1224 PE=4 SV=1 | Q7A5Q0 Q7A5Q0_STAAN | -1.2 | -1.2 | -1.2 |
| 3 | Elongation factor G OS=Staphylococcus aureus (strain N315) GN=fusA PE=1 SV=2 | P68789 EFG_STAAN | -1.2 | -1.1 | -1.15 |
| 12 | Cell division protein ftsZ OS=Staphylococcus aureus (strain N315) GN=ftsZ PE=1 SV=1 | P99108 FTSZ_STAAN | -1.1 | -1.2 | -1.15 |
| 36 | 50S ribosomal protein L21 OS=Staphylococcus aureus (strain N315) GN=rplU PE=1 SV=1 | Q7A583 RL21_STAAN | -1 | -1.1 | -1.05 |
| 51 | 50S ribosomal protein L14 OS=Staphylococcus aureus (strain N315) GN=rplN PE=1 SV=1 | Q7A463 RL14_STAAN | -1 | -1.1 | -1.05 |
| 72 | Glycyl-tRNA synthetase OS=Staphylococcus aureus (strain N315) GN=glyQS PE=1 SV=1 | P99129 SYG_STAAN | -0.9 | -1 | -0.95 |
| 33 | Aspartyl/glutamyl-tRNA(Asn/Gln) amidotransferase subunit B OS=Staphylococcus aureus (strain N315) GN=gatB PE=1 SV=1 | P99169 GATB_STAAN | -1 | -0.8 | -0.9 |
| 49 | ATP synthase subunit alpha OS=Staphylococcus aureus (strain N315) GN=atpA PE=1 SV=1 | P99111 ATPA_STAAN | -0.8 | -0.8 | -0.8 |

| | | | | | |
|----|---|---------------------|---------------|----------------------|--------------|
| 56 | DNA-directed RNA polymerase subunit beta OS=Staphylococcus aureus (strain N315) GN=rpoB PE=1 SV=1 | P60278 RPOB_STAAN | -0.8 | -0.8 | -0.8 |
| 16 | 30S ribosomal protein S2 OS=Staphylococcus aureus (strain N315) GN=rpsB PE=1 SV=1 | P66544 RS2_STAAN | -0.8 | -0.7 | -0.75 |
| 30 | 50S ribosomal protein L19 OS=Staphylococcus aureus (strain N315) GN=rplS PE=1 SV=1 | P66083 RL19_STAAN | -0.7 | -0.7 | -0.7 |
| 60 | Cell division protein ftsA OS=Staphylococcus aureus (strain N315) GN=ftsA PE=1 SV=1 | P63765 FTSA_STAAN | -0.6 | -0.8 | -0.7 |
| 14 | Serine hydroxymethyltransferase OS=Staphylococcus aureus (strain N315) GN=glyA PE=1 SV=1 | P99091 GLYA_STAAN | -0.7 | -0.5 | -0.6 |
| 26 | Bifunctional autolysin OS=Staphylococcus aureus (strain N315) GN=atl PE=1 SV=1 | Q99V41 ATL_STAAN | -0.4 | -0.4 | -0.4 |
| 27 | Uncharacterized protein SA0829 OS=Staphylococcus aureus (strain N315) GN=SA0829 PE=1 SV=1 | Q7A6H3 Y829_STAAN | No Values | No Values | |
| 31 | D-lactate dehydrogenase OS=Staphylococcus aureus (strain N315) GN=ldhD PE=1 SV=1 | P99116 LDHD_STAAN | No Values | No Values | |
| 38 | Q7A7W3 Q7A7W3_STAAN | Q7A7W3 Q7A7W3_STAAN | Value Missing | Value Missing | |
| 39 | ATP-dependent Clp protease ATP-binding subunit clpL OS=Staphylococcus aureus (strain N315) GN=clpL PE=1 SV=1 | Q7A3F4 CLPL_STAAN | No Values | No Values | |
| 41 | Phosphoribosylaminoimidazole-succinocarboxamide synthase OS=Staphylococcus aureus (strain N315) GN=purC PE=1 SV=1 | P99064 PUR7_STAAN | No Values | No Values | |
| 44 | 50S ribosomal protein L3 OS=Staphylococcus aureus (strain N315) GN=rplC PE=1 SV=1 | P60449 RL3_STAAN | No Values | No Values | |
| 46 | 50S ribosomal protein L6 OS=Staphylococcus aureus (strain N315) GN=rplF PE=1 SV=1 | Q7A466 RL6_STAAN | No Values | No Values | |
| 54 | Aerobic glycerol-3-phosphate dehydrogenase OS=Staphylococcus aureus (strain N315) GN=glpD PE=1 SV=2 | Q7A5V7 GLPD_STAAN | No Values | No Values | |
| 55 | 2-oxoglutarate dehydrogenase E1 component OS=Staphylococcus aureus (strain N315) GN=odhA PE=1 SV=1 | Q99U74 ODO1_STAAN | No Values | No Values | |
| 63 | (3R)-hydroxymyristoyl-[acyl-carrier-protein] dehydratase OS=Staphylococcus aureus (strain N315) GN=fabZ PE=3 SV=1 | P64108 FABZ_STAAN | No Values | No Values | |
| 67 | 30S ribosomal protein S5 OS=Staphylococcus aureus (strain N315) GN=rpsE PE=1 SV=1 | P66579 RS5_STAAN | Value Missing | Value Missing | |
| 68 | 1-pyrroline-5-carboxylate dehydrogenase OS=Staphylococcus aureus (strain N315) GN=rocA PE=1 SV=1 | P99076 ROCA_STAAN | No Values | No Values | |
| 71 | P99119 LDH2_STAAN | P99119 LDH2_STAAN | No Values | No Values | |
| 78 | Ribonuclease J 2 OS=Staphylococcus aureus (strain N315) GN=SA1118 PE=1 SV=1 | Q7A5X6 RNJ2_STAAN | No Values | No Values | |
| 80 | Naphthoate synthase OS=Staphylococcus aureus (strain N315) GN=menB PE=1 SV=1 | Q7A6A9 MENB_STAAN | No Values | No Values | |

| | | | | |
|----|--|----------------------------|---------------|----------------------|
| 83 | Formate acetyltransferase OS=Staphylococcus aureus (strain N315) GN=pflB PE=1 SV=1 | Q7A7X6 PFLB_STAAN | Value Missing | Value Missing |
| 84 | Pyruvate dehydrogenase E1 component subunit alpha OS=Staphylococcus aureus (strain N315) GN=pdhA PE=1 SV=1 | Q820A6 ODPA_STAAN | No Values | No Values |
| 85 | ATP-dependent Clp protease ATP-binding subunit clpC OS=Staphylococcus aureus (strain N315) GN=clpC PE=1 SV=1 | Q7A797 RANDOM_CLPC_STAAN-R | Value Missing | Value Missing |

Table A10. Complete list of intracellular proteins identified from the USA 100 adaptive mutant at 8 hours.

| # | Identified Proteins (66) | Accession Number | Fold Change from WT | | Average Fold Change |
|----|---|---------------------|---------------------|------|---------------------|
| 54 | Formate acetyltransferase OS=Staphylococcus aureus (strain USA300) GN=pflB PE=3 SV=1 | Q2FK44 PFLB_STAA3 | -2 | -2.6 | -2.3 |
| 18 | Alcohol dehydrogenase OS=Staphylococcus aureus (strain USA300) GN=adh PE=3 SV=1 | Q2FJ31 ADH_STAA3 | -2.1 | -1.9 | -2 |
| 24 | Aconitate hydratase OS=Staphylococcus aureus (strain USA300) GN=acnA PE=4 SV=1 | Q2FH85 Q2FH85_STAA3 | -1.3 | -1.1 | -1.2 |
| 9 | Formate--tetrahydrofolate ligase OS=Staphylococcus aureus (strain USA300) GN=fhs PE=3 SV=1 | Q2FG06 FTHS_STAA3 | -1.2 | -1.1 | -1.15 |
| 36 | Putative universal stress protein SAUSA300_1656 OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1656 PE=3 SV=1 | Q2FG28 Y1656_STAA3 | -1.2 | -1.1 | -1.15 |
| 65 | Pyruvate carboxylase OS=Staphylococcus aureus (strain USA300) GN=pyc PE=4 SV=1 | Q2FHW6 Q2FHW6_STAA3 | -1 | -0.8 | -0.9 |
| 52 | Cysteine synthase OS=Staphylococcus aureus (strain USA300) GN=cysK PE=3 SV=1 | Q2FJC8 Q2FJC8_STAA3 | -0.9 | -0.6 | -0.75 |
| 42 | Glucose-6-phosphate isomerase OS=Staphylococcus aureus (strain USA300) GN=pgi PE=3 SV=1 | Q2FIB3 G6PI_STAA3 | -0.7 | -0.7 | -0.7 |
| 56 | Phosphoenolpyruvate carboxykinase [ATP] OS=Staphylococcus aureus (strain USA300) GN=pckA PE=3 SV=1 | Q2FFV5 PCKA_STAA3 | -0.9 | -0.5 | -0.7 |
| 40 | Succinyl-CoA ligase [ADP-forming] subunit beta OS=Staphylococcus aureus (strain USA300) GN=sucC PE=3 SV=1 | Q2FHJ3 SUCC_STAA3 | -0.7 | -0.6 | -0.65 |
| 50 | 6-phosphogluconate dehydrogenase, decarboxylating OS=Staphylococcus aureus (strain USA300) GN=gnd PE=3 SV=1 | Q2FGM3 Q2FGM3_STAA3 | -0.7 | -0.5 | -0.6 |
| 62 | NAD-specific glutamate dehydrogenase OS=Staphylococcus aureus (strain USA300) GN=gudB PE=3 SV=1 | Q2FIB7 Q2FIB7_STAA3 | -0.7 | -0.5 | -0.6 |
| 32 | Succinyl-CoA ligase [ADP-forming] subunit alpha OS=Staphylococcus aureus (strain USA300) GN=sucD PE=3 SV=1 | Q2FHJ2 Q2FHJ2_STAA3 | -0.6 | -0.5 | -0.55 |
| 8 | Enolase OS=Staphylococcus aureus (strain USA300) GN=eno PE=3 SV=1 | Q2FIL7 ENO_STAA3 | -0.6 | -0.4 | -0.5 |
| 51 | Dihydrolipoamide acetyltransferase OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0995 PE=3 SV=1 | Q2FHY5 Q2FHY5_STAA3 | 0.2 | -1.1 | -0.45 |

| | | | | | |
|----|--|---------------------|------|------|--------------|
| 26 | Dihydrolipoyllysine-residue succinyltransferase component of 2-oxoglutarate dehydrogenase complex OS=Staphylococcus aureus (strain USA300) GN=odhB PE=3 SV=1 | Q2FH26 ODO2_STAA3 | -0.6 | -0.3 | -0.45 |
| 6 | Inosine-5'-monophosphate dehydrogenase OS=Staphylococcus aureus (strain USA300) GN=guAB PE=3 SV=1 | Q2FJM6 IMDH_STAA3 | -0.5 | -0.3 | -0.4 |
| 5 | Pyruvate dehydrogenase E1 component, beta subunit OS=Staphylococcus aureus (strain USA300) GN=pdhB PE=4 SV=1 | Q2FHY6 Q2FHY6_STAA3 | -0.4 | -0.3 | -0.35 |
| 43 | 30S ribosomal protein S1 OS=Staphylococcus aureus (strain USA300) GN=rpsA PE=4 SV=1 | Q2FGW6 Q2FGW6_STAA3 | -0.4 | -0.3 | -0.35 |
| 3 | Dihydrolipoyl dehydrogenase OS=Staphylococcus aureus (strain USA300) GN=lpdA PE=3 SV=1 | Q2FHY4 Q2FHY4_STAA3 | -0.3 | -0.2 | -0.25 |
| 14 | L-lactate dehydrogenase 1 OS=Staphylococcus aureus (strain USA300) GN=ldh1 PE=3 SV=2 | Q2FK29 LDH1_STAA3 | -0.3 | -0.2 | -0.25 |
| 23 | Catalase OS=Staphylococcus aureus (strain USA300) GN=katA PE=3 SV=1 | Q2FH99 CATA_STAA3 | -0.3 | -0.2 | -0.25 |
| 16 | Malate:quinone-oxidoreductase OS=Staphylococcus aureus (strain USA300) GN=mqo PE=3 SV=1 | Q2FDQ3 Q2FDQ3_STAA3 | -0.3 | -0.1 | -0.2 |
| 25 | Glutamine synthetase OS=Staphylococcus aureus (strain USA300) GN=glnA PE=3 SV=1 | Q2FHD0 Q2FHD0_STAA3 | -0.3 | -0.1 | -0.2 |
| 30 | Ferritin OS=Staphylococcus aureus (strain USA300) GN=ftnA PE=3 SV=1 | Q2FFK2 FTN_STAA3 | -0.3 | -0.1 | -0.2 |
| 47 | NADH dehydrogenase-like protein SAUSA300_0844 OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0844 PE=3 SV=1 | Q2FID4 Y844_STAA3 | -0.3 | 0 | -0.15 |
| 13 | Phosphoglycerate kinase OS=Staphylococcus aureus (strain USA300) GN=pgk PE=3 SV=1 | Q2FIM0 PGK_STAA3 | -0.2 | 0 | -0.1 |
| 46 | Bifunctional protein fold OS=Staphylococcus aureus (strain USA300) GN=fold PE=3 SV=1 | Q2FI15 FOLD_STAA3 | -0.2 | 0 | -0.1 |
| 66 | Isocitrate dehydrogenase [NADP] OS=Staphylococcus aureus (strain USA300) GN=icd PE=3 SV=1 | Q2FG43 Q2FG43_STAA3 | -0.1 | 0 | -0.05 |
| 39 | ATP synthase subunit beta OS=Staphylococcus aureus (strain USA300) GN=atpD PE=3 SV=1 | Q2FF24 ATPB_STAA3 | 0 | 0 | 0 |
| 20 | Pyruvate dehydrogenase E1 component, alpha subunit OS=Staphylococcus aureus (strain USA300) GN=pdhA PE=4 SV=1 | Q2FHY7 Q2FHY7_STAA3 | -0.1 | 0.1 | 0 |
| 33 | DNA-binding protein HU OS=Staphylococcus aureus (strain USA300) GN=hup PE=3 SV=1 | Q2FGW9 Q2FGW9_STAA3 | -0.1 | 0.1 | 0 |
| 34 | DNA-directed RNA polymerase subunit beta OS=Staphylococcus aureus (strain USA300) GN=rpoB PE=3 SV=2 | Q2FJ98 RPOB_STAA3 | -0.1 | 0.1 | 0 |
| 64 | Phosphoenolpyruvate-protein phosphotransferase OS=Staphylococcus aureus (strain USA300) GN=ptsI PE=3 SV=1 | Q2FHZ6 Q2FHZ6_STAA3 | -0.1 | 0.3 | 0.1 |
| 4 | Glyceraldehyde-3-phosphate dehydrogenase, type I OS=Staphylococcus aureus (strain USA300) GN=gap PE=3 SV=1 | Q2FIM1 Q2FIM1_STAA3 | 0 | 0.2 | 0.1 |
| 38 | GTP-sensing transcriptional pleiotropic repressor codY OS=Staphylococcus aureus (strain USA300) GN=codY PE=3 SV=1 | Q2FHI3 CODY_STAA3 | 0 | 0.2 | 0.1 |

| | | | | | |
|----|--|---------------------|-----|-----|-------------|
| 12 | Pyruvate kinase OS=Staphylococcus aureus (strain USA300) GN=pyk PE=3 SV=1 | Q2FG40 KPYK_STAA3 | 0.1 | 0.2 | 0.15 |
| 63 | 30S ribosomal protein S9 OS=Staphylococcus aureus (strain USA300) GN=rpsI PE=3 SV=1 | Q2FES2 RS9_STAA3 | 0.1 | 0.2 | 0.15 |
| 11 | DNA-directed RNA polymerase subunit beta' OS=Staphylococcus aureus (strain USA300) GN=rpoC PE=3 SV=2 | Q2FJ97 RPOC_STAA3 | 0.1 | 0.3 | 0.2 |
| 60 | DNA polymerase III, beta subunit OS=Staphylococcus aureus (strain USA300) GN=dnaN PE=3 SV=1 | Q2FKQ4 Q2FKQ4_STAA3 | 0.1 | 0.3 | 0.2 |
| 28 | 50S ribosomal protein L2 OS=Staphylococcus aureus (strain USA300) GN=rplB PE=3 SV=1 | Q2FEP2 RL2_STAA3 | 0.3 | 0.2 | 0.25 |
| 37 | Glycyl-tRNA synthetase OS=Staphylococcus aureus (strain USA300) GN=glyQS PE=3 SV=1 | Q2FGF8 SYG_STAA3 | 0.2 | 0.3 | 0.25 |
| 22 | Alkyl hydroperoxide reductase subunit C OS=Staphylococcus aureus (strain USA300) GN=ahpC PE=3 SV=1 | Q2FJN4 AHPC_STAA3 | 0.3 | 0.3 | 0.3 |
| 7 | Alkaline shock protein 23 OS=Staphylococcus aureus (strain USA300) GN=asp23 PE=3 SV=1 | Q2FEV0 ASP23_STAA3 | 0.2 | 0.4 | 0.3 |
| 2 | Elongation factor G OS=Staphylococcus aureus (strain USA300) GN=fusA PE=3 SV=3 | Q2FJ93 EFG_STAA3 | 0.3 | 0.4 | 0.35 |
| 48 | 50S ribosomal protein L14 OS=Staphylococcus aureus (strain USA300) GN=rplN PE=3 SV=1 | Q2FEP9 RL14_STAA3 | 0.4 | 0.4 | 0.4 |
| 55 | UPF0457 protein SAUSA300_2132 OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_2132 PE=3 SV=1 | Q2FEV9 Y2132_STAA3 | 0.4 | 0.4 | 0.4 |
| 31 | 30S ribosomal protein S5 OS=Staphylococcus aureus (strain USA300) GN=rpsE PE=3 SV=1 | Q2FEQ6 RS5_STAA3 | 0.3 | 0.5 | 0.4 |
| 19 | Transketolase OS=Staphylococcus aureus (strain USA300) GN=tkt PE=4 SV=1 | Q2FH92 Q2FH92_STAA3 | 0.4 | 0.5 | 0.45 |
| 53 | Alkyl hydroperoxide reductase, subunit F OS=Staphylococcus aureus (strain USA300) GN=ahpF PE=3 SV=1 | Q2FJN5 Q2FJN5_STAA3 | 0.4 | 0.6 | 0.5 |
| 21 | 50S ribosomal protein L1 OS=Staphylococcus aureus (strain USA300) GN=rplA PE=3 SV=1 | Q2FJA2 RL1_STAA3 | 0.5 | 0.6 | 0.55 |
| 57 | 50S ribosomal protein L13 OS=Staphylococcus aureus (strain USA300) GN=rplM PE=3 SV=1 | Q2FES1 RL13_STAA3 | 0.4 | 0.7 | 0.55 |
| 27 | 50S ribosomal protein L3 OS=Staphylococcus aureus (strain USA300) GN=rplC PE=3 SV=1 | Q2FEN9 RL3_STAA3 | 0.5 | 0.7 | 0.6 |
| 1 | Elongation factor Tu OS=Staphylococcus aureus (strain USA300) GN=tuf PE=3 SV=1 | Q2FJ92 EFTU_STAA3 | 0.6 | 0.7 | 0.65 |
| 15 | Cell division protein ftsZ OS=Staphylococcus aureus (strain USA300) GN=ftsZ PE=3 SV=1 | Q2FHQ1 Q2FHQ1_STAA3 | 0.6 | 0.7 | 0.65 |
| 17 | Serine hydroxymethyltransferase OS=Staphylococcus aureus (strain USA300) GN=glyA PE=3 SV=1 | Q2FF15 GLYA_STAA3 | 0.6 | 0.7 | 0.65 |
| 35 | D-lactate dehydrogenase OS=Staphylococcus aureus (strain USA300) GN=ddh PE=3 SV=1 | Q2FDY1 Q2FDY1_STAA3 | 0.6 | 0.9 | 0.75 |

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|----|---|---------------------|---------------|---------------|-------------|
| 49 | ATP synthase subunit alpha OS=Staphylococcus aureus (strain USA300) GN=atpA PE=3 SV=1 | Q2FF22 ATPA_STAA3 | 0.7 | 1 | 0.85 |
| 10 | Chaperone protein dnaK OS=Staphylococcus aureus (strain USA300) GN=dnaK PE=2 SV=1 | Q2FGE3 DNAK_STAA3 | 1 | 1.1 | 1.05 |
| 29 | 30S ribosomal protein S2 OS=Staphylococcus aureus (strain USA300) GN=rpsB PE=3 SV=1 | Q2FHI2 RS2_STAA3 | 1 | 1.1 | 1.05 |
| 61 | Probable transglycosylase isaA OS=Staphylococcus aureus (strain USA300) GN=isaA PE=3 SV=1 | Q2FDT8 ISAA_STAA3 | 1.2 | 1.7 | 1.45 |
| 41 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_2473 PE=4 SV=1 | Q2FDX1 Q2FDX1_STAA3 | 2.2 | 2.8 | 2.5 |
| 44 | 50S ribosomal protein L6 OS=Staphylococcus aureus (strain USA300) GN=rplF PE=3 SV=1 | Q2FEQ4 RL6_STAA3 | No Values | No Values | |
| 45 | Glucosamine--fructose-6-phosphate aminotransferase (Isomerizing) OS=Staphylococcus aureus (strain USA300) GN=gImS PE=3 SV=1 | Q2FEX8 Q2FEX8_STAA3 | No Values | No Values | |
| 59 | Transcription termination factor NusA OS=Staphylococcus aureus (strain USA300) GN=nusA PE=4 SV=1 | Q2FHH2 Q2FHH2_STAA3 | No Values | No Values | |
| 58 | Glyceraldehyde-3-phosphate dehydrogenase, type I OS=Staphylococcus aureus (strain USA300) GN=gap PE=3 SV=1 | Q2FG50 Q2FG50_STAA3 | Value Missing | Value Missing | |

Table A11. Complete list of intracellular proteins identified from the USA 300 adaptive mutant at 8 hours.

| # | Identified Proteins (796) | Accession Number | Fold Change from WT |
|-----|---|---------------------|---------------------|
| 213 | Probable molybdate-binding protein OS=Staphylococcus aureus (strain N315) GN=modA PE=4 SV=1 | Q99RZ3 Q99RZ3_STAAN | -4.4 |
| 30 | Lipase 2 (lip2) | Q7A7P2 LIP2_STAAN | -3.7 |
| 161 | Phosphoribosylaminoimidazole-succinocarboxamide synthase OS=Staphylococcus aureus (strain N315) GN=purC PE=1 SV=1 | P99064 PUR7_STAAN | -3.5 |
| 290 | ATP synthase subunit delta OS=Staphylococcus aureus (strain N315) GN=atpH PE=1 SV=1 | P99109 ATPD_STAAN | -3.5 |
| 251 | Seryl-tRNA synthetase OS=Staphylococcus aureus (strain N315) GN=serS PE=1 SV=1 | P99178 SYS_STAAN | -3.3 |
| 318 | SA0916 protein OS=Staphylococcus aureus (strain N315) GN=SA0916 PE=1 SV=1 | Q7A696 Q7A696_STAAN | -3.3 |
| 493 | Carbamate kinase 1 OS=Staphylococcus aureus (strain N315) GN=arcC1 PE=1 SV=1 | Q7A627 ARCC1_STAAN | -3.3 |
| 33 | Immunoglobulin-binding protein (sbi) | Q99RL2 SBL_STAAN | -3.2 |
| 248 | Bifunctional protein pyrR OS=Staphylococcus aureus (strain N315) GN=pyrR PE=1 SV=1 | P65944 PYRR_STAAN | -3.2 |
| 577 | PTS system glucoside-specific EIICBA component OS=Staphylococcus aureus (strain N315) GN=glcB PE=1 SV=1 | Q7A3G4 PTU3C_STAAN | -3.2 |
| 103 | Ferritin OS=Staphylococcus aureus (strain N315) GN=ftnA PE=1 SV=1 | Q7A4R2 FTN_STAAN | -3.1 |
| 114 | Phosphoribosylamine--glycine ligase OS=Staphylococcus aureus (strain N315) GN=purD PE=1 SV=1 | P65896 PUR2_STAAN | -3.1 |
| 167 | Deoxyribose-phosphate aldolase 2 OS=Staphylococcus aureus (strain N315) GN=deoC2 PE=1 SV=1 | P99174 DEOC2_STAAN | -3.1 |

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|-----|--|----------------------|------|
| 386 | SA0537 protein OS=Staphylococcus aureus (strain N315) GN=SA0537 PE=1 SV=1 | Q7A765 Q7A765_STAAN | -3.1 |
| 413 | UvrABC system protein A OS=Staphylococcus aureus (strain N315) GN=uvrA PE=1 SV=1 | P63383 UVRA_ST_AAN | -3.1 |
| 32 | Phosphoribosylformylglycinamide synthase 2 (purL) | P65901 PURL_ST_AAN | -3 |
| 49 | Dihydrolipoyllysine-residue acetyltransferase component of pyruvate dehydrogenase complex (pdhC) | P65636 ODP2_ST_AAN | -3 |
| 106 | L-lactate dehydrogenase 1 OS=Staphylococcus aureus (strain N315) GN=ldhA PE=1 SV=1 | P65256 LDH1_ST_AAN | -3 |
| 199 | PTS system glucose-specific EIICBA component OS=Staphylococcus aureus (strain N315) GN=ptsG PE=1 SV=1 | Q7A807 PTG3C_S_TAAN | -3 |
| 282 | SA0243 protein OS=Staphylococcus aureus (strain N315) GN=SA0243 PE=4 SV=1 | Q7A7V2 Q7A7V2_STAAN | -3 |
| 320 | Putative uncharacterized protein SA2101 OS=Staphylococcus aureus (strain N315) GN=SA2101 PE=4 SV=1 | Q7A414 Q7A414_STAAN | -3 |
| 457 | Uncharacterized lipoprotein SA2158 OS=Staphylococcus aureus (strain N315) GN=SA2158 PE=1 SV=1 | Q7A3W5 Y2158_S_TAAN | -3 |
| 84 | Bifunctional purine biosynthesis protein purH (purH) | P67544 PUR9_STAAN | -2.9 |
| 100 | Ornithine aminotransferase 2 OS=Staphylococcus aureus (strain N315) GN=rocD2 PE=1 SV=1 | P60298 OAT2_ST_AAN | -2.9 |
| 120 | Pyrimidine-nucleoside phosphorylase OS=Staphylococcus aureus (strain N315) GN=pdp PE=1 SV=2 | Q7A4D0 PDP_STAAN | -2.9 |
| 198 | Phosphoribosylaminoimidazole carboxylase ATPase subunit OS=Staphylococcus aureus (strain N315) GN=purK PE=1 SV=1 | Q7A695 PURK_ST_AAN | -2.9 |
| 264 | Probable malate:quinone oxidoreductase 1 OS=Staphylococcus aureus (strain N315) GN=mqo1 PE=1 SV=1 | P65422 MQO1_ST_AAN | -2.9 |
| 266 | Glutamate-1-semialdehyde 2,1-aminomutase 1 OS=Staphylococcus aureus (strain N315) GN=hemL1 PE=1 SV=1 | P99096 GSA1_ST_AAN | -2.9 |
| 324 | SA0248 protein OS=Staphylococcus aureus (strain N315) GN=SA0248 PE=4 SV=1 | Q7A7U7 Q7A7U7_STAAN | -2.9 |
| 419 | Tyrosyl-tRNA synthetase OS=Staphylococcus aureus (strain N315) GN=tyrS PE=1 SV=1 | Q7A537 SYY_STAAN | -2.9 |
| 9 | Probable malate:quinone oxidoreductase 2 (mqo2) | P99115 MQO2_ST_AAN | -2.8 |
| 16 | Dihydrolipoyl dehydrogenase (pdhD) | P99084 DLHD_ST_AAN | -2.8 |
| 34 | SA0587 protein (SA0587) | Q7A719 Q7A719_STAAN | -2.8 |
| 73 | Immunodominant staphylococcal antigen B (isaB) | Q7A377 ISAB_ST_AAN | -2.8 |
| 127 | Ribose-phosphate pyrophosphokinase OS=Staphylococcus aureus (strain N315) GN=prs PE=1 SV=1 | P65237 KPRS_ST_AAN | -2.8 |
| 221 | ATP synthase subunit b OS=Staphylococcus aureus (strain N315) GN=atpF PE=1 SV=1 | Q7A4E7 ATPF_ST_AAN | -2.8 |
| 253 | ATP synthase gamma chain OS=Staphylococcus aureus (strain N315) GN=atpG PE=1 SV=1 | Q7A4E8 ATPG_ST_AAN | -2.8 |
| 274 | SA2302 protein OS=Staphylococcus aureus (strain N315) GN=SA2302 PE=4 SV=1 | Q7A3I7 Q7A3I7_S_TAAN | -2.8 |
| 286 | 50S ribosomal protein L20 OS=Staphylococcus aureus (strain N315) GN=rplT PE=1 SV=1 | P66108 RL20_STAAN | -2.8 |
| 480 | Argininosuccinate synthase OS=Staphylococcus aureus (strain N315) GN=argG PE=3 SV=1 | P63645 ASSY_ST_AAN | -2.8 |
| 35 | 50S ribosomal protein L5 (rpIE) | Q7A465 RL5_STAAN | -2.7 |
| 56 | SA0295 protein (SA0295) | Q7A7Q2 Q7A7Q2_STAAN | -2.7 |
| 145 | L-lactate dehydrogenase 2 OS=Staphylococcus aureus (strain N315) GN=idhB PE=1 | P99119 LDH2_ST | -2.7 |

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|-----|--|----------------------|------|
| | SV=1 | AAN | |
| 307 | Putative uncharacterized protein SA0618 OS=Staphylococcus aureus (strain N315) GN=SA0618 PE=4 SV=1 | Q7A6Z0 Q7A6Z0_STAAN | -2.7 |
| 326 | Putative uncharacterized protein SAS081 OS=Staphylococcus aureus (strain N315) GN=SA2054.1 PE=4 SV=1 | Q7A450 Q7A450_STAAN | -2.7 |
| 387 | DNA topoisomerase 4 subunit A OS=Staphylococcus aureus (strain N315) GN=parC PE=1 SV=1 | Q93KF4 PARC_ST_AAN | -2.7 |
| 394 | Putative uncharacterized protein SA2171 OS=Staphylococcus aureus (strain N315) GN=SA2171 PE=4 SV=1 | Q7A3V3 Q7A3V3_STAAN | -2.7 |
| 406 | D-alanine--poly(phosphoribitol) ligase subunit 2 OS=Staphylococcus aureus (strain N315) GN=dltC PE=3 SV=1 | P0A019 DLTC_ST_AAN | -2.7 |
| 462 | Ornithine carbamoyltransferase, catabolic OS=Staphylococcus aureus (strain N315) GN=arcB PE=1 SV=1 | P65602 OTCC_ST_AAN | -2.7 |
| 570 | Putative uncharacterized protein SA1649 OS=Staphylococcus aureus (strain N315) GN=SA1649 PE=4 SV=1 | Q7A4W5 Q7A4W5_STAAN | -2.7 |
| 632 | Branched-chain alpha-keto acid dehydrogenase E1 OS=Staphylococcus aureus (strain N315) GN=bfmBAA PE=4 SV=1 | Q7A5F7 Q7A5F7_STAAN | -2.7 |
| 38 | Carbamoyl-phosphate synthase large chain (carB) | P63740 CARB_ST_AAN | -2.6 |
| 71 | NADH dehydrogenase-like protein SA0802 (SA0802) | Q7A6J4 Y802_ST_AAN | -2.6 |
| 146 | 50S ribosomal protein L14 OS=Staphylococcus aureus (strain N315) GN=rplN PE=1 SV=1 | Q7A463 RL14_ST_AAN | -2.6 |
| 162 | SA1224 protein OS=Staphylococcus aureus (strain N315) GN=SA1224 PE=4 SV=1 | Q7A5Q0 Q7A5Q0_STAAN | -2.6 |
| 183 | GTPase obg OS=Staphylococcus aureus (strain N315) GN=obg PE=1 SV=1 | Q7A584 OBG_ST_AAN | -2.6 |
| 197 | 2,3-bisphosphoglycerate-independent phosphoglycerate mutase OS=Staphylococcus aureus (strain N315) GN=gpmI PE=1 SV=1 | P64270 GPMI_ST_AAN | -2.6 |
| 334 | SA0589 protein OS=Staphylococcus aureus (strain N315) GN=SA0589 PE=4 SV=1 | Q7A717 Q7A717_STAAN | -2.6 |
| 347 | Glycerol kinase OS=Staphylococcus aureus (strain N315) GN=glpK PE=1 SV=1 | P99113 GLPK_ST_AAN | -2.6 |
| 441 | SA1606 protein OS=Staphylococcus aureus (strain N315) GN=SA1606 PE=1 SV=1 | Q7A4Z8 Q7A4Z8_STAAN | -2.6 |
| 455 | Phosphoribosylformylglycinamide synthase 1 OS=Staphylococcus aureus (strain N315) GN=purQ PE=1 SV=1 | P99166 PURQ_ST_AAN | -2.6 |
| 612 | Putative uncharacterized protein SA0637 OS=Staphylococcus aureus (strain N315) GN=SA0637 PE=4 SV=1 | Q7A6X4 Q7A6X4_STAAN | -2.6 |
| 729 | SA0682 protein OS=Staphylococcus aureus (strain N315) GN=SA0682 PE=3 SV=1 | Q7A6T5 Q7A6T5_STAAN | -2.6 |
| 44 | D-lactate dehydrogenase (ldhD) | P99116 LDHD_ST_AAN | -2.5 |
| 94 | Asparaginyl-tRNA synthetase OS=Staphylococcus aureus (strain N315) GN=asnS PE=1 SV=1 | P67572 SYN_STA_AN | -2.5 |
| 279 | GTP-binding protein engA OS=Staphylococcus aureus (strain N315) GN=engA PE=1 SV=1 | P64060 ENGA_ST_AAN | -2.5 |
| 364 | SA1989 protein OS=Staphylococcus aureus (strain N315) GN=SA1989 PE=1 SV=1 | Q7A492 Q7A492_STAAN | -2.5 |
| 415 | SA1749 protein OS=Staphylococcus aureus (strain N315) GN=SA1749 PE=4 SV=1 | Q7A4N0 Q7A4N0_STAAN | -2.5 |
| 469 | Kanamycin nucleotidyltransferase OS=Staphylococcus aureus (strain N315) GN=aadD PE=4 SV=1 | Q7A8D0 Q7A8D0_STAAN | -2.5 |
| 477 | Protein-export membrane protein SecDF OS=Staphylococcus aureus (strain N315) GN=secF PE=4 SV=1 | Q7A586 Q7A586_STAAN | -2.5 |
| 617 | UPF0297 protein SA1445 OS=Staphylococcus aureus (strain N315) GN=SA1445 PE=1 SV=1 | P60359 Y1445_ST_AAN | -2.5 |
| 667 | Putative uncharacterized protein SA0814 OS=Staphylococcus aureus (strain N315) GN=SA0814 PE=4 SV=1 | Q7A6I2 Q7A6I2_S_TAAN | -2.5 |

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| 6 | Formate acetyltransferase (pflB) | Q7A7X6 PFLB_ST AAN | -2.4 |
| 53 | Protein translocase subunit secA 1 (secA1) | Q7A6R5 SECA1_S TAAN | -2.4 |
| 54 | ATP synthase subunit alpha (atpA) | P99111 ATPA_ST AAN | -2.4 |
| 66 | Probable quinol oxidase subunit 2 (qoxA) | Q7A698 QOX2_ST AAN | -2.4 |
| 116 | 50S ribosomal protein L19 OS=Staphylococcus aureus (strain N315) GN=rplS PE=1 SV=1 | P66083 RL19_STA AN | -2.4 |
| 139 | Phosphate acetyltransferase OS=Staphylococcus aureus (strain N315) GN=pta PE=1 SV=1 | P99092 PTA_STA AN | -2.4 |
| 340 | Putative uncharacterized protein SA0933 OS=Staphylococcus aureus (strain N315) GN=SA0933 PE=4 SV=1 | Q7A687 Q7A687_ STAAN | -2.4 |
| 356 | GTP pyrophosphokinase OS=Staphylococcus aureus (strain N315) GN=relA PE=1 SV=2 | Q99TL8 RELA_ST AAN | -2.4 |
| 450 | Virulence factor esxA OS=Staphylococcus aureus (strain N315) GN=esxA PE=1 SV=1 | ESXA_STAAN (+1) | -2.4 |
| 573 | Molybdopterin synthase sulfur carrier subunit OS=Staphylococcus aureus (strain N315) GN=moaD PE=1 SV=1 | Q7A441 MOAD_S TAAN | -2.4 |
| 631 | SA2201 protein OS=Staphylococcus aureus (strain N315) GN=SA2201 PE=3 SV=1 | Q7A3S5 Q7A3S5_ STAAN | -2.4 |
| 82 | Fructose-bisphosphate aldolase (fba) | P99075 ALF2_STA AN | -2.3 |
| 83 | PBP2 (pbp2) | Q7A5K8 Q7A5K8_ STAAN | -2.3 |
| 96 | 50S ribosomal protein L13 OS=Staphylococcus aureus (strain N315) GN=rplM PE=1 SV=1 | Q7A473 RL13_ST AAN | -2.3 |
| 137 | 2,3-bisphosphoglycerate-dependent phosphoglycerate mutase OS=Staphylococcus aureus (strain N315) GN=gpmA PE=1 SV=1 | P99153 GPMA_ST AAN | -2.3 |
| 140 | Probable catabolite control protein A OS=Staphylococcus aureus (strain N315) GN=ccpA PE=1 SV=1 | P99175 CCPA_ST AAN | -2.3 |
| 142 | N-acetylmuramoyl-L-alanine amidase sle1 OS=Staphylococcus aureus (strain N315) GN=sle1 PE=1 SV=1 | Q7A7E0 SLE1_ST AAN | -2.3 |
| 220 | Acetoin(diacetyl) reductase OS=Staphylococcus aureus (strain N315) GN=butA PE=1 SV=1 | P99120 BUTA_ST AAN | -2.3 |
| 223 | Ffh protein OS=Staphylococcus aureus (strain N315) GN=ffh PE=4 SV=1 | Q7A5Z0 Q7A5Z0_ STAAN | -2.3 |
| 332 | DNA polymerase I OS=Staphylococcus aureus (strain N315) GN=polA PE=3 SV=1 | Q7A565 Q7A565_ STAAN | -2.3 |
| 363 | DegV domain-containing protein SA1258 OS=Staphylococcus aureus (strain N315) GN=SA1258 PE=1 SV=1 | P67371 Y1258_ST AAN | -2.3 |
| 384 | Putative uncharacterized protein SA1933 OS=Staphylococcus aureus (strain N315) GN=SA1933 PE=4 SV=1 | Q7A4D3 Q7A4D3_ STAAN | -2.3 |
| 393 | Carbamoyl-phosphate synthase small chain OS=Staphylococcus aureus (strain N315) GN=carA PE=1 SV=1 | P99147 CARA_ST AAN | -2.3 |
| 420 | 50S ribosomal protein L24 OS=Staphylococcus aureus (strain N315) GN=rplX PE=1 SV=1 | P60735 RL24_STA AN | -2.3 |
| 491 | Amidophosphoribosyltransferase OS=Staphylococcus aureus (strain N315) GN=purF PE=1 SV=1 | P99164 PUR1_STA AN | -2.3 |
| 506 | Glycerol-3-phosphate dehydrogenase [NAD(P)+] OS=Staphylococcus aureus (strain N315) GN=gpsA PE=1 SV=1 | P64191 GPDA_ST AAN | -2.3 |
| 621 | Putative uncharacterized protein SA1168 OS=Staphylococcus aureus (strain N315) GN=SA1168 PE=4 SV=1 | Q7A5T3 Q7A5T3_ STAAN | -2.3 |
| 785 | Ribonuclease 3 OS=Staphylococcus aureus (strain N315) GN=rnc PE=1 SV=1 | P66668 RNC_STA AN | -2.3 |
| 18 | ATP synthase subunit beta (atpD) | P99112 ATPB_ST AAN | -2.2 |
| 40 | Aconitate hydratase (acnA) | P99148 ACON_ST | -2.2 |

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| 51 | 50S ribosomal protein L1 (rplA) | Q99W68 RL1_STA AN | -2.2 |
| 69 | 50S ribosomal protein L6 (rplF) | Q7A466 RL6_STA AN | -2.2 |
| 77 | Glucose-6-phosphate isomerase (pgi) | P99078 G6PI_STA AN | -2.2 |
| 92 | Succinate dehydrogenase flavoprotein subunit OS=Staphylococcus aureus (strain N315) GN=sdhA PE=4 SV=1 | Q7A642 Q7A642_ STAAN | -2.2 |
| 104 | Formate--tetrahydrofolate ligase OS=Staphylococcus aureus (strain N315) GN=fhs PE=1 SV=1 | Q7A535 FTHS_ST AAN | -2.2 |
| 105 | Aerobic glycerol-3-phosphate dehydrogenase OS=Staphylococcus aureus (strain N315) GN=glpD PE=1 SV=2 | Q7A5V7 GLPD_S TAAN | -2.2 |
| 115 | Threonyl-tRNA synthetase OS=Staphylococcus aureus (strain N315) GN=thrS PE=1 SV=1 | P67585 SYT_STA AN | -2.2 |
| 130 | 50S ribosomal protein L22 OS=Staphylococcus aureus (strain N315) GN=rplV PE=1 SV=1 | Q7A460 RL22_ST AAN | -2.2 |
| 141 | NAD-specific glutamate dehydrogenase OS=Staphylococcus aureus (strain N315) GN=gluD PE=1 SV=1 | Q7A6H8 DHE2_ST AAN | -2.2 |
| 156 | Transcription termination-antitermination factor OS=Staphylococcus aureus (strain N315) GN=nusA PE=4 SV=1 | Q7A5Y2 Q7A5Y2_ STAAN | -2.2 |
| 157 | 50S ribosomal protein L4 OS=Staphylococcus aureus (strain N315) GN=rplD PE=1 SV=1 | P61059 RL4_STA AN | -2.2 |
| 180 | Adenylosuccinate lyase OS=Staphylococcus aureus (strain N315) GN=purB PE=1 SV=1 | Q7A4Q3 PUR8_ST AAN | -2.2 |
| 196 | SA1599 protein OS=Staphylococcus aureus (strain N315) GN=SA1599 PE=4 SV=1 | Q7A501 Q7A501_ STAAN | -2.2 |
| 205 | HTH-type transcriptional regulator mgrA OS=Staphylococcus aureus (strain N315) GN=mgrA PE=1 SV=3 | Q7A6X2 MGRA_S TAAN | -2.2 |
| 230 | UPF0355 protein SA0372 OS=Staphylococcus aureus (strain N315) GN=SA0372 PE=1 SV=1 | Q7A7I6 UP355_ST AAN | -2.2 |
| 247 | ATP-dependent Clp protease ATP-binding subunit clpX OS=Staphylococcus aureus (strain N315) GN=clpX PE=1 SV=1 | P63790 CLPX_ST AAN | -2.2 |
| 268 | Putative uncharacterized protein SA0633 OS=Staphylococcus aureus (strain N315) GN=SA0633 PE=4 SV=1 | Q7A6X7 Q7A6X7_ STAAN | -2.2 |
| 283 | Putative uncharacterized protein SA0919 OS=Staphylococcus aureus (strain N315) GN=SA0919 PE=4 SV=1 | Q7A694 Q7A694_ STAAN | -2.2 |
| 305 | Acetyl-coenzyme A carboxylase carboxyl transferase subunit alpha OS=Staphylococcus aureus (strain N315) GN=accA PE=1 SV=1 | Q7A558 ACCA_ST AAN | -2.2 |
| 333 | Putative uncharacterized protein SA1331 OS=Staphylococcus aureus (strain N315) GN=SA1331 PE=1 SV=1 | Q7A5H1 Q7A5H1_ STAAN | -2.2 |
| 362 | Serine-protein kinase rsbW OS=Staphylococcus aureus (strain N315) GN=rsbW PE=1 SV=1 | P0A0H7 RSBW_S TAAN | -2.2 |
| 411 | SA1585 protein OS=Staphylococcus aureus (strain N315) GN=SA1585 PE=4 SV=1 | Q7A512 Q7A512_ STAAN | -2.2 |
| 454 | Cytidylate kinase OS=Staphylococcus aureus (strain N315) GN=cmk PE=3 SV=1 | P63806 KCY_STA AN | -2.2 |
| 481 | Uncharacterized peptidase SA1530 OS=Staphylococcus aureus (strain N315) GN=SA1530 PE=1 SV=2 | Q7A552 Y1530_ST AAN | -2.2 |
| 519 | UPF0173 metal-dependent hydrolase SA1529 OS=Staphylococcus aureus (strain N315) GN=SA1529 PE=1 SV=1 | P99149 Y1529_ST AAN | -2.2 |
| 536 | SA0658 protein OS=Staphylococcus aureus (strain N315) GN=SA0658 PE=4 SV=1 | Q7A6V6 Q7A6V6_ STAAN | -2.2 |
| 598 | SA1450 protein OS=Staphylococcus aureus (strain N315) GN=SA1450 PE=4 SV=1 | Q7A595 Q7A595_ STAAN | -2.2 |
| 691 | UvrABC system protein B OS=Staphylococcus aureus (strain N315) GN=uvrB PE=1 SV=1 | P67425 UVRB_ST AAN | -2.2 |
| 718 | (3R)-hydroxymyristoyl-[acyl-carrier-protein] dehydratase OS=Staphylococcus aureus (strain N315) GN=fabZ PE=3 SV=1 | P64108 FABZ_ST AAN | -2.2 |

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| 7 | Penicillin binding protein 2 prime (mecA) | Q7A8C6 Q7A8C6_STAAN | -2.1 |
| 39 | 1-pyrroline-5-carboxylate dehydrogenase (rocA) | P99076 ROCA_STAAN | -2.1 |
| 50 | 30S ribosomal protein S5 (rpsE) | P66579 RS5_STAA_N | -2.1 |
| 65 | Transketolase (tkt) | P99161 TKT_STAAN | -2.1 |
| 68 | 30S ribosomal protein S11 (rpsK) | P66357 RS11_STAAN | -2.1 |
| 86 | Cell division protein (ftsA) | P63765 FTSA_STAAN | -2.1 |
| 88 | Translation initiation factor IF-2 (infB) | P65134 IF2_STAAN | -2.1 |
| 147 | Naphthoate synthase OS=Staphylococcus aureus (strain N315) GN=menB PE=1 SV=1 | Q7A6A9 MENB_STAAN | -2.1 |
| 159 | Uncharacterized protein SA1069 OS=Staphylococcus aureus (strain N315) GN=SA1069 PE=1 SV=1 | Q7A5Z4 Y1069_STAAN | -2.1 |
| 160 | Copper chaperone copZ OS=Staphylococcus aureus (strain N315) GN=copZ PE=1 SV=1 | Q7A3E5 COPZ_STAAN | -2.1 |
| 172 | SA0859 protein OS=Staphylococcus aureus (strain N315) GN=SA0859 PE=1 SV=1 | Q7A6E5 Q7A6E5_STAAN | -2.1 |
| 176 | 6-phosphofructokinase OS=Staphylococcus aureus (strain N315) GN=pfkA PE=1 SV=1 | P99165 K6PF_STAAN | -2.1 |
| 217 | 50S ribosomal protein L21 OS=Staphylococcus aureus (strain N315) GN=rplU PE=1 SV=1 | Q7A583 RL21_STAAN | -2.1 |
| 225 | Xanthine phosphoribosyltransferase OS=Staphylococcus aureus (strain N315) GN=xpt PE=1 SV=1 | Q7A7I5 XPT_STAAN | -2.1 |
| 276 | Trans-2-enoyl-ACP reductase OS=Staphylococcus aureus (strain N315) GN=fabI PE=4 SV=1 | Q7A6D8 Q7A6D8_STAAN | -2.1 |
| 299 | 30S ribosomal protein S18 OS=Staphylococcus aureus (strain N315) GN=rpsR PE=1 SV=1 | P66468 RS18_STAAN | -2.1 |
| 304 | Urocanate hydratase OS=Staphylococcus aureus (strain N315) GN=hutU PE=1 SV=1 | P67417 HUTU_STAAN | -2.1 |
| 350 | SA1969 protein OS=Staphylococcus aureus (strain N315) GN=SA1969 PE=4 SV=1 | Q7A4A8 Q7A4A8_STAAN | -2.1 |
| 369 | 30S ribosomal protein S17 OS=Staphylococcus aureus (strain N315) GN=rpsQ PE=1 SV=1 | Q7A462 RS17_STAAN | -2.1 |
| 379 | Putative uncharacterized protein SA2309 OS=Staphylococcus aureus (strain N315) GN=SA2309 PE=4 SV=1 | Q7A3I0 Q7A3I0_STAAN | -2.1 |
| 381 | Aminoacyltransferase femB OS=Staphylococcus aureus (strain N315) GN=femB PE=1 SV=1 | P0A0A7 FEMB_STAAN | -2.1 |
| 400 | SA0884 protein OS=Staphylococcus aureus (strain N315) GN=SA0884 PE=4 SV=1 | Q7A6C5 Q7A6C5_STAAN | -2.1 |
| 404 | Anti-sigma-B factor antagonist OS=Staphylococcus aureus (strain N315) GN=rsbV PE=1 SV=1 | P66838 RSBV_STAAN | -2.1 |
| 432 | SA1054 protein OS=Staphylococcus aureus (strain N315) GN=SA1054 PE=4 SV=1 | Q7A605 Q7A605_STAAN | -2.1 |
| 436 | Putative uncharacterized protein SAS053 OS=Staphylococcus aureus (strain N315) GN=SA1670.1 PE=4 SV=1 | Q7A4U6 Q7A4U6_STAAN | -2.1 |
| 488 | ATP-dependent DNA helicase perA OS=Staphylococcus aureus (strain N315) GN=perA PE=1 SV=1 | P64319 PCRA_STAAN | -2.1 |
| 496 | Putative uncharacterized protein SA1534 OS=Staphylococcus aureus (strain N315) GN=SA1534 PE=4 SV=1 | Q7A550 Q7A550_STAAN | -2.1 |
| 503 | Putative uncharacterized protein SA2247 OS=Staphylococcus aureus (strain N315) GN=SA2247 PE=4 SV=1 | Q7A3N9 Q7A3N9_STAAN | -2.1 |
| 563 | Probable ribokinase OS=Staphylococcus aureus (strain N315) GN=rbsK PE=3 SV=1 | Q7A7T7 Q7A7T7_STAAN | -2.1 |
| 640 | Putative uncharacterized protein SA1455 OS=Staphylococcus aureus (strain N315) | Q7A590 Q7A590_ | -2.1 |

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| | GN=SA1455 PE=4 SV=1 | STAAN | |
| 663 | Uridine kinase OS=Staphylococcus aureus (strain N315) GN=udk PE=1 SV=1 | P67411 URK_STA AN | -2.1 |
| 698 | P0A0I2 SECE_STAAN | P0A0I2 SECE_ST AAN | -2.1 |
| 26 | DNA-directed RNA polymerase subunit beta' (rpoC) | P60285 RPOC_ST AAN | -2 |
| 45 | Putative universal stress protein SA1532 (SA1532) | Q7A551 Y1532_ST AAN | -2 |
| 62 | ATP-dependent Clp protease ATP-binding subunit (clpL) | Q7A3F4 CLPL_ST AAN | -2 |
| 64 | Catalase (katA) | Q7A5T2 CATA_S TAAN | -2 |
| 107 | UPF0342 protein SA1663 OS=Staphylococcus aureus (strain N315) GN=SA1663 PE=1 SV=1 | Q7A4V3 Y1663_S TAAN | -2 |
| 164 | SA0351 protein OS=Staphylococcus aureus (strain N315) GN=SA0351 PE=4 SV=1 | Q7A7K4 Q7A7K4_ STAAN | -2 |
| 170 | Putative uncharacterized protein SA1607 OS=Staphylococcus aureus (strain N315) GN=SA1607 PE=4 SV=1 | Q7A4Z7 Q7A4Z7_ STAAN | -2 |
| 178 | UPF0356 protein SA0941 OS=Staphylococcus aureus (strain N315) GN=SA0941 PE=3 SV=2 | Q99V08 Y941_ST AAN | -2 |
| 208 | SA2119 protein OS=Staphylococcus aureus (strain N315) GN=SA2119 PE=1 SV=1 | Q7A3Z5_STAAN | -2 |
| 210 | Citrate synthase II OS=Staphylococcus aureus (strain N315) GN=citZ PE=1 SV=1 | Q7A561 Q7A561_ STAAN | -2 |
| 249 | 30S ribosomal protein S10 OS=Staphylococcus aureus (strain N315) GN=rpsJ PE=1 SV=1 | P66334 RS10_STA AN | -2 |
| 252 | Putative 2-hydroxyacid dehydrogenase SA2098 OS=Staphylococcus aureus (strain N315) GN=SA2098 PE=1 SV=1 | Q7A417 Y2098_ST AAN | -2 |
| 261 | Extracellular matrix protein-binding protein emp OS=Staphylococcus aureus (strain N315) GN=emp PE=1 SV=1 | Q7A6P4 EMP_ST AAN | -2 |
| 267 | SA1524 protein OS=Staphylococcus aureus (strain N315) GN=SA1524 PE=3 SV=1 | Q7A556 Q7A556_ STAAN | -2 |
| 308 | Uncharacterized oxidoreductase SA2266 OS=Staphylococcus aureus (strain N315) GN=SA2266 PE=1 SV=1 | Q7A3L9 Y2266_S TAAN | -2 |
| 309 | ATP-dependent protease ATPase subunit HslU OS=Staphylococcus aureus (strain N315) GN=hslU PE=1 SV=1 | P63797 HSLU_ST AAN | -2 |
| 313 | Putative phosphotransferase SA1392 OS=Staphylococcus aureus (strain N315) GN=SA1392 PE=3 SV=1 | P67200 Y1392_ST AAN | -2 |
| 316 | Uncharacterized epimerase/dehydratase SA0511 OS=Staphylococcus aureus (strain N315) GN=SA0511 PE=1 SV=1 | Q7A788 Y511_ST AAN | -2 |
| 342 | Uncharacterized N-acetyltransferase SA1019 OS=Staphylococcus aureus (strain N315) GN=SA1019 PE=1 SV=1 | Q99UT4 Y1019_S TAAN | -2 |
| 408 | Lipoyl synthase OS=Staphylococcus aureus (strain N315) GN=lipA PE=1 SV=1 | P65286 LIPA_STA AN | -2 |
| 486 | Putative uncharacterized protein SA0319 OS=Staphylococcus aureus (strain N315) GN=SA0319 PE=4 SV=1 | Q7A7N3 Q7A7N3_ STAAN | -2 |
| 495 | Glutathione peroxidase homolog BsaA OS=Staphylococcus aureus (strain N315) GN=bsaA PE=1 SV=1 | P99097 BSAA_ST AAN | -2 |
| 509 | Putative uncharacterized protein SA2143 OS=Staphylococcus aureus (strain N315) GN=SA2143 PE=4 SV=1 | Q7A3X9 Q7A3X9_ STAAN | -2 |
| 560 | Pyrimidine nucleoside transport protein OS=Staphylococcus aureus (strain N315) GN=nupC PE=4 SV=1 | Q7A7A0 Q7A7A0_ STAAN | -2 |
| 594 | 30S ribosomal protein S14 type Z OS=Staphylococcus aureus (strain N315) GN=rpsZ PE=3 SV=1 | P66412 RS14Z_ST AAN | -2 |
| 603 | SA1155 protein OS=Staphylococcus aureus (strain N315) GN=SA1155 PE=4 SV=1 | Q7A5U5 Q7A5U5_ STAAN | -2 |
| 645 | UPF0039 protein SA0906 OS=Staphylococcus aureus (strain N315) GN=SA0906 PE=3 SV=1 | P0A0M7 Y906_ST AAN | -2 |

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| 671 | SA2166 protein OS=Staphylococcus aureus (strain N315) GN=SA2166 PE=4 SV=1 | Q7A3V7 Q7A3V7_STAAN | -2 |
| 673 | SA0572 protein OS=Staphylococcus aureus (strain N315) GN=SA0572 PE=4 SV=1 | Q7A733 Q7A733_STAAN | -2 |
| 730 | Putative uncharacterized protein SA0626 OS=Staphylococcus aureus (strain N315) GN=SA0626 PE=4 SV=1 | Q7A6Y4 Q7A6Y4_STAAN | -2 |
| 12 | Pyruvate kinase (pyk) | Q7A559 KPYK_ST AAN | -1.9 |
| 23 | Cysteine synthase (cysK) | P63871 CYSK_ST AAN | -1.9 |
| 36 | Phosphoglycerate kinase (pgk) | P99135 PGK_STA AN | -1.9 |
| 47 | Pyruvate dehydrogenase E1 component subunit alpha (pdhA) | Q820A6 ODPA_ST AAN | -1.9 |
| 59 | 50S ribosomal protein L2 (rplB) | P60432 RL2_STA AN | -1.9 |
| 60 | Acetate kinase (ackA) | Q99TF2 ACKA_ST AAN | -1.9 |
| 67 | UPF0478 protein SA1560 (SA1560) | Q7A531 Y1560_ST AAN | -1.9 |
| 78 | Isocitrate dehydrogenase [NADP] (icd) | P99167 IDH_STA AN | -1.9 |
| 80 | DNA polymerase III subunit beta (dnan) | P99103 DPO3B_ST AAN | -1.9 |
| 85 | Putative aldehyde dehydrogenase SA1924 (SA1924) | Q7A4D8 ALD1_ST AAN | -1.9 |
| 93 | 30S ribosomal protein S7 OS=Staphylococcus aureus (strain N315) GN=rpsG PE=1 SV=1 | P66616 RS7_STAA N | -1.9 |
| 126 | 6-phosphogluconate dehydrogenase, decarboxylating OS=Staphylococcus aureus (strain N315) GN=gnd PE=1 SV=1 | P63334 6PGD_ST AAN | -1.9 |
| 128 | 30S ribosomal protein S13 OS=Staphylococcus aureus (strain N315) GN=rpsM PE=1 SV=1 | P66388 RS13_STA AN | -1.9 |
| 134 | Prolyl-tRNA synthetase OS=Staphylococcus aureus (strain N315) GN=proS PE=1 SV=1 | Q7A5Y3 SYP_STA AN | -1.9 |
| 138 | 30S ribosomal protein S12 OS=Staphylococcus aureus (strain N315) GN=rpsL PE=1 SV=1 | P0A0G8 RS12_ST AAN | -1.9 |
| 144 | 30S ribosomal protein S8 OS=Staphylococcus aureus (strain N315) GN=rpsH PE=1 SV=1 | P66630 RS8_STAA N | -1.9 |
| 151 | Phosphoglucomamine mutase OS=Staphylococcus aureus (strain N315) GN=glmM PE=1 SV=1 | P99087 GLMM_ST AAN | -1.9 |
| 171 | Putative dipeptidase SA1572 OS=Staphylococcus aureus (strain N315) GN=SA1572 PE=1 SV=1 | Q7A522 PEPVL_STAAN | -1.9 |
| 174 | Putative aldehyde dehydrogenase AldA OS=Staphylococcus aureus (strain N315) GN=aldA PE=1 SV=1 | Q7A825 ALDA_ST AAN | -1.9 |
| 188 | SA0959 protein OS=Staphylococcus aureus (strain N315) GN=SA0959 PE=4 SV=1 | Q7A671 Q7A671_STAAN | -1.9 |
| 204 | UPF0477 protein SA0873 OS=Staphylococcus aureus (strain N315) GN=SA0873 PE=1 SV=1 | Q7A6D4 Y873_ST AAN | -1.9 |
| 209 | 50S ribosomal protein L23 OS=Staphylococcus aureus (strain N315) GN=rplW PE=1 SV=1 | Q7A459 RL23_ST AAN | -1.9 |
| 214 | Succinate dehydrogenase iron-sulfur protein subunit OS=Staphylococcus aureus (strain N315) GN=sdhB PE=4 SV=1 | Q99UV7 Q99UV7_STAAN | -1.9 |
| 228 | Probable thiol peroxidase OS=Staphylococcus aureus (strain N315) GN=tpx PE=1 SV=1 | P99146 TPX_STA AN | -1.9 |
| 291 | SA1387 protein OS=Staphylococcus aureus (strain N315) GN=SA1387 PE=4 SV=1 | Q7A5D2 Q7A5D2_STAAN | -1.9 |
| 294 | Glucokinase OS=Staphylococcus aureus (strain N315) GN=glcK PE=4 SV=1 | Q7A5D8 Q7A5D8_STAAN | -1.9 |
| 306 | UPF0051 protein SA0778 OS=Staphylococcus aureus (strain N315) GN=SA0778 PE=1 | Q7A6L4 Y778_ST | -1.9 |

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| | SV=1 | AAN | |
| 322 | Transcriptional regulatory protein srrA OS=Staphylococcus aureus (strain N315) GN=srrA PE=1 SV=1 | Q7A5H6 SRRA_STAAN | -1.9 |
| 345 | GTP-binding protein era homolog OS=Staphylococcus aureus (strain N315) GN=era PE=1 SV=1 | P64085 ERA_STAAN | -1.9 |
| 360 | SA1548 protein OS=Staphylococcus aureus (strain N315) GN=SA1548 PE=4 SV=1 | Q7A539 Q7A539_STAAN | -1.9 |
| 377 | SA0317 protein OS=Staphylococcus aureus (strain N315) GN=SA0317 PE=4 SV=1 | Q7A7N5 Q7A7N5_STAAN | -1.9 |
| 378 | SA2202 protein OS=Staphylococcus aureus (strain N315) GN=SA2202 PE=4 SV=1 | Q99RL6 Q99RL6_STAAN | -1.9 |
| 391 | Methionyl-tRNA formyltransferase OS=Staphylococcus aureus (strain N315) GN=fmt PE=1 SV=1 | P99127 FMT_STAAN | -1.9 |
| 392 | Mannitol-1-phosphate 5-dehydrogenase OS=Staphylococcus aureus (strain N315) GN=mtlD PE=1 SV=1 | P99140 MTLD_STAAN | -1.9 |
| 399 | PhoH protein OS=Staphylococcus aureus (strain N315) GN=phoH PE=4 SV=1 | Q7A5C7 Q7A5C7_STAAN | -1.9 |
| 412 | Acetyl-CoA synthetase OS=Staphylococcus aureus (strain N315) GN=acsA PE=4 SV=1 | Q99TD1 Q99TD1_STAAN | -1.9 |
| 466 | Fructose specific permease OS=Staphylococcus aureus (strain N315) GN=fruA PE=4 SV=1 | Q7A6V9 Q7A6V9_STAAN | -1.9 |
| 475 | UDP-N-acetylglucosamine 1-carboxyvinyltransferase 2 OS=Staphylococcus aureus (strain N315) GN=murA2 PE=1 SV=1 | P65457 MURA2_STAAN | -1.9 |
| 485 | Putative uncharacterized protein SA1242 OS=Staphylococcus aureus (strain N315) GN=SA1242 PE=4 SV=1 | Q7A5N6 Q7A5N6_STAAN | -1.9 |
| 568 | Probable DNA-directed RNA polymerase subunit delta OS=Staphylococcus aureus (strain N315) GN=rpoE PE=1 SV=1 | P66715 RPOE_STAAN | -1.9 |
| 627 | 50S ribosomal protein L32 OS=Staphylococcus aureus (strain N315) GN=rpmF PE=1 SV=1 | P66210 RL32_STAAN | -1.9 |
| 629 | Dihydrofolate reductase OS=Staphylococcus aureus (strain N315) GN=folA PE=1 SV=2 | P99079 DYR_STAAN | -1.9 |
| 647 | 50S ribosomal protein L9 OS=Staphylococcus aureus (strain N315) GN=rplI PE=1 SV=1 | P66318 RL9_STAAN | -1.9 |
| 660 | Membrane-associated protein tcaA OS=Staphylococcus aureus (strain N315) GN=tcaA PE=2 SV=1 | Q7A3X6 TCAA_STAAN | -1.9 |
| 672 | Putative uncharacterized protein SA1068 OS=Staphylococcus aureus (strain N315) GN=SA1068 PE=4 SV=1 | Q7A5Z5 Q7A5Z5_STAAN | -1.9 |
| 687 | Putative uncharacterized protein SA1086 OS=Staphylococcus aureus (strain N315) GN=SA1086 PE=4 SV=1 | Q7A5Y9 Q7A5Y9_STAAN | -1.9 |
| 767 | Putative uncharacterized protein SA1062 OS=Staphylococcus aureus (strain N315) GN=SA1062 PE=4 SV=1 | Q7A5Z9 Q7A5Z9_STAAN | -1.9 |
| 1 | Elongation factor Tu (tuf) | P99152 EFTU_STAAN | -1.8 |
| 2 | Bifunctional autolysin (atl) | Q99V41 ATL_STAAN | -1.8 |
| 29 | Pyruvate dehydrogenase E1 component subunit beta (pdhB) | P99063 ODPB_STAAN | -1.8 |
| 48 | Aspartyl/glutamyl-tRNA(Asn/Gln) amidotransferase subunit B (gatB) | P99169 GATB_STAAN | -1.8 |
| 58 | Glutamyl-tRNA(Gln) amidotransferase subunit A (gatA) | P63489 GATA_STAAN | -1.8 |
| 75 | Ribonucleoside-diphosphate reductase (nrdE) | Q7A6T2 Q7A6T2_STAAN | -1.8 |
| 122 | SA1745 protein OS=Staphylococcus aureus (strain N315) GN=SA1745 PE=4 SV=1 | Q7A4N5 Q7A4N5_STAAN | -1.8 |
| 129 | DNA-directed RNA polymerase subunit alpha OS=Staphylococcus aureus (strain N315) GN=rpoA PE=1 SV=1 | P66706 RPOA_STAAN | -1.8 |
| 148 | Pyridoxal biosynthesis lyase pdxS OS=Staphylococcus aureus (strain N315) GN=pdxS PE=1 SV=1 | P60798 PDXS_STAAN | -1.8 |

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| 166 | Succinyl-CoA ligase [ADP-forming] subunit alpha OS=Staphylococcus aureus (strain N315) GN=sucD PE=1 SV=1 | P99070 SUCD_ST AAN | -1.8 |
| 179 | Glycine cleavage system H protein OS=Staphylococcus aureus (strain N315) GN=gcvH PE=1 SV=1 | P64214 GCSH_ST AAN | -1.8 |
| 219 | D-alanine aminotransferase OS=Staphylococcus aureus (strain N315) GN=dat PE=1 SV=1 | P99090 DAAA_ST AAN | -1.8 |
| 229 | 3-oxoacyl-[acyl-carrier-protein] synthase 2 OS=Staphylococcus aureus (strain N315) GN=fabF PE=1 SV=1 | Q7A6F8 FABF_ST AAN | -1.8 |
| 233 | Putative 8-amino-7-oxononanoate synthase/2-amino-3-ketobutyrate coenzyme A ligase OS=Staphylococcus aureus (strain N315) GN=SA0508 PE=1 SV=1 | P60120 BIKB_STA AN | -1.8 |
| 235 | D-alanine--poly(phosphoribitol) ligase subunit 1 OS=Staphylococcus aureus (strain N315) GN=dltA PE=1 SV=1 | P99107 DLTA_ST AAN | -1.8 |
| 241 | 30S ribosomal protein S6 OS=Staphylococcus aureus (strain N315) GN=rpsF PE=1 SV=1 | P99142 RS6_STA N | -1.8 |
| 245 | Uridylate kinase OS=Staphylococcus aureus (strain N315) GN=pyrH PE=1 SV=1 | P65936 PYRH_ST AAN | -1.8 |
| 257 | Chaperone protein hchA OS=Staphylococcus aureus (strain N315) GN=hchA PE=1 SV=1 | P64313 HCHA_ST AAN | -1.8 |
| 280 | CTP synthase OS=Staphylococcus aureus (strain N315) GN=pyrG PE=1 SV=1 | P99072 PYRG_ST AAN | -1.8 |
| 285 | D-alanine--D-alanine ligase OS=Staphylococcus aureus (strain N315) GN=dll PE=1 SV=1 | P63892 DDL_STA AN | -1.8 |
| 293 | Putative NAD(P)H nitroreductase SA2311 OS=Staphylococcus aureus (strain N315) GN=SA2311 PE=1 SV=1 | Q7A3H8 Y2311_S TAAN | -1.8 |
| 300 | 30S ribosomal protein S9 OS=Staphylococcus aureus (strain N315) GN=rpsI PE=1 SV=1 | P66646 RS9_STA N | -1.8 |
| 302 | 50S ribosomal protein L31 type B OS=Staphylococcus aureus (strain N315) GN=rpmE2 PE=1 SV=1 | P66196 RL31B_ST AAN | -1.8 |
| 311 | Imidazolonepropionase OS=Staphylococcus aureus (strain N315) GN=hutI PE=1 SV=1 | P64418 HUTI_STA N | -1.8 |
| 329 | 50S ribosomal protein L29 OS=Staphylococcus aureus (strain N315) GN=rpmC PE=1 SV=1 | P66173 RL29_STA N | -1.8 |
| 358 | Putative uncharacterized protein SA1657 OS=Staphylococcus aureus (strain N315) GN=SA1657 PE=4 SV=1 | Q7A4V9 Q7A4V9_ STAAN | -1.8 |
| 361 | PTS system EIIBC component SA0186 OS=Staphylococcus aureus (strain N315) GN=SA0186 PE=1 SV=1 | Q7A804 PTXBC_S TAAN | -1.8 |
| 366 | Ribonuclease J 2 OS=Staphylococcus aureus (strain N315) GN=SA1118 PE=1 SV=1 | Q7A5X6 R NJ2_ST AAN | -1.8 |
| 383 | Hypoxanthine-guanine phosphoribosyltransferase OS=Staphylococcus aureus (strain N315) GN=hpt PE=1 SV=1 | P99085 HPRT_ST AAN | -1.8 |
| 398 | 30S ribosomal protein S16 OS=Staphylococcus aureus (strain N315) GN=rpsP PE=1 SV=1 | P66440 RS16_STA N | -1.8 |
| 459 | Glutamate-1-semialdehyde 2,1-aminomutase 2 OS=Staphylococcus aureus (strain N315) GN=hemL2 PE=1 SV=1 | Q7A4T5 GSA2_ST AAN | -1.8 |
| 473 | Leucyl-tRNA synthetase OS=Staphylococcus aureus (strain N315) GN=leuS PE=1 SV=1 | P67513 SYL_STA N | -1.8 |
| 499 | 30S ribosomal protein S20 OS=Staphylococcus aureus (strain N315) GN=rpsT PE=1 SV=1 | Q7A5C0 RS20_ST AAN | -1.8 |
| 624 | Response regulator protein vraR OS=Staphylococcus aureus (strain N315) GN=vraR PE=1 SV=1 | Q7A4R9 VRAR_S TAAN | -1.8 |
| 652 | Protein nagD homolog OS=Staphylococcus aureus (strain N315) GN=nagD PE=3 SV=1 | Q7A6K4 NAGD_S TAAN | -1.8 |
| 701 | Putative uncharacterized protein SA1453 OS=Staphylococcus aureus (strain N315) GN=SA1453 PE=4 SV=1 | Q7A592 Q7A592_ STAAN | -1.8 |
| 17 | Protein map (map) | P69775 MAP1_ST AAN | -1.7 |
| 24 | Fructose-bisphosphate aldolase class 1 (fda) | P99117 ALF1_STA N | -1.7 |
| 42 | UPF0365 protein SA1402 (SA1402) | Q7A5C5 Y1402_S | -1.7 |

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| 57 | Uncharacterized protein SA0829 (SA0829) | Q7A6H3 Y829_ST AAN | -1.7 |
| 79 | Glutamine synthetase (glnA) | P99095 GLNA_ST AAN | -1.7 |
| 98 | 60 kDa chaperonin OS=Staphylococcus aureus (strain N315) GN=groL PE=1 SV=1 | P99083 CH60_STA AN | -1.7 |
| 99 | Triosephosphate isomerase OS=Staphylococcus aureus (strain N315) GN=tpiA PE=1 SV=1 | P99133 TPIS_STA AN | -1.7 |
| 101 | 50S ribosomal protein L10 OS=Staphylococcus aureus (strain N315) GN=rplJ PE=1 SV=1 | P99155 RL10_STA AN | -1.7 |
| 113 | Septation ring formation regulator ezra OS=Staphylococcus aureus (strain N315) GN=ezrA PE=1 SV=1 | P64003 EZRA_ST AAN | -1.7 |
| 119 | GTP-sensing transcriptional pleiotropic repressor codY OS=Staphylococcus aureus (strain N315) GN=codY PE=1 SV=1 | P63844 CODY_ST AAN | -1.7 |
| 143 | Protein recA OS=Staphylococcus aureus (strain N315) GN=recA PE=1 SV=1 | P68844 RECA_ST AAN | -1.7 |
| 149 | 50S ribosomal protein L7/L12 OS=Staphylococcus aureus (strain N315) GN=rplL PE=1 SV=1 | P99154 RL7_STA AN | -1.7 |
| 152 | Putative uncharacterized protein SA1986 OS=Staphylococcus aureus (strain N315) GN=SA1986 PE=4 SV=1 | Q7A493 Q7A493_ STAAN | -1.7 |
| 193 | Putative uncharacterized protein SA0359 OS=Staphylococcus aureus (strain N315) GN=SA0359 PE=4 SV=1 | Q7A7J8 Q7A7J8_S TAAN | -1.7 |
| 200 | Putative uncharacterized protein SA1528 OS=Staphylococcus aureus (strain N315) GN=SA1528 PE=4 SV=1 | Q7A553 Q7A553_ STAAN | -1.7 |
| 232 | Transcription antitermination protein nusG OS=Staphylococcus aureus (strain N315) GN=nusG PE=1 SV=1 | P0A096 NUSG_ST AAN | -1.7 |
| 236 | Glycerol phosphate lipoteichoic acid synthase OS=Staphylococcus aureus (strain N315) GN=ItaS PE=1 SV=1 | Q7A6U1 LTAS_ST AAN | -1.7 |
| 254 | Elastin-binding protein ebpS OS=Staphylococcus aureus (strain N315) GN=ebpS PE=1 SV=3 | Q7A516 EBPS_ST AAN | -1.7 |
| 263 | UDP-N-acetylglucosamine--D-glutamate ligase OS=Staphylococcus aureus (strain N315) GN=murD PE=1 SV=1 | P0A090 MURD_S TAAN | -1.7 |
| 270 | Arginyl-tRNA synthetase OS=Staphylococcus aureus (strain N315) GN=argS PE=1 SV=1 | Q99W05 SYR_ST AAN | -1.7 |
| 272 | Orotidine 5'-phosphate decarboxylase OS=Staphylococcus aureus (strain N315) GN=pyrF PE=1 SV=1 | P99145 PYRF_ST AAN | -1.7 |
| 277 | Alcohol-acetaldehyde dehydrogenase OS=Staphylococcus aureus (strain N315) GN=adhE PE=4 SV=1 | Q7A843 Q7A843_ STAAN | -1.7 |
| 317 | 50S ribosomal protein L17 OS=Staphylococcus aureus (strain N315) GN=rplQ PE=1 SV=1 | Q7A469 RL17_ST AAN | -1.7 |
| 390 | Translation initiation factor IF-3 OS=Staphylococcus aureus (strain N315) GN=infC PE=1 SV=1 | P65140 IF3_STAA N | -1.7 |
| 395 | Putative uncharacterized protein SA1946 OS=Staphylococcus aureus (strain N315) GN=SA1946 PE=1 SV=1 | Q7A4C4 Q7A4C4_ STAAN | -1.7 |
| 421 | SA1565 protein OS=Staphylococcus aureus (strain N315) GN=SA1565 PE=4 SV=1 | Q7A527 Q7A527_ STAAN | -1.7 |
| 433 | Cystathione gamma-synthase OS=Staphylococcus aureus (strain N315) GN=metB PE=3 SV=1 | Q99WE2 Q99WE2 _STAAN | -1.7 |
| 437 | Phosphate acyltransferase OS=Staphylococcus aureus (strain N315) GN=plsX PE=1 SV=1 | P65739 PLSX_STA AN | -1.7 |
| 446 | Putative uncharacterized protein SA1840 OS=Staphylococcus aureus (strain N315) GN=SA1840 PE=1 SV=1 | Q7A4J0 Q7A4J0_S TAAN | -1.7 |
| 500 | Ribosomal RNA small subunit methyltransferase H OS=Staphylococcus aureus (strain N315) GN=rsmH PE=1 SV=1 | P60392 RSMH_ST AAN | -1.7 |
| 514 | Putative uncharacterized protein SA0635 OS=Staphylococcus aureus (strain N315) GN=SA0635 PE=4 SV=1 | Q7A6X5 Q7A6X5_ STAAN | -1.7 |
| 555 | Putative uncharacterized protein SA1464 OS=Staphylococcus aureus (strain N315) GN=SA1464 PE=4 SV=1 | Q7A585 Q7A585_ STAAN | -1.7 |

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| 579 | SA0675 protein OS=Staphylococcus aureus (strain N315) GN=SA0675 PE=4 SV=1 | Q7A6U0 Q7A6U0_STAAN | -1.7 |
| 628 | tRNA modification GTPase mnmE OS=Staphylococcus aureus (strain N315) GN=mnmE PE=3 SV=1 | P66972 MNME_ST_AAN | -1.7 |
| 669 | Chaperone protein dnaJ OS=Staphylococcus aureus (strain N315) GN=dnaJ PE=1 SV=1 | P63971 DNAJ_ST_AAN | -1.7 |
| 11 | Cell division protein ftsZ (ftsZ) | P99108 FTSZ_STAAN | -1.6 |
| 27 | Staphylococcal secretory antigen (ssaA2) | Q7A423 SSAA2_S_TAAN | -1.6 |
| 72 | DNA-directed RNA polymerase subunit beta (rpoB) | P60278 RPOB_ST_AAN | -1.6 |
| 90 | Trigger factor OS=Staphylococcus aureus (strain N315) GN=tig PE=1 SV=1 | P99080 TIG_STAAN | -1.6 |
| 121 | Putative formate dehydrogenase SA2102 OS=Staphylococcus aureus (strain N315) GN=SA2102 PE=1 SV=1 | Q99RW4 FDHL_STAAN | -1.6 |
| 175 | Adenylosuccinate synthetase OS=Staphylococcus aureus (strain N315) GN=purA PE=1 SV=1 | P99099 PURA_ST_AAN | -1.6 |
| 181 | Putative uncharacterized protein SA1263 OS=Staphylococcus aureus (strain N315) GN=SA1263 PE=4 SV=1 | Q7A5M5 Q7A5M5_STAAN | -1.6 |
| 182 | UDP-N-acetylglucosamine 1-carboxyvinyltransferase 1 OS=Staphylococcus aureus (strain N315) GN=murA1 PE=1 SV=1 | P84058 MURA1_STAAN | -1.6 |
| 239 | Putative uncharacterized protein SA1743 OS=Staphylococcus aureus (strain N315) GN=SA1743 PE=1 SV=1 | Q7A4N7 Q7A4N7_STAAN | -1.6 |
| 242 | Chaperone protein clpB OS=Staphylococcus aureus (strain N315) GN=clpB PE=1 SV=1 | Q7A6G6 CLPB_ST_AAN | -1.6 |
| 281 | Thioredoxin reductase OS=Staphylococcus aureus (strain N315) GN=trxR PE=1 SV=1 | P99101 TRXB_ST_AAN | -1.6 |
| 298 | DNA gyrase subunit A OS=Staphylococcus aureus (strain N315) GN=gyrA PE=1 SV=1 | Q99XG5 GYRA_STAAN | -1.6 |
| 314 | Ribosome-recycling factor OS=Staphylococcus aureus (strain N315) GN=frr PE=1 SV=1 | P99130 RRF_STAAN | -1.6 |
| 328 | Putative septation protein spoVG OS=Staphylococcus aureus (strain N315) GN=spoVG PE=1 SV=2 | Q7A7B5 SP5G_ST_AAN | -1.6 |
| 365 | Aspartate semialdehyde dehydrogenase OS=Staphylococcus aureus (strain N315) GN=asd PE=3 SV=1 | Q7A5P8 Q7A5P8_STAAN | -1.6 |
| 397 | Branched-chain alpha-keto acid dehydrogenase E2 OS=Staphylococcus aureus (strain N315) GN=bmfBB PE=3 SV=1 | Q7A5F9 Q7A5F9_STAAN | -1.6 |
| 414 | 10 kDa chaperonin OS=Staphylococcus aureus (strain N315) GN=groS PE=1 SV=1 | P99104 CH10_STAAN | -1.6 |
| 470 | Putative uncharacterized protein SAS056 OS=Staphylococcus aureus (strain N315) GN=SA1738.1 PE=4 SV=1 | Q7A4P2 Q7A4P2_STAAN | -1.6 |
| 483 | Pyrroline-5-carboxylate reductase OS=Staphylococcus aureus (strain N315) GN=proC PE=1 SV=1 | Q7A5G8 P5CR_STAAN | -1.6 |
| 511 | Arginase OS=Staphylococcus aureus (strain N315) GN=arg PE=1 SV=1 | P60088 ARGI_STAAN | -1.6 |
| 539 | SA2056 protein OS=Staphylococcus aureus (strain N315) GN=SA2056 PE=4 SV=1 | Q7A448 Q7A448_STAAN | -1.6 |
| 540 | Menaquinone biosynthesis methyltransferase ubiE OS=Staphylococcus aureus (strain N315) GN=ubiE PE=1 SV=1 | P67062 UBIE_STAAN | -1.6 |
| 554 | 50S ribosomal protein L28 OS=Staphylococcus aureus (strain N315) GN=rpmB PE=3 SV=1 | P66153 RL28_STAAN | -1.6 |
| 585 | Uncharacterized protein SA1737 OS=Staphylococcus aureus (strain N315) GN=SA1737 PE=1 SV=1 | Q7A4P4 Y1737_STAAN | -1.6 |
| 593 | Single-stranded DNA-binding protein OS=Staphylococcus aureus (strain N315) GN=ssb PE=4 SV=1 | Q7A7K2_STAAN(+1) | -1.6 |
| 680 | Ribosome-binding factor A OS=Staphylococcus aureus (strain N315) GN=rbfA PE=1 SV=1 | P65967 RBFA_STAAN | -1.6 |
| 3 | Elongation factor G (fusA) | P68789 EFG_STA | -1.5 |

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| 10 | Inosine-5'-monophosphate dehydrogenase (guAB) | P99106 IMDH_ST AAN | -1.5 |
| 19 | Enolase (eno) | P99088 ENO_STA AN | -1.5 |
| 25 | 30S ribosomal protein S2 (rpsB) | P66544 RS2_STAA N | -1.5 |
| 28 | 30S ribosomal protein S3 (rpsC) | P66553 RS3_STAA N | -1.5 |
| 55 | Alkyl hydroperoxide reductase subunit C (ahpC) | P99074 AHPC_ST AAN | -1.5 |
| 74 | Phosphocarrier protein HPr (ptsH) | P99143 PTHP_STA AN | -1.5 |
| 76 | GMP synthase [glutamine-hydrolyzing] (guaA) | P99105 GUAA_ST AAN | -1.5 |
| 91 | Lysyl-tRNA synthetase OS=Staphylococcus aureus (strain N315) GN=lysS PE=1 SV=1 | P67610 SYK_STA AN | -1.5 |
| 102 | Probable branched-chain-amino-acid aminotransferase OS=Staphylococcus aureus (strain N315) GN=ilvE PE=1 SV=1 | P99138 ILVE_STA AN | -1.5 |
| 108 | 50S ribosomal protein L3 OS=Staphylococcus aureus (strain N315) GN=rplC PE=1 SV=1 | P60449 RL3_STA AN | -1.5 |
| 125 | Bifunctional protein fold OS=Staphylococcus aureus (strain N315) GN=fold PE=1 SV=1 | Q7A697 FOLD_ST AAN | -1.5 |
| 133 | Succinyl-CoA ligase [ADP-forming] subunit beta OS=Staphylococcus aureus (strain N315) GN=sucC PE=1 SV=1 | P99071 SUCC_ST AAN | -1.5 |
| 165 | UPF0133 protein SA0437 OS=Staphylococcus aureus (strain N315) GN=SA0437 PE=1 SV=1 | P99126 Y437_STA AN | -1.5 |
| 186 | S-adenosylmethionine synthase OS=Staphylococcus aureus (strain N315) GN=metK PE=1 SV=1 | P66767 METK_ST AAN | -1.5 |
| 195 | 50S ribosomal protein L18 OS=Staphylococcus aureus (strain N315) GN=rplR PE=1 SV=1 | Q7A467 RL18_ST AAN | -1.5 |
| 202 | Glyceraldehyde-3-phosphate dehydrogenase 2 OS=Staphylococcus aureus (strain N315) GN=gapA2 PE=1 SV=1 | P99067 G3P2_STA AN | -1.5 |
| 215 | Glutamyl-tRNA synthetase OS=Staphylococcus aureus (strain N315) GN=gltX PE=1 SV=1 | P99170 SYE_STA AN | -1.5 |
| 222 | Putative uncharacterized protein SA1661 OS=Staphylococcus aureus (strain N315) GN=SA1661 PE=4 SV=1 | Q7A4V5 Q7A4V5_ STAAN | -1.5 |
| 224 | Putative peptidyl-prolyl cis-trans isomerase OS=Staphylococcus aureus (strain N315) GN=SA0815 PE=1 SV=1 | Q7A6I1 PPI1_STA AN | -1.5 |
| 238 | Aspartyl-tRNA synthetase OS=Staphylococcus aureus (strain N315) GN=aspS PE=1 SV=1 | P67015 SYD_STA AN | -1.5 |
| 250 | Uracil phosphoribosyltransferase OS=Staphylococcus aureus (strain N315) GN=upp PE=1 SV=1 | P67396 UPP_STA AN | -1.5 |
| 258 | DNA gyrase subunit B OS=Staphylococcus aureus (strain N315) GN=gyrB PE=1 SV=2 | P66937 GYRB_ST AAN | -1.5 |
| 287 | 30S ribosomal protein S4 OS=Staphylococcus aureus (strain N315) GN=rpsD PE=1 SV=1 | P66563 RS4_STAA N | -1.5 |
| 327 | Putative uncharacterized protein SA1668 OS=Staphylococcus aureus (strain N315) GN=SA1668 PE=4 SV=1 | Q7A4U8 Q7A4U8_ STAAN | -1.5 |
| 335 | UDP-N-acetylmuramoyl-L-alanyl-D-glutamate--L-lysine ligase OS=Staphylococcus aureus (strain N315) GN=murE PE=1 SV=1 | P65480 MURE_ST AAN | -1.5 |
| 346 | Peptide methionine sulfoxide reductase msrA 2 OS=Staphylococcus aureus (strain N315) GN=msrA2 PE=1 SV=1 | P65446 MSRA2_S_ TAAN | -1.5 |
| 352 | SA1243 protein OS=Staphylococcus aureus (strain N315) GN=SA1243 PE=4 SV=1 | Q7A5N5 Q7A5N5_ STAAN | -1.5 |
| 374 | SA0758 protein OS=Staphylococcus aureus (strain N315) GN=SA0758 PE=4 SV=1 | Q7A6M7 Q7A6M7_ _STAAN | -1.5 |
| 401 | Mannitol-specific phosphotransferase enzyme IIA component OS=Staphylococcus aureus (strain N315) GN=mtlF PE=3 SV=2 | P0A0D8 PTMA_S TAAN | -1.5 |

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| 403 | Dephospho-CoA kinase OS=Staphylococcus aureus (strain N315) GN=coaE PE=1 SV=1 | P63831 COAE_ST AAN | -1.5 |
| 428 | UDP-N-acetylmuramoyl-tripeptide--D-alanyl-D-alanine ligase OS=Staphylococcus aureus (strain N315) GN=murF PE=3 SV=1 | Q7A4F9 Q7A4F9_STAAN | -1.5 |
| 449 | (Dimethylallyl)adenosine tRNA methylthiotransferase miaB OS=Staphylococcus aureus (strain N315) GN=miaB PE=1 SV=1 | Q7A5W3 MIAB_S TAAN | -1.5 |
| 508 | RNA polymerase sigma factor rpoD OS=Staphylococcus aureus (strain N315) GN=rpoD PE=1 SV=1 | Q99TT5 RPOD_ST AAN | -1.5 |
| 517 | Conserved virulence factor B OS=Staphylococcus aureus (strain N315) GN=cvfB PE=1 SV=1 | Q7A5Q1 CVFB_S TAAN | -1.5 |
| 557 | UPF0312 protein SA2479 OS=Staphylococcus aureus (strain N315) GN=SA2479 PE=1 SV=1 | Q7A339 Y2479_ST AAN | -1.5 |
| 699 | GMP reductase OS=Staphylococcus aureus (strain N315) GN=guAC PE=1 SV=1 | P60563 GUAC_ST AAN | -1.5 |
| 761 | Methicillin resistance mecR1 protein OS=Staphylococcus aureus (strain N315) GN=mecR1 PE=1 SV=1 | P0A0B0 MECR_S TAAN | -1.5 |
| 769 | SA0777 protein OS=Staphylococcus aureus (strain N315) GN=SA0777 PE=4 SV=1 | Q7A6L5 Q7A6L5_STAAN | -1.5 |
| 21 | Glyceraldehyde-3-phosphate dehydrogenase 1 (gapA1) | P99136 G3P1_STA AN | -1.4 |
| 109 | Phosphoenolpyruvate-protein phosphotransferase OS=Staphylococcus aureus (strain N315) GN=ptsI PE=1 SV=1 | Q99V14 PT1_STA AN | -1.4 |
| 110 | Putative uncharacterized protein SA1698 OS=Staphylococcus aureus (strain N315) GN=SA1698 PE=4 SV=1 | Q7A4S0 Q7A4S0_STAAN | -1.4 |
| 118 | Putative uncharacterized protein SA0775 OS=Staphylococcus aureus (strain N315) GN=SA0775 PE=4 SV=1 | Q7A6L6 Q7A6L6_STAAN | -1.4 |
| 154 | Serine hydroxymethyltransferase OS=Staphylococcus aureus (strain N315) GN=glyA PE=1 SV=1 | P99091 GLYA_ST AAN | -1.4 |
| 191 | SA1549 protein OS=Staphylococcus aureus (strain N315) GN=SA1549 PE=4 SV=1 | Q7A538 Q7A538_STAAN | -1.4 |
| 237 | 50S ribosomal protein L30 OS=Staphylococcus aureus (strain N315) GN=rpmD PE=1 SV=1 | RL30_STAAN (+1) | -1.4 |
| 262 | 50S ribosomal protein L16 OS=Staphylococcus aureus (strain N315) GN=rplP PE=1 SV=1 | Q7A461 RL16_ST AAN | -1.4 |
| 265 | Alanyl-tRNA synthetase OS=Staphylococcus aureus (strain N315) GN=alaS PE=1 SV=1 | P67011 SYA_STA AN | -1.4 |
| 292 | Aspartyl/glutamyl-tRNA(Asn/Gln) amidotransferase subunit C OS=Staphylococcus aureus (strain N315) GN=gatC PE=1 SV=1 | P68808 GATC_ST AAN | -1.4 |
| 315 | Signal transduction protein TRAP OS=Staphylococcus aureus (strain N315) GN=traP PE=1 SV=1 | Q7A4W3 TRAP_S TAAN | -1.4 |
| 319 | Acetate-CoA ligase OS=Staphylococcus aureus (strain N315) GN=SA2402 PE=4 SV=1 | Q7A3A2 Q7A3A2_STAAN | -1.4 |
| 343 | DNA-directed RNA polymerase subunit omega OS=Staphylococcus aureus (strain N315) GN=rp0Z PE=1 SV=1 | P66726 RPOZ_ST AAN | -1.4 |
| 388 | Putative uncharacterized protein SAS040 OS=Staphylococcus aureus (strain N315) GN=SA1154.1 PE=4 SV=1 | Q7A5U6 Q7A5U6_STAAN | -1.4 |
| 418 | UPF0637 protein SA0957 OS=Staphylococcus aureus (strain N315) GN=SA0957 PE=1 SV=1 | Q99UZ6 Y957_ST AAN | -1.4 |
| 447 | Branched-chain alpha-keto acid dehydrogenase E1 OS=Staphylococcus aureus (strain N315) GN=bfmBAB PE=4 SV=1 | Q7A5F8 Q7A5F8_STAAN | -1.4 |
| 489 | Lipase 1 OS=Staphylococcus aureus (strain N315) GN=lip1 PE=3 SV=2 | P65289 LIP1_STA AN | -1.4 |
| 492 | Organic hydroperoxide resistance protein-like OS=Staphylococcus aureus (strain N315) GN=SA0755 PE=1 SV=1 | Q7A6M9 OHRL_S TAAN | -1.4 |
| 501 | Methionine aminopeptidase OS=Staphylococcus aureus (strain N315) GN=map PE=1 SV=1 | P99121 AMPM_ST AAN | -1.4 |
| 43 | Glycyl-tRNA synthetase (glyQS) | P99129 SYG_STA AN | -1.3 |
| 87 | UPF0457 protein SA1975.1 (SA1975.1) | Q99S93 Y197A_ST | -1.3 |

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| 95 | Cell-division protein OS=Staphylococcus aureus (strain N315) GN=ftsH PE=4 SV=1 | Q7A7A5 Q7A7A5_STAAN | -1.3 |
| 117 | Putative uncharacterized protein SAS030 OS=Staphylococcus aureus (strain N315) GN=SA0930.1 PE=4 SV=1 | Q7A690 Q7A690_STAAN | -1.3 |
| 123 | Putative uncharacterized protein SA1671 OS=Staphylococcus aureus (strain N315) GN=SA1671 PE=1 SV=1 | Q7A4U5 Q7A4U5_STAAN | -1.3 |
| 132 | Foldase protein prsA OS=Staphylococcus aureus (strain N315) GN=prsA PE=1 SV=1 | P60748 PRSA_ST_AAN | -1.3 |
| 155 | Alkyl hydroperoxide reductase subunit F OS=Staphylococcus aureus (strain N315) GN=ahpF PE=1 SV=1 | P99118 AHPF_ST_AAN | -1.3 |
| 168 | Uncharacterized hydrolase SA2367 OS=Staphylococcus aureus (strain N315) GN=SA2367 PE=1 SV=1 | Q7A3C4 Y2367_S_TAAN | -1.3 |
| 190 | Translation initiation factor IF-1 OS=Staphylococcus aureus (strain N315) GN=infA PE=1 SV=1 | P65119 IF1_STAA_N | -1.3 |
| 194 | SA2095 protein OS=Staphylococcus aureus (strain N315) GN=SA2095 PE=4 SV=1 | Q7A420 Q7A420_STAAN | -1.3 |
| 203 | 3-oxoacyl-[acyl-carrier-protein] reductase OS=Staphylococcus aureus (strain N315) GN=fabG PE=1 SV=1 | P99093 FABG_ST_AAN | -1.3 |
| 227 | Adenylate kinase OS=Staphylococcus aureus (strain N315) GN=adk PE=1 SV=1 | P99062 KAD_STA_AN | -1.3 |
| 255 | Dihydrolipoylysine-residue succinyltransferase component of 2-oxoglutarate dehydrogenase complex OS=Staphylococcus aureus (strain N315) GN=odhB PE=1 SV=1 | Q7A5N4 ODO2_S_TAAN | -1.3 |
| 338 | Probable uridylyltransferase SA1974 OS=Staphylococcus aureus (strain N315) GN=SA1974 PE=1 SV=1 | Q7A4A4 URTF_ST_AAN | -1.3 |
| 373 | Elongation factor P OS=Staphylococcus aureus (strain N315) GN=efp PE=1 SV=1 | P99066 EFP_STAA_N | -1.3 |
| 382 | Staphopain A OS=Staphylococcus aureus (strain N315) GN=sspP PE=3 SV=1 | P65826 SSPP_STA_AN | -1.3 |
| 402 | HTH-type transcriptional regulator sarR OS=Staphylococcus aureus (strain N315) GN=sarR PE=1 SV=3 | Q7A425 SARR_ST_AAN | -1.3 |
| 435 | 50S ribosomal protein L33_1 OS=Staphylococcus aureus (strain N315) GN=rpmG1 PE=3 SV=1 | P66228 RL331_ST_AAN | -1.3 |
| 440 | Hit-like protein involved in cell-cycle regulation OS=Staphylococcus aureus (strain N315) GN=hit PE=4 SV=1 | Q7A4W0 Q7A4W0_STAAN | -1.3 |
| 505 | Putative uncharacterized protein SAS027 OS=Staphylococcus aureus (strain N315) GN=SA0884.1 PE=4 SV=1 | Q7A6C4 Q7A6C4_STAAN | -1.3 |
| 556 | Cold shock protein cspB OS=Staphylococcus aureus (strain N315) GN=cspB PE=3 SV=1 | Q7A326 Q7A326_STAAN | -1.3 |
| 633 | Uncharacterized protein SA1186 OS=Staphylococcus aureus (strain N315) GN=SA1186 PE=1 SV=1 | Q7A5S4 Y1186_ST_AAN | -1.3 |
| 5 | DNA-binding protein HU (hup) | Q7A5J1 DBH_STA_AN | -1.2 |
| 14 | 30S ribosomal protein S1 (rpsA) | Q7A5J0 RS1_STA_AN | -1.2 |
| 37 | Thioredoxin (trxA) | P99122 THIO_STA_AN | -1.2 |
| 81 | SA0774 protein (SA0774) | Q7A6L7 Q7A6L7_STAAN | -1.2 |
| 124 | Polyribonucleotide nucleotidyltransferase OS=Staphylococcus aureus (strain N315) GN=pnp PE=1 SV=1 | Q7A5X7 PNP_STA_AN | -1.2 |
| 177 | 2-oxoglutarate dehydrogenase E1 component OS=Staphylococcus aureus (strain N315) GN=odhA PE=1 SV=1 | Q99U74 ODO1_ST_AAN | -1.2 |
| 207 | Methionyl-tRNA synthetase OS=Staphylococcus aureus (strain N315) GN=metG PE=1 SV=1 | P67579 SYM_STA_AN | -1.2 |
| 297 | Regulatory protein msrR OS=Staphylococcus aureus (strain N315) GN=msrR PE=1 SV=1 | Q99Q02 MSRR_ST_AAN | -1.2 |

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| 351 | Glucose-6-phosphate 1-dehydrogenase OS=Staphylococcus aureus (strain N315) GN=SA1336 PE=3 SV=1 | Q7A5G7 Q7A5G7_STAAN | -1.2 |
| 375 | NH(3)-dependent NAD(+) synthetase OS=Staphylococcus aureus (strain N315) GN=nadE PE=1 SV=1 | P99150 NADE_ST_AAN | -1.2 |
| 430 | Peptide methionine sulfoxide reductase msrB OS=Staphylococcus aureus (strain N315) GN=msrB PE=1 SV=1 | P99065 MSRB_ST_AAN | -1.2 |
| 443 | Redox-sensing transcriptional repressor rex OS=Staphylococcus aureus (strain N315) GN=rex PE=3 SV=1 | P60386 REX_STAAN | -1.2 |
| 543 | Chromosome segregation SMC protein OS=Staphylococcus aureus (strain N315) GN=smc PE=4 SV=1 | Q7A5Z2 Q7A5Z2_STAAN | -1.2 |
| 136 | Putative uncharacterized protein SA0570 OS=Staphylococcus aureus (strain N315) GN=SA0570 PE=4 SV=1 | Q7A735 Q7A735_STAAN | -1.1 |
| 295 | Malonyl CoA-acyl carrier protein transacylase OS=Staphylococcus aureus (strain N315) GN=fabD PE=1 SV=1 | Q7A5Z3 FABD_ST_AAN | -1.1 |
| 301 | Transcription elongation factor greA OS=Staphylococcus aureus (strain N315) GN=greA PE=1 SV=1 | P99156 GREA_ST_AAN | -1.1 |
| 344 | 30S ribosomal protein S19 OS=Staphylococcus aureus (strain N315) GN=rpsS PE=1 SV=1 | P66494 RS19_STAAN | -1.1 |
| 348 | Probable cysteine desulfurase OS=Staphylococcus aureus (strain N315) GN=csd PE=1 SV=1 | P99177 CSD_STAAN | -1.1 |
| 359 | S-ribosylhomocysteine lyase OS=Staphylococcus aureus (strain N315) GN=luxS PE=1 SV=1 | P65330 LUXS_ST_AAN | -1.1 |
| 368 | Probable glycine dehydrogenase [decarboxylating] subunit 2 OS=Staphylococcus aureus (strain N315) GN=gcvPB PE=1 SV=1 | P99168 GCSPB_ST_AAN | -1.1 |
| 464 | SA1035 protein OS=Staphylococcus aureus (strain N315) GN=SA1035 PE=1 SV=1 | Q7A612 Q7A612_STAAN | -1.1 |
| 465 | Putative uncharacterized protein SA2262 OS=Staphylococcus aureus (strain N315) GN=SA2262 PE=4 SV=1 | Q7A3M3 Q7A3M3_STAAN | -1.1 |
| 526 | Low molecular weight protein-tyrosine-phosphatase ptpA OS=Staphylococcus aureus (strain N315) GN=ptpA PE=1 SV=1 | Q7A4S1 PTPA_ST_AAN | -1.1 |
| 550 | Probable transglycosylase sceD OS=Staphylococcus aureus (strain N315) GN=sceD PE=2 SV=1 | Q7A4F2 SCED_ST_AAN | -1.1 |
| 578 | OppF protein OS=Staphylococcus aureus (strain N315) GN=oppF PE=4 SV=1 | Q7A6F3 Q7A6F3_STAAN | -1.1 |
| 618 | 3-phosphoshikimate 1-carboxyvinyltransferase OS=Staphylococcus aureus (strain N315) GN=aroA PE=1 SV=1 | P63585 AROA_ST_AAN | -1.1 |
| 620 | SA1475 protein OS=Staphylococcus aureus (strain N315) GN=SA1475 PE=4 SV=1 | Q7A581 Q7A581_STAAN | -1.1 |
| 646 | Aminomethyltransferase OS=Staphylococcus aureus (strain N315) GN=gcvT PE=1 SV=1 | P64225 GCST_ST_AAN | -1.1 |
| 4 | UPF0337 protein SA0772 (SA0772) | Q7A6L9 Y772_ST_AAN | -1 |
| 41 | Acyl carrier protein (acpP) | P0A002 ACP_STAAN | -1 |
| 46 | Uncharacterized leukocidin-like protein 2 (SA1813) | Q99SN7 LUKL2_STAAN | -1 |
| 89 | Probable manganese-dependent inorganic pyrophosphatase (ppaC) | P65753 PPAC_ST_AAN | -1 |
| 185 | 50S ribosomal protein L11 OS=Staphylococcus aureus (strain N315) GN=rplK PE=1 SV=2 | P0A0F2 RL11_ST_AAN | -1 |
| 442 | Homoserine dehydrogenase OS=Staphylococcus aureus (strain N315) GN=dhoM PE=3 SV=1 | Q7A5T6 Q7A5T6_STAAN | -1 |
| 467 | Cysteinyl-tRNA synthetase OS=Staphylococcus aureus (strain N315) GN=cysS PE=1 SV=1 | Q99W73 SYC_ST_AAN | -1 |
| 504 | Bla regulator protein blaR1 OS=Staphylococcus aureus (strain N315) GN=blaR1 PE=4 SV=1 | Q9AC79 Q9AC79_STAAN | -1 |
| 523 | FMN-dependent NADPH-azoreductase OS=Staphylococcus aureus (strain N315) GN=azo1 PE=1 SV=1 | Q7A782 AZO1_ST_AAN | -1 |
| 548 | tRNA uridine 5-carboxymethylaminomethyl modification enzyme mnmg | P64230 MNMG_S | -1 |

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| | OS=Staphylococcus aureus (strain N315) GN=mnmG PE=1 SV=1 | TAAN | |
| 613 | UPF0447 protein SA0544 OS=Staphylococcus aureus (strain N315) GN=SA0544 PE=1 SV=1 | Q7A759 Y544_ST AAN | -1 |
| 716 | Putative trmH family tRNA/rRNA methyltransferase OS=Staphylococcus aureus (strain N315) GN=SA0490 PE=1 SV=1 | Q7A794 TRMHL_ STAAN | -1 |
| 746 | UPF0154 protein SA1178 OS=Staphylococcus aureus (strain N315) GN=SA1178 PE=1 SV=1 | P67291 Y1178_ST AAN | -1 |
| 750 | SA0605 protein OS=Staphylococcus aureus (strain N315) GN=SA0605 PE=4 SV=1 | Q7A701 Q7A701_ STAAN | -1 |
| 8 | Alkaline shock protein 23 (asp23) | P99157 ASP23_ST AAN | -0.9 |
| 111 | 50S ribosomal protein L27 OS=Staphylococcus aureus (strain N315) GN=rpmA PE=1 SV=1 | P66133 RL27_STA AN | -0.9 |
| 112 | SA2327 protein OS=Staphylococcus aureus (strain N315) GN=SA2327 PE=4 SV=1 | Q7A3G3 Q7A3G3_ STAAN | -0.9 |
| 163 | ATP-dependent Clp protease ATP-binding subunit clpC OS=Staphylococcus aureus (strain N315) GN=clpC PE=1 SV=1 | Q7A797 CLPC_ST AAN | -0.9 |
| 192 | 3-hexulose-6-phosphate synthase OS=Staphylococcus aureus (strain N315) GN=SA0528 PE=1 SV=1 | Q7A774 HPS_STA AN | -0.9 |
| 246 | Valyl-tRNA synthetase OS=Staphylococcus aureus (strain N315) GN=valS PE=1 SV=1 | Q99TJ8 SYV_STA AN | -0.9 |
| 310 | Probable glycine dehydrogenase [decarboxylating] subunit 1 OS=Staphylococcus aureus (strain N315) GN=gcvPA PE=1 SV=1 | P64218 GCSPA_S TAAN | -0.9 |
| 380 | Ribonucleoside-diphosphate reductase minor subunit OS=Staphylococcus aureus (strain N315) GN=nrdF PE=4 SV=1 | Q7A6T1 Q7A6T1_ STAAN | -0.9 |
| 490 | SA1558 protein OS=Staphylococcus aureus (strain N315) GN=SA1558 PE=4 SV=1 | Q7A533 Q7A533_ STAAN | -0.9 |
| 522 | Probable ctpA-like serine protease OS=Staphylococcus aureus (strain N315) GN=SA1253 PE=1 SV=1 | Q7A5M9 CTPAL_ STAAN | -0.9 |
| 527 | Putative uncharacterized protein SA0936 OS=Staphylococcus aureus (strain N315) GN=SA0936 PE=4 SV=1 | Q7A686 Q7A686_ STAAN | -0.9 |
| 600 | Putative uncharacterized protein SA1293 OS=Staphylococcus aureus (strain N315) GN=SA1293 PE=4 SV=1 | Q7A5J9 Q7A5J9_S TAAN | -0.9 |
| 766 | Threonine synthase OS=Staphylococcus aureus (strain N315) GN=thrC PE=4 SV=1 | Q7A5T5 Q7A5T5_ STAAN | -0.9 |
| 97 | Phosphoenolpyruvate carboxykinase [ATP] OS=Staphylococcus aureus (strain N315) GN=pckA PE=1 SV=1 | P99128 PCKA_ST AAN | -0.8 |
| 189 | 2-C-methyl-D-erythritol 4-phosphate cytidylyltransferase 2 OS=Staphylococcus aureus (strain N315) GN=ispD2 PE=1 SV=1 | Q7A7V0 ISPD2_S TAAN | -0.8 |
| 405 | Cold-shock protein C OS=Staphylococcus aureus (strain N315) GN=cspC PE=3 SV=1 | Q7A6P1 Q7A6P1_ STAAN | -0.8 |
| 422 | Glucose-specific phosphotransferase enzyme IIA component OS=Staphylococcus aureus (strain N315) GN=err PE=1 SV=1 | P60857 PTGA_ST AAN | -0.8 |
| 478 | ATP-binding cassette transporter A OS=Staphylococcus aureus (strain N315) GN=SA0599 PE=4 SV=1 | Q7A708 Q7A708_ STAAN | -0.8 |
| 623 | Iron-regulated ABC transporter siderophore-binding protein SirA OS=Staphylococcus aureus (strain N315) GN=sirA PE=4 SV=1 | Q7A869 Q7A869_ STAAN | -0.8 |
| 135 | Transcriptional regulator sarA OS=Staphylococcus aureus (strain N315) GN=sarA PE=1 SV=3 | Q7A732 SARA_ST AAN | -0.7 |
| 206 | General stress protein 20U OS=Staphylococcus aureus (strain N315) GN=dps PE=3 SV=1 | Q7A4C8 Q7A4C8_ STAAN | -0.7 |
| 212 | Uncharacterized protein SA0707 OS=Staphylococcus aureus (strain N315) GN=SA0707 PE=1 SV=1 | Q7A6R6 Y707_ST AAN | -0.7 |
| 303 | UPF0082 protein SA0624 OS=Staphylococcus aureus (strain N315) GN=SA0624 PE=1 SV=1 | P67182 Y624_STA AN | -0.7 |
| 532 | Penicillin-binding protein 1 OS=Staphylococcus aureus (strain N315) GN=pbpA PE=4 SV=1 | Q7A619 Q7A619_ STAAN | -0.7 |
| 602 | Putative uncharacterized protein SA1593 OS=Staphylococcus aureus (strain N315) GN=SA1593 PE=4 SV=1 | Q99T94 Q99T94_S TAAN | -0.7 |

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| 711 | Putative uncharacterized protein SA2221 OS=Staphylococcus aureus (strain N315) GN=SA2221 PE=4 SV=1 | Q7A3R1 Q7A3R1_STAAN | -0.7 |
| 712 | Aminopeptidase ampS OS=Staphylococcus aureus (strain N315) GN=ampS PE=4 SV=1 | Q7A4S3 Q7A4S3_STAAN | -0.7 |
| 717 | Na(+)/H(+) antiporter subunit E1 OS=Staphylococcus aureus (strain N315) GN=mnhE1 PE=1 SV=1 | P60689 MNHE1_S_TAAN | -0.7 |
| 153 | Isoleucyl-tRNA synthetase OS=Staphylococcus aureus (strain N315) GN=ileS PE=1 SV=1 | P67509 SYI_STAA_N | -0.6 |
| 158 | Putative uncharacterized protein SA1573 OS=Staphylococcus aureus (strain N315) GN=SA1573 PE=4 SV=1 | Q7A521 Q7A521_STAAN | -0.6 |
| 169 | Probable DEAD-box ATP-dependent RNA helicase SA1885 OS=Staphylococcus aureus (strain N315) GN=SA1885 PE=1 SV=1 | Q7A4G0 Y1885_S_TAAN | -0.6 |
| 289 | Superoxide dismutase [Mn/Fe] 1 OS=Staphylococcus aureus (strain N315) GN=sodA PE=1 SV=1 | P99098 SODM1_S_TAAN | -0.6 |
| 367 | SA0691 protein OS=Staphylococcus aureus (strain N315) GN=SA0691 PE=4 SV=1 | Q7A6S7 Q7A6S7_STAAN | -0.6 |
| 448 | Epimerase family protein SA0724 OS=Staphylococcus aureus (strain N315) GN=SA0724 PE=1 SV=1 | Q7A6Q5 Y724_ST_AAN | -0.6 |
| 476 | SA1563 protein OS=Staphylococcus aureus (strain N315) GN=SA1563 PE=1 SV=1 | Q7A529 Q7A529_STAAN | -0.6 |
| 705 | Putative uncharacterized protein SA0711 OS=Staphylococcus aureus (strain N315) GN=SA0711 PE=4 SV=1 | Q7A6R2 Q7A6R2_STAAN | -0.6 |
| 187 | Cell cycle protein gpsB OS=Staphylococcus aureus (strain N315) GN=gpsB PE=1 SV=1 | Q7A5L1 GPSB_ST_AAN | -0.5 |
| 284 | Superoxide dismutase [Mn/Fe] 2 OS=Staphylococcus aureus (strain N315) GN=sodM PE=1 SV=1 | P66831 SODM2_S_TAAN | -0.5 |
| 479 | Aminoacyltransferase femA OS=Staphylococcus aureus (strain N315) GN=femA PE=1 SV=1 | Q7A5R3 FEMA_S_TAAN | -0.5 |
| 482 | HTH-type transcriptional regulator sarS OS=Staphylococcus aureus (strain N315) GN=sarS PE=1 SV=1 | Q7A872 SARS_ST_AAN | -0.5 |
| 582 | Putative uncharacterized protein SA0695 OS=Staphylococcus aureus (strain N315) GN=SA0695 PE=4 SV=1 | Q7A6S4 Q7A6S4_STAAN | -0.5 |
| 625 | SA0422 protein OS=Staphylococcus aureus (strain N315) GN=SA0422 PE=4 SV=1 | Q7A7E1 Q7A7E1_STAAN | -0.5 |
| 715 | Peptide deformylase OS=Staphylococcus aureus (strain N315) GN=def PE=1 SV=1 | P99077 DEF_STAAN | -0.5 |
| 271 | FMN-dependent NADH-azoreductase OS=Staphylococcus aureus (strain N315) GN=azoR PE=1 SV=1 | Q99X11 AZOR_ST_AAN | -0.4 |
| 552 | Lytic regulatory protein truncated with Tn554 OS=Staphylococcus aureus (strain N315) GN=truncated-SA PE=4 SV=1 | Q99SB2 Q99SB2_STAAN | -0.4 |
| 553 | Clumping factor A OS=Staphylococcus aureus (strain N315) GN=clfA PE=1 SV=1 | Q99VJ4 CLFA_ST_AAN | -0.4 |
| 20 | Chaperone protein dnaK (dnaK) | P99110 DNAK_ST_AAN | -0.3 |
| 321 | Hydroxamate siderophore binding lipoprotein OS=Staphylococcus aureus (strain N315) GN=fhuD2 PE=4 SV=1 | Q7A433 Q7A433_STAAN | -0.3 |
| 664 | Methylenetetrahydrofolate--tRNA-(uracil-5-)-methyltransferase trmFO OS=Staphylococcus aureus (strain N315) GN=trmFO PE=1 SV=1 | P64235 TRMFO_S_TAAN | -0.3 |
| 752 | Putative uncharacterized protein SA2267 OS=Staphylococcus aureus (strain N315) GN=SA2267 PE=4 SV=1 | Q99RF4 Q99RF4_STAAN | -0.3 |
| 765 | Putative uncharacterized protein SA1957 OS=Staphylococcus aureus (strain N315) GN=SA1957 PE=4 SV=1 | Q7A4B6 Q7A4B6_STAAN | -0.2 |
| 31 | SA2437 protein (SA2437) | Q7A371 Q7A371_STAAN | -0.1 |
| 216 | SA1979 protein OS=Staphylococcus aureus (strain N315) GN=SA1979 PE=1 SV=1 | Q7A499 Q7A499_STAAN | -0.1 |
| 288 | 2',3'-cyclic-nucleotide 2'-phosphodiesterase OS=Staphylococcus aureus (strain N315) GN=cvfA PE=1 SV=1 | P67278 CNPD_ST_AAN | -0.1 |
| 444 | Anti repressor OS=Staphylococcus aureus (strain N315) GN=SA1801 PE=4 SV=1 | Q99SP8 Q99SP8_S | -0.1 |

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| 545 | Putative uncharacterized protein SA1274 OS=Staphylococcus aureus (strain N315) GN=SA1274 PE=4 SV=1 | Q7A5L6 Q7A5L6_STAAN | -0.1 |
| 22 | Probable transglycosylase isaA (isaA) | P99160 ISAA_STAAN | 0 |
| 735 | Heme-degrading monooxygenase isdl OS=Staphylococcus aureus (strain N315) GN=isdl PE=1 SV=1 | Q7A827 ISDI_STAAN | 0 |
| 275 | UPF0435 protein SA1696 OS=Staphylococcus aureus (strain N315) GN=SA1696 PE=1 SV=1 | Q7A4S2 Y1696_STAAN | 0.1 |
| 575 | Putative uncharacterized protein SA0943 OS=Staphylococcus aureus (strain N315) GN=SA0943 PE=4 SV=1 | Q7A681 Q7A681_STAAN | 0.1 |
| 708 | SA1343 protein OS=Staphylococcus aureus (strain N315) GN=SA1343 PE=4 SV=1 | Q7A5G2 Q7A5G2_STAAN | 0.1 |
| 325 | 6,7-dimethyl-8-ribityllumazine synthase OS=Staphylococcus aureus (strain N315) GN=ribH PE=1 SV=1 | P99141 RISB_STAAN | 0.2 |
| 15 | Elongation factor Ts (tsf) | P99171 EFTS_STAAN | 0.4 |
| 218 | 50S ribosomal protein L25 OS=Staphylococcus aureus (strain N315) GN=rplY PE=1 SV=1 | Q7A7B3 RL25_STAAN | 0.4 |
| 52 | Putative uncharacterized protein SAS049 (SA1451.1) | Q7A594 Q7A594_STAAN | 0.5 |
| 63 | Putative uncharacterized protein SA2323 (SA2323) | Q7A3G7 Q7A3G7_STAAN | 0.5 |
| 259 | UPF0337 protein SA1452 OS=Staphylococcus aureus (strain N315) GN=SA1452 PE=1 SV=1 | Q7A593 Y1452_STAAN | 0.7 |
| 355 | GTP cyclohydrolase folE2 OS=Staphylococcus aureus (strain N315) GN=folE2 PE=1 SV=1 | Q7A777 GCH4_STAAN | 0.8 |
| 547 | Delta-hemolysin OS=Staphylococcus aureus (strain N315) GN=hld PE=1 SV=2 | P0A0M2 HLD_STAAN | 0.8 |
| 240 | SA0246 protein OS=Staphylococcus aureus (strain N315) GN=SA0246 PE=4 SV=1 | Q7A7U9 Q7A7U9_STAAN | No Values |
| 312 | UDP-N-acetyl muramate-L-alanine ligase OS=Staphylococcus aureus (strain N315) GN=murC PE=1 SV=1 | P65475 MURC_STAAN | No Values |
| 353 | Pseudouridine synthase OS=Staphylococcus aureus (strain N315) GN=SA1040 PE=3 SV=1 | Q7A610 Q7A610_STAAN | No Values |
| 385 | Probable cytosol aminopeptidase OS=Staphylococcus aureus (strain N315) GN=ampA PE=4 SV=1 | Q7A6J3 Q7A6J3_STAAN | No Values |
| 396 | Aldehyde dehydrogenase OS=Staphylococcus aureus (strain N315) GN=aldH PE=4 SV=1 | Q7A4P5 Q7A4P5_STAAN | No Values |
| 407 | Fumarate hydratase class II OS=Staphylococcus aureus (strain N315) GN=fumC PE=1 SV=1 | P64173 FUMC_STAAN | No Values |
| 416 | Putative uncharacterized protein SA0908 OS=Staphylococcus aureus (strain N315) GN=SA0908 PE=4 SV=1 | Q7A6A3 Q7A6A3_STAAN | No Values |
| 424 | Bleomycin resistance protein OS=Staphylococcus aureus (strain N315) GN=ble PE=1 SV=2 | Q7A8D1 BLE_STAAN | No Values |
| 425 | Protein grpE OS=Staphylococcus aureus (strain N315) GN=grpE PE=1 SV=1 | P99086 GRPE_STAAN | No Values |
| 434 | Putative uncharacterized protein SAS010 OS=Staphylococcus aureus (strain N315) GN=SA0359.1 PE=4 SV=1 | Q7A7J7 Q7A7J7_STAAN | No Values |
| 453 | Exodeoxyribonuclease 7 small subunit OS=Staphylococcus aureus (strain N315) GN=xseB PE=3 SV=1 | P67461 EX7S_STAAN | No Values |
| 456 | Serine-aspartate repeat-containing protein D OS=Staphylococcus aureus (strain N315) GN=sdrD PE=1 SV=1 | Q7A780 SDRD_STAAN | No Values |
| 460 | Putative uncharacterized protein SA1277 OS=Staphylococcus aureus (strain N315) GN=SA1277 PE=4 SV=1 | Q7A5L3 Q7A5L3_STAAN | No Values |
| 468 | 50S ribosomal protein L15 OS=Staphylococcus aureus (strain N315) GN=rplO PE=1 SV=1 | P0A0F6 RL15_STAAN | No Values |
| 471 | 30S ribosomal protein S15 OS=Staphylococcus aureus (strain N315) GN=rpsO PE=1 SV=1 | Q7A5X8 RS15_STAAN | No Values |

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| 497 | Methionine import ATP-binding protein MetN 2 OS=Staphylococcus aureus (strain N315) GN=metN2 PE=1 SV=1 | Q7A6M2 METN2_STAAN | No Values |
| 498 | Putative uncharacterized protein SA1363 OS=Staphylococcus aureus (strain N315) GN=SA1363 PE=4 SV=1 | Q7A5E8 Q7A5E8_STAAN | No Values |
| 502 | SA0182 protein OS=Staphylococcus aureus (strain N315) GN=SA0182 PE=1 SV=1 | Q7A808 Q7A808_STAAN | No Values |
| 510 | SA1559 protein OS=Staphylococcus aureus (strain N315) GN=SA1559 PE=4 SV=1 | Q7A532 Q7A532_STAAN | No Values |
| 513 | Protein kinase OS=Staphylococcus aureus (strain N315) GN=SA1063 PE=4 SV=1 | Q7A5Z8 Q7A5Z8_STAAN | No Values |
| 516 | SA2140 protein OS=Staphylococcus aureus (strain N315) GN=SA2140 PE=4 SV=1 | Q7A3Y2 Q7A3Y2_STAAN | No Values |
| 518 | 3-methyl-2-oxobutanoate hydroxymethyltransferase OS=Staphylococcus aureus (strain N315) GN=panB PE=1 SV=1 | P65656 PANB_ST_AAN | No Values |
| 525 | ATP synthase epsilon chain OS=Staphylococcus aureus (strain N315) GN=atpC PE=1 SV=1 | P63665 ATPE_ST_AAN | No Values |
| 528 | SA2346 protein OS=Staphylococcus aureus (strain N315) GN=SA2346 PE=4 SV=1 | Q7A3E4 Q7A3E4_STAAN | No Values |
| 529 | Uncharacterized protein SA0370 OS=Staphylococcus aureus (strain N315) GN=SA0370 PE=1 SV=1 | P60855 Y370_STAAN | No Values |
| 531 | Coenzyme A disulfide reductase OS=Staphylococcus aureus (strain N315) GN=cdr PE=1 SV=3 | Q7A6H1 CDR_ST_AAN | No Values |
| 533 | Molybdopterin molybdenumtransferase OS=Staphylococcus aureus (strain N315) GN=moeA PE=1 SV=1 | P99139 MOEA_ST_AAN | No Values |
| 535 | Putative uncharacterized protein SA1031 OS=Staphylococcus aureus (strain N315) GN=SA1031 PE=3 SV=1 | Q7A616 Q7A616_STAAN | No Values |
| 537 | SA1121 protein OS=Staphylococcus aureus (strain N315) GN=SA1121 PE=3 SV=1 | Q7A5X4 Q7A5X4_STAAN | No Values |
| 538 | Putative uncharacterized protein SA2160 OS=Staphylococcus aureus (strain N315) GN=SA2160 PE=4 SV=1 | Q7A3W3 Q7A3W3_STAAN | No Values |
| 541 | Adenine phosphoribosyltransferase OS=Staphylococcus aureus (strain N315) GN=apt PE=1 SV=1 | P68779 APT_STAAN | No Values |
| 542 | SA1311 protein OS=Staphylococcus aureus (strain N315) GN=SA1311 PE=4 SV=1 | Q7A5I7 Q7A5I7_STAAN | No Values |
| 546 | SA2434 protein OS=Staphylococcus aureus (strain N315) GN=SA2434 PE=4 SV=1 | Q7A374 Q7A374_STAAN | No Values |
| 558 | SA2332 protein OS=Staphylococcus aureus (strain N315) GN=SA2332 PE=4 SV=1 | Q7A3F8 Q7A3F8_STAAN | No Values |
| 561 | 2,3,4,5-tetrahydropyridine-2,6-dicarboxylate N-acetyltransferase OS=Staphylococcus aureus (strain N315) GN=dapH PE=3 SV=1 | Q7A5P7 DAPH_ST_AAN | No Values |
| 566 | TelA-like protein SA1238 OS=Staphylococcus aureus (strain N315) GN=SA1238 PE=1 SV=1 | P60108 TELL_STAAN | No Values |
| 567 | Putative uncharacterized protein SA2374 OS=Staphylococcus aureus (strain N315) GN=SA2374 PE=4 SV=1 | Q7A3B7 Q7A3B7_STAAN | No Values |
| 571 | Putative uncharacterized protein SA0721 OS=Staphylococcus aureus (strain N315) GN=SA0721 PE=4 SV=1 | Q7A6Q7 Q7A6Q7_STAAN | No Values |
| 576 | Chorismate synthase OS=Staphylococcus aureus (strain N315) GN=aroC PE=3 SV=1 | P63614 AROC_ST_AAN | No Values |
| 580 | PurR protein OS=Staphylococcus aureus (strain N315) GN=purR PE=4 SV=1 | Q7A7B7 Q7A7B7_STAAN | No Values |
| 583 | DNA topoisomerase 1 OS=Staphylococcus aureus (strain N315) GN=topA PE=1 SV=1 | Q7A5Y5 TOP1_ST_AAN | No Values |
| 584 | SA2200 protein OS=Staphylococcus aureus (strain N315) GN=SA2200 PE=4 SV=1 | Q7A3S6 Q7A3S6_STAAN | No Values |
| 590 | SA2490 protein OS=Staphylococcus aureus (strain N315) GN=SA2490 PE=1 SV=1 | Q7A331 Q7A331_STAAN | No Values |
| 591 | Putative uncharacterized protein SA1454 OS=Staphylococcus aureus (strain N315) GN=SA1454 PE=4 SV=1 | Q7A591 Q7A591_STAAN | No Values |
| 596 | Nucleoside-triphosphatase OS=Staphylococcus aureus (strain N315) GN=SA0998 PE=1 | P99094 NTPA_ST | No Values |

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| | SV=1 | AAN | |
| 597 | Purine nucleoside phosphorylase OS=Staphylococcus aureus (strain N315) GN=deoD PE=1 SV=1 | Q7A4C9 Q7A4C9_STAAN | No Values |
| 599 | UPF0473 protein SA1443 OS=Staphylococcus aureus (strain N315) GN=SA1443 PE=1 SV=1 | Q7A598 Y1443_ST AAN | No Values |
| 601 | Glycolytic operon regulator OS=Staphylococcus aureus (strain N315) GN=gapR PE=4 SV=1 | Q7A6Q3 Q7A6Q3_STAAN | No Values |
| 608 | Putative uncharacterized protein SA1405 OS=Staphylococcus aureus (strain N315) GN=SA1405 PE=4 SV=1 | Q7A5C4 Q7A5C4_STAAN | No Values |
| 609 | Putative uncharacterized protein SA1451 OS=Staphylococcus aureus (strain N315) GN=SA1451 PE=4 SV=1 | Q99TM6 Q99TM6_STAAN | No Values |
| 610 | Sensor protein srrB OS=Staphylococcus aureus (strain N315) GN=srrB PE=1 SV=2 | Q7A5H7 SRRB_ST AAN | No Values |
| 611 | Phosphoglucomutase OS=Staphylococcus aureus (strain N315) GN=pgcA PE=1 SV=2 | PGCA_STAAN | No Values |
| 619 | Putative uncharacterized protein SAS054 OS=Staphylococcus aureus (strain N315) GN=SA1692.1 PE=4 SV=1 | Q7A4S5 Q7A4S5_STAAN | No Values |
| 626 | SA0247 protein OS=Staphylococcus aureus (strain N315) GN=SA0247 PE=4 SV=1 | Q7A7U8 Q7A7U8_STAAN | No Values |
| 630 | SA2244 protein OS=Staphylococcus aureus (strain N315) GN=SA2244 PE=4 SV=1 | Q7A3P2 Q7A3P2_STAAN | No Values |
| 636 | UPF0349 protein SA0800 OS=Staphylococcus aureus (strain N315) GN=SA0800 PE=3 SV=1 | Q7A6J6 Y800_ST AAN | No Values |
| 638 | Glycine betaine transporter OS=Staphylococcus aureus (strain N315) GN=opuD PE=4 SV=1 | Q99UC9 Q99UC9_STAAN | No Values |
| 639 | Glutamate racemase OS=Staphylococcus aureus (strain N315) GN=murI PE=1 SV=1 | P63638 MURI_ST AAN | No Values |
| 641 | Putative uncharacterized protein SA1795 OS=Staphylococcus aureus (strain N315) GN=SA1795 PE=4 SV=1 | Q99SQ6 Q99SQ6_STAAN | No Values |
| 642 | DNA ligase OS=Staphylococcus aureus (strain N315) GN=ligA PE=3 SV=1 | Q7A4Q5 DNLJ_ST AAN | No Values |
| 643 | SA2498 protein OS=Staphylococcus aureus (strain N315) GN=SA2498 PE=4 SV=1 | Q7A321 Q7A321_STAAN | No Values |
| 644 | SA0817 protein OS=Staphylococcus aureus (strain N315) GN=SA0817 PE=1 SV=1 | Q7A6H9 Q7A6H9_STAAN | No Values |
| 650 | SA1566 protein OS=Staphylococcus aureus (strain N315) GN=SA1566 PE=4 SV=1 | Q7A526 Q7A526_STAAN | No Values |
| 651 | Alpha-D-1,4-glucosidase OS=Staphylococcus aureus (strain N315) GN=malA PE=1 SV=1 | Q7A5G5 Q7A5G5_STAAN | No Values |
| 653 | Putative uncharacterized protein SA0696 OS=Staphylococcus aureus (strain N315) GN=SA0696 PE=1 SV=1 | Q7A6S3 Q7A6S3_STAAN | No Values |
| 654 | Putative uncharacterized protein SA0529 OS=Staphylococcus aureus (strain N315) GN=SA0529 PE=4 SV=1 | Q7A773 Q7A773_STAAN | No Values |
| 655 | SA0165 protein OS=Staphylococcus aureus (strain N315) GN=SA0165 PE=4 SV=1 | Q7A821 Q7A821_STAAN | No Values |
| 657 | Alanine dehydrogenase 2 OS=Staphylococcus aureus (strain N315) GN=ald2 PE=1 SV=1 | Q99TF4 DHA2_ST AAN | No Values |
| 658 | SA1216 protein OS=Staphylococcus aureus (strain N315) GN=SA1216 PE=4 SV=1 | Q7A5Q5 Q7A5Q5_STAAN | No Values |
| 659 | UTP--glucose-1-phosphate uridylyltransferase OS=Staphylococcus aureus (strain N315) GN=gtaB PE=1 SV=1 | Q7A3J9 GTAB_ST AAN | No Values |
| 668 | Glucosamine--fructose-6-phosphate aminotransferase [isomerizing] OS=Staphylococcus aureus (strain N315) GN=glmS PE=1 SV=2 | GLMS_STAAN | No Values |
| 676 | Bifunctional protein glmU OS=Staphylococcus aureus (strain N315) GN=glmU PE=1 SV=1 | Q7A7B4 GLMU_ST AAN | No Values |
| 677 | SA0229 protein OS=Staphylococcus aureus (strain N315) GN=SA0229 PE=4 SV=1 | Q7A7W6 Q7A7W6_STAAN | No Values |
| 678 | PTS enzyme II, phosphoenolpyruvate-dependent, trehalose-specific OS=Staphylococcus aureus (strain N315) GN=treP PE=4 SV=1 | Q7A7D1 Q7A7D1_STAAN | No Values |

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| 681 | SA0557 protein OS=Staphylococcus aureus (strain N315) GN=SA0557 PE=4 SV=1 | Q7A747 Q7A747_STAAN | No Values |
| 683 | SA2170 protein OS=Staphylococcus aureus (strain N315) GN=SA2170 PE=4 SV=1 | Q7A3V4 Q7A3V4_STAAN | No Values |
| 684 | Transcription-repair-coupling factor OS=Staphylococcus aureus (strain N315) GN=mfd PE=1 SV=1 | Q7A7B2 MFD_ST_AAN | No Values |
| 688 | SA0677 protein OS=Staphylococcus aureus (strain N315) GN=SA0677 PE=4 SV=1 | Q7A6T8 Q7A6T8_STAAN | No Values |
| 689 | SA2248 protein OS=Staphylococcus aureus (strain N315) GN=SA2248 PE=4 SV=1 | Q7A3N8 Q7A3N8_STAAN | No Values |
| 690 | UDP-N-acetylglucosamine 2-epimerase OS=Staphylococcus aureus (strain N315) GN=mnaA PE=3 SV=1 | Q7A4E3 Q7A4E3_STAAN | No Values |
| 692 | SA2240 protein OS=Staphylococcus aureus (strain N315) GN=SA2240 PE=3 SV=1 | Q7A3P6 Q7A3P6_STAAN | No Values |
| 693 | Putative uncharacterized protein SA1966 OS=Staphylococcus aureus (strain N315) GN=SA1966 PE=4 SV=1 | Q7A4B0 Q7A4B0_STAAN | No Values |
| 694 | Transcriptional repressor nrdR OS=Staphylococcus aureus (strain N315) GN=nrdR PE=3 SV=1 | P67316 NRDR_ST_AAN | No Values |
| 695 | Uroporphyrinogen decarboxylase OS=Staphylococcus aureus (strain N315) GN=hemE PE=1 SV=1 | P67420 DCUP_ST_AAN | No Values |
| 696 | SA0902 protein OS=Staphylococcus aureus (strain N315) GN=SA0902 PE=3 SV=1 | Q7A6A5 Q7A6A5_STAAN | No Values |
| 697 | SA2099 protein OS=Staphylococcus aureus (strain N315) GN=SA2099 PE=4 SV=1 | Q7A416 Q7A416_STAAN | No Values |
| 702 | Pseudouridine synthase OS=Staphylococcus aureus (strain N315) GN=rluB PE=3 SV=1 | Q7A5H5 Q7A5H5_STAAN | No Values |
| 707 | Putative uncharacterized protein SA0013 OS=Staphylococcus aureus (strain N315) GN=SA0013 PE=4 SV=1 | Q7A8E3 Q7A8E3_STAAN | No Values |
| 709 | Putative uncharacterized protein SAS032 OS=Staphylococcus aureus (strain N315) GN=SA0959.1 PE=4 SV=1 | Q7A670 Q7A670_STAAN | No Values |
| 710 | Formimidoylglutamase OS=Staphylococcus aureus (strain N315) GN=hutG PE=1 SV=1 | P99158 HUTG_ST_AAN | No Values |
| 713 | Probable GTP-binding protein engB OS=Staphylococcus aureus (strain N315) GN=engB PE=1 SV=1 | P64071 ENG_B_ST_AAN | No Values |
| 714 | Putative uncharacterized protein SA2298 OS=Staphylococcus aureus (strain N315) GN=SA2298 PE=4 SV=1 | Q7A3J0 Q7A3J0_S_TAAN | No Values |
| 719 | Delta-aminolevulinic acid dehydratase OS=Staphylococcus aureus (strain N315) GN=hemB PE=1 SV=1 | P64334 HEM2_ST_AAN | No Values |
| 721 | Serine acetyltransferase OS=Staphylococcus aureus (strain N315) GN=cysE PE=1 SV=1 | P67765 CYSE_ST_AAN | No Values |
| 723 | SA2436 protein OS=Staphylococcus aureus (strain N315) GN=SA2436 PE=4 SV=1 | Q7A372 Q7A372_STAAN | No Values |
| 724 | Diacylglycerol kinase OS=Staphylococcus aureus (strain N315) GN=dagK PE=3 SV=1 | Q7A4Q8 DAGK_S_TAAN | No Values |
| 725 | Putative uncharacterized protein SA1546 OS=Staphylococcus aureus (strain N315) GN=SA1546 PE=4 SV=1 | Q7A541 Q7A541_STAAN | No Values |
| 726 | SA1291 protein OS=Staphylococcus aureus (strain N315) GN=SA1291 PE=4 SV=1 | Q7A5K1 Q7A5K1_STAAN | No Values |
| 727 | Putative uncharacterized protein SA1017 OS=Staphylococcus aureus (strain N315) GN=SA1017 PE=4 SV=1 | Q7A623 Q7A623_STAAN | No Values |
| 731 | SA0590 protein OS=Staphylococcus aureus (strain N315) GN=SA0590 PE=4 SV=1 | Q7A716 Q7A716_STAAN | No Values |
| 732 | Protein esaA OS=Staphylococcus aureus (strain N315) GN=esaA PE=3 SV=1 | Q7A7S3 ESAA_ST_AAN | No Values |
| 733 | SA0270 protein OS=Staphylococcus aureus (strain N315) GN=SA0270 PE=4 SV=1 | Q7A7S5_STAAN(+1) | No Values |
| 734 | Ribonuclease R OS=Staphylococcus aureus (strain N315) GN=rnr PE=4 SV=1 | Q99VK1 Q99VK1_STAAN | No Values |
| 736 | Putative uncharacterized protein SA0447 OS=Staphylococcus aureus (strain N315) | Q7A7C1 Q7A7C1_ | No Values |

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| | GN=SA0447 PE=4 SV=1 | STAAN | |
| 737 | UPF0403 protein SA1261 OS=Staphylococcus aureus (strain N315) GN=SA1261 PE=1 SV=1 | Q7A5M6 Y1261_S TAAN | No Values |
| 738 | Uncharacterized lipoprotein SA2273 OS=Staphylococcus aureus (strain N315) GN=SA2273 PE=1 SV=1 | Q7A3L3 Y2273_S TAAN | No Values |
| 739 | DNA polymerase III polC-type OS=Staphylococcus aureus (strain N315) GN=polC PE=1 SV=1 | P63982 DPO3_ST AAN | No Values |
| 741 | HmrA protein OS=Staphylococcus aureus (strain N315) GN=hmrA PE=4 SV=1 | Q99Q45 Q99Q45_ STAAN | No Values |
| 742 | Putative uncharacterized protein SA2238 OS=Staphylococcus aureus (strain N315) GN=SA2238 PE=4 SV=1 | Q99R12 Q99R12_S TAAN | No Values |
| 743 | Queuine tRNA-ribosyltransferase OS=Staphylococcus aureus (strain N315) GN=tgt PE=1 SV=1 | P66905 TGT_STA AN | No Values |
| 744 | Streptomycin 3"-adenylyltransferase OS=Staphylococcus aureus (strain N315) GN=ant1 PE=1 SV=1 | P0A0D1 S3AD_ST AAN | No Values |
| 745 | 5-methyltetrahydropteroylglutamate--homocysteine methyltransferase OS=Staphylococcus aureus (strain N315) GN=metE PE=3 SV=1 | P65343 METE_ST AAN | No Values |
| 748 | Glycine betaine/carnitine/choline ABC transporter opuCC OS=Staphylococcus aureus (strain N315) GN=opuCC PE=4 SV=1 | Q7A3Q0 Q7A3Q0_ STAAN | No Values |
| 749 | Putative uncharacterized protein SA2224 OS=Staphylococcus aureus (strain N315) GN=SA2224 PE=4 SV=1 | Q7A3Q8 Q7A3Q8_ STAAN | No Values |
| 751 | SA0530 protein OS=Staphylococcus aureus (strain N315) GN=SA0530 PE=4 SV=1 | Q7A772 Q7A772_ STAAN | No Values |
| 753 | Putative uncharacterized protein SA1403 OS=Staphylococcus aureus (strain N315) GN=SA1403 PE=4 SV=1 | Q99TS2 Q99TS2_S TAAN | No Values |
| 756 | Ribosomal RNA small subunit methyltransferase G OS=Staphylococcus aureus (strain N315) GN=rsmG PE=3 SV=1 | P64240 RSMG_ST AAN | No Values |
| 757 | Acetyl-coenzyme A carboxylase carboxyl transferase subunit beta OS=Staphylococcus aureus (strain N315) GN=accD PE=1 SV=1 | Q7A557 ACCD_ST AAN | No Values |
| 758 | Porphobilinogen deaminase OS=Staphylococcus aureus (strain N315) GN=hemC PE=1 SV=1 | P64341 HEM3_ST AAN | No Values |
| 760 | Peptide methionine sulfoxide reductase msrA 1 OS=Staphylococcus aureus (strain N315) GN=msrA1 PE=1 SV=1 | P0A082 MSRA1_S TAAN | No Values |
| 762 | Glycine betaine aldehyde dehydrogenase gbsA OS=Staphylococcus aureus (strain N315) GN=gbsA PE=4 SV=1 | Q7A399 Q7A399_ STAAN | No Values |
| 763 | Preprotein translocase subunit secY OS=Staphylococcus aureus (strain N315) GN=secY PE=1 SV=1 | Q7A468 SECY_ST AAN | No Values |
| 764 | Putative uncharacterized protein SA1985 OS=Staphylococcus aureus (strain N315) GN=SA1985 PE=4 SV=1 | Q7A494 Q7A494_ STAAN | No Values |
| 768 | Putative uncharacterized protein SA1018 OS=Staphylococcus aureus (strain N315) GN=SA1018 PE=4 SV=1 | Q7A622 Q7A622_ STAAN | No Values |
| 772 | Serine-aspartate repeat-containing protein E OS=Staphylococcus aureus (strain N315) GN=sdrE PE=1 SV=1 | Q99W46 SDRE_ST AAN | No Values |
| 773 | Peptidase T OS=Staphylococcus aureus (strain N315) GN=pepT PE=3 SV=1 | P65806 PEPT_STA AN | No Values |
| 775 | DNA topoisomerase 3 OS=Staphylococcus aureus (strain N315) GN=topB PE=3 SV=1 | Q7A455 TOP3_ST AAN | No Values |
| 776 | Ferrodoxin--NADP reductase OS=Staphylococcus aureus (strain N315) GN=SA2162 PE=1 SV=2 | Q7A3W1 FENR_S TAAN | No Values |
| 777 | SA0849 protein OS=Staphylococcus aureus (strain N315) GN=SA0849 PE=4 SV=1 | Q7A6F2 Q7A6F2_ STAAN | No Values |
| 779 | SA2194 protein OS=Staphylococcus aureus (strain N315) GN=SA2194 PE=3 SV=1 | Q7A3T2 RANDO M_Q7A3T2_STAA N-R | No Values |
| 780 | Putative uncharacterized protein SA0673 OS=Staphylococcus aureus (strain N315) GN=SA0673 PE=4 SV=1 | Q7A6U2 Q7A6U2_ STAAN | No Values |
| 781 | Guanylate kinase OS=Staphylococcus aureus (strain N315) GN=gmk PE=1 SV=1 | P99176 KGUA_ST AAN | No Values |

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| 782 | Glycerol uptake facilitator OS=Staphylococcus aureus (strain N315) GN=glpF PE=3 SV=1 | Q7A5V8 Q7A5V8_STAAN | No Values |
| 783 | Putative uncharacterized protein SA0960 OS=Staphylococcus aureus (strain N315) GN=SA0960 PE=4 SV=1 | Q7A669 Q7A669_STAAN | No Values |
| 784 | Putative uncharacterized protein SA1742 OS=Staphylococcus aureus (strain N315) GN=SA1742 PE=4 SV=1 | Q7A4N8 Q7A4N8_STAAN | No Values |
| 786 | MutS2 protein OS=Staphylococcus aureus (strain N315) GN=mutS2 PE=1 SV=1 | P65496 MUTS2_S_TAAN | No Values |
| 787 | SA2324 protein OS=Staphylococcus aureus (strain N315) GN=SA2324 PE=4 SV=1 | Q7A3G6 Q7A3G6_STAAN | No Values |
| 788 | SA1562 protein OS=Staphylococcus aureus (strain N315) GN=SA1562 PE=4 SV=1 | Q7A530 Q7A530_STAAN | No Values |
| 789 | 2-succinyl-5-enolpyruvyl-6-hydroxy-3-cyclohexene-1-carboxylate synthase OS=Staphylococcus aureus (strain N315) GN=mend PE=3 SV=1 | Q7A6B1 MEND_S_TAAN | No Values |
| 790 | Sensor protein kinase walkK OS=Staphylococcus aureus (strain N315) GN=walkK PE=1 SV=1 | Q7A8E0 WALK_S_TAAN | No Values |
| 792 | Thymidylate synthase OS=Staphylococcus aureus (strain N315) GN=thyA PE=3 SV=1 | P67047 TYSY_ST_AAN | No Values |
| 793 | UPF0124 protein SA1030 OS=Staphylococcus aureus (strain N315) GN=SA1030 PE=3 SV=1 | Q7A617 Y1030_ST_AAN | No Values |
| 794 | DNA polymerase III gamma and tau subunits OS=Staphylococcus aureus (strain N315) GN=dnaX PE=4 SV=1 | Q7A7C7 Q7A7C7_STAAN | No Values |
| 795 | Dehydrosqualene desaturase OS=Staphylococcus aureus (strain N315) GN=crtN PE=1 SV=1 | Q7A3E2 CRTN_ST_AAN | No Values |
| 796 | Pantothenate synthetase OS=Staphylococcus aureus (strain N315) GN=panC PE=1 SV=1 | P65659 PANC_ST_AAN | No Values |
| 354 | Putative uncharacterized protein SA0771 OS=Staphylococcus aureus (strain N315) GN=SA0771 PE=4 SV=1 | Q7A6M0 Q7A6M0_STAAN | Reference Missing |
| 569 | SA2422 protein OS=Staphylococcus aureus (strain N315) GN=SA2422 PE=4 SV=1 | Q7A383 Q7A383_STAAN | Reference Missing |
| 662 | Primosomal protein OS=Staphylococcus aureus (strain N315) GN=dnaI PE=4 SV=1 | Q7A568 Q7A568_STAAN | Reference Missing |
| 13 | Cold shock protein (cspA) | Q7A5P3 CSPA_ST_AAN | Value Missing |
| 61 | Glucosamine--fructose-6-phosphate aminotransferase [isomerizing] (glmS) | P64228 GLMS_ST_AAN | Value Missing |
| 70 | Uncharacterized leukocidin-like protein 1 (SA1812) | Q7A4L0 LUKL1_ST_TAAN | Value Missing |
| 131 | Immunoglobulin G-binding protein A OS=Staphylococcus aureus (strain N315) GN=spa PE=1 SV=1 | SPA_STAAN | Value Missing |
| 150 | Phosphoribosylformylglycinamide cyclo-ligase OS=Staphylococcus aureus (strain N315) GN=purM PE=1 SV=1 | P99163 PUR5_STAAN | Value Missing |
| 173 | Alcohol dehydrogenase OS=Staphylococcus aureus (strain N315) GN=adh PE=1 SV=1 | Q7A742 ADH_ST_AAN | Value Missing |
| 184 | Pyruvate carboxylase OS=Staphylococcus aureus (strain N315) GN=pycA PE=4 SV=1 | Q7A666 Q7A666_STAAN | Value Missing |
| 201 | Threonine dehydratase catabolic OS=Staphylococcus aureus (strain N315) GN=tdcB PE=1 SV=1 | Q7A5L8 THD2_ST_AAN | Value Missing |
| 211 | Alpha-Hemolysin OS=Staphylococcus aureus (strain N315) GN=SA1007 PE=4 SV=1 | Q7A632 Q7A632_STAAN | Value Missing |
| 226 | SA0231 protein OS=Staphylococcus aureus (strain N315) GN=SA0231 PE=1 SV=1 | Q7A7W3 Q7A7W3_STAAN | Value Missing |
| 231 | Probable quinol oxidase subunit 1 OS=Staphylococcus aureus (strain N315) GN=qoxB PE=1 SV=1 | Q7A699 QOX1_ST_AAN | Value Missing |
| 234 | UDP-N-acetylglucosamine--N-acetylmuramyl-(pentapeptide) pyrophosphoryl-undecaprenol N-acetylglucosamine transferase OS=Staphylococcus aureus (strain N315) GN=murG PE=1 SV=1 | P65482 MURG_ST_AAN | Value Missing |
| 243 | Poly D-alanine transfer protein OS=Staphylococcus aureus (strain N315) GN=dltD PE=4 SV=1 | Q7A6K0 Q7A6K0_STAAN | Value Missing |

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| 244 | Transcriptional regulatory protein walR OS=Staphylococcus aureus (strain N315) GN=walR PE=1 SV=2 | Q7A8E1 WALR_STAAN | Value Missing |
| 256 | SA0759 protein OS=Staphylococcus aureus (strain N315) GN=SA0759 PE=4 SV=1 | Q7A6M6 Q7A6M6_STAAN | Value Missing |
| 260 | SA1000 protein OS=Staphylococcus aureus (strain N315) GN=SA1000 PE=4 SV=1 | Q7A639 Q7A639_STAAN | Value Missing |
| 269 | Transcription termination factor Rho OS=Staphylococcus aureus (strain N315) GN=rho PE=4 SV=1 | Q99SD7 Q99SD7_STAAN | Value Missing |
| 273 | 3-hydroxy-3-methylglutaryl CoA synthase OS=Staphylococcus aureus (strain N315) GN=mvaS PE=1 SV=1 | Q7A3F6 Q7A3F6_STAAN | Value Missing |
| 278 | Accessory gene regulator protein A OS=Staphylococcus aureus (strain N315) GN=agrA PE=1 SV=1 | P0A0I5 AGRA_ST_AAN | Value Missing |
| 296 | Putative uncharacterized protein SA0663 OS=Staphylococcus aureus (strain N315) GN=SA0663 PE=4 SV=1 | Q7A6V1 Q7A6V1_STAAN | Value Missing |
| 323 | SA0969 protein OS=Staphylococcus aureus (strain N315) GN=SA0969 PE=4 SV=1 | Q7A661 Q7A661_STAAN | Value Missing |
| 330 | UDP-N-acetylenolpyruvylglucosamine reductase OS=Staphylococcus aureus (strain N315) GN=murB PE=1 SV=1 | P65463 MURB_ST_AAN | Value Missing |
| 331 | Aminoacyltransferase femX OS=Staphylococcus aureus (strain N315) GN=femX PE=1 SV=1 | Q7A447 FEMX_ST_AAN | Value Missing |
| 336 | Dihydroorotate OS=Staphylococcus aureus (strain N315) GN=pyrC PE=1 SV=1 | P65906 PYRC_ST_AAN | Value Missing |
| 337 | Chromosomal replication initiator protein dnaA OS=Staphylococcus aureus (strain N315) GN=dnaA PE=1 SV=1 | P68866 DNAA_ST_AAN | Value Missing |
| 339 | Putative uncharacterized protein SA1868 OS=Staphylococcus aureus (strain N315) GN=SA1868 PE=4 SV=1 | Q7A4H1 Q7A4H1_STAAN | Value Missing |
| 341 | Putative uncharacterized protein SA0606 OS=Staphylococcus aureus (strain N315) GN=SA0606 PE=1 SV=1 | Q7A700 Q7A700_STAAN | Value Missing |
| 349 | SA2375 protein OS=Staphylococcus aureus (strain N315) GN=SA2375 PE=3 SV=1 | Q7A3B6 Q7A3B6_STAAN | Value Missing |
| 357 | Nucleoside diphosphate kinase OS=Staphylococcus aureus (strain N315) GN=ndk PE=1 SV=1 | NDK_STAAN | Value Missing |
| 370 | Putative uncharacterized protein SA0517 OS=Staphylococcus aureus (strain N315) GN=SA0517 PE=1 SV=1 | Q7A783 Q7A783_STAAN | Value Missing |
| 371 | Probable acetyl-CoA acyltransferase OS=Staphylococcus aureus (strain N315) GN=SA0342 PE=1 SV=1 | Q7A7L2 THLA_ST_AAN | Value Missing |
| 372 | Ferrochelatase OS=Staphylococcus aureus (strain N315) GN=hemH PE=1 SV=1 | P64125 HEMH_ST_AAN | Value Missing |
| 376 | Alpha-acetolactate synthase OS=Staphylococcus aureus (strain N315) GN=alsS PE=4 SV=1 | Q7A481 Q7A481_STAAN | Value Missing |
| 389 | Protein fmtA OS=Staphylococcus aureus (strain N315) GN=fmtA PE=1 SV=1 | Q7A6A2 FMTA_SSTAAN | Value Missing |
| 409 | Phosphopentomutase OS=Staphylococcus aureus (strain N315) GN=deoB PE=1 SV=1 | P99100 DEOB_ST_AAN | Value Missing |
| 410 | SigmaB regulation protein RsbU OS=Staphylococcus aureus (strain N315) GN=rsbU PE=4 SV=1 | Q7A4H0 Q7A4H0_STAAN | Value Missing |
| 417 | Xaa-Pro dipeptidase OS=Staphylococcus aureus (strain N315) GN=SA1360 PE=3 SV=1 | Q99TW4 Q99TW4_STAAN | Value Missing |
| 423 | ATP-dependent Clp protease proteolytic subunit OS=Staphylococcus aureus (strain N315) GN=clpP PE=1 SV=1 | P99089 CLPP_STAAN | Value Missing |
| 426 | SA1626 protein OS=Staphylococcus aureus (strain N315) GN=SA1626 PE=4 SV=1 | Q7A4Y5 Q7A4Y5_STAAN (+1) | Value Missing |
| 427 | Ribonuclease J 1 OS=Staphylococcus aureus (strain N315) GN=SA0940 PE=1 SV=1 | Q7A682 RNJ1_ST_AAN | Value Missing |
| 429 | D-3-phosphoglycerate dehydrogenase OS=Staphylococcus aureus (strain N315) GN=serA PE=4 SV=1 | Q7A542 Q7A542_STAAN | Value Missing |
| 431 | Phosphoribosylglycinamide formyltransferase OS=Staphylococcus aureus (strain N315) GN=purN PE=1 SV=1 | P99162 PUR3_STAAN | Value Missing |
| 438 | Ornithine carbamoyltransferase OS=Staphylococcus aureus (strain N315) GN=argF | P99073 OTC_STA | Value |

| | PE=1 SV=1 | AN | Missing |
|-----|--|-------------------------|------------------|
| 439 | Alanine dehydrogenase 1 OS= <i>Staphylococcus aureus</i> (strain N315) GN=ald1 PE=1 SV=1 | P99151 DHA1_ST AAN | Value Missing |
| 445 | Peptide chain release factor 3 OS= <i>Staphylococcus aureus</i> (strain N315) GN=prfC PE=1 SV=1 | Q99V72 RF3_STA AN | Value Missing |
| 451 | DNA repair protein OS= <i>Staphylococcus aureus</i> (strain N315) GN=recN PE=4 SV=1 | Q7A5F5 Q7A5F5_ STAAN | Value Missing |
| 452 | HTH-type transcriptional regulator rot OS= <i>Staphylococcus aureus</i> (strain N315) GN=rot PE=1 SV=2 | Q7A514 ROT_STA AN | Value Missing |
| 458 | Glycine betaine/carnitine/choline ABC transporter opuCA OS= <i>Staphylococcus aureus</i> (strain N315) GN=opuCA PE=4 SV=1 | Q7A3P8 Q7A3P8_ STAAN | Value Missing |
| 461 | Putative uncharacterized protein SA1161 OS= <i>Staphylococcus aureus</i> (strain N315) GN=SA1161 PE=4 SV=1 | Q7A5T9 Q7A5T9_ STAAN | Value Missing |
| 463 | SA2297 protein OS= <i>Staphylococcus aureus</i> (strain N315) GN=SA2297 PE=4 SV=1 | Q7A3J1_STAAN (+1) | Value Missing |
| 472 | tRNA pseudouridine synthase B OS= <i>Staphylococcus aureus</i> (strain N315) GN=truB PE=1 SV=1 | P65855 TRUB_ST AAN | Value Missing |
| 474 | Alkaline phosphatase synthesis transcriptional regulatory protein OS= <i>Staphylococcus aureus</i> (strain N315) GN=phoP PE=4 SV=1 | Q7A562 Q7A562_ STAAN | Value Missing |
| 484 | Putative uncharacterized protein SA1364 OS= <i>Staphylococcus aureus</i> (strain N315) GN=SA1364 PE=4 SV=1 | Q7A5E7 Q7A5E7_ STAAN | Value Missing |
| 487 | SA2156 protein OS= <i>Staphylococcus aureus</i> (strain N315) GN=SA2156 PE=4 SV=1 | Q7A3W7 Q7A3W7_ STAAN | Value Missing |
| 494 | HPr kinase/phosphorylase OS= <i>Staphylococcus aureus</i> (strain N315) GN=hprK PE=1 SV=1 | P60701 HPRK_ST AAN | Value Missing |
| 507 | DNA topoisomerase 4 subunit B OS= <i>Staphylococcus aureus</i> (strain N315) GN=parE PE=1 SV=1 | P66939 PARE_ST AAN | Value Missing |
| 512 | Arginine deiminase OS= <i>Staphylococcus aureus</i> (strain N315) GN=arcA PE=1 SV=1 | P63554 ARCA_ST AAN | Value Missing |
| 515 | Histidine protein kinase saeS OS= <i>Staphylococcus aureus</i> (strain N315) GN=saeS PE=1 SV=1 | Q7A6V4 SAES_ST AAN | Value Missing |
| 520 | Accessory gene regulator C OS= <i>Staphylococcus aureus</i> (strain N315) GN=agrC PE=4 SV=1 | Q7A4I6 Q7A4I6_S TAAN | Value Missing |
| 521 | Putative uncharacterized protein SA1423 OS= <i>Staphylococcus aureus</i> (strain N315) GN=SA1423 PE=4 SV=1 | Q7A5B3 Q7A5B3_ STAAN | Value Missing |
| 524 | Glutamine amidotransferase subunit pdxT OS= <i>Staphylococcus aureus</i> (strain N315) GN=pdxT PE=1 SV=1 | Q7A7A1 PDXT_S TAAN | Value Missing |
| 530 | SA1708 protein OS= <i>Staphylococcus aureus</i> (strain N315) GN=SA1708 PE=4 SV=1 | Q7A4R3 Q7A4R3_ STAAN | Value Missing |
| 534 | Protoporphyrinogen oxidase OS= <i>Staphylococcus aureus</i> (strain N315) GN=hemY PE=4 SV=1 | Q7A4W4 Q7A4W4_ STAAN | Value Missing |
| 544 | Putative uncharacterized protein SA1662 OS= <i>Staphylococcus aureus</i> (strain N315) GN=SA1662 PE=4 SV=1 | Q7A4V4_STAAN | Value Missing |
| 549 | Phenylalanyl-tRNA synthetase beta chain OS= <i>Staphylococcus aureus</i> (strain N315) GN=pheT PE=1 SV=1 | P67041 SYFB_ST AAN | Value Missing |
| 551 | SA0791 protein OS= <i>Staphylococcus aureus</i> (strain N315) GN=SA0791 PE=4 SV=1 | Q7A6K3 Q7A6K3_ STAAN | Value Missing |
| 559 | SA2278 protein OS= <i>Staphylococcus aureus</i> (strain N315) GN=SA2278 PE=4 SV=1 | Q7A3K8 Q7A3K8_ STAAN | Value Missing |
| 562 | Cmp-binding-factor 1 OS= <i>Staphylococcus aureus</i> (strain N315) GN=cbf1 PE=4 SV=1 | Q7A4V6 Q7A4V6_ STAAN | Value Missing |
| 564 | UPF0316 protein SA1727 OS= <i>Staphylococcus aureus</i> (strain N315) GN=SA1727 PE=1 SV=1 | P61544 Y1727_ST AAN | Value Missing |
| 565 | Putative uncharacterized protein SA1426 OS= <i>Staphylococcus aureus</i> (strain N315) GN=SA1426 PE=4 SV=1 | Q7A5B1 Q7A5B1_ STAAN | Value Missing |
| 572 | Penicillin binding protein 4 OS= <i>Staphylococcus aureus</i> (strain N315) GN=pbp4 PE=3 SV=1 | Q7A709 Q7A709_ STAAN | Value Missing |
| 574 | Putative uncharacterized protein SA0513 OS= <i>Staphylococcus aureus</i> (strain N315) GN=SA0513 PE=4 SV=1 | Q7A787 Q7A787_ STAAN | Value Missing |

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|-----|--|---------------------|---------------|
| 581 | tRNA-specific 2-thiouridylase mnmA OS=Staphylococcus aureus (strain N315) GN=mnmA PE=1 SV=1 | Q99TM8 MNMA_STAAN | Value Missing |
| 586 | Thymidylate kinase OS=Staphylococcus aureus (strain N315) GN=tmk PE=3 SV=1 | P65249 KTHY_ST AAN | Value Missing |
| 587 | GTP-binding protein lepA OS=Staphylococcus aureus (strain N315) GN=lepA PE=1 SV=1 | P65272 LEPA_ST AAN | Value Missing |
| 588 | DNA mismatch repair protein mutL OS=Staphylococcus aureus (strain N315) GN=mutL PE=1 SV=1 | P65492 MUTL_ST AAN | Value Missing |
| 589 | Aspartate carbamoyltransferase OS=Staphylococcus aureus (strain N315) GN=pyrB PE=1 SV=1 | P65618 PYRB_ST AAN | Value Missing |
| 592 | Penicillin-binding protein 3 OS=Staphylococcus aureus (strain N315) GN=pbp3 PE=4 SV=1 | Q7A5D5 Q7A5D5_STAAN | Value Missing |
| 595 | SA0357 protein OS=Staphylococcus aureus (strain N315) GN=SA0357 PE=4 SV=1 | Q7A7K0 Q7A7K0_STAAN | Value Missing |
| 604 | Fibrinogen-binding protein OS=Staphylococcus aureus (strain N315) GN=fib PE=1 SV=1 | P68800 FIB_STAA N | Value Missing |
| 605 | 4,4'-diaponeurosporene oxidase OS=Staphylococcus aureus (strain N315) GN=crtP PE=1 SV=1 | Q7A3D9 CRTP_ST AAN | Value Missing |
| 606 | SA2243 protein OS=Staphylococcus aureus (strain N315) GN=SA2243 PE=4 SV=1 | Q7A3P3_STAAN (+1) | Value Missing |
| 607 | SA2103 protein OS=Staphylococcus aureus (strain N315) GN=SA2103 PE=4 SV=1 | Q7A413 Q7A413_STAAN | Value Missing |
| 614 | Membrane protein oxaA OS=Staphylococcus aureus (strain N315) GN=oxaA PE=1 SV=1 | P65629 OXAA_ST AAN | Value Missing |
| 615 | SA1329 protein OS=Staphylococcus aureus (strain N315) GN=SA1329 PE=4 SV=1 | Q7A5H3 Q7A5H3_STAAN | Value Missing |
| 616 | Competence-damage inducible protein cinA OS=Staphylococcus aureus (strain N315) GN=cinA PE=4 SV=1 | Q7A5W9 Q7A5W9_STAAN | Value Missing |
| 622 | Putative uncharacterized protein SA0449 OS=Staphylococcus aureus (strain N315) GN=SA0449 PE=4 SV=1 | Q7A7C0 Q7A7C0_STAAN | Value Missing |
| 634 | OppD protein OS=Staphylococcus aureus (strain N315) GN=oppD PE=4 SV=1 | Q7A6F4 Q7A6F4_STAAN | Value Missing |
| 635 | Putative uncharacterized protein SA0832 OS=Staphylococcus aureus (strain N315) GN=SA0832 PE=4 SV=1 | Q7A6H0 Q7A6H0_STAAN | Value Missing |
| 637 | Transcriptional regulator ctsR OS=Staphylococcus aureus (strain N315) GN=ctsR PE=1 SV=1 | Q7A799 CTSR_ST AAN | Value Missing |
| 648 | Ribose-5-phosphate isomerase A OS=Staphylococcus aureus (strain N315) GN=rpiA PE=3 SV=1 | P66695 RPIA_STAA N | Value Missing |
| 649 | Putative uncharacterized protein SA2090 OS=Staphylococcus aureus (strain N315) GN=SA2090 PE=4 SV=1 | Q7A424 Q7A424_STAAN | Value Missing |
| 656 | SA2132 protein OS=Staphylococcus aureus (strain N315) GN=SA2132 PE=4 SV=1 | Q99RT2 Q99RT2_STAAN | Value Missing |
| 661 | 2-dehydropantoate 2-reductase OS=Staphylococcus aureus (strain N315) GN=SA2232 PE=3 SV=1 | Q7A3Q3 Q7A3Q3_STAAN | Value Missing |
| 665 | Putative uncharacterized protein SA0184 OS=Staphylococcus aureus (strain N315) GN=SA0184 PE=4 SV=1 | Q7A806 Q7A806_STAAN | Value Missing |
| 666 | Gamma-hemolysin component B OS=Staphylococcus aureus (strain N315) GN=hlgB PE=1 SV=1 | P0A075 HLGB_ST AAN | Value Missing |
| 670 | Mannose-6-phosphate isomerase OS=Staphylococcus aureus (strain N315) GN=pmi PE=3 SV=1 | Q7A373 Q7A373_STAAN | Value Missing |
| 674 | SA0566 protein OS=Staphylococcus aureus (strain N315) GN=SA0566 PE=4 SV=1 | Q7A739 Q7A739_STAAN | Value Missing |
| 675 | Putative uncharacterized protein SA0561 OS=Staphylococcus aureus (strain N315) GN=SA0561 PE=4 SV=1 | Q7A743 Q7A743_STAAN | Value Missing |
| 679 | Putative uncharacterized protein SA0954 OS=Staphylococcus aureus (strain N315) GN=SA0954 PE=4 SV=1 | Q7A675 Q7A675_STAAN | Value Missing |
| 682 | Peptide chain release factor 1 OS=Staphylococcus aureus (strain N315) GN=prfA PE=3 SV=1 | P66019 RF1_STAA N | Value Missing |
| 685 | Putative uncharacterized protein SA0739 OS=Staphylococcus aureus (strain N315) | Q7A6P8 Q7A6P8_ | Value |

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|-----|--|----------------------|---------------|
| | GN=SA0739 PE=4 SV=1 | STAAN | Missing |
| 686 | Putative zinc metalloprotease SA1105 OS=Staphylococcus aureus (strain N315) GN=SA1105 PE=1 SV=1 | P63333 Y1105_ST AAN | Value Missing |
| 700 | Putative uncharacterized protein SA1942 OS=Staphylococcus aureus (strain N315) GN=SA1942 PE=4 SV=1 | Q7A4C7 Q7A4C7_STAAN | Value Missing |
| 703 | SA0958 protein OS=Staphylococcus aureus (strain N315) GN=SA0958 PE=4 SV=1 | Q7A673 Q7A673_STAAN | Value Missing |
| 704 | SA0734 protein OS=Staphylococcus aureus (strain N315) GN=SA0734 PE=4 SV=1 | Q7A6Q0 Q7A6Q0_STAAN | Value Missing |
| 706 | Putative uncharacterized protein SA0296 OS=Staphylococcus aureus (strain N315) GN=SA0296 PE=4 SV=1 | Q7A7Q1 Q7A7Q1_STAAN | Value Missing |
| 720 | Undecaprenyl-diphosphatase OS=Staphylococcus aureus (strain N315) GN=uppP PE=3 SV=1 | P67391 UPPP_STA AN | Value Missing |
| 722 | Carbamate kinase 2 OS=Staphylococcus aureus (strain N315) GN=arcC2 PE=1 SV=1 | P99069 ARCC2_S TAAN | Value Missing |
| 728 | SA0895 protein OS=Staphylococcus aureus (strain N315) GN=SA0895 PE=4 SV=1 | Q7A6B2 Q7A6B2_STAAN | Value Missing |
| 740 | Urease accessory protein ureG OS=Staphylococcus aureus (strain N315) GN=ureG PE=1 SV=1 | Q7A427 UREG_ST AAN | Value Missing |
| 747 | Orotate phosphoribosyltransferase OS=Staphylococcus aureus (strain N315) GN=pyrE PE=1 SV=1 | PYRE_STAAN (+1) | Value Missing |
| 754 | Sulfite reductase flavoprotein OS=Staphylococcus aureus (strain N315) GN=SA2413 PE=3 SV=1 | Q7A392 Q7A392_STAAN | Value Missing |
| 755 | SA1699 protein OS=Staphylococcus aureus (strain N315) GN=SA1699 PE=4 SV=1 | Q99SZ8 Q99SZ8_S TAAN | Value Missing |
| 759 | Putative uncharacterized protein SA1672 OS=Staphylococcus aureus (strain N315) GN=SA1672 PE=4 SV=1 | Q7A4U4 Q7A4U4_STAAN | Value Missing |
| 770 | Putative uncharacterized protein SA0601 OS=Staphylococcus aureus (strain N315) GN=SA0601 PE=3 SV=1 | Q7A705 Q7A705_STAAN | Value Missing |
| 771 | NADPH-dependent oxidoreductase OS=Staphylococcus aureus (strain N315) GN=nfrA PE=3 SV=1 | Q7A7J0 NFRA_ST AAN | Value Missing |
| 774 | Putative uncharacterized protein SA1526 OS=Staphylococcus aureus (strain N315) GN=SA1526 PE=4 SV=1 | Q7A555 Q7A555_STAAN | Value Missing |
| 778 | 30S ribosomal protein S5 OS=Staphylococcus aureus (strain N315) GN=rpsE PE=1 SV=1 | RS5_STAAN | Value Missing |
| 791 | Dihydrolipoyl dehydrogenase OS=Staphylococcus aureus (strain N315) GN=SA1349 PE=3 SV=1 | Q7A5F6 Q7A5F6_STAAN | Value Missing |

Table A12. Complete list of intracellular proteins identified from the USA 100 adaptive mutant at 15 hours.

| # | Identified Proteins (791) | Accession Number | Fold Change from WT |
|-----|--|---------------------|---------------------|
| 47 | Uncharacterized leukocidin-like protein 2 OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1975 PE=3 SV=1 | Q2FFA2 LUKL2_STAA3 | -4.4 |
| 67 | Uncharacterized leukocidin-like protein 1 OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1974 PE=3 SV=1 | Q2FFA3 LUKL1_STAA3 | -4.4 |
| 429 | Glycosyl transferase, group 1 family protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0939 PE=4 SV=1 | Q2FI41 Q2FI41_STAA3 | -4.4 |
| 428 | Proline dehydrogenase OS=Staphylococcus aureus (strain USA300) GN=putA PE=4 SV=1 | Q2FFX4 Q2FFX4_STAA3 | -4.3 |
| 671 | Hydrolase, alpha/beta hydrolase fold family OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0604 PE=4 SV=1 | Q2FJ21 Q2FJ21_STAA3 | -4.1 |

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|-----|---|---------------------|------|
| 338 | Dihydroxyacetone kinase, DhaL subunit OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0637 PE=4 SV=1 | Q2FIY8 Q2FIY8_STAA3 | -4 |
| 521 | Accessory gene regulator protein C OS=Staphylococcus aureus (strain USA300) GN=agrC PE=4 SV=1 | Q2FF86 Q2FF86_STAA3 | -3.8 |
| 205 | PTS system glucose-specific EIICBA component OS=Staphylococcus aureus (strain USA300) GN=ptsG PE=3 SV=1 | Q2FK73 PTG3C_STAA3 | -3.6 |
| 436 | Alanine dehydrogenase 1 OS=Staphylococcus aureus (strain USA300) GN=ald1 PE=3 SV=1 | Q2FH00 DHA1_STAA3 | -3.6 |
| 552 | UPF0316 protein SAUSA300_1892 OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1892 PE=3 SV=1 | Q2FFI4 Y1892_STAA3 | -3.6 |
| 587 | Putative staphylococcal enterotoxin OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0370 PE=4 SV=1 | Q2FJP4 Q2FJP4_STAA3 | -3.5 |
| 31 | Phosphoribosylformylglycinamide synthase 2 OS=Staphylococcus aureus (strain USA300) GN=purL PE=3 SV=1 | Q2FI09 PURL_STAA3 | -3.4 |
| 244 | Uracil phosphoribosyltransferase OS=Staphylococcus aureus (strain USA300) GN=upp PE=3 SV=1 | Q2FF16 UPP_STAA3 | -3.4 |
| 579 | GTP-binding protein lepA OS=Staphylococcus aureus (strain USA300) GN=lepA PE=3 SV=1 | Q2FGD9 LEPA_STAA3 | -3.4 |
| 269 | Hydroxymethylglutaryl-CoA synthase OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_2484 PE=4 SV=1 | Q2FDW0 Q2FDW0_STAA3 | -3.3 |
| 392 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_2328 PE=4 SV=1 | Q2FEB5 Q2FEB5_STAA3 | -3.3 |
| 453 | Glutamate-1-semialdehyde 2,1-aminomutase 2 OS=Staphylococcus aureus (strain USA300) GN=hemL2 PE=3 SV=1 | Q2FFN1 GSA2_STAA3 | -3.3 |
| 8 | Formate acetyltransferase OS=Staphylococcus aureus (strain USA300) GN=pflB PE=3 SV=1 | Q2FK44 PFLB_STAA3 | -3.2 |
| 65 | Probable quinol oxidase subunit 2 OS=Staphylococcus aureus (strain USA300) GN=qoxA PE=3 SV=1 | Q2FI17 QOX2_STAA3 | -3.2 |
| 305 | ATP-dependent hsl protease ATP-binding subunit hslU OS=Staphylococcus aureus (strain USA300) GN=hslU PE=3 SV=1 | Q2FHI4 HSLU_STAA3 | -3.2 |
| 319 | Accessory gene regulator protein A OS=Staphylococcus aureus (strain USA300) GN=agrA PE=4 SV=1 | Q2FF85 Q2FF85_STAA3 | -3.2 |
| 534 | AcrB/AcrD/AcrF family protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_2213 PE=4 SV=1 | Q2FEN0 Q2FEN0_STAA3 | -3.2 |
| 662 | Uridine kinase OS=Staphylococcus aureus (strain USA300) GN=udk PE=3 SV=1 | Q2FGB5 URK_STAA3 | -3.2 |
| 146 | Phosphoribosylformylglycinamide cyclo-ligase OS=Staphylococcus aureus (strain USA300) GN=purM PE=3 SV=1 | Q2FI07 PUR5_STAA3 | -3.1 |
| 278 | Putative teichoic acid biosynthesis protein B OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0247 PE=4 SV=1 | Q2FK17 Q2FK17_STAA3 | -3.1 |
| 297 | Putative lipoprotein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0693 PE=4 SV=1 | Q2FIT2 Q2FIT2_STAA3 | -3.1 |

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|-----|---|---------------------|------|
| 327 | Aminoacyltransferase femX OS=Staphylococcus aureus (strain USA300) GN=femX PE=3 SV=1 | Q2FEM9 FEMX_STAA3 | -3.1 |
| 339 | Chromosomal replication initiator protein dnaA OS=Staphylococcus aureus (strain USA300) GN=dnaA PE=3 SV=1 | Q2FKQ5 DNAA_STAA3 | -3.1 |
| 361 | Hydrolase, haloacid dehalogenase-like family OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0544 PE=4 SV=1 | Q2FJ81 Q2FJ81_STAA3 | -3.1 |
| 411 | Lipoyl synthase OS=Staphylococcus aureus (strain USA300) GN=lipA PE=3 SV=1 | Q2FIE9 LIPA_STAA3 | -3.1 |
| 61 | Glucosamine--fructose-6-phosphate aminotransferase (Isomerizing) OS=Staphylococcus aureus (strain USA300) GN=glmS PE=3 SV=1 | Q2FEX8 Q2FEX8_STAA3 | -3 |
| 171 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1729 PE=4 SV=1 | Q2FFV7 Q2FFV7_STAA3 | -3 |
| 116 | Phosphoribosylamine--glycine ligase OS=Staphylococcus aureus (strain USA300) GN=purD PE=3 SV=1 | Q2FI04 Q2FI04_STAA3 | -2.9 |
| 148 | Pyridoxal biosynthesis lyase pdxS OS=Staphylococcus aureus (strain USA300) GN=pdxS PE=3 SV=1 | Q2FJC1 PDXS_STAA3 | -2.9 |
| 200 | Glyceraldehyde-3-phosphate dehydrogenase, type I OS=Staphylococcus aureus (strain USA300) GN=gap PE=3 SV=1 | Q2FG50 Q2FG50_STAA3 | -2.9 |
| 333 | ABC transporter ATP-binding protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0620 PE=4 SV=1 | Q2FJ05 Q2FJ05_STAA3 | -2.9 |
| 442 | DNA repair protein RecN OS=Staphylococcus aureus (strain USA300) GN=recN PE=4 SV=1 | Q2FGL4 Q2FGL4_STAA3 | -2.9 |
| 228 | Probable quinol oxidase subunit 1 OS=Staphylococcus aureus (strain USA300) GN=qoxB PE=3 SV=1 | Q2FI18 QOX1_STAA3 | -2.8 |
| 270 | Alcohol dehydrogenase, iron-containing OS=Staphylococcus aureus (strain USA300) GN=adhE PE=4 SV=1 | Q2FKB2 Q2FKB2_STAA3 | -2.8 |
| 452 | Oxidoreductase, aldo/keto reductase family OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0688 PE=4 SV=1 | Q2FIT7 Q2FIT7_STAA3 | -2.8 |
| 471 | Protein-export membrane protein SecF OS=Staphylococcus aureus (strain USA300) GN=secF PE=4 SV=1 | Q2FG90 Q2FG90_STAA3 | -2.8 |
| 668 | Chaperone protein dnaJ OS=Staphylococcus aureus (strain USA300) GN=dnaJ PE=3 SV=1 | Q2FGE4 DNAJ_STAA3 | -2.8 |
| 159 | Phosphoribosylaminoimidazole-succinocarboxamide synthase OS=Staphylococcus aureus (strain USA300) GN=purC PE=3 SV=1 | Q2FI12 PUR7_STAA3 | -2.7 |
| 271 | ABC transporter, ATP-binding protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_2453 PE=4 SV=1 | Q2FDZ1 Q2FDZ1_STAA3 | -2.7 |
| 357 | Ribonuclease J 2 OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1168 PE=3 SV=2 | Q2FHG3 RNJ2_STAA3 | -2.7 |
| 225 | Acetoin(Diacetyl) reductase OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0129 PE=3 SV=1 | Q2FKD2 Q2FKD2_STAA3 | -2.6 |
| 232 | ATP synthase subunit delta OS=Staphylococcus aureus (strain USA300) GN=atpH PE=3 SV=1 | Q2FF21 ATPD_STAA3 | -2.6 |

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|-----|--|------------------------------|------|
| 276 | UPF0637 protein SAUSA300_1006 OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1006 PE=3 SV=1 | Q2FHX4 Y1006_STAA3 | -2.6 |
| 341 | Dihydroorotate dehydrogenase OS=Staphylococcus aureus (strain USA300) GN=pyrD PE=3 SV=1 | Q2FDR8 Q2FDR8_STAA3 | -2.6 |
| 359 | Glycosyl transferase, group 2 family protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0252 PE=4 SV=1 | Q2FK12 Q2FK12_STAA3 | -2.6 |
| 383 | Staphopain A OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1890 PE=4 SV=1 | Q2FFI6 Q2FFI6_STAA3 | -2.6 |
| 404 | HTH-type transcriptional regulator sarR OS=Staphylococcus aureus (strain USA300) GN=sarR PE=3 SV=3 | Q2FEJ8 SARR_STAA3 | -2.6 |
| 752 | Dihydroxyacetone kinase, DhaK subunit OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0636 PE=4 SV=1 | Q2FIY9 Q2FIY9_STAA3 | -2.6 |
| 759 | RNA methyltransferase OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1805 PE=4 SV=1 | Q2FFP0 Q2FFP0_STAA3 | -2.6 |
| 788 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_2378 PE=4 SV=1 | Q2FE65 RANDOM_Q2FE65_STAA3-R | -2.6 |
| 15 | Cold shock protein cspA OS=Staphylococcus aureus (strain USA300) GN=cspA PE=3 SV=1 | Q2FH36 CSPA_STAA3 | -2.5 |
| 35 | 50S ribosomal protein L5 OS=Staphylococcus aureus (strain USA300) GN=rplE PE=3 SV=1 | Q2FEQ1 RL5_STAA3 | -2.5 |
| 55 | ATP synthase subunit alpha OS=Staphylococcus aureus (strain USA300) GN=atpA PE=3 SV=1 | Q2FF22 ATPA_STAA3 | -2.5 |
| 154 | L-lactate dehydrogenase 2 OS=Staphylococcus aureus (strain USA300) GN=ldh2 PE=3 SV=1 | Q2FDQ7 LDH2_STAA3 | -2.5 |
| 235 | UDP-N-acetylglucosamine--N-acetylmuramyl-(pentapeptide) pyrophosphoryl-undecaprenol N-acetylglucosamine transferase OS=Staphylococcus aureus (strain USA300) GN=murG PE=3 SV=1 | Q2FH20 MURG_STAA3 | -2.5 |
| 330 | Oxidoreductase, aldo/keto reductase family OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1450 PE=4 SV=1 | Q2FGN2 Q2FGN2_STAA3 | -2.5 |
| 387 | Phosphomethylpyrimidine kinase OS=Staphylococcus aureus (strain USA300) GN=thiD PE=4 SV=1 | Q2FJ63 Q2FJ63_STAA3 | -2.5 |
| 426 | Amidophosphoribosyltransferase OS=Staphylococcus aureus (strain USA300) GN=purF PE=4 SV=1 | Q2FI08 Q2FI08_STAA3 | -2.5 |
| 450 | Cytidylate kinase OS=Staphylococcus aureus (strain USA300) GN=cmk PE=4 SV=1 | Q2FGW4 Q2FGW4_STAA3 | -2.5 |
| 516 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0278 PE=4 SV=1 | Q2FJY6 Q2FJY6_STAA3 | -2.5 |
| 582 | Aspartate carbamoyltransferase OS=Staphylococcus aureus (strain USA300) GN=pyrB PE=3 SV=1 | Q2FHN8 PYRB_STAA3 | -2.5 |
| 603 | Membrane protein oxaA OS=Staphylococcus aureus (strain USA300) GN=oxaA PE=3 SV=1 | Q2FF36 OXAA_STAA3 | -2.5 |
| 32 | ABC transporter, substrate-binding protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0618 PE=3 SV=1 | Q2FJ07 Q2FJ07_STAA3 | -2.4 |

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| 39 | Carbamoyl-phosphate synthase large chain OS=Staphylococcus aureus (strain USA300) GN=carB PE=3 SV=1 | Q2FHN5 CARB_STAA3 | -2.4 |
| 196 | Phosphoribosylaminoimidazole carboxylase, ATPase subunit OS=Staphylococcus aureus (strain USA300) GN=purK PE=4 SV=1 | Q2FI13 Q2FI13_STAA3 | -2.4 |
| 217 | ATP synthase subunit b OS=Staphylococcus aureus (strain USA300) GN=atpF PE=3 SV=1 | Q2FF20 ATPF_STAA3 | -2.4 |
| 249 | Bifunctional protein pyrR OS=Staphylococcus aureus (strain USA300) GN=pyrR PE=3 SV=1 | Q2FHP0 PYRR_STAA3 | -2.4 |
| 334 | Dihydroorotate OS=Staphylococcus aureus (strain USA300) GN=pyrC PE=3 SV=1 | Q2FHN7 Q2FHN7_STAA3 | -2.4 |
| 440 | Glycine betaine/carnitine/choline ABC transporter ATP-binding protein OS=Staphylococcus aureus (strain USA300) GN=opuC PE=4 SV=1 | Q2FE50 Q2FE50_STAA3 | -2.4 |
| 486 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0331 PE=4 SV=1 | Q2FJT3 Q2FJT3_STAA3 | -2.4 |
| 496 | Carbamate kinase 1 OS=Staphylococcus aureus (strain USA300) GN=arcC1 PE=3 SV=1 | Q2FHR7 ARCC1_STAA3 | -2.4 |
| 559 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1780 PE=4 SV=1 | Q2FFR5 Q2FFR5_STAA3 | -2.4 |
| 699 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1583 PE=4 SV=1 | Q2FGA0 Q2FGA0_STAA3 | -2.4 |
| 53 | Protein translocase subunit secA 1 OS=Staphylococcus aureus (strain USA300) GN=secA1 PE=3 SV=1 | Q2FIN8 SECA1_STAA3 | -2.3 |
| 89 | Bifunctional purine biosynthesis protein purH OS=Staphylococcus aureus (strain USA300) GN=purH PE=3 SV=1 | Q2FI05 PUR9_STAA3 | -2.3 |
| 138 | Catabolite control protein A OS=Staphylococcus aureus (strain USA300) GN=ccpA PE=4 SV=1 | Q2FG02 Q2FG02_STAA3 | -2.3 |
| 188 | Putative serine protease HtrA OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1674 PE=4 SV=1 | Q2FG10 Q2FG10_STAA3 | -2.3 |
| 354 | Serine-protein kinase rsbW OS=Staphylococcus aureus (strain USA300) GN=rsbW PE=3 SV=1 | Q2FF59 RSBW_STAA3 | -2.3 |
| 399 | Methionyl-tRNA formyltransferase OS=Staphylococcus aureus (strain USA300) GN=fmt PE=3 SV=1 | Q2FHM2 FMT_STAA3 | -2.3 |
| 696 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_2093 PE=4 SV=1 | Q2FEY9 Q2FEY9_STAA3 | -2.3 |
| 71 | Ribonucleoside-diphosphate reductase OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0716 PE=3 SV=1 | Q2FIQ9 Q2FIQ9_STAA3 | -2.2 |
| 336 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0982 PE=4 SV=1 | Q2FHZ8 Q2FHZ8_STAA3 | -2.2 |
| 390 | Fmt protein OS=Staphylococcus aureus (strain USA300) GN=fmt PE=4 SV=1 | Q2FI21 Q2FI21_STAA3 | -2.2 |
| 523 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1554 PE=4 SV=1 | Q2FGC9 Q2FGC9_STAA3 | -2.2 |

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| 548 | Pyrimidine nucleoside transport protein OS=Staphylococcus aureus (strain USA300) GN=nupC PE=4 SV=1 | Q2FJB9 Q2FJB9_STAA3 | -2.2 |
| 557 | ABC transporter, permease protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_2358 PE=3 SV=1 | Q2FE85 Q2FE85_STAA3 | -2.2 |
| 621 | tRNA modification GTPase mnmE OS=Staphylococcus aureus (strain USA300) GN=mnmE PE=3 SV=1 | Q2FDE8 MNME_STAA3 | -2.2 |
| 737 | Heme-degrading monooxygenase isdI OS=Staphylococcus aureus (strain USA300) GN=isdI PE=3 SV=1 | Q2FK96 ISDI_STAA3 | -2.2 |
| 9 | Penicillin-binding protein 2' OS=Staphylococcus aureus (strain USA300) GN=mecA PE=4 SV=1 | Q2FKM6 Q2FKM6_STAA3 | -2.1 |
| 19 | ATP synthase subunit beta OS=Staphylococcus aureus (strain USA300) GN=atpD PE=3 SV=1 | Q2FF24 ATPB_STAA3 | -2.1 |
| 29 | 30S ribosomal protein S3 OS=Staphylococcus aureus (strain USA300) GN=rpsC PE=3 SV=1 | Q2FEP5 RS3_STAA3 | -2.1 |
| 136 | 2,3-bisphosphoglycerate-dependent phosphoglycerate mutase OS=Staphylococcus aureus (strain USA300) GN=gpmA PE=3 SV=1 | Q2FE81 GPMA_STAA3 | -2.1 |
| 160 | Alcohol dehydrogenase OS=Staphylococcus aureus (strain USA300) GN=adh PE=3 SV=1 | Q2FJ31 ADH_STAA3 | -2.1 |
| 223 | Xanthine phosphoribosyltransferase OS=Staphylococcus aureus (strain USA300) GN=xpt PE=3 SV=1 | Q2FJM8 XPT_STAA3 | -2.1 |
| 230 | Putative pyridoxal phosphate-dependent acyltransferase OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0535 PE=3 SV=1 | Q2FJ90 Q2FJ90_STAA3 | -2.1 |
| 251 | Putative arsenate reductase OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0790 PE=4 SV=1 | Q2FII8 Q2FII8_STAA3 | -2.1 |
| 282 | 50S ribosomal protein L20 OS=Staphylococcus aureus (strain USA300) GN=rplT PE=3 SV=1 | Q2FG58 RL20_STAA3 | -2.1 |
| 315 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_2212 PE=4 SV=1 | Q2FEN1 Q2FEN1_STAA3 | -2.1 |
| 371 | ATP-binding protein, Mrp/Nbp35 family OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_2125 PE=4 SV=1 | Q2FEW6 Q2FEW6_STAA3 | -2.1 |
| 403 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1223 PE=4 SV=1 | Q2FHA8 Q2FHA8_STAA3 | -2.1 |
| 412 | Phosphopentomutase OS=Staphylococcus aureus (strain USA300) GN=deoB PE=3 SV=1 | Q2FKC0 DEOB_STAA3 | -2.1 |
| 504 | Putative lipoprotein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_2403 PE=4 SV=1 | Q2FE40 Q2FE40_STAA3 | -2.1 |
| 506 | 3-phosphoshikimate 1-carboxyvinyltransferase OS=Staphylococcus aureus (strain USA300) GN=aroA PE=3 SV=1 | Q2FGX6 AROA_STAA3 | -2.1 |
| 508 | Glycerol-3-phosphate dehydrogenase [NAD(P)+] OS=Staphylococcus aureus (strain USA300) GN=gpsA PE=3 SV=1 | Q2FGW8 GPDA_STAA3 | -2.1 |
| 729 | Amino acid/peptide transporter (Peptide:H ⁺ symporter) OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0712 PE=3 SV=1 | Q2FIR3 Q2FIR3_STAA3 | -2.1 |

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| 11 | Malate:quinone-oxidoreductase OS=Staphylococcus aureus (strain USA300) GN=mqo PE=3 SV=1 | Q2FDQ3 Q2FDQ3_STAA3 | -2 |
| 42 | UPF0365 protein SAUSA300_1533 OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1533 PE=3 SV=1 | Q2FGF0 Y1533_STAA3 | -2 |
| 46 | Putative universal stress protein SAUSA300_1656 OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1656 PE=3 SV=1 | Q2FG28 Y1656_STAA3 | -2 |
| 48 | 50S ribosomal protein L1 OS=Staphylococcus aureus (strain USA300) GN=rplA PE=3 SV=1 | Q2FJA2 RL1_STAA3 | -2 |
| 68 | UPF0478 protein SAUSA300_1685 OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1685 PE=3 SV=1 | Q2FFZ9 Y1685_STAA3 | -2 |
| 73 | NADH dehydrogenase-like protein SAUSA300_0844 OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0844 PE=3 SV=1 | Q2FID4 Y844_STAA3 | -2 |
| 179 | GTPase obg OS=Staphylococcus aureus (strain USA300) GN=obg PE=3 SV=1 | Q2FG83 OBG_STAA3 | -2 |
| 209 | Succinate dehydrogenase, iron-sulfur protein OS=Staphylococcus aureus (strain USA300) GN=sdhB PE=4 SV=1 | Q2FHT2 Q2FHT2_STAA3 | -2 |
| 262 | Transcription termination factor Rho OS=Staphylococcus aureus (strain USA300) GN=rho PE=4 SV=1 | Q2FF07 Q2FF07_STAA3 | -2 |
| 285 | Elastin-binding protein ebpS OS=Staphylococcus aureus (strain USA300) GN=ebpS PE=3 SV=3 | Q2FGW1 EBPS_STAA3 | -2 |
| 301 | Trans-2-enoyl-ACP reductase OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0912 PE=4 SV=1 | Q2FI66 Q2FI66_STAA3 | -2 |
| 316 | Putative AMP-binding enzyme OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_2542 PE=4 SV=1 | Q2FDQ2 Q2FDQ2_STAA3 | -2 |
| 317 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_2257 PE=4 SV=1 | Q2FEI6 Q2FEI6_STAA3 | -2 |
| 344 | Glucose-6-phosphate 1-dehydrogenase OS=Staphylococcus aureus (strain USA300) GN=zwf PE=3 SV=1 | Q2FGM8 Q2FGM8_STAA3 | -2 |
| 437 | Ornithine carbamoyltransferase OS=Staphylococcus aureus (strain USA300) GN=argF PE=3 SV=1 | Q2FHR8 Q2FHR8_STAA3 | -2 |
| 485 | Hydrolase, MutT/nudix family OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_2432 PE=4 SV=1 | Q2FE12 Q2FE12_STAA3 | -2 |
| 490 | ATP-dependent DNA helicase, PcrA OS=Staphylococcus aureus (strain USA300) GN=pcrA PE=4 SV=1 | Q2FFJ0 Q2FFJ0_STAA3 | -2 |
| 491 | Mur ligase family protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1873 PE=4 SV=1 | Q2FFK3 Q2FFK3_STAA3 | -2 |
| 517 | Histidine protein kinase saeS OS=Staphylococcus aureus (strain USA300) GN=saeS PE=3 SV=1 | Q2FIT5 SAES_STAA3 | -2 |
| 641 | Putative lipoprotein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0769 PE=4 SV=1 | Q2FIK9 Q2FIK9_STAA3 | -2 |
| 670 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1118 PE=4 SV=1 | Q2FHL3 Q2FHL3_STAA3 | -2 |

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| 750 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1240 PE=4 SV=1 | Q2FH91 Q2FH91_STAA3 | -2 |
| 37 | Triacylglycerol lipase OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0320 PE=4 SV=1 | Q2FJU4 Q2FJU4_STAA3 | -1.9 |
| 78 | Isocitrate dehydrogenase [NADP] OS=Staphylococcus aureus (strain USA300) GN=icd PE=3 SV=1 | Q2FG43 Q2FG43_STAA3 | -1.9 |
| 91 | Translation initiation factor IF-2 OS=Staphylococcus aureus (strain USA300) GN=infB PE=3 SV=1 | Q2FHG9 IF2_STAA3 | -1.9 |
| 94 | Asparaginyl-tRNA synthetase OS=Staphylococcus aureus (strain USA300) GN=asnS PE=3 SV=1 | Q2FGY6 SYN_STAA3 | -1.9 |
| 103 | Formate--tetrahydrofolate ligase OS=Staphylococcus aureus (strain USA300) GN=fhs PE=3 SV=1 | Q2FG06 FTHS_STAA3 | -1.9 |
| 109 | 50S ribosomal protein L3 OS=Staphylococcus aureus (strain USA300) GN=rplC PE=3 SV=1 | Q2FEN9 RL3_STAA3 | -1.9 |
| 130 | Ribose-phosphate pyrophosphokinase OS=Staphylococcus aureus (strain USA300) GN=prs PE=3 SV=1 | Q2FJE1 Q2FJE1_STAA3 | -1.9 |
| 155 | 50S ribosomal protein L4 OS=Staphylococcus aureus (strain USA300) GN=rplD PE=3 SV=1 | Q2FEP0 RL4_STAA3 | -1.9 |
| 156 | Uncharacterized protein SAUSA300_1119 OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1119 PE=4 SV=1 | Q2FHL2 Y1119_STAA3 | -1.9 |
| 210 | UPF0477 protein SAUSA300_0916 OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0916 PE=3 SV=1 | Q2FI62 Y916_STAA3 | -1.9 |
| 264 | Glutamate-1-semialdehyde 2,1-aminomutase 1 OS=Staphylococcus aureus (strain USA300) GN=hemL1 PE=3 SV=1 | Q2FG69 GSA1_STAA3 | -1.9 |
| 273 | ATP synthase gamma chain OS=Staphylococcus aureus (strain USA300) GN=atpG PE=3 SV=1 | Q2FF23 Q2FF23_STAA3 | -1.9 |
| 300 | Threonine dehydratase catabolic OS=Staphylococcus aureus (strain USA300) GN=tdcB PE=3 SV=1 | Q2FH01 THD2_STAA3 | -1.9 |
| 311 | Putative phosphotransferase SAUSA300_1523 OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1523 PE=3 SV=1 | Q2FGG0 Y1523_STAA3 | -1.9 |
| 355 | DegV family protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1318 PE=4 SV=1 | Q2FH13 Q2FH13_STAA3 | -1.9 |
| 388 | Hypoxanthine phosphoribosyltransferase OS=Staphylococcus aureus (strain USA300) GN=hpt PE=4 SV=1 | Q2FJD1 Q2FJD1_STAA3 | -1.9 |
| 497 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1658 PE=4 SV=1 | Q2FG26 Q2FG26_STAA3 | -1.9 |
| 551 | Ribokinase OS=Staphylococcus aureus (strain USA300) GN=rbsK PE=3 SV=1 | Q2FK02 Q2FK02_STAA3 | -1.9 |
| 567 | tRNA-specific 2-thiouridylase mnmA OS=Staphylococcus aureus (strain USA300) GN=mnmA PE=3 SV=2 | Q2FGA5 MNMA_STAA3 | -1.9 |
| 666 | Mannose-6-phosphate isomerase, class I OS=Staphylococcus aureus (strain USA300) GN=manA PE=3 SV=1 | Q2FDL7 Q2FDL7_STAA3 | -1.9 |

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| 697 | Delta-hemolysin OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1988 PE=4 SV=1 | Q2FF89 Q2FF89_STAA3 | -1.9 |
| 751 | Orotate phosphoribosyltransferase OS=Staphylococcus aureus (strain USA300) GN=pyrE PE=3 SV=1 | Q2FHN3 Q2FHN3_STAA3 | -1.9 |
| 70 | 30S ribosomal protein S11 OS=Staphylococcus aureus (strain USA300) GN=rpsK PE=3 SV=1 | Q2FER4 RS11_STAA3 | -1.8 |
| 81 | DNA polymerase III, beta subunit OS=Staphylococcus aureus (strain USA300) GN=dnaN PE=3 SV=1 | Q2FKQ4 Q2FKQ4_STAA3 | -1.8 |
| 92 | Succinate dehydrogenase, flavoprotein subunit OS=Staphylococcus aureus (strain USA300) GN=sdhA PE=4 SV=1 | Q2FHT3 Q2FHT3_STAA3 | -1.8 |
| 125 | 50S ribosomal protein L19 OS=Staphylococcus aureus (strain USA300) GN=rplS PE=3 SV=1 | Q2FHJ7 RL19_STAA3 | -1.8 |
| 167 | ABC transporter, ATP-binding protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1285 PE=4 SV=1 | Q2FH46 Q2FH46_STAA3 | -1.8 |
| 204 | Transcriptional regulator, MarR family OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0672 PE=4 SV=1 | Q2FIV3 Q2FIV3_STAA3 | -1.8 |
| 216 | Oxidoreductase, short chain dehydrogenase/reductase family OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_2275 PE=4 SV=1 | Q2FEG8 Q2FEG8_STAA3 | -1.8 |
| 220 | Signal recognition particle protein OS=Staphylococcus aureus (strain USA300) GN=ffh PE=4 SV=1 | Q2FHK1 Q2FHK1_STAA3 | -1.8 |
| 237 | D-alanine-activating enzyme/D-alanine-D-alanyl, dltD protein OS=Staphylococcus aureus (strain USA300) GN=dltD PE=4 SV=1 | Q2FIE0 Q2FIE0_STAA3 | -1.8 |
| 247 | Extracellular matrix protein-binding protein emp OS=Staphylococcus aureus (strain USA300) GN=emp PE=3 SV=1 | Q2FIK4 EMP_STAA3 | -1.8 |
| 292 | Putative NADP-dependent malic enzyme OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1648 PE=3 SV=1 | Q2FG36 Q2FG36_STAA3 | -1.8 |
| 294 | GTP-binding protein engA OS=Staphylococcus aureus (strain USA300) GN=engA PE=3 SV=1 | Q2FGW7 ENGA_STAA3 | -1.8 |
| 304 | Urocanate hydratase OS=Staphylococcus aureus (strain USA300) GN=hutU PE=4 SV=1 | Q2FEG5 Q2FEG5_STAA3 | -1.8 |
| 306 | UPF0051 protein SAUSA300_0822 OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0822 PE=3 SV=1 | Q2FIF6 Y822_STAA3 | -1.8 |
| 340 | DNA-directed RNA polymerase subunit omega OS=Staphylococcus aureus (strain USA300) GN=rpoZ PE=3 SV=1 | Q2FHM8 RPOZ_STAA3 | -1.8 |
| 367 | Putative thioredoxin OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0789 PE=4 SV=1 | Q2FI9 Q2FI9_STAA3 | -1.8 |
| 568 | Oligopeptide ABC transporter, ATP-binding protein OS=Staphylococcus aureus (strain USA300) GN=oppF PE=4 SV=1 | Q2FI88 Q2FI88_STAA3 | -1.8 |
| 585 | Single-stranded DNA-binding protein OS=Staphylococcus aureus (strain USA300) GN=ssb PE=4 SV=1 | Q2FJP7 Q2FJP7_STAA3 | -1.8 |
| 586 | 30S ribosomal protein S14 type Z OS=Staphylococcus aureus (strain USA300) GN=rpsZ PE=3 SV=2 | Q2FEQ2 RS14Z_STAA3 | -1.8 |

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| 590 | Aminotransferase, class V OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1579 PE=3 SV=1 | Q2FGA4 Q2FGA4_STAA3 | -1.8 |
| 766 | Threonine synthase OS=Staphylococcus aureus (strain USA300) GN=thrC PE=3 SV=1 | Q2FHA4 Q2FHA4_STAA3 | -1.8 |
| 40 | 1-pyrroline-5-carboxylate dehydrogenase OS=Staphylococcus aureus (strain USA300) GN=rocA PE=3 SV=1 | Q2FDV3 ROCA_STAA3 | -1.7 |
| 62 | 50S ribosomal protein L2 OS=Staphylococcus aureus (strain USA300) GN=rplB PE=3 SV=1 | Q2FEP2 RL2_STAA3 | -1.7 |
| 104 | Aerobic glycerol-3-phosphate dehydrogenase OS=Staphylococcus aureus (strain USA300) GN=glpD PE=3 SV=1 | Q2FHD8 GLPD_STAA3 | -1.7 |
| 105 | Ornithine aminotransferase OS=Staphylococcus aureus (strain USA300) GN=rocD PE=3 SV=1 | Q2FIB8 Q2FIB8_STAA3 | -1.7 |
| 133 | Prolyl-tRNA synthetase OS=Staphylococcus aureus (strain USA300) GN=proS PE=3 SV=1 | Q2FHH5 SYP_STAA3 | -1.7 |
| 137 | 30S ribosomal protein S12 OS=Staphylococcus aureus (strain USA300) GN=rpsL PE=3 SV=1 | Q2FJ95 RS12_STAA3 | -1.7 |
| 150 | Phosphoglucomamine mutase OS=Staphylococcus aureus (strain USA300) GN=glmM PE=3 SV=1 | Q2FEX1 GLMM_STAA3 | -1.7 |
| 152 | Protein recA OS=Staphylococcus aureus (strain USA300) GN=recA PE=3 SV=1 | Q2FHF3 Q2FHF3_STAA3 | -1.7 |
| 181 | Adenylosuccinate synthetase OS=Staphylococcus aureus (strain USA300) GN=purA PE=3 SV=1 | Q2FKN9 Q2FKN9_STAA3 | -1.7 |
| 187 | Translation initiation factor IF-1 OS=Staphylococcus aureus (strain USA300) GN=infA PE=3 SV=1 | Q2FER1 IF1_STAA3 | -1.7 |
| 221 | Putative peptidyl-prolyl cis-trans isomerase OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0857 PE=3 SV=1 | Q2FIC1 PPI1_STAA3 | -1.7 |
| 255 | DNA gyrase subunit B OS=Staphylococcus aureus (strain USA300) GN=gyrB PE=3 SV=3 | Q2FKQ1 GYRB_STAA3 | -1.7 |
| 256 | ATP-dependent Clp protease ATP-binding subunit clpX OS=Staphylococcus aureus (strain USA300) GN=clpX PE=3 SV=1 | Q2FG62 CLPX_STAA3 | -1.7 |
| 261 | Malate:quinone-oxidoreductase OS=Staphylococcus aureus (strain USA300) GN=mqo PE=3 SV=1 | Q2FED1 Q2FED1_STAA3 | -1.7 |
| 382 | UDP-N-acetylglucosamyl-tripeptide--D-alanyl-D-alanine ligase OS=Staphylococcus aureus (strain USA300) GN=murF PE=3 SV=1 | Q2FF44 Q2FF44_STAA3 | -1.7 |
| 384 | 2-oxoisovalerate dehydrogenase, E2 component, dihydrolipoamide acetyltransferase OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1464 PE=3 SV=1 | Q2FGL8 Q2FGL8_STAA3 | -1.7 |
| 435 | Acetyl-coenzyme A synthetase OS=Staphylococcus aureus (strain USA300) GN=acsA PE=4 SV=1 | Q2FG05 Q2FG05_STAA3 | -1.7 |
| 482 | Pyrroline-5-carboxylate reductase OS=Staphylococcus aureus (strain USA300) GN=proc PE=4 SV=1 | Q2FGN0 Q2FGN0_STAA3 | -1.7 |
| 519 | Conserved virulence factor B OS=Staphylococcus aureus (strain USA300) GN=cvfB PE=3 SV=1 | Q2FH47 CVFB_STAA3 | -1.7 |

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| 560 | Chromosome segregation protein SMC OS=Staphylococcus aureus (strain USA300) GN=smc PE=4 SV=1 | Q2FHK4 Q2FHK4_STAA3 | -1.7 |
| 574 | Uncharacterized protein SAUSA300_1902 OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1902 PE=3 SV=1 | Q2FFH4 Y1902_STAA3 | -1.7 |
| 625 | 2-oxoisovalerate dehydrogenase, E1 component, alpha subunit OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1466 PE=4 SV=1 | Q2FGL6 Q2FGL6_STAA3 | -1.7 |
| 719 | RNA methyltransferase, TrmH family, group 3 OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0517 PE=4 SV=1 | Q2FJA8 Q2FJA8_STAA3 | -1.7 |
| 727 | Na(+)/H(+) antiporter subunit E1 OS=Staphylococcus aureus (strain USA300) GN=mnhE1 PE=3 SV=1 | Q2FIC7 MNHE1_STAA3 | -1.7 |
| 731 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0657 PE=4 SV=1 | Q2FIW8 Q2FIW8_STAA3 | -1.7 |
| 14 | Pyruvate kinase OS=Staphylococcus aureus (strain USA300) GN=pyk PE=3 SV=1 | Q2FG40 KPYK_STAA3 | -1.6 |
| 26 | Fructose-bisphosphate aldolase class 1 OS=Staphylococcus aureus (strain USA300) GN=fda PE=3 SV=1 | Q2FDQ4 ALF1_STAA3 | -1.6 |
| 63 | Acetate kinase OS=Staphylococcus aureus (strain USA300) GN=ackA PE=3 SV=1 | Q2FG27 ACKA_STAA3 | -1.6 |
| 88 | Cell division protein ftsA OS=Staphylococcus aureus (strain USA300) GN=ftsA PE=4 SV=1 | Q2FHQ2 Q2FHQ2_STAA3 | -1.6 |
| 96 | 50S ribosomal protein L13 OS=Staphylococcus aureus (strain USA300) GN=rplM PE=3 SV=1 | Q2FES1 RL13_STAA3 | -1.6 |
| 101 | 50S ribosomal protein L10 OS=Staphylococcus aureus (strain USA300) GN=rplJ PE=3 SV=1 | Q2FJA1 RL10_STAA3 | -1.6 |
| 108 | L-lactate dehydrogenase 1 OS=Staphylococcus aureus (strain USA300) GN=ldh1 PE=3 SV=2 | Q2FK29 LDH1_STAA3 | -1.6 |
| 131 | 30S ribosomal protein S13 OS=Staphylococcus aureus (strain USA300) GN=rpsM PE=3 SV=1 | Q2FER3 RS13_STAA3 | -1.6 |
| 142 | 50S ribosomal protein L14 OS=Staphylococcus aureus (strain USA300) GN=rplN PE=3 SV=1 | Q2FEP9 RL14_STAA3 | -1.6 |
| 168 | Succinyl-CoA ligase [ADP-forming] subunit alpha OS=Staphylococcus aureus (strain USA300) GN=sucD PE=3 SV=1 | Q2FHJ2 Q2FHJ2_STAA3 | -1.6 |
| 184 | GTP-binding protein OS=Staphylococcus aureus (strain USA300) GN=typA PE=4 SV=1 | Q2FHX1 Q2FHX1_STAA3 | -1.6 |
| 208 | Citrate synthase II OS=Staphylococcus aureus (strain USA300) GN=gltA PE=3 SV=1 | Q2FG42 Q2FG42_STAA3 | -1.6 |
| 241 | 30S ribosomal protein S6 OS=Staphylococcus aureus (strain USA300) GN=rpsF PE=3 SV=1 | Q2FJP8 RS6_STAA3 | -1.6 |
| 274 | 30S ribosomal protein S4 OS=Staphylococcus aureus (strain USA300) GN=rpsD PE=3 SV=1 | Q2FG18 RS4_STAA3 | -1.6 |
| 281 | D-alanine--D-alanine ligase OS=Staphylococcus aureus (strain USA300) GN=ddl PE=3 SV=1 | Q2FF43 DDL_STAA3 | -1.6 |

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| 307 | UPF0082 protein SAUSA300_0655 OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0655 PE=3 SV=1 | Q2FIX0 Y655_STAA3 | -1.6 |
| 308 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0649 PE=4 SV=1 | Q2FIX6 Q2FIX6_STAA3 | -1.6 |
| 342 | GTP pyrophosphokinase OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1590 PE=3 SV=1 | Q2FG93 Q2FG93_STAA3 | -1.6 |
| 343 | GTP-binding protein era homolog OS=Staphylococcus aureus (strain USA300) GN=era PE=3 SV=1 | Q2FGF6 ERA_STAA3 | -1.6 |
| 381 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_2085 PE=4 SV=1 | Q2FEZ7 Q2FEZ7_STAA3 | -1.6 |
| 427 | D-3-phosphoglycerate dehydrogenase OS=Staphylococcus aureus (strain USA300) GN=serA PE=3 SV=1 | Q2FG14 Q2FG14_STAA3 | -1.6 |
| 542 | D-isomer specific 2-hydroxyacid dehydrogenase OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0834 PE=3 SV=1 | Q2FIE4 Q2FIE4_STAA3 | -1.6 |
| 558 | Probable DNA-directed RNA polymerase subunit delta OS=Staphylococcus aureus (strain USA300) GN=rpoE PE=3 SV=1 | Q2FF00 RPOE_STAA3 | -1.6 |
| 644 | PTS system glucoside-specific EIICBA component OS=Staphylococcus aureus (strain USA300) GN=glcB PE=3 SV=1 | Q2FDW8 PTU3C_STAA3 | -1.6 |
| 682 | Putative membrane-associated zinc metalloprotease OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1155 PE=3 SV=1 | Q2FHH6 Q2FHH6_STAA3 | -1.6 |
| 1 | Elongation factor Tu OS=Staphylococcus aureus (strain USA300) GN=tuf PE=3 SV=1 | Q2FJ92 EFTU_STAA3 | -1.5 |
| 27 | DNA-directed RNA polymerase subunit beta' OS=Staphylococcus aureus (strain USA300) GN=rpoC PE=3 SV=2 | Q2FJ97 RPOC_STAA3 | -1.5 |
| 30 | Pyruvate dehydrogenase E1 component, beta subunit OS=Staphylococcus aureus (strain USA300) GN=pdhB PE=4 SV=1 | Q2FHY6 Q2FHY6_STAA3 | -1.5 |
| 54 | 30S ribosomal protein S5 OS=Staphylococcus aureus (strain USA300) GN=rpsE PE=3 SV=1 | Q2FEQ6 RS5_STAA3 | -1.5 |
| 58 | 5'-nucleotidase, lipoprotein e(P4) family OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0307 PE=4 SV=1 | Q2FJV7 Q2FJV7_STAA3 | -1.5 |
| 72 | DNA-directed RNA polymerase subunit beta OS=Staphylococcus aureus (strain USA300) GN=rpoB PE=3 SV=2 | Q2FJ98 RPOB_STAA3 | -1.5 |
| 98 | Phosphoenolpyruvate carboxykinase [ATP] OS=Staphylococcus aureus (strain USA300) GN=pckA PE=3 SV=1 | Q2FFV5 PCKA_STAA3 | -1.5 |
| 110 | Threonyl-tRNA synthetase OS=Staphylococcus aureus (strain USA300) GN=thrS PE=3 SV=1 | Q2FG54 SYT_STAA3 | -1.5 |
| 114 | Putative formate dehydrogenase SAUSA300_2258 OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_2258 PE=3 SV=1 | Q2FEI5 FDHL_STAA3 | -1.5 |
| 115 | Septation ring formation regulator ezra OS=Staphylococcus aureus (strain USA300) GN=ezrA PE=3 SV=1 | Q2FG20 EZRA_STAA3 | -1.5 |
| 118 | Pyrimidine-nucleoside phosphorylase OS=Staphylococcus aureus (strain USA300) GN=pdp PE=3 SV=2 | Q2FEZ3 PDP_STAA3 | -1.5 |

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| 124 | Succinyl-CoA ligase [ADP-forming] subunit beta OS=Staphylococcus aureus (strain USA300) GN=sucC PE=3 SV=1 | Q2FHJ3 SUCC_STAA3 | -1.5 |
| 161 | Alkyl hydroperoxide reductase, subunit F OS=Staphylococcus aureus (strain USA300) GN=ahpF PE=3 SV=1 | Q2FJN5 Q2FJN5_STAA3 | -1.5 |
| 162 | Putative dipeptidase SAUSA300_1697 OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1697 PE=3 SV=1 | Q2FFY7 PEPVL_STAA3 | -1.5 |
| 164 | GTP-binding protein YchF OS=Staphylococcus aureus (strain USA300) GN=ychF PE=4 SV=1 | Q2FJQ0 Q2FJQ0_STAA3 | -1.5 |
| 165 | UPF0133 protein SAUSA300_0453 OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0453 PE=3 SV=1 | Q2FJG3 Y453_STAA3 | -1.5 |
| 180 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1323 PE=4 SV=1 | Q2FH08 Q2FH08_STAA3 | -1.5 |
| 183 | Pyruvate carboxylase OS=Staphylococcus aureus (strain USA300) GN=pyc PE=4 SV=1 | Q2FHW6 Q2FHW6_STAA3 | -1.5 |
| 252 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0385 PE=4 SV=1 | Q2FJM9 Q2FJM9_STAA3 | -1.5 |
| 254 | Seryl-tRNA synthetase OS=Staphylococcus aureus (strain USA300) GN=serS PE=3 SV=1 | Q2FKP7 SYS_STAA3 | -1.5 |
| 260 | 50S ribosomal protein L16 OS=Staphylococcus aureus (strain USA300) GN=rplP PE=3 SV=1 | Q2FEP6 RL16_STAA3 | -1.5 |
| 320 | Staphylococcal respiratory response protein, SrrA OS=Staphylococcus aureus (strain USA300) GN=srrA PE=4 SV=1 | Q2FGP0 Q2FGP0_STAA3 | -1.5 |
| 321 | Glycerophosphoryl diester phosphodiesterase family protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1020 PE=4 SV=1 | Q2FHW0 Q2FHW0_STAA3 | -1.5 |
| 351 | PTS system EIIBC component SAUSA300_0194 OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0194 PE=3 SV=1 | Q2FK70 PTXBC_STAA3 | -1.5 |
| 377 | Nucleoside diphosphate kinase OS=Staphylococcus aureus (strain USA300) GN=ndk PE=3 SV=2 | Q2FGX3 NDK_STAA3 | -1.5 |
| 400 | Carbamoyl-phosphate synthase, small subunit OS=Staphylococcus aureus (strain USA300) GN=carA PE=3 SV=1 | Q2FHN6 Q2FHN6_STAA3 | -1.5 |
| 402 | Phosphate starvation-induced protein, PhoH family OS=Staphylococcus aureus (strain USA300) GN=phoH PE=4 SV=1 | Q2FGF2 Q2FGF2_STAA3 | -1.5 |
| 409 | Oxidoreductase, aldo/keto reductase family OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1728 PE=4 SV=1 | Q2FFV8 Q2FFV8_STAA3 | -1.5 |
| 413 | 10 kDa chaperonin OS=Staphylococcus aureus (strain USA300) GN=groS PE=3 SV=1 | Q2FF94 CH10_STAA3 | -1.5 |
| 425 | Ribonuclease J 1 OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0989 PE=3 SV=1 | Q2FHZ1 RNJ1_STAA3 | -1.5 |
| 441 | (Dimethylallyl)adenosine tRNA methylthiotransferase miaB OS=Staphylococcus aureus (strain USA300) GN=miaB PE=3 SV=1 | Q2FHE6 MIAB_STAA3 | -1.5 |
| 565 | HAD-superfamily hydrolase, subfamily IA, variant 1 OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0540 PE=4 SV=1 | Q2FJ85 Q2FJ85_STAA3 | -1.5 |

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| 575 | Uncharacterized lipoprotein SAUSA300_2315 OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_2315 PE=4 SV=1 | Q2FEC8 Y2315_STAA3 | -1.5 |
| 601 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0668 PE=4 SV=1 | Q2FIV7 Q2FIV7_STAA3 | -1.5 |
| 637 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1585 PE=4 SV=1 | Q2FG98 Q2FG98_STAA3 | -1.5 |
| 639 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1082 PE=3 SV=1 | Q2FHP9 Q2FHP9_STAA3 | -1.5 |
| 12 | Inosine-5'-monophosphate dehydrogenase OS=Staphylococcus aureus (strain USA300) GN=guAB PE=3 SV=1 | Q2FJM6 IMDH_STAA3 | -1.4 |
| 41 | Aconitate hydratase OS=Staphylococcus aureus (strain USA300) GN=acnA PE=4 SV=1 | Q2FH85 Q2FH85_STAA3 | -1.4 |
| 50 | Aspartyl/glutamyl-tRNA(Asn/Gln) amidotransferase subunit B OS=Staphylococcus aureus (strain USA300) GN=gatB PE=3 SV=1 | Q2FFJ6 GATB_STAA3 | -1.4 |
| 69 | 50S ribosomal protein L6 OS=Staphylococcus aureus (strain USA300) GN=rplF PE=3 SV=1 | Q2FEQ4 RL6_STAA3 | -1.4 |
| 74 | Immunodominant staphylococcal antigen B OS=Staphylococcus aureus (strain USA300) GN=isaB PE=3 SV=1 | Q2FDM1 ISAB_STAA3 | -1.4 |
| 174 | UPF0356 protein SAUSA300_0990 OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0990 PE=3 SV=1 | Q2FHZ0 Y990_STAA3 | -1.4 |
| 191 | Dehydrogenase family protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_2251 PE=4 SV=1 | Q2FEJ2 Q2FEJ2_STAA3 | -1.4 |
| 234 | Aspartyl-tRNA synthetase OS=Staphylococcus aureus (strain USA300) GN=aspS PE=3 SV=1 | Q2FG97 SYD_STAA3 | -1.4 |
| 246 | Uridylate kinase OS=Staphylococcus aureus (strain USA300) GN=pyrH PE=3 SV=1 | Q2FHI0 PYRH_STAA3 | -1.4 |
| 259 | Chaperone protein hchA OS=Staphylococcus aureus (strain USA300) GN=hchA PE=3 SV=1 | Q2FJ89 HCHA_STAA3 | -1.4 |
| 272 | CTP synthase OS=Staphylococcus aureus (strain USA300) GN=pyrG PE=3 SV=1 | Q2FF01 PYRG_STAA3 | -1.4 |
| 288 | DNA gyrase subunit A OS=Staphylococcus aureus (strain USA300) GN=gyrA PE=3 SV=1 | Q2FKQ0 GYRA_STAA3 | -1.4 |
| 322 | Uncharacterized epimerase/dehydratase SAUSA300_0538 OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0538 PE=3 SV=1 | Q2FJ87 Y538_STAA3 | -1.4 |
| 360 | 30S ribosomal protein S17 OS=Staphylococcus aureus (strain USA300) GN=rpsQ PE=3 SV=1 | Q2FEP8 R\$17_STAA3 | -1.4 |
| 373 | Glycerol kinase OS=Staphylococcus aureus (strain USA300) GN=glpK PE=3 SV=1 | Q2FHD9 GLPK_STAA3 | -1.4 |
| 378 | Lipoate-protein ligase A family protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0930 PE=4 SV=1 | Q2FI50 Q2FI50_STAA3 | -1.4 |
| 391 | Cold shock protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0777 PE=3 SV=1 | Q2FIK1 Q2FIK1_STAA3 | -1.4 |

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| 420 | Phosphopantethenoylcysteine decarboxylase/phosphopantethenate--cysteine ligase OS=Staphylococcus aureus (strain USA300) GN=coaBC PE=4 SV=1 | Q2FHM7 Q2FHM7_STAA3 | -1.4 |
| 472 | Phosphate acyltransferase OS=Staphylococcus aureus (strain USA300) GN=plsX PE=3 SV=1 | Q2FHK9 PLSX_STAA3 | -1.4 |
| 473 | ABC transporter, ATP-binding protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0630 PE=4 SV=1 | Q2FIZ5 Q2FIZ5_STAA3 | -1.4 |
| 475 | Methicillin resistance protein FemA OS=Staphylococcus aureus (strain USA300) GN=femA PE=4 SV=1 | Q2FH62 Q2FH62_STAA3 | -1.4 |
| 505 | Uncharacterized oxidoreductase SAUSA300_2422 OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_2422 PE=3 SV=1 | Q2FE21 Y2422_STAA3 | -1.4 |
| 515 | Decarboxylase family protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0666 PE=4 SV=1 | Q2FIV9 Q2FIV9_STAA3 | -1.4 |
| 578 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1793 PE=4 SV=1 | Q2FFQ2 Q2FFQ2_STAA3 | -1.4 |
| 669 | Menaquinone biosynthesis methyltransferase ubiE OS=Staphylococcus aureus (strain USA300) GN=ubiE PE=4 SV=1 | Q2FGX1 Q2FGX1_STAA3 | -1.4 |
| 687 | UvrABC system protein B OS=Staphylococcus aureus (strain USA300) GN=uvrB PE=3 SV=1 | Q2FIN5 Q2FIN5_STAA3 | -1.4 |
| 25 | 30S ribosomal protein S2 OS=Staphylococcus aureus (strain USA300) GN=rpsB PE=3 SV=1 | Q2FHI2 RS2_STAA3 | -1.3 |
| 33 | Immunoglobulin-binding protein sbi OS=Staphylococcus aureus (strain USA300) GN=sbi PE=3 SV=1 | Q2FE79 SBI_STAA3 | -1.3 |
| 49 | Pyruvate dehydrogenase E1 component, alpha subunit OS=Staphylococcus aureus (strain USA300) GN=pdhA PE=4 SV=1 | Q2FHY7 Q2FHY7_STAA3 | -1.3 |
| 60 | ATP-dependent Clp protease ATP-binding subunit clpL OS=Staphylococcus aureus (strain USA300) GN=clpL PE=3 SV=1 | Q2FDV8 CLPL_STAA3 | -1.3 |
| 95 | 30S ribosomal protein S7 OS=Staphylococcus aureus (strain USA300) GN=rpsG PE=3 SV=2 | Q2FJ94 RS7_STAA3 | -1.3 |
| 112 | 50S ribosomal protein L27 OS=Staphylococcus aureus (strain USA300) GN=rpmA PE=3 SV=1 | Q2FG82 RL27_STAA3 | -1.3 |
| 121 | Bifunctional protein fold OS=Staphylococcus aureus (strain USA300) GN=fold PE=3 SV=1 | Q2FI15 FOLD_STAA3 | -1.3 |
| 126 | 50S ribosomal protein L22 OS=Staphylococcus aureus (strain USA300) GN=rplV PE=3 SV=1 | Q2FEP4 RL22_STAA3 | -1.3 |
| 140 | Phosphate acetyltransferase OS=Staphylococcus aureus (strain USA300) GN=pta PE=4 SV=1 | Q2FJ55 Q2FJ55_STAA3 | -1.3 |
| 153 | Transcription termination factor NusA OS=Staphylococcus aureus (strain USA300) GN=nusA PE=4 SV=1 | Q2FHH2 Q2FHH2_STAA3 | -1.3 |
| 186 | 2-C-methyl-D-erythritol 4-phosphate cytidylyltransferase OS=Staphylococcus aureus (strain USA300) GN=ispD PE=3 SV=1 | Q2FK15 ISPD_STAA3 | -1.3 |
| 195 | Immunoglobulin G binding protein A OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0113 PE=3 SV=1 | Q2FKE8 Q2FKE8_STAA3 | -1.3 |

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| 243 | 30S ribosomal protein S10 OS=Staphylococcus aureus (strain USA300) GN=rpsJ PE=3 SV=1 | Q2FEN8 RS10_STAA3 | -1.3 |
| 332 | UDP-N-acetylenolpyruvoylglucosamine reductase OS=Staphylococcus aureus (strain USA300) GN=murB PE=3 SV=1 | Q2FIQ3 MURB_STAA3 | -1.3 |
| 350 | 1-acyl-sn-glycerol-3-phosphate acyltransferases OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1673 PE=4 SV=1 | Q2FG11 Q2FG11_STAA3 | -1.3 |
| 352 | Phosphoribosylaminoimidazole carboxylase, catalytic subunit OS=Staphylococcus aureus (strain USA300) GN=purE PE=4 SV=1 | Q2FI14 Q2FI14_STAA3 | -1.3 |
| 379 | Ribonucleoside-diphosphate reductase, beta subunit OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0717 PE=4 SV=1 | Q2FIQ8 Q2FIQ8_STAA3 | -1.3 |
| 380 | Phosphoribosylglycinamide formyltransferase OS=Staphylococcus aureus (strain USA300) GN=purN PE=4 SV=1 | Q2FI06 Q2FI06_STAA3 | -1.3 |
| 385 | Methicillin resistance protein FemB OS=Staphylococcus aureus (strain USA300) GN=femB PE=4 SV=1 | Q2FH61 Q2FH61_STAA3 | -1.3 |
| 408 | Sigma-B regulation protein OS=Staphylococcus aureus (strain USA300) GN=rsbU PE=4 SV=1 | Q2FF57 Q2FF57_STAA3 | -1.3 |
| 627 | Uncharacterized protein SAUSA300_1248 OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1248 PE=3 SV=1 | Q2FH83 Y1248_STAA3 | -1.3 |
| 658 | 50S ribosomal protein L9 OS=Staphylococcus aureus (strain USA300) GN=rplI PE=3 SV=1 | Q2FKP1 RL9_STAA3 | -1.3 |
| 660 | 2-dehydropantoate 2-reductase OS=Staphylococcus aureus (strain USA300) GN=panE PE=3 SV=1 | Q2FE55 Q2FE55_STAA3 | -1.3 |
| 20 | Enolase OS=Staphylococcus aureus (strain USA300) GN=eno PE=3 SV=1 | Q2FIL7 ENO_STAA3 | -1.2 |
| 122 | ABC transporter, ATP-binding protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1911 PE=4 SV=1 | Q2FFG5 Q2FFG5_STAA3 | -1.2 |
| 123 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1804 PE=4 SV=1 | Q2FFP1 Q2FFP1_STAA3 | -1.2 |
| 139 | NAD-specific glutamate dehydrogenase OS=Staphylococcus aureus (strain USA300) GN=gudB PE=3 SV=1 | Q2FIB7 Q2FIB7_STAA3 | -1.2 |
| 145 | Isoleucyl-tRNA synthetase OS=Staphylococcus aureus (strain USA300) GN=ileS PE=3 SV=1 | Q2FHP4 SYI_STAA3 | -1.2 |
| 170 | Probable DEAD-box ATP-dependent RNA helicase SAUSA300_2037 OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_2037 PE=3 SV=1 | Q2FF45 Y2037_STAA3 | -1.2 |
| 175 | Adenylosuccinate lyase OS=Staphylococcus aureus (strain USA300) GN=purB PE=3 SV=1 | Q2FFI7 PUR8_STAA3 | -1.2 |
| 182 | S-adenosylmethionine synthase OS=Staphylococcus aureus (strain USA300) GN=metK PE=3 SV=1 | Q2FFV6 METK_STAA3 | -1.2 |
| 194 | 2,3-bisphosphoglycerate-independent phosphoglycerate mutase OS=Staphylococcus aureus (strain USA300) GN=gpmI PE=3 SV=1 | Q2FIL8 Q2FIL8_STAA3 | -1.2 |
| 218 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1792 PE=4 SV=1 | Q2FFQ3 Q2FFQ3_STAA3 | -1.2 |

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| 233 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1909 PE=4 SV=1 | Q2FFG7 Q2FFG7_STAA3 | -1.2 |
| 267 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0664 PE=4 SV=1 | Q2FIW1 Q2FIW1_STAA3 | -1.2 |
| 298 | 30S ribosomal protein S9 OS=Staphylococcus aureus (strain USA300) GN=rpsI PE=3 SV=1 | Q2FES2 RS9_STAA3 | -1.2 |
| 329 | DNA polymerase I OS=Staphylococcus aureus (strain USA300) GN=polA PE=3 SV=1 | Q2FG47 Q2FG47_STAA3 | -1.2 |
| 348 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1788 PE=4 SV=1 | Q2FFQ7 Q2FFQ7_STAA3 | -1.2 |
| 375 | Putative oxidoreductase OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0329 PE=4 SV=1 | Q2FJT5 Q2FJT5_STAA3 | -1.2 |
| 456 | Ornithine carbamoyltransferase OS=Staphylococcus aureus (strain USA300) GN=arcB PE=3 SV=1 | Q2FDM5 Q2FDM5_STAA3 | -1.2 |
| 469 | UDP-N-acetylglucosamine 1-carboxyvinyltransferase OS=Staphylococcus aureus (strain USA300) GN=murA PE=3 SV=1 | Q2FF04 Q2FF04_STAA3 | -1.2 |
| 476 | S-adenosyl-L-methionine-dependent methyltransferase mraW OS=Staphylococcus aureus (strain USA300) GN=mraW PE=3 SV=2 | Q2FHQ8 MRAW_STAA3 | -1.2 |
| 483 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1495 PE=4 SV=1 | Q2FGI8 Q2FGI8_STAA3 | -1.2 |
| 511 | Multidrug resistance protein A, drug resistance transporter OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_2299 PE=4 SV=1 | Q2FEE4 Q2FEE4_STAA3 | -1.2 |
| 522 | UPF0173 metal-dependent hydrolase SAUSA300_1653 OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1653 PE=3 SV=1 | Q2FG31 Y1653_STAA3 | -1.2 |
| 531 | Penicillin-binding protein 1 OS=Staphylococcus aureus (strain USA300) GN=pbpA PE=4 SV=1 | Q2FHQ6 Q2FHQ6_STAA3 | -1.2 |
| 589 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1720 PE=4 SV=1 | Q2FFW5 Q2FFW5_STAA3 | -1.2 |
| 610 | UPF0297 protein SAUSA300_1574 OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1574 PE=3 SV=1 | Q2FGA9 Y1574_STAA3 | -1.2 |
| 617 | DNA-binding response regulator OS=Staphylococcus aureus (strain USA300) GN=vraR PE=4 SV=1 | Q2FFL1 Q2FFL1_STAA3 | -1.2 |
| 654 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0956 PE=4 SV=1 | Q2FI24 Q2FI24_STAA3 | -1.2 |
| 18 | Dihydrolipoyl dehydrogenase OS=Staphylococcus aureus (strain USA300) GN=lpdA PE=3 SV=1 | Q2FHY4 Q2FHY4_STAA3 | -1.1 |
| 56 | Glutamyl-tRNA(Gln) amidotransferase subunit A OS=Staphylococcus aureus (strain USA300) GN=gatA PE=3 SV=1 | Q2FFJ5 GATA_STAA3 | -1.1 |
| 100 | Triosephosphate isomerase OS=Staphylococcus aureus (strain USA300) GN=tpiA PE=3 SV=1 | Q2FIL9 TPIS_STAA3 | -1.1 |
| 102 | Ferritin OS=Staphylococcus aureus (strain USA300) GN=ftnA PE=3 SV=1 | Q2FFK2 FTN_STAA3 | -1.1 |

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| 111 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1863 PE=4 SV=1 | Q2FFL3 Q2FFL3_STAA3 | -1.1 |
| 143 | 30S ribosomal protein S8 OS=Staphylococcus aureus (strain USA300) GN=rpsH PE=3 SV=1 | Q2FEQ3 RS8_STAA3 | -1.1 |
| 149 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_2144 PE=4 SV=1 | Q2FEU8 Q2FEU8_STAA3 | -1.1 |
| 202 | 50S ribosomal protein L23 OS=Staphylococcus aureus (strain USA300) GN=rplW PE=3 SV=1 | Q2FEP1 RL23_STAA3 | -1.1 |
| 213 | 50S ribosomal protein L21 OS=Staphylococcus aureus (strain USA300) GN=rplU PE=3 SV=1 | Q2FG80 RL21_STAA3 | -1.1 |
| 248 | Putative 2-hydroxyacid dehydrogenase SAUSA300_2254 OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_2254 PE=3 SV=1 | Q2FEI9 Y2254_STAA3 | -1.1 |
| 386 | DNA topoisomerase IV, subunit A OS=Staphylococcus aureus (strain USA300) GN=parC PE=4 SV=1 | Q2FH80 Q2FH80_STAA3 | -1.1 |
| 394 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_2097 PE=4 SV=1 | Q2FEY5 Q2FEY5_STAA3 | -1.1 |
| 414 | Aminotransferase OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1916 PE=4 SV=1 | Q2FFG0 Q2FFG0_STAA3 | -1.1 |
| 459 | 2-oxoisovalerate dehydrogenase, E1 component, beta subunit OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1465 PE=4 SV=1 | Q2FGL7 Q2FGL7_STAA3 | -1.1 |
| 502 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1494 PE=4 SV=1 | Q2FGI9 Q2FGI9_STAA3 | -1.1 |
| 509 | RNA polymerase sigma factor OS=Staphylococcus aureus (strain USA300) GN=rpoD PE=3 SV=1 | Q2FGG2 Q2FGG2_STAA3 | -1.1 |
| 545 | Preprotein translocase, YajC subunit OS=Staphylococcus aureus (strain USA300) GN=yajC PE=4 SV=1 | Q2FG89 Q2FG89_STAA3 | -1.1 |
| 594 | Cardiolipin synthetase OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1216 PE=4 SV=1 | Q2FHB5 Q2FHB5_STAA3 | -1.1 |
| 602 | UPF0447 protein SAUSA300_0569 OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0569 PE=3 SV=1 | Q2FJ56 Y569_STAA3 | -1.1 |
| 714 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1230 PE=4 SV=1 | Q2FHA1 Q2FHA1_STAA3 | -1.1 |
| 17 | 30S ribosomal protein S1 OS=Staphylococcus aureus (strain USA300) GN=rpsA PE=4 SV=1 | Q2FGW6 Q2FGW6_STAA3 | -1 |
| 59 | Uncharacterized protein SAUSA300_0871 OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0871 PE=3 SV=1 | Q2FIA7 Y871_STAA3 | -1 |
| 77 | GMP synthase [glutamine-hydrolyzing] OS=Staphylococcus aureus (strain USA300) GN=guaA PE=3 SV=1 | Q2FJM5 GUAA_STAA3 | -1 |
| 85 | Putative aldehyde dehydrogenase SAUSA300_2076 OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_2076 PE=3 SV=1 | Q2FF06 ALD1_STAA3 | -1 |
| 87 | Probable manganese-dependent inorganic pyrophosphatase OS=Staphylococcus aureus (strain USA300) GN=ppaC PE=3 SV=1 | Q2FFH6 PPAC_STAA3 | -1 |

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| 93 | Lysyl-tRNA synthetase OS=Staphylococcus aureus (strain USA300) GN=lysS PE=3 SV=1 | Q2FJC3 SYK_STAA3 | -1 |
| 120 | Polyribonucleotide nucleotidyltransferase OS=Staphylococcus aureus (strain USA300) GN=pnp PE=3 SV=1 | Q2FHG4 PNP_STAA3 | -1 |
| 127 | DNA-directed RNA polymerase subunit alpha OS=Staphylococcus aureus (strain USA300) GN=rpoA PE=3 SV=1 | Q2FER5 RPOA_STAA3 | -1 |
| 147 | 50S ribosomal protein L7/L12 OS=Staphylococcus aureus (strain USA300) GN=rpL7 PE=3 SV=1 | Q2FJA0 RL7_STAA3 | -1 |
| 163 | ATP-dependent Clp protease ATP-binding subunit clpC OS=Staphylococcus aureus (strain USA300) GN=clpC PE=3 SV=1 | Q2FJB5 CLPC_STAA3 | -1 |
| 169 | Oligoendopeptidase F OS=Staphylococcus aureus (strain USA300) GN=pepF PE=4 SV=1 | Q2FI76 Q2FI76_STAA3 | -1 |
| 199 | 6-phosphofructokinase OS=Staphylococcus aureus (strain USA300) GN=pfkA PE=3 SV=1 | Q2FG39 Q2FG39_STAA3 | -1 |
| 253 | Putative flavohemoprotein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0234 PE=3 SV=1 | Q2FK30 Q2FK30_STAA3 | -1 |
| 279 | Phosphoribosylformylglycinamide synthase OS=Staphylococcus aureus (strain USA300) GN=purS PE=4 SV=1 | Q2FI11 Q2FI11_STAA3 | -1 |
| 283 | ATP-dependent RNA helicase, DEAD/DEAH box family OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1518 PE=4 SV=1 | Q2FGG5 Q2FGG5_STAA3 | -1 |
| 345 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1304 PE=4 SV=1 | Q2FH27 Q2FH27_STAA3 | -1 |
| 432 | 50S ribosomal protein L33_2 OS=Staphylococcus aureus (strain USA300) GN=rpmG2 PE=3 SV=1 | Q2FGH2 RL332_STAA3 | -1 |
| 467 | tRNA pseudouridine synthase B OS=Staphylococcus aureus (strain USA300) GN=truB PE=3 SV=1 | Q2FHG7 TRUB_STAA3 | -1 |
| 638 | ABC transporter, ATP-binding protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0704 PE=4 SV=1 | Q2FIS1 Q2FIS1_STAA3 | -1 |
| 656 | Protein nagD homolog OS=Staphylococcus aureus (strain USA300) GN=nagD PE=3 SV=1 | Q2FIE5 NAGD_STAA3 | -1 |
| 667 | Transporter, CorA family OS=Staphylococcus aureus (strain USA300) GN=cobI PE=4 SV=1 | Q2FEC0 Q2FEC0_STAA3 | -1 |
| 717 | Peptide deformylase OS=Staphylococcus aureus (strain USA300) GN=def PE=3 SV=1 | Q2FHY9 Q2FHY9_STAA3 | -1 |
| 5 | Elongation factor G OS=Staphylococcus aureus (strain USA300) GN=fusA PE=3 SV=3 | Q2FJ93 EFG_STAA3 | -0.9 |
| 13 | Cell division protein ftsZ OS=Staphylococcus aureus (strain USA300) GN=ftsZ PE=3 SV=1 | Q2FHQ1 Q2FHQ1_STAA3 | -0.9 |
| 64 | Catalase OS=Staphylococcus aureus (strain USA300) GN=katA PE=3 SV=1 | Q2FH99 CATA_STAA3 | -0.9 |
| 83 | Penicillin binding protein 2 OS=Staphylococcus aureus (strain USA300) GN=pbp2 PE=4 SV=1 | Q2FGZ0 Q2FGZ0_STAA3 | -0.9 |

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| 106 | Branched-chain-amino-acid aminotransferase OS=Staphylococcus aureus (strain USA300) GN=ilvE PE=3 SV=1 | Q2FJ86 Q2FJ86_STAA3 | -0.9 |
| 129 | Phosphoenolpyruvate-protein phosphotransferase OS=Staphylococcus aureus (strain USA300) GN=ptsI PE=3 SV=1 | Q2FHZ6 Q2FHZ6_STAA3 | -0.9 |
| 178 | UDP-N-acetylglucosamine 1-carboxyvinyltransferase 1 OS=Staphylococcus aureus (strain USA300) GN=murA PE=3 SV=1 | Q2FF27 Q2FF27_STAA3 | -0.9 |
| 198 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1652 PE=4 SV=1 | Q2FG32 Q2FG32_STAA3 | -0.9 |
| 203 | 3-oxoacyl-(Acyl-carrier-protein) reductase OS=Staphylococcus aureus (strain USA300) GN=fabG PE=3 SV=1 | Q2FHK7 Q2FHK7_STAA3 | -0.9 |
| 219 | D-alanine aminotransferase OS=Staphylococcus aureus (strain USA300) GN=dat PE=3 SV=1 | Q2FFY8 Q2FFY8_STAA3 | -0.9 |
| 222 | Methionyl-tRNA synthetase OS=Staphylococcus aureus (strain USA300) GN=metS PE=3 SV=1 | Q2FJF2 Q2FJF2_STAA3 | -0.9 |
| 258 | Arginyl-tRNA synthetase OS=Staphylococcus aureus (strain USA300) GN=argS PE=3 SV=1 | Q2FJ29 SYR_STAA3 | -0.9 |
| 275 | Orotidine 5'-phosphate decarboxylase OS=Staphylococcus aureus (strain USA300) GN=pyrF PE=3 SV=1 | Q2FHN4 PYRF_STAA3 | -0.9 |
| 290 | Putative NAD(P)H nitroreductase SAUSA300_2462 OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_2462 PE=3 SV=1 | Q2FDY2 Y2462_STAA3 | -0.9 |
| 325 | Ribosomal large subunit pseudouridine synthase, RluD subfamily OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1800 PE=4 SV=1 | Q2FFP5 Q2FFP5_STAA3 | -0.9 |
| 326 | Putative septation protein spoVG OS=Staphylococcus aureus (strain USA300) GN=spoVG PE=3 SV=1 | Q2FJE4 SP5G_STAA3 | -0.9 |
| 405 | Dephospho-CoA kinase OS=Staphylococcus aureus (strain USA300) GN=coaE PE=3 SV=1 | Q2FG49 COAE_STAA3 | -0.9 |
| 433 | Redox-sensing transcriptional repressor rex OS=Staphylococcus aureus (strain USA300) GN=rex PE=3 SV=1 | Q2FF78 REX_STAA3 | -0.9 |
| 434 | HIT family protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1787 PE=4 SV=1 | Q2FFQ8 Q2FFQ8_STAA3 | -0.9 |
| 609 | Rod shape-determining protein MreC OS=Staphylococcus aureus (strain USA300) GN=mreC PE=4 SV=1 | Q2FG78 Q2FG78_STAA3 | -0.9 |
| 3 | Autolysin OS=Staphylococcus aureus (strain USA300) GN=atl PE=4 SV=1 | Q2FI25 Q2FI25_STAA3 | -0.8 |
| 24 | Cysteine synthase OS=Staphylococcus aureus (strain USA300) GN=cysK PE=3 SV=1 | Q2FJC8 Q2FJC8_STAA3 | -0.8 |
| 57 | Alkyl hydroperoxide reductase subunit C OS=Staphylococcus aureus (strain USA300) GN=ahpC PE=3 SV=1 | Q2FJN4 AHPC_STAA3 | -0.8 |
| 82 | FeS assembly ATPase SufC OS=Staphylococcus aureus (strain USA300) GN=sufC PE=4 SV=1 | Q2FIG0 Q2FIG0_STAA3 | -0.8 |
| 99 | 60 kDa chaperonin OS=Staphylococcus aureus (strain USA300) GN=groL PE=3 SV=1 | Q2FF95 CH60_STAA3 | -0.8 |

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| 135 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0602 PE=4 SV=1 | Q2FJ23 Q2FJ23_STAA3 | -0.8 |
| 177 | Glycine cleavage system H protein OS=Staphylococcus aureus (strain USA300) GN=gcvH PE=3 SV=1 | Q2FII7 GCSH_STAA3 | -0.8 |
| 231 | Transcription antitermination protein nusG OS=Staphylococcus aureus (strain USA300) GN=nusG PE=3 SV=1 | Q2FJA4 Q2FJA4_STAA3 | -0.8 |
| 295 | Peptide methionine sulfoxide reductase regulator MsrR OS=Staphylococcus aureus (strain USA300) GN=msrR PE=4 SV=1 | Q2FH74 Q2FH74_STAA3 | -0.8 |
| 417 | Tyrosyl-tRNA synthetase OS=Staphylococcus aureus (strain USA300) GN=tyrS PE=3 SV=1 | Q2FG09 SYY_STAA3 | -0.8 |
| 451 | Phosphoribosylformylglycinamide synthase 1 OS=Staphylococcus aureus (strain USA300) GN=purQ PE=3 SV=1 | Q2FI10 PURQ_STAA3 | -0.8 |
| 470 | Phenylalanyl-tRNA synthetase (Beta subunit) OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1688 PE=4 SV=1 | Q2FFZ6 Q2FFZ6_STAA3 | -0.8 |
| 480 | Uncharacterized peptidase SAUSA300_1654 OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1654 PE=3 SV=1 | Q2FG30 Y1654_STAA3 | -0.8 |
| 538 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1333 PE=4 SV=1 | Q2FGZ8 Q2FGZ8_STAA3 | -0.8 |
| 787 | Dihydrolipoyl dehydrogenase OS=Staphylococcus aureus (strain USA300) GN=lpdA PE=3 SV=1 | Q2FGL5 Q2FGL5_STAA3 | -0.8 |
| 43 | Glycyl-tRNA synthetase OS=Staphylococcus aureus (strain USA300) GN=glyQS PE=3 SV=1 | Q2FGF8 SYG_STAA3 | -0.7 |
| 76 | Transketolase OS=Staphylococcus aureus (strain USA300) GN=tkt PE=4 SV=1 | Q2FH92 Q2FH92_STAA3 | -0.7 |
| 97 | Putative cell division protein FtsH OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0489 PE=4 SV=1 | Q2FJD0 Q2FJD0_STAA3 | -0.7 |
| 117 | FeS assembly protein SufD OS=Staphylococcus aureus (strain USA300) GN=sufD PE=4 SV=1 | Q2FIF9 Q2FIF9_STAA3 | -0.7 |
| 119 | GTP-sensing transcriptional pleiotropic repressor codY OS=Staphylococcus aureus (strain USA300) GN=codY PE=3 SV=1 | Q2FHI3 CODY_STAA3 | -0.7 |
| 128 | 6-phosphogluconate dehydrogenase, decarboxylating OS=Staphylococcus aureus (strain USA300) GN=gnd PE=3 SV=1 | Q2FGM3 Q2FGM3_STAA3 | -0.7 |
| 158 | 2-oxoglutarate dehydrogenase E1 component OS=Staphylococcus aureus (strain USA300) GN=odhA PE=3 SV=1 | Q2FH25 ODO1_STAA3 | -0.7 |
| 193 | Transaldolase OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1725 PE=3 SV=1 | Q2FFW0 Q2FFW0_STAA3 | -0.7 |
| 211 | Uncharacterized protein SAUSA300_0736 OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0736 PE=3 SV=1 | Q2FIN9 Y736_STAA3 | -0.7 |
| 238 | 50S ribosomal protein L30 OS=Staphylococcus aureus (strain USA300) GN=rpmD PE=3 SV=1 | Q2FEQ7 RL30_STAA3 | -0.7 |
| 245 | Valyl-tRNA synthetase OS=Staphylococcus aureus (strain USA300) GN=valS PE=3 SV=1 | Q2FG72 SYV_STAA3 | -0.7 |

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| 265 | Alanyl-tRNA synthetase OS=Staphylococcus aureus (strain USA300) GN=alaS PE=3 SV=1 | Q2FGA8 SYA_STAA3 | -0.7 |
| 335 | Acetyltransferase, GNAT family OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1070 PE=4 SV=1 | Q2FHR1 Q2FHR1_STAA3 | -0.7 |
| 353 | Alcohol dehydrogenase, zinc-containing OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_2147 PE=4 SV=1 | Q2FEU5 Q2FEU5_STAA3 | -0.7 |
| 356 | Aspartate semialdehyde dehydrogenase OS=Staphylococcus aureus (strain USA300) GN=asd PE=3 SV=1 | Q2FH44 Q2FH44_STAA3 | -0.7 |
| 376 | Acetyltransferase family protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_2460 PE=4 SV=1 | Q2FDY4 Q2FDY4_STAA3 | -0.7 |
| 422 | ATP-dependent Clp protease proteolytic subunit OS=Staphylococcus aureus (strain USA300) GN=clpP PE=3 SV=1 | Q2FIM5 CLPP_STAA3 | -0.7 |
| 500 | Epiemerase family protein SAUSA300_0753 OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0753 PE=3 SV=1 | Q2FIM4 Y753_STAA3 | -0.7 |
| 563 | Molybdopterin converting factor, subunit 1 OS=Staphylococcus aureus (strain USA300) GN=moaD PE=4 SV=1 | Q2FEM2 Q2FEM2_STAA3 | -0.7 |
| 631 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0874 PE=4 SV=1 | Q2FIA4 Q2FIA4_STAA3 | -0.7 |
| 701 | GMP reductase OS=Staphylococcus aureus (strain USA300) GN=guaC PE=3 SV=1 | Q2FH96 GUAC_STAA3 | -0.7 |
| 79 | Glucose-6-phosphate isomerase OS=Staphylococcus aureus (strain USA300) GN=pgi PE=3 SV=1 | Q2FIB3 G6PI_STAA3 | -0.6 |
| 86 | UPF0457 protein SAUSA300_2132 OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_2132 PE=3 SV=1 | Q2FEV9 Y2132_STAA3 | -0.6 |
| 166 | Uncharacterized hydrolase SAUSA300_2518 OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_2518 PE=3 SV=1 | Q2FDS6 Y2518_STAA3 | -0.6 |
| 197 | Putative lipoprotein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0372 PE=4 SV=1 | Q2FJP2 Q2FJP2_STAA3 | -0.6 |
| 224 | Alcohol dehydrogenase, zinc-containing OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0250 PE=4 SV=1 | Q2FK14 Q2FK14_STAA3 | -0.6 |
| 236 | Chaperone clpB OS=Staphylococcus aureus (strain USA300) GN=clpB PE=3 SV=1 | Q2FIA1 Q2FIA1_STAA3 | -0.6 |
| 250 | Fibrinogen-binding protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1052 PE=4 SV=1 | Q2FHS8 Q2FHS8_STAA3 | -0.6 |
| 287 | 2',3'-cyclic-nucleotide 2'-phosphodiesterase OS=Staphylococcus aureus (strain USA300) GN=cvfA PE=3 SV=1 | Q2FHF2 CNPD_STAA3 | -0.6 |
| 364 | 30S ribosomal protein S19 OS=Staphylococcus aureus (strain USA300) GN=rpsS PE=3 SV=1 | Q2FEP3 RS19_STAA3 | -0.6 |
| 370 | Probable uridyltransferase SAUSA300_2130 OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_2130 PE=3 SV=1 | Q2FEW1 URTF_STAA3 | -0.6 |
| 444 | PTS system, mannitol specific IIA component OS=Staphylococcus aureus (strain USA300) GN=mtlA PE=4 SV=1 | Q2FEX5 Q2FEX5_STAA3 | -0.6 |

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| 460 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_2418 PE=4 SV=1 | Q2FE25 Q2FE25_STAA3 | -0.6 |
| 498 | Glutathione peroxidase OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1197 PE=3 SV=1 | Q2FHD4 Q2FHD4_STAA3 | -0.6 |
| 566 | Putative lipoprotein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0992 PE=4 SV=1 | Q2FHY8 Q2FHY8_STAA3 | -0.6 |
| 583 | Bifunctional protein glmU OS=Staphylococcus aureus (strain USA300) GN=glmU PE=3 SV=1 | Q2FJE2 GLMU_STAA3 | -0.6 |
| 592 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1351 PE=4 SV=1 | Q2FGY0 Q2FGY0_STAA3 | -0.6 |
| 606 | Competence/damage-inducible protein cinA OS=Staphylococcus aureus (strain USA300) GN=cinA PE=4 SV=1 | Q2FHF4 Q2FHF4_STAA3 | -0.6 |
| 36 | Phosphoglycerate kinase OS=Staphylococcus aureus (strain USA300) GN=pgk PE=3 SV=1 | Q2FIM0 PGK_STAA3 | -0.5 |
| 51 | Dihydrolipoamide acetyltransferase OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0995 PE=3 SV=1 | Q2FHY5 Q2FHY5_STAA3 | -0.5 |
| 90 | Trigger factor OS=Staphylococcus aureus (strain USA300) GN=tig PE=3 SV=1 | Q2FG61 TIG_STAA3 | -0.5 |
| 289 | Aspartyl/glutamyl-tRNA(Asn/Gln) amidotransferase subunit C OS=Staphylococcus aureus (strain USA300) GN=gatC PE=3 SV=1 | Q2FFJ4 GATC_STAA3 | -0.5 |
| 415 | Excinuclease ABC, A subunit OS=Staphylococcus aureus (strain USA300) GN=uvrA PE=3 SV=1 | Q2FIN4 Q2FIN4_STAA3 | -0.5 |
| 431 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0373 PE=4 SV=1 | Q2FJP1 Q2FJP1_STAA3 | -0.5 |
| 443 | Cystathionine gamma-synthase OS=Staphylococcus aureus (strain USA300) GN=metB PE=3 SV=1 | Q2FJI1 Q2FJI1_STAA3 | -0.5 |
| 477 | Lytic regulatory protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_2100 PE=4 SV=1 | Q2FEY2 Q2FEY2_STAA3 | -0.5 |
| 501 | 30S ribosomal protein S20 OS=Staphylococcus aureus (strain USA300) GN=rpsT PE=3 SV=1 | Q2FGD8 RS20_STAA3 | -0.5 |
| 754 | Sulfite reductase flavoprotein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_2554 PE=3 SV=1 | Q2FDP0 Q2FDP0_STAA3 | -0.5 |
| 22 | Glyceraldehyde-3-phosphate dehydrogenase, type I OS=Staphylococcus aureus (strain USA300) GN=gap PE=3 SV=1 | Q2FIM1 Q2FIM1_STAA3 | -0.4 |
| 132 | Foldase protein prsA OS=Staphylococcus aureus (strain USA300) GN=prsA PE=3 SV=1 | Q2FFQ5 PRSA_STAA3 | -0.4 |
| 151 | Serine hydroxymethyltransferase OS=Staphylococcus aureus (strain USA300) GN=glyA PE=3 SV=1 | Q2FF15 GLYA_STAA3 | -0.4 |
| 214 | Glutamyl-tRNA synthetase OS=Staphylococcus aureus (strain USA300) GN=gltX PE=3 SV=1 | Q2FJB2 SYE_STAA3 | -0.4 |
| 229 | D-alanine--poly(phosphoribitol) ligase subunit 1 OS=Staphylococcus aureus (strain USA300) GN=dltA PE=3 SV=1 | Q2FIE3 DLTA_STAA3 | -0.4 |

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| 239 | 3-oxoacyl-(Acyl-carrier-protein) synthase II OS=Staphylococcus aureus (strain USA300) GN=fabF PE=3 SV=1 | Q2FI92 Q2FI92_STAA3 | -0.4 |
| 240 | Glycerol phosphate lipoteichoic acid synthase OS=Staphylococcus aureus (strain USA300) GN=ItaS PE=3 SV=1 | Q2FIS2 LTAS_STAA3 | -0.4 |
| 277 | Thioredoxin reductase OS=Staphylococcus aureus (strain USA300) GN=trxB PE=3 SV=1 | Q2FIM9 Q2FIM9_STAA3 | -0.4 |
| 313 | Ribosome-recycling factor OS=Staphylococcus aureus (strain USA300) GN=frr PE=3 SV=1 | Q2FHH9 RRF_STAA3 | -0.4 |
| 318 | Iron compound ABC transporter, iron compound-binding protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_2235 PE=4 SV=1 | Q2FEK8 Q2FEK8_STAA3 | -0.4 |
| 323 | 50S ribosomal protein L29 OS=Staphylococcus aureus (strain USA300) GN=rpmC PE=4 SV=1 | Q2FEP7 Q2FEP7_STAA3 | -0.4 |
| 337 | UDP-N-acetylglucosaminyldolichol-phosphate-D-glucosaminide-4-epimerase OS=Staphylococcus aureus (strain USA300) GN=murE PE=3 SV=1 | Q2FI59 MURE_STAA3 | -0.4 |
| 421 | Putative thioredoxin OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1690 PE=4 SV=1 | Q2FFZ4 Q2FFZ4_STAA3 | -0.4 |
| 535 | Nitroreductase family protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1986 PE=4 SV=1 | Q2FF91 Q2FF91_STAA3 | -0.4 |
| 544 | 50S ribosomal protein L28 OS=Staphylococcus aureus (strain USA300) GN=rpmB PE=3 SV=1 | Q2FHL4 RL28_STAA3 | -0.4 |
| 596 | Putative transcriptional regulator OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_2259 PE=4 SV=1 | Q2FEI4 Q2FEI4_STAA3 | -0.4 |
| 599 | Fibrinogen-binding protein OS=Staphylococcus aureus (strain USA300) GN=efb PE=4 SV=1 | Q2FHS5 Q2FHS5_STAA3 | -0.4 |
| 607 | Arginine deiminase OS=Staphylococcus aureus (strain USA300) GN=arcA PE=3 SV=1 | Q2FDM4 Q2FDM4_STAA3 | -0.4 |
| 44 | Acyl carrier protein OS=Staphylococcus aureus (strain USA300) GN=acpP PE=3 SV=1 | Q2FHK6 ACP_STAA3 | -0.3 |
| 189 | Cell cycle protein gpsB OS=Staphylococcus aureus (strain USA300) GN=gpsB PE=3 SV=1 | Q2FGZ4 GPSB_STAA3 | -0.3 |
| 445 | HTH-type transcriptional regulator rot OS=Staphylococcus aureus (strain USA300) GN=rot PE=3 SV=1 | Q2FFX6 Q2FFX6_STAA3 | -0.3 |
| 448 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1803 PE=4 SV=1 | Q2FFP2 Q2FFP2_STAA3 | -0.3 |
| 464 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1904 PE=4 SV=1 | Q2FFH2 Q2FFH2_STAA3 | -0.3 |
| 546 | Cold shock protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_2639 PE=3 SV=1 | Q2FDF5 Q2FDF5_STAA3 | -0.3 |
| 550 | Cmp-binding-factor 1 OS=Staphylococcus aureus (strain USA300) GN=cbf1 PE=4 SV=1 | Q2FFQ4 Q2FFQ4_STAA3 | -0.3 |
| 564 | N utilization substance protein B homolog OS=Staphylococcus aureus (strain USA300) GN=nusB PE=3 SV=1 | Q2FGK9 NUSB_STAA3 | -0.3 |

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| 626 | Dihydrofolate reductase OS=Staphylococcus aureus (strain USA300) GN=folA PE=3 SV=1 | Q2FH12 Q2FH12_STAA3 | -0.3 |
| 80 | Glutamine synthetase OS=Staphylococcus aureus (strain USA300) GN=glnA PE=3 SV=1 | Q2FHD0 Q2FHD0_STAA3 | -0.2 |
| 144 | Naphthoate synthase OS=Staphylococcus aureus (strain USA300) GN=menB PE=4 SV=1 | Q2FI32 Q2FI32_STAA3 | -0.2 |
| 173 | Putative aldehyde dehydrogenase AldA OS=Staphylococcus aureus (strain USA300) GN=aldA PE=3 SV=1 | Q2FK94 ALDA_STAA3 | -0.2 |
| 190 | 3-hexulose-6-phosphate synthase OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0555 PE=3 SV=1 | Q2FJ70 HPS_STAA3 | -0.2 |
| 192 | 50S ribosomal protein L18 OS=Staphylococcus aureus (strain USA300) GN=rplR PE=3 SV=1 | Q2FEQ5 RL18_STAA3 | -0.2 |
| 299 | Transcription elongation factor greA OS=Staphylococcus aureus (strain USA300) GN=greA PE=3 SV=1 | Q2FGB6 GREA_STAA3 | -0.2 |
| 302 | 30S ribosomal protein S18 OS=Staphylococcus aureus (strain USA300) GN=rpsR PE=3 SV=1 | Q2FP6 RS18_STAA3 | -0.2 |
| 312 | Probable glycine dehydrogenase [decarboxylating] subunit 1 OS=Staphylococcus aureus (strain USA300) GN=gcvPA PE=3 SV=1 | Q2FGI6 GCSPA_STAA3 | -0.2 |
| 314 | 50S ribosomal protein L17 OS=Staphylococcus aureus (strain USA300) GN=rplQ PE=3 SV=1 | Q2FER6 RL17_STAA3 | -0.2 |
| 347 | ABC transporter, substrate-binding protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0798 PE=4 SV=1 | Q2FII0 Q2FII0_STAA3 | -0.2 |
| 368 | Amino acid ABC transporter, amino acid-binding protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_2359 PE=4 SV=1 | Q2FE84 Q2FE84_STAA3 | -0.2 |
| 424 | Homoserine dehydrogenase OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1226 PE=3 SV=1 | Q2FHA5 Q2FHA5_STAA3 | -0.2 |
| 430 | Peptide methionine sulfoxide reductase msrB OS=Staphylococcus aureus (strain USA300) GN=msrB PE=3 SV=1 | Q2FH15 MSRB_STAA3 | -0.2 |
| 447 | PTS system, glucose-specific IIA component OS=Staphylococcus aureus (strain USA300) GN=crr PE=4 SV=1 | Q2FH16 Q2FH16_STAA3 | -0.2 |
| 479 | Argininosuccinate synthase OS=Staphylococcus aureus (strain USA300) GN=argG PE=3 SV=1 | Q2FIB4 ASSY_STAA3 | -0.2 |
| 484 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1303 PE=4 SV=1 | Q2FH28 Q2FH28_STAA3 | -0.2 |
| 495 | Organic hydroperoxide resistance protein-like OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0786 PE=3 SV=1 | Q2FIJ2 OHRL_STAA3 | -0.2 |
| 52 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1581 PE=4 SV=1 | Q2FGA2 Q2FGA2_STAA3 | -0.1 |
| 113 | Pyruvate oxidase OS=Staphylococcus aureus (strain USA300) GN=cidC PE=3 SV=1 | Q2FDW7 Q2FDW7_STAA3 | -0.1 |
| 207 | Molybdenum ABC transporter, molybdenum-binding protein ModA OS=Staphylococcus aureus (strain USA300) GN=modA PE=4 SV=1 | Q2FEL3 Q2FEL3_STAA3 | -0.1 |

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| 212 | Iron compound ABC transporter, iron compound-binding protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_2136 PE=4 SV=1 | Q2FEV5 Q2FEV5_STAA3 | -0.1 |
| 366 | Elongation factor P OS=Staphylococcus aureus (strain USA300) GN=efp PE=3 SV=1 | Q2FGJ3 EFP_STAA3 | -0.1 |
| 406 | Anti-sigma factor antagonist OS=Staphylococcus aureus (strain USA300) GN=rsbV PE=3 SV=1 | Q2FF58 Q2FF58_STAA3 | -0.1 |
| 461 | Fructose specific permease OS=Staphylococcus aureus (strain USA300) GN=fruA PE=4 SV=1 | Q2FIU0 Q2FIU0_STAA3 | -0.1 |
| 466 | Leucyl-tRNA synthetase OS=Staphylococcus aureus (strain USA300) GN=leuS PE=3 SV=1 | Q2FFY0 SYL_STAA3 | -0.1 |
| 487 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0985 PE=4 SV=1 | Q2FHZ5 Q2FHZ5_STAA3 | -0.1 |
| 562 | Penicillin-binding protein 4 OS=Staphylococcus aureus (strain USA300) GN=pbp4 PE=3 SV=1 | Q2FIZ6 Q2FIZ6_STAA3 | -0.1 |
| 629 | 50S ribosomal protein L32 OS=Staphylococcus aureus (strain USA300) GN=rpmF PE=3 SV=1 | Q2FHV3 RL32_STAA3 | -0.1 |
| 7 | DNA-binding protein HU OS=Staphylococcus aureus (strain USA300) GN=hup PE=3 SV=1 | Q2FGW9 Q2FGW9_STAA3 | 0 |
| 84 | Fructose bisphosphate aldolase OS=Staphylococcus aureus (strain USA300) GN=fba PE=4 SV=1 | Q2FF03 Q2FF03_STAA3 | 0 |
| 226 | Adenylate kinase OS=Staphylococcus aureus (strain USA300) GN=adk PE=3 SV=1 | Q2FER0 Q2FER0_STAA3 | 0 |
| 303 | 50S ribosomal protein L31 type B OS=Staphylococcus aureus (strain USA300) GN=rpmE2 PE=3 SV=1 | Q2FF08 RL31B_STAA3 | 0 |
| 309 | Signal transduction protein TRAP OS=Staphylococcus aureus (strain USA300) GN=traP PE=3 SV=1 | Q2FFR1 TRAP_STAA3 | 0 |
| 481 | Staphylococcal accessory regulator OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0114 PE=4 SV=1 | Q2FKE7 Q2FKE7_STAA3 | 0 |
| 541 | Phenylalanyl-tRNA synthetase beta chain OS=Staphylococcus aureus (strain USA300) GN=pheT PE=3 SV=1 | Q2FHU2 SYFB_STAA3 | 0 |
| 580 | Penicillin-binding protein 3 OS=Staphylococcus aureus (strain USA300) GN=pbp3 PE=4 SV=1 | Q2FGH1 Q2FGH1_STAA3 | 0 |
| 615 | Iron compound ABC transporter, iron compound-binding protein SirA OS=Staphylococcus aureus (strain USA300) GN=sirA PE=4 SV=1 | Q2FKE4 Q2FKE4_STAA3 | 0 |
| 711 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_2378 PE=4 SV=1 | Q2FE65 Q2FE65_STAA3 | 0 |
| 6 | UPF0337 protein SAUSA300_0816 OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0816 PE=3 SV=1 | Q2FIG2 Y816_STAA3 | 0.1 |
| 21 | Chaperone protein dnaK OS=Staphylococcus aureus (strain USA300) GN=dnaK PE=2 SV=1 | Q2FGE3 DNAK_STAA3 | 0.1 |
| 107 | UPF0342 protein SAUSA300_1795 OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1795 PE=3 SV=1 | Q2FFQ0 Y1795_STAA3 | 0.1 |

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| 157 | Copper chaperone copZ OS=Staphylococcus aureus (strain USA300) GN=copZ PE=3 SV=1 | Q2FDU9 COPZ_STAA3 | 0.1 |
| 227 | Thiol peroxidase OS=Staphylococcus aureus (strain USA300) GN=tpx PE=4 SV=1 | Q2FG25 Q2FG25_STAA3 | 0.1 |
| 268 | FMN-dependent NADH-azoreductase OS=Staphylococcus aureus (strain USA300) GN=azoR PE=3 SV=1 | Q2FK58 AZOR_STAA3 | 0.1 |
| 293 | Glucokinase OS=Staphylococcus aureus (strain USA300) GN=glk PE=4 SV=1 | Q2FGH6 Q2FGH6_STAA3 | 0.1 |
| 419 | 50S ribosomal protein L24 OS=Staphylococcus aureus (strain USA300) GN=rplX PE=3 SV=1 | Q2FEQ0 RL24_STAA3 | 0.1 |
| 458 | Putative cell-division initiation protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1086 PE=4 SV=1 | Q2FHP5 Q2FHP5_STAA3 | 0.1 |
| 647 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_2246 PE=4 SV=1 | Q2FEJ7 Q2FEJ7_STAA3 | 0.1 |
| 722 | (3R)-hydroxymyristoyl-[acyl-carrier-protein] dehydratase OS=Staphylococcus aureus (strain USA300) GN=fabZ PE=3 SV=1 | Q2FF28 FABZ_STAA3 | 0.1 |
| 34 | N-acetylmuramoyl-L-alanine amidase domain protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_2579 PE=4 SV=1 | Q2FDL5 Q2FDL5_STAA3 | 0.2 |
| 185 | 50S ribosomal protein L11 OS=Staphylococcus aureus (strain USA300) GN=rplK PE=3 SV=3 | Q2FJA3 RL11_STAA3 | 0.2 |
| 215 | 50S ribosomal protein L25 OS=Staphylococcus aureus (strain USA300) GN=rplY PE=3 SV=1 | Q2FJE0 RL25_STAA3 | 0.2 |
| 389 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1215 PE=4 SV=1 | Q2FHB6 Q2FHB6_STAA3 | 0.2 |
| 492 | Chorismate mutase/phospho-2-dehydro-3-deoxyheptonate aldolase OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1683 PE=4 SV=1 | Q2FG01 Q2FG01_STAA3 | 0.2 |
| 507 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0931 PE=4 SV=1 | Q2FI49 Q2FI49_STAA3 | 0.2 |
| 683 | Putative GTP-binding protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1136 PE=4 SV=1 | Q2FHJ5 Q2FHJ5_STAA3 | 0.2 |
| 771 | NADPH-dependent oxidoreductase OS=Staphylococcus aureus (strain USA300) GN=nfra PE=3 SV=1 | Q2FJN3 NFRA_STAA3 | 0.2 |
| 10 | Alkaline shock protein 23 OS=Staphylococcus aureus (strain USA300) GN=asp23 PE=3 SV=1 | Q2FEV0 ASP23_STAA3 | 0.3 |
| 172 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1698 PE=4 SV=1 | Q2FFY6 Q2FFY6_STAA3 | 0.3 |
| 286 | Dihydrolipoylysine-residue succinyltransferase component of 2-oxoglutarate dehydrogenase complex OS=Staphylococcus aureus (strain USA300) GN=odhB PE=3 SV=1 | Q2FH26 ODO2_STAA3 | 0.3 |
| 401 | 30S ribosomal protein S16 OS=Staphylococcus aureus (strain USA300) GN=rpsP PE=3 SV=1 | Q2FHK0 RS16_STAA3 | 0.3 |
| 768 | SUF system FeS assembly protein, NifU family OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0821 PE=4 SV=1 | Q2FIF7 Q2FIF7_STAA3 | 0.3 |

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| 28 | Secretory antigen SsaA OS=Staphylococcus aureus (strain USA300) GN=ssaA PE=4 SV=1 | Q2FEJ4 Q2FEJ4_STAA3 | 0.4 |
| 141 | N-acetylmuramoyl-L-alanine amidase sle1 OS=Staphylococcus aureus (strain USA300) GN=sle1 PE=3 SV=1 | Q2FJH7 SLE1_STAA3 | 0.4 |
| 324 | 6,7-dimethyl-8-ribityllumazine synthase OS=Staphylococcus aureus (strain USA300) GN=ribH PE=3 SV=1 | Q2FFX3 RISB_STAA3 | 0.4 |
| 393 | Mannitol-1-phosphate 5-dehydrogenase OS=Staphylococcus aureus (strain USA300) GN=mtlD PE=3 SV=1 | Q2FEX4 MTLD_STAA3 | 0.4 |
| 398 | Translation initiation factor IF-3 OS=Staphylococcus aureus (strain USA300) GN=infC PE=3 SV=1 | Q2FG56 IF3_STAA3 | 0.4 |
| 407 | D-alanine--poly(phosphoribitol) ligase subunit 2 OS=Staphylococcus aureus (strain USA300) GN=dltC PE=3 SV=1 | Q2FIE1 DLTC_STAA3 | 0.4 |
| 489 | Triacylglycerol lipase OS=Staphylococcus aureus (strain USA300) GN=lip PE=4 SV=1 | Q2FDJ1 Q2FDJ1_STAA3 | 0.4 |
| 618 | NLPA lipoprotein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0437 PE=4 SV=1 | Q2FJH8 Q2FJH8_STAA3 | 0.4 |
| 38 | Thioredoxin OS=Staphylococcus aureus (strain USA300) GN=trxA PE=3 SV=1 | Q2FHT6 THIO_STAA3 | 0.5 |
| 396 | NH(3)-dependent NAD(+) synthetase OS=Staphylococcus aureus (strain USA300) GN=nadE PE=3 SV=1 | Q2FFI3 NADE_STAA3 | 0.5 |
| 571 | Putative lipoprotein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0724 PE=4 SV=1 | Q2FIQ1 Q2FIQ1_STAA3 | 0.5 |
| 75 | Phosphocarrier protein HPr OS=Staphylococcus aureus (strain USA300) GN=ptsH PE=4 SV=1 | Q2FHZ7 Q2FHZ7_STAA3 | 0.6 |
| 134 | Transcriptional regulator sarA OS=Staphylococcus aureus (strain USA300) GN=sarA PE=3 SV=1 | Q2FJ20 SARA_STAA3 | 0.6 |
| 310 | Acetyl-coenzyme A carboxylase carboxyl transferase subunit alpha OS=Staphylococcus aureus (strain USA300) GN=accA PE=1 SV=1 | Q2FG38 ACCA_STAA3 | 0.6 |
| 624 | Probable transglycosylase sceD OS=Staphylococcus aureus (strain USA300) GN=sceD PE=2 SV=1 | Q2FF31 SCED_STAA3 | 0.6 |
| 296 | Malonyl CoA-acyl carrier protein transacylase OS=Staphylococcus aureus (strain USA300) GN=fabD PE=4 SV=1 | Q2FHK8 Q2FHK8_STAA3 | 0.7 |
| 540 | tRNA uridine 5-carboxymethylaminomethyl modification enzyme mnmG OS=Staphylococcus aureus (strain USA300) GN=mnmG PE=3 SV=2 | Q2FDE9 MNMG_STAA3 | 0.7 |
| 372 | Methionine-S-sulfoxide reductase OS=Staphylococcus aureus (strain USA300) GN=msrA PE=3 SV=1 | Q2FH14 Q2FH14_STAA3 | 0.8 |
| 503 | Methionine aminopeptidase OS=Staphylococcus aureus (strain USA300) GN=map PE=3 SV=1 | Q2FFK7 Q2FFK7_STAA3 | 0.8 |
| 619 | Clumping factor A OS=Staphylococcus aureus (strain USA300) GN=clfA PE=3 SV=1 | Q2FIK6 Q2FIK6_STAA3 | 0.8 |
| 23 | Probable transglycosylase isaA OS=Staphylococcus aureus (strain USA300) GN=isaA PE=3 SV=1 | Q2FDT8 ISAA_STAA3 | 0.9 |

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| 45 | D-lactate dehydrogenase OS=Staphylococcus aureus (strain USA300) GN=ddh PE=3 SV=1 | Q2FDY1 Q2FDY1_STAA3 | 0.9 |
| 263 | UPF0435 protein SAUSA300_1861 OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1861 PE=3 SV=2 | Q2FFL5 Y1861_STAA3 | 0.9 |
| 349 | S-ribosylhomocysteine lyase OS=Staphylococcus aureus (strain USA300) GN=luxS PE=3 SV=1 | Q2FEZ4 LUXS_STAA3 | 0.9 |
| 478 | Carboxyl-terminal protease OS=Staphylococcus aureus (strain USA300) GN=ctpA PE=3 SV=1 | Q2FH18 Q2FH18_STAA3 | 0.9 |
| 659 | Membrane-associated protein tcaA OS=Staphylococcus aureus (strain USA300) GN=tcaA PE=3 SV=1 | Q2FEE1 TCAA_STAA3 | 0.9 |
| 358 | Transferrin receptor OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0721 PE=4 SV=1 | Q2FIQ4 Q2FIQ4_STAA3 | 1 |
| 418 | Probable glycine dehydrogenase [decarboxylating] subunit 2 OS=Staphylococcus aureus (strain USA300) GN=gcvPB PE=3 SV=1 | Q2FGI7 GCSPB_STAA3 | 1 |
| 525 | Glutamine amidotransferase subunit pdxT OS=Staphylococcus aureus (strain USA300) GN=pdxT PE=3 SV=1 | Q2FJC0 PDXT_STAA3 | 1 |
| 713 | Aminopeptidase PepS OS=Staphylococcus aureus (strain USA300) GN=pepS PE=4 SV=1 | Q2FFL6 Q2FFL6_STAA3 | 1 |
| 66 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_2473 PE=4 SV=1 | Q2FDX1 Q2FDX1_STAA3 | 1.1 |
| 266 | UDP-N-acetylmuramoylalanine--D-glutamate ligase OS=Staphylococcus aureus (strain USA300) GN=murD PE=3 SV=1 | Q2FHQ4 MURD_STAA3 | 1.1 |
| 206 | General stress protein 20U OS=Staphylococcus aureus (strain USA300) GN=dps PE=3 SV=1 | Q2FEZ0 Q2FEZ0_STAA3 | 1.3 |
| 363 | Imidazolonepropionase OS=Staphylococcus aureus (strain USA300) GN=hutI PE=3 SV=1 | Q2FEG6 HUTI_STAA3 | 1.5 |
| 16 | Elongation factor Ts OS=Staphylococcus aureus (strain USA300) GN=tsf PE=3 SV=1 | Q2FHI1 EFTS_STAA3 | 1.6 |
| 284 | Superoxide dismutase [Mn/Fe] 1 OS=Staphylococcus aureus (strain USA300) GN=sodA PE=3 SV=1 | Q2FGH0 SODM1_STAA3 | 1.6 |
| 513 | Arginase OS=Staphylococcus aureus (strain USA300) GN=rocF PE=3 SV=1 | Q2FEW8 Q2FEW8_STAA3 | 1.7 |
| 374 | GTP cyclohydrolase folE2 OS=Staphylococcus aureus (strain USA300) GN=folE2 PE=3 SV=1 | Q2FJ74 GCH4_STAA3 | 1.8 |
| 462 | Cysteinyl-tRNA synthetase OS=Staphylococcus aureus (strain USA300) GN=cysS PE=3 SV=1 | Q2FJB0 SYC_STAA3 | 1.8 |
| 2 | Antibacterial protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1067 PE=4 SV=1 | Q2FHR4 Q2FHR4_STAA3 | 2.2 |
| 280 | Superoxide dismutase [Mn/Fe] 2 OS=Staphylococcus aureus (strain USA300) GN=sodM PE=3 SV=1 | Q2FKC6 SODM2_STAA3 | 2.2 |
| 4 | Antibacterial protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1068 PE=4 SV=1 | Q2FHR3 Q2FHR3_STAA3 | 2.7 |

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| 257 | UPF0337 protein SAUSA300_1582 OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1582 PE=3 SV=1 | Q2FGA1 Y1582_STAA3 | 2.7 |
| 438 | Phi77 ORF014-like protein, phage anti-repressor protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1966 PE=4 SV=1 | Q2FFB1 Q2FFB1_STAA3 | 2.9 |
| 176 | Deoxyribose-phosphate aldolase OS=Staphylococcus aureus (strain USA300) GN=deoC PE=3 SV=1 | Q2FKC1 Q2FKC1_STAA3 | No Values |
| 291 | UDP-N-acetyl muramate-L-alanine ligase OS=Staphylococcus aureus (strain USA300) GN=murC PE=3 SV=1 | Q2FFZ8 MURC_STAA3 | No Values |
| 331 | Pseudouridine synthase OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1090 PE=3 SV=1 | Q2FHP1 Q2FHP1_STAA3 | No Values |
| 397 | Fumarate hydratase, class II OS=Staphylococcus aureus (strain USA300) GN=fumC PE=4 SV=1 | Q2FFP4 Q2FFP4_STAA3 | No Values |
| 410 | Cytosol aminopeptidase OS=Staphylococcus aureus (strain USA300) GN=ampA PE=3 SV=1 | Q2FID3 Q2FID3_STAA3 | No Values |
| 446 | Exodeoxyribonuclease 7 small subunit OS=Staphylococcus aureus (strain USA300) GN=xseB PE=3 SV=1 | Q2FGL1 EX7S_STAA3 | No Values |
| 449 | Protein grpE OS=Staphylococcus aureus (strain USA300) GN=grpE PE=3 SV=1 | Q2FGE2 GRPE_STAA3 | No Values |
| 454 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1336 PE=4 SV=1 | Q2FGZ5 Q2FGZ5_STAA3 | No Values |
| 463 | 50S ribosomal protein L15 OS=Staphylococcus aureus (strain USA300) GN=rplO PE=3 SV=1 | Q2FEQ8 RL15_STAA3 | No Values |
| 465 | 30S ribosomal protein S15 OS=Staphylococcus aureus (strain USA300) GN=rpsO PE=3 SV=1 | Q2FHG5 RS15_STAA3 | No Values |
| 474 | Serine-aspartate repeat-containing protein D OS=Staphylococcus aureus (strain USA300) GN=sdrD PE=3 SV=1 | Q2FJ78 SDRD_STAA3 | No Values |
| 488 | L-lactate permease OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_2313 PE=4 SV=1 | Q2FED0 Q2FED0_STAA3 | No Values |
| 494 | Putative zinc-binding dehydrogenase OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_2317 PE=4 SV=1 | Q2FEC6 Q2FEC6_STAA3 | No Values |
| 512 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1684 PE=4 SV=1 | Q2FG00 Q2FG00_STAA3 | No Values |
| 518 | Esterase-like protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_2296 PE=4 SV=1 | Q2FEE7 Q2FEE7_STAA3 | No Values |
| 520 | 3-methyl-2-oxobutanoate hydroxymethyltransferase OS=Staphylococcus aureus (strain USA300) GN=panB PE=3 SV=2 | Q2FDR0 PANB_STAA3 | No Values |
| 526 | ATP synthase epsilon chain OS=Staphylococcus aureus (strain USA300) GN=atpC PE=3 SV=1 | Q2FF25 ATPE_STAA3 | No Values |
| 528 | D-isomer specific 2-hydroxyacid dehydrogenase family protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_2496 PE=3 SV=1 | Q2FDU8 Q2FDU8_STAA3 | No Values |
| 529 | Coenzyme A disulfide reductase OS=Staphylococcus aureus (strain USA300) GN=cdr PE=3 SV=1 | Q2FIA5 CDR_STAA3 | No Values |

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| 530 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0383 PE=4 SV=1 | Q2FJN1 Q2FJN1_STAA3 | No Values |
| 532 | Molybdopterin biosynthesis protein A OS=Staphylococcus aureus (strain USA300) GN=moeA PE=4 SV=1 | Q2FEL9 Q2FEL9_STAA3 | No Values |
| 533 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1171 PE=3 SV=1 | Q2FHG0 Q2FHG0_STAA3 | No Values |
| 536 | Adenine phosphoribosyltransferase OS=Staphylococcus aureus (strain USA300) GN=apt PE=3 SV=1 | Q2FG92 APT_STAA3 | No Values |
| 543 | Methionine import ATP-binding protein MetN 2 OS=Staphylococcus aureus (strain USA300) GN=metN2 PE=3 SV=1 | Q2FII2 METN2_STAA3 | No Values |
| 547 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_2482 PE=4 SV=1 | Q2FDW2 Q2FDW2_STAA3 | No Values |
| 549 | 2,3,4,5-tetrahydropyridine-2,6-dicarboxylate N-acetyltransferase OS=Staphylococcus aureus (strain USA300) GN=dapH PE=3 SV=1 | Q2FH41 DAPH_STAA3 | No Values |
| 554 | TelA-like protein SAUSA300_1299 OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1299 PE=3 SV=1 | Q2FH32 TELL_STAA3 | No Values |
| 561 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0749 PE=4 SV=1 | Q2FIM7 Q2FIM7_STAA3 | No Values |
| 572 | DNA topoisomerase 1 OS=Staphylococcus aureus (strain USA300) GN=topA PE=3 SV=2 | Q2FHI8 TOP1_STAA3 | No Values |
| 573 | ABC transporter, ATP-binding protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_2357 PE=4 SV=1 | Q2FE86 Q2FE86_STAA3 | No Values |
| 576 | Putative N-acetyltransferase OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_2631 PE=3 SV=1 | Q2FDG3 Q2FDG3_STAA3 | No Values |
| 581 | DNA mismatch repair protein mutL OS=Staphylococcus aureus (strain USA300) GN=mutL PE=3 SV=1 | Q2FHE2 MUTL_STAA3 | No Values |
| 588 | Purine nucleoside phosphorylase OS=Staphylococcus aureus (strain USA300) GN=deoD PE=3 SV=1 | Q2FEZ1 Q2FEZ1_STAA3 | No Values |
| 591 | UPF0473 protein SAUSA300_1572 OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1572 PE=3 SV=1 | Q2FGB1 Y1572_STAA3 | No Values |
| 593 | Glycolytic operon regulator OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0755 PE=4 SV=1 | Q2FIM2 Q2FIM2_STAA3 | No Values |
| 598 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1536 PE=4 SV=1 | Q2FGE7 Q2FGE7_STAA3 | No Values |
| 600 | Sensor protein OS=Staphylococcus aureus (strain USA300) GN=srrB PE=3 SV=1 | Q2FGP1 Q2FGP1_STAA3 | No Values |
| 614 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0173 PE=4 SV=1 | Q2FK91 Q2FK91_STAA3 | No Values |
| 616 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1180 PE=4 SV=1 | Q2FHF1 Q2FHF1_STAA3 | No Values |
| 620 | Putative teichoic acid biosynthesis protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0251 PE=4 SV=1 | Q2FK13 Q2FK13_STAA3 | No Values |

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| 628 | Glycine betaine transporter opuD OS=Staphylococcus aureus (strain USA300) GN=opuD PE=4 SV=1 | Q2FH86 Q2FH86_STAA3 | No Values |
| 632 | UPF0349 protein SAUSA300_0842 OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0842 PE=3 SV=1 | Q2FID6 Y842_STAA3 | No Values |
| 635 | Glutamate racemase OS=Staphylococcus aureus (strain USA300) GN=murI PE=3 SV=1 | Q2FHT1 MURI_STAA3 | No Values |
| 636 | PhiPVL ORF41-like protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1961 PE=4 SV=1 | Q2FFB6 Q2FFB6_STAA3 | No Values |
| 640 | DNA ligase OS=Staphylococcus aureus (strain USA300) GN=ligA PE=3 SV=1 | Q2FFJ1 DNLJ_STAA3 | No Values |
| 643 | Putative chromosome partitioning protein, ParB family OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_2643 PE=4 SV=1 | Q2FDF1 Q2FDF1_STAA3 | No Values |
| 648 | Glutamyl-aminopeptidase OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1691 PE=4 SV=1 | Q2FFZ3 Q2FFZ3_STAA3 | No Values |
| 650 | Bacterial luciferase family protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1580 PE=4 SV=1 | Q2FGA3 Q2FGA3_STAA3 | No Values |
| 652 | Alpha glucosidase OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1456 PE=3 SV=1 | Q2FGM6 Q2FGM6_STAA3 | No Values |
| 653 | Oligoendopeptidase F OS=Staphylococcus aureus (strain USA300) GN=pepF PE=4 SV=1 | Q2FH53 Q2FH53_STAA3 | No Values |
| 674 | ABC transporter, substrate-binding protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0231 PE=4 SV=1 | Q2FK33 Q2FK33_STAA3 | No Values |
| 675 | PTS system, trehalose-specific IIBC component OS=Staphylococcus aureus (strain USA300) GN=trep PE=4 SV=1 | Q2FJG8 Q2FJG8_STAA3 | No Values |
| 679 | Transcription-repair-coupling factor OS=Staphylococcus aureus (strain USA300) GN=mfd PE=3 SV=1 | Q2FJD8 MFD_STAA3 | No Values |
| 680 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_2327 PE=4 SV=1 | Q2FEB6 Q2FEB6_STAA3 | No Values |
| 681 | Phosphoglucomutase OS=Staphylococcus aureus (strain USA300) GN=pgcA PE=3 SV=2 | Q2FE11 PGCA_STAA3 | No Values |
| 684 | Putative osmoprotectant ABC transporter, ATP-binding protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0706 PE=4 SV=1 | Q2FIR9 Q2FIR9_STAA3 | No Values |
| 685 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_2404 PE=4 SV=1 | Q2FE39 Q2FE39_STAA3 | No Values |
| 686 | UDP-N-acetylglucosamine 2-epimerase OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_2065 PE=3 SV=1 | Q2FF17 Q2FF17_STAA3 | No Values |
| 688 | Para-nitrobenzyl esterase OS=Staphylococcus aureus (strain USA300) GN=pnbA PE=3 SV=1 | Q2FE47 Q2FE47_STAA3 | No Values |
| 689 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_2112 PE=4 SV=1 | Q2FEX0 Q2FEX0_STAA3 | No Values |
| 690 | Transcriptional repressor nrdR OS=Staphylococcus aureus (strain USA300) GN=nrdR PE=3 SV=1 | Q2FG51 NRDR_STAA3 | No Values |

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| 691 | UTP--glucose-1-phosphate uridylyltransferase OS=Staphylococcus aureus (strain USA300) GN=gtaB PE=3 SV=2 | Q2FE05 GTAB_STAA3 | No Values |
| 692 | Uroporphyrinogen decarboxylase OS=Staphylococcus aureus (strain USA300) GN=hemE PE=3 SV=1 | Q2FFR2 DCUP_STAA3 | No Values |
| 693 | Aminotransferase, class I OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0952 PE=3 SV=1 | Q2FI28 Q2FI28_STAA3 | No Values |
| 694 | Indole-3-pyruvate decarboxylase OS=Staphylococcus aureus (strain USA300) GN=ipdC PE=3 SV=1 | Q2FK74 Q2FK74_STAA3 | No Values |
| 695 | Monoxygenase family protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_2255 PE=4 SV=1 | Q2FEI8 Q2FEI8_STAA3 | No Values |
| 703 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0814 PE=4 SV=1 | Q2FIG4 Q2FIG4_STAA3 | No Values |
| 704 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0740 PE=4 SV=1 | Q2FIN6 Q2FIN6_STAA3 | No Values |
| 706 | DHH subfamily 1 protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0014 PE=4 SV=1 | Q2FKP2 Q2FKP2_STAA3 | No Values |
| 707 | Acetyltransferase, GNAT family OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0451 PE=4 SV=1 | Q2FJG5 Q2FJG5_STAA3 | No Values |
| 709 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1010 PE=4 SV=1 | Q2FHX0 Q2FHX0_STAA3 | No Values |
| 710 | Acetyl-CoA carboxylase, biotin carboxylase OS=Staphylococcus aureus (strain USA300) GN=accC PE=4 SV=1 | Q2FGC0 Q2FGC0_STAA3 | No Values |
| 712 | Formimidoylglutamase OS=Staphylococcus aureus (strain USA300) GN=hutG PE=3 SV=1 | Q2FEG2 HUTG_STAA3 | No Values |
| 715 | Probable GTP-binding protein engB OS=Staphylococcus aureus (strain USA300) GN=engB PE=3 SV=1 | Q2FG63 ENGB_STAA3 | No Values |
| 716 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_2447 PE=4 SV=1 | Q2FDZ7 Q2FDZ7_STAA3 | No Values |
| 718 | NADH-dependent flavin oxidoreductase OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0859 PE=4 SV=1 | Q2FIB9 Q2FIB9_STAA3 | No Values |
| 720 | Putative phage infection protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_2578 PE=4 SV=1 | Q2FDL6 Q2FDL6_STAA3 | No Values |
| 723 | Diacylglycerol kinase OS=Staphylococcus aureus (strain USA300) GN=dagK PE=3 SV=1 | Q2FFJ7 DAGK_STAA3 | No Values |
| 724 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1671 PE=4 SV=1 | Q2FG13 Q2FG13_STAA3 | No Values |
| 725 | Delta-aminolevulinic acid dehydratase OS=Staphylococcus aureus (strain USA300) GN=hemB PE=3 SV=1 | Q2FG68 Q2FG68_STAA3 | No Values |
| 726 | Glycosyl transferase, group 1 family protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1349 PE=4 SV=1 | Q2FGY2 Q2FGY2_STAA3 | No Values |
| 728 | Ribonuclease R OS=Staphylococcus aureus (strain USA300) GN=rnr PE=3 SV=1 | Q2FIL3 Q2FIL3_STAA3 | No Values |

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| 732 | Iron-dependent repressor OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0621 PE=4 SV=1 | Q2FJ04 Q2FJ04_STAA3 | No Values |
| 733 | SIS domain protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0556 PE=4 SV=1 | Q2FJ69 Q2FJ69_STAA3 | No Values |
| 734 | Serine acetyltransferase OS=Staphylococcus aureus (strain USA300) GN=cysE PE=4 SV=1 | Q2FJB1 Q2FJB1_STAA3 | No Values |
| 735 | Putative membrane protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0279 PE=4 SV=1 | Q2FJY5 Q2FJY5_STAA3 | No Values |
| 738 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0466 PE=4 SV=1 | Q2FJF3 Q2FJF3_STAA3 | No Values |
| 739 | UPF0403 protein SAUSA300_1321 OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1321 PE=3 SV=1 | Q2FH10 Y1321_STAA3 | No Values |
| 741 | DNA polymerase III polC-type OS=Staphylococcus aureus (strain USA300) GN=polC PE=3 SV=1 | Q2FHH4 DPO3_STAA3 | No Values |
| 742 | Putative peptidase OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_2087 PE=4 SV=1 | Q2FEZ5 Q2FEZ5_STAA3 | No Values |
| 743 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_2394 PE=4 SV=1 | Q2FE49 Q2FE49_STAA3 | No Values |
| 744 | Queuine tRNA-ribosyltransferase OS=Staphylococcus aureus (strain USA300) GN=tgt PE=3 SV=1 | Q2FG88 TGT_STAA3 | No Values |
| 745 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_2527 PE=4 SV=1 | Q2FDR7 Q2FDR7_STAA3 | No Values |
| 746 | Glycine betaine/carnitine/choline ABC transporter OS=Staphylococcus aureus (strain USA300) GN=opuC PE=4 SV=1 | Q2FE52 Q2FE52_STAA3 | No Values |
| 747 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_2381 PE=4 SV=1 | Q2FE62 Q2FE62_STAA3 | No Values |
| 748 | tRNA (guanine-N(7)-)methyltransferase OS=Staphylococcus aureus (strain USA300) GN=trmB PE=3 SV=1 | Q2FFZ0 TRMB_STAA3 | No Values |
| 749 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1534 PE=4 SV=1 | Q2FGE9 Q2FGE9_STAA3 | No Values |
| 753 | HAD-superfamily hydrolase, subfamily IA, variant 1 OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0557 PE=4 SV=1 | Q2FJ68 Q2FJ68_STAA3 | No Values |
| 755 | Ribosomal RNA small subunit methyltransferase G OS=Staphylococcus aureus (strain USA300) GN=rsmG PE=3 SV=1 | Q2FDF0 RSMG_STAA3 | No Values |
| 757 | Acetyl-coenzyme A carboxylase carboxyl transferase subunit beta OS=Staphylococcus aureus (strain USA300) GN=accD PE=3 SV=1 | Q2FG37 ACCD_STAA3 | No Values |
| 758 | Porphobilinogen deaminase OS=Staphylococcus aureus (strain USA300) GN=hemC PE=3 SV=1 | Q2FG66 HEM3_STAA3 | No Values |
| 760 | Thymidylate synthase OS=Staphylococcus aureus (strain USA300) GN=thyA PE=3 SV=1 | Q2FH11 TYSY_STAA3 | No Values |
| 761 | Glycine betaine aldehyde dehydrogenase OS=Staphylococcus aureus (strain USA300) GN=betB PE=3 SV=1 | Q2FDP8 Q2FDP8_STAA3 | No Values |

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| 762 | Preprotein translocase subunit secY OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_2184 PE=3 SV=1 | Q2FEQ9 Q2FEQ9_STAA3 | No Values |
| 763 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_2143 PE=4 SV=1 | Q2FEU9 Q2FEU9_STAA3 | No Values |
| 765 | Peptide methionine sulfoxide reductase MsrA OS=Staphylococcus aureus (strain USA300) GN=msrA PE=3 SV=1 | Q2FH75 Q2FH75_STAA3 | No Values |
| 767 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1069 PE=4 SV=1 | Q2FHR2 Q2FHR2_STAA3 | No Values |
| 770 | Serine-aspartate repeat-containing protein E OS=Staphylococcus aureus (strain USA300) GN=sdrE PE=3 SV=1 | Q2FJ77 SDRE_STAA3 | No Values |
| 772 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1650 PE=4 SV=1 | Q2FG34 Q2FG34_STAA3 | No Values |
| 773 | Peptidase T OS=Staphylococcus aureus (strain USA300) GN=pepT PE=3 SV=1 | Q2FIP8 PEPT_STAA3 | No Values |
| 774 | DNA topoisomerase 3 OS=Staphylococcus aureus (strain USA300) GN=topB PE=3 SV=1 | Q2FEN5 TOP3_STAA3 | No Values |
| 775 | Oligopeptide ABC transporter, substrate-binding protein OS=Staphylococcus aureus (strain USA300) GN=oppA PE=4 SV=1 | Q2FI87 Q2FI87_STAA3 | No Values |
| 776 | Putative lipoprotein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0079 PE=4 SV=1 | Q2FKI1 Q2FKI1_STAA3 | No Values |
| 777 | Ferrodoxin–NADP reductase OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_2319 PE=3 SV=1 | Q2FEC4 FENR_STAA3 | No Values |
| 778 | Urea amidolyase-related protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0702 PE=4 SV=1 | Q2FIS3 Q2FIS3_STAA3 | No Values |
| 779 | Guanylate kinase OS=Staphylococcus aureus (strain USA300) GN=gmk PE=3 SV=1 | Q2FHM9 KGUA_STAA3 | No Values |
| 780 | Glycerol uptake facilitator OS=Staphylococcus aureus (strain USA300) GN=glpF PE=3 SV=1 | Q2FHE0 Q2FHE0_STAA3 | No Values |
| 781 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1011 PE=4 SV=1 | Q2FHW9 Q2FHW9_STAA3 | No Values |
| 782 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1908 PE=4 SV=1 | Q2FFG8 Q2FFG8_STAA3 | No Values |
| 783 | FtsK/SpoIIIE family protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1687 PE=4 SV=1 | Q2FFZ7 Q2FFZ7_STAA3 | No Values |
| 784 | MutS2 protein OS=Staphylococcus aureus (strain USA300) GN=mutS2 PE=3 SV=1 | Q2FHT7 MUTS2_STAA3 | No Values |
| 785 | 2-succinyl-5-enolpyruvyl-6-hydroxy-3-cyclohexene-1-carboxylate synthase OS=Staphylococcus aureus (strain USA300) GN=menD PE=3 SV=1 | Q2FI34 MEND_STAA3 | No Values |
| 786 | Sensor protein kinase walK OS=Staphylococcus aureus (strain USA300) GN=walK PE=3 SV=1 | Q2FKN7 WALK_STAA3 | No Values |
| 789 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1081 PE=4 SV=1 | Q2FHQ0 Q2FHQ0_STAA3 | No Values |

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| 790 | DNA polymerase III, gamma and tau subunits OS=Staphylococcus aureus (strain USA300) GN=dnaX PE=4 SV=1 | Q2FJG4 Q2FJG4_STAA3 | No Values |
| 791 | Pantothenate synthetase OS=Staphylococcus aureus (strain USA300) GN=panC PE=3 SV=1 | Q2FDR1 PANC_STAA3 | No Values |
| 346 | Cysteine desulfurases, SufS subfamily subfamily OS=Staphylococcus aureus (strain USA300) GN=sufS PE=3 SV=1 | Q2FIF8 Q2FIF8_STAA3 | Reference Missing |
| 395 | Aldehyde dehydrogenase OS=Staphylococcus aureus (strain USA300) GN=aldA2 PE=3 SV=1 | Q2FFH5 Q2FFH5_STAA3 | Reference Missing |
| 455 | Transcriptional regulator OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0958 PE=4 SV=1 | Q2FI22 Q2FI22_STAA3 | Reference Missing |
| 499 | HPr kinase/phosphorylase OS=Staphylococcus aureus (strain USA300) GN=hprK PE=3 SV=1 | Q2FIN3 HPRK_STAA3 | Reference Missing |
| 524 | FMN-dependent NADPH-azoreductase OS=Staphylococcus aureus (strain USA300) GN=azo1 PE=3 SV=1 | Q2FJ80 AZO1_STAA3 | Reference Missing |
| 605 | Transcriptional regulator, Fur family OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1448 PE=4 SV=1 | Q2FGN4 Q2FGN4_STAA3 | Reference Missing |
| 630 | Oligopeptide ABC transporter, ATP-binding protein OS=Staphylococcus aureus (strain USA300) GN=oppD PE=4 SV=1 | Q2FI89 Q2FI89_STAA3 | Reference Missing |
| 663 | Methylenetetrahydrofolate--tRNA-(uracil-5)-methyltransferase trmFO OS=Staphylococcus aureus (strain USA300) GN=trmFO PE=3 SV=1 | Q2FHI7 TRMFO_STAA3 | Reference Missing |
| 672 | Putative iron compound ABC transporter, iron compound-binding protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0598 PE=4 SV=1 | Q2FJ27 Q2FJ27_STAA3 | Reference Missing |
| 677 | Ribosome-binding factor A OS=Staphylococcus aureus (strain USA300) GN=rbfA PE=3 SV=1 | Q2FHG8 RBFA_STAA3 | Reference Missing |
| 708 | Peptidase, M20/M25/M40 family OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1460 PE=4 SV=1 | Q2FGM2 Q2FGM2_STAA3 | Reference Missing |
| 730 | Undecaprenyl-diphosphatase OS=Staphylococcus aureus (strain USA300) GN=uppP PE=3 SV=1 | Q2FIV6 UPPP_STAA3 | Reference Missing |
| 201 | Alpha-hemolysin OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1058 PE=4 SV=1 | Q2FHS2 Q2FHS2_STAA3 | Value Missing |
| 242 | Transcriptional regulatory protein walR OS=Staphylococcus aureus (strain USA300) GN=walR PE=3 SV=1 | Q2FKN8 WALR_STAA3 | Value Missing |
| 328 | S1 RNA binding domain protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_2021 PE=4 SV=1 | Q2FF61 Q2FF61_STAA3 | Value Missing |
| 362 | Probable acetyl-CoA acyltransferase OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0355 PE=3 SV=1 | Q2FJQ9 THLA_STAA3 | Value Missing |
| 365 | Ferrochelatase OS=Staphylococcus aureus (strain USA300) GN=hemH PE=3 SV=1 | Q2FFR3 Q2FFR3_STAA3 | Value Missing |
| 369 | Alpha-acetolactate synthase OS=Staphylococcus aureus (strain USA300) GN=alsS PE=3 SV=1 | Q2FES6 Q2FES6_STAA3 | Value Missing |
| 416 | Proline dipeptidase OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1491 PE=3 SV=1 | Q2FGJ2 Q2FGJ2_STAA3 | Value Missing |

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| 423 | Type I restriction-modification system, M subunit OS=Staphylococcus aureus (strain USA300) GN=hsdM PE=4 SV=1 | Q2FFT5 Q2FFT5_STAA3 (+1) | Value Missing |
| 439 | Peptide chain release factor 3 OS=Staphylococcus aureus (strain USA300) GN=prfC PE=3 SV=1 | Q2FI57 RF3_STAA3 | Value Missing |
| 457 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_2446 PE=4 SV=1 | Q2FDZ8 Q2FDZ8_STAA3 | Value Missing |
| 468 | Alkaline phosphatase synthesis transcriptional regulatory protein PhoP OS=Staphylococcus aureus (strain USA300) GN=phoP PE=4 SV=1 | Q2FG44 Q2FG44_STAA3 | Value Missing |
| 493 | Chorismate synthase OS=Staphylococcus aureus (strain USA300) GN=aroC PE=3 SV=1 | Q2FGX4 AROC_STAA3 | Value Missing |
| 510 | DNA topoisomerase IV, subunit B OS=Staphylococcus aureus (strain USA300) GN=parE PE=3 SV=1 | Q2FH81 Q2FH81_STAA3 | Value Missing |
| 514 | Protein kinase OS=Staphylococcus aureus (strain USA300) GN=pknB PE=4 SV=1 | Q2FHL8 Q2FHL8_STAA3 | Value Missing |
| 527 | Low molecular weight protein-tyrosine-phosphatase ptpA OS=Staphylococcus aureus (strain USA300) GN=ptpA PE=3 SV=1 | Q2FFL4 PTPA_STAA3 | Value Missing |
| 537 | Pyridine nucleotide-disulfide oxidoreductase OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1369 PE=4 SV=1 | Q2FGW2 Q2FGW2_STAA3 | Value Missing |
| 539 | Phosphotransferase system, fructose-specific IIABC component OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_2576 PE=4 SV=1 | Q2FDL8 Q2FDL8_STAA3 | Value Missing |
| 553 | Hydrolase, HAD-superfamily, subfamily IIIA OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1557 PE=4 SV=1 | Q2FGC6 Q2FGC6_STAA3 | Value Missing |
| 555 | Panton-Valentine leukocidin, LukF-PV OS=Staphylococcus aureus (strain USA300) GN=lukF-PV PE=4 SV=1 | Q2FGV0 Q2FGV0_STAA3 | Value Missing |
| 556 | Tributyrin esterase OS=Staphylococcus aureus (strain USA300) GN=estA PE=4 SV=1 | Q2FDN0 Q2FDN0_STAA3 | Value Missing |
| 569 | Aldo/keto reductase family protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0589 PE=4 SV=1 | Q2FJ36 Q2FJ36_STAA3 | Value Missing |
| 570 | Pur operon repressor OS=Staphylococcus aureus (strain USA300) GN=purR PE=4 SV=1 | Q2FJE6 Q2FJE6_STAA3 | Value Missing |
| 577 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_2525 PE=4 SV=1 | Q2FDR9 Q2FDR9_STAA3 | Value Missing |
| 584 | Thymidylate kinase OS=Staphylococcus aureus (strain USA300) GN=tmk PE=3 SV=1 | Q2FJG0 KTHY_STAA3 | Value Missing |
| 595 | 4,4'-diaponeurosporene oxidase OS=Staphylococcus aureus (strain USA300) GN=crtP PE=3 SV=1 | Q2FDU3 CRTP_STAA3 | Value Missing |
| 597 | Protoporphyrinogen oxidase OS=Staphylococcus aureus (strain USA300) GN=hemG PE=4 SV=1 | Q2FFR4 Q2FFR4_STAA3 | Value Missing |
| 604 | ABC transporter, ATP-binding protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_2399 PE=4 SV=1 | Q2FE44 Q2FE44_STAA3 | Value Missing |
| 608 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1857 PE=4 SV=1 | Q2FFL9 Q2FFL9_STAA3 | Value Missing |

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| 611 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0812 PE=4 SV=1 | Q2FIG6 Q2FIG6_STAA3 | Value Missing |
| 612 | Hydrolase, TatD family OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0468 PE=4 SV=1 | Q2FJF1 Q2FJF1_STAA3 | Value Missing |
| 613 | 5-methyltetrahydropteroylglutamate--homocysteine methyltransferase OS=Staphylococcus aureus (strain USA300) GN=metE PE=3 SV=1 | Q2FJQ7 METE_STAA3 | Value Missing |
| 622 | Hydroxymethylglutaryl-CoA reductase OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_2483 PE=3 SV=1 | Q2FDW1 Q2FDW1_STAA3 | Value Missing |
| 623 | Glutamyl-aminopeptidase OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_2400 PE=4 SV=1 | Q2FE43 Q2FE43_STAA3 | Value Missing |
| 633 | Carboxylesterase OS=Staphylococcus aureus (strain USA300) GN=est PE=4 SV=1 | Q2FIL4 Q2FIL4_STAA3 | Value Missing |
| 634 | Transcriptional regulator ctsR OS=Staphylococcus aureus (strain USA300) GN=ctsR PE=3 SV=1 | Q2FJB8 CTSR_STAA3 | Value Missing |
| 642 | Universal stress protein family OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0067 PE=4 SV=1 | Q2FKJ2 Q2FKJ2_STAA3 | Value Missing |
| 645 | ABC transporter, ATP-binding protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_2288 PE=4 SV=1 | Q2FEF5 Q2FEF5_STAA3 | Value Missing |
| 646 | Ribose 5-phosphate isomerase A OS=Staphylococcus aureus (strain USA300) GN=rpiA PE=3 SV=1 | Q2FEG0 Q2FEG0_STAA3 | Value Missing |
| 649 | Alanine dehydrogenase 2 OS=Staphylococcus aureus (strain USA300) GN=ald2 PE=3 SV=1 | Q2FG29 DHA2_STAA3 | Value Missing |
| 651 | Aminomethyltransferase OS=Staphylococcus aureus (strain USA300) GN=gcvT PE=3 SV=1 | Q2FGI5 GCST_STAA3 | Value Missing |
| 655 | Isochorismate synthase family protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0945 PE=4 SV=1 | Q2FI35 Q2FI35_STAA3 | Value Missing |
| 657 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0725 PE=4 SV=1 | Q2FIQ0 Q2FIQ0_STAA3 | Value Missing |
| 661 | Primosomal protein Dnal OS=Staphylococcus aureus (strain USA300) GN=dnal PE=4 SV=1 | Q2FG53 Q2FG53_STAA3 | Value Missing |
| 664 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0192 PE=4 SV=1 | Q2FK72 Q2FK72_STAA3 | Value Missing |
| 665 | Gamma-hemolysin component B OS=Staphylococcus aureus (strain USA300) GN=hlgB PE=4 SV=1 | Q2FE76 Q2FE76_STAA3 | Value Missing |
| 673 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0593 PE=4 SV=1 | Q2FJ32 Q2FJ32_STAA3 | Value Missing |
| 676 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1003 PE=4 SV=1 | Q2FHX7 Q2FHX7_STAA3 | Value Missing |
| 678 | Peptide chain release factor 1 OS=Staphylococcus aureus (strain USA300) GN=prfA PE=3 SV=1 | Q2FF10 RF1_STAA3 | Value Missing |
| 698 | ATPase, AAA family OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1584 PE=4 SV=1 | Q2FG99 Q2FG99_STAA3 | Value Missing |

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| 700 | Pseudouridine synthase OS=Staphylococcus aureus (strain USA300) GN=rluB PE=3 SV=1 | Q2FGN9 Q2FGN9_STAA3 | Value Missing |
| 702 | Inositol monophosphatase family protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1007 PE=4 SV=1 | Q2FHX3 Q2FHX3_STAA3 | Value Missing |
| 705 | ABC transporter, permease protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0308 PE=4 SV=1 | Q2FJV6 Q2FJV6_STAA3 | Value Missing |
| 721 | Carbamate kinase 2 OS=Staphylococcus aureus (strain USA300) GN=arcC2 PE=3 SV=1 | Q2FDM7 ARCC2_STAA3 | Value Missing |
| 736 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0042 PE=4 SV=1 | Q2FKL6 Q2FKL6_STAA3 | Value Missing |
| 740 | Urease accessory protein ureG OS=Staphylococcus aureus (strain USA300) GN=ureG PE=3 SV=1 | Q2FEK0 UREG_STAA3 | Value Missing |
| 756 | Putative membrane protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_1864 PE=3 SV=1 | Q2FFL2 Q2FFL2_STAA3 | Value Missing |
| 764 | Haloacid dehalogenase-like hydrolase OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_2102 PE=4 SV=1 | Q2FEY0 Q2FEY0_STAA3 | Value Missing |
| 769 | Putative uncharacterized protein OS=Staphylococcus aureus (strain USA300) GN=SAUSA300_0632 PE=3 SV=1 | Q2FIZ3 Q2FIZ3_STAA3 | Value Missing |

Table A13. Complete list of intracellular proteins identified from the USA 300 adaptive mutant at 15 hours.

Appendix C. Phyre results.

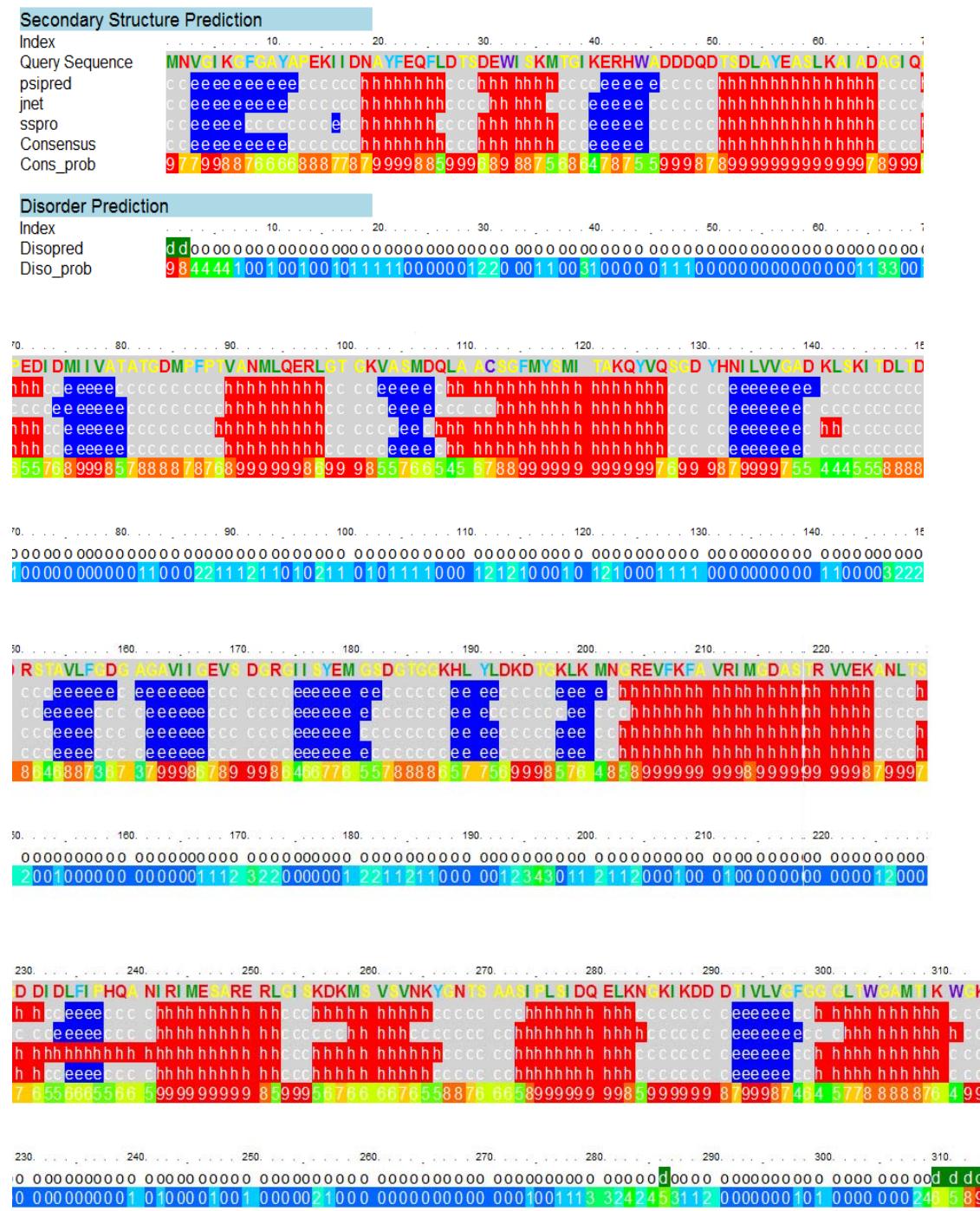


Figure A1. Results of QuickPhyre analysis of COL (top) and USA 100 635 (bottom) amino acid sequences and predicted structures. Red = predicted α -helix. Blue = predicted β -pleated sheet.