Matrix Biology Highlights
Edited by Maria Gubbiotti and Tom Neill

1. Biglycan hungers to curtail kidney inflammation and damage

Reference | Poluzzi, C., Nastase, M.V., Zeng-Brouwers, J., Roedig, H., Hsieh, L.T.H., Michaelis, J.B., Buhl, E.M., Rezende, F., Manavski, Y., Bleich, A., Boor, P., Brandes, R.P., Pfeilschifter, J., Stelzer, E.H.K., Munch, C., Dikic, I., Brandts, C., Iozzo, R.V., Wygrecka, M., and Schaefer, L. Biglycan evokes autophagy in macrophages via a novel CD44/Toll-like receptor 4 signaling axis in ischemia/reperfusion injury. 2019. *Kidney International*. 95:540-562.

Biglycan is a canonical small leucine-rich proteoglycan that acts as a danger signal to recruit macrophages to sites of inflammation via engagement of Toll-like receptors (TLR) 2/4. The utilization of different co-receptors, such as CD14, alters biglycan function to ultimately dictate whether biglycan induces pro- or anti-inflammatory states. In this recently published article by Poluzzi *et al*, the authors sought additional biglycan co-receptors that could differentially modulate biglycan signaling. They discovered that mice stably over-expressing soluble biglycan had greater numbers of autophagic macrophages with enhanced autophagic flux (Fig. 1). Mechanistically, employing mice with genetic ablations of TLR/4, CD14, or CD44 the authors elegantly demonstrated a functional *in vivo* dependency of TL4 interacting with CD44. In a mouse model of renal ischemia/ reperfusion injury (IRI), transient overexpression of biglycan enhanced M1 macrophage recruitment in the kidney of CD44 wildtype and null mice, but not in kidneys lacking CD14. The interaction of biglycan/CD44 increased autophagic flux of the M1 macrophages while concurrently increasing M2 macrophages and reducing tubular damage from IRI. Collectively, the authors have demonstrated that biglycan interacting with CD44 evokes a proautophagic signaling cascade in renal macrophages to curtail kidney inflammation and damage.

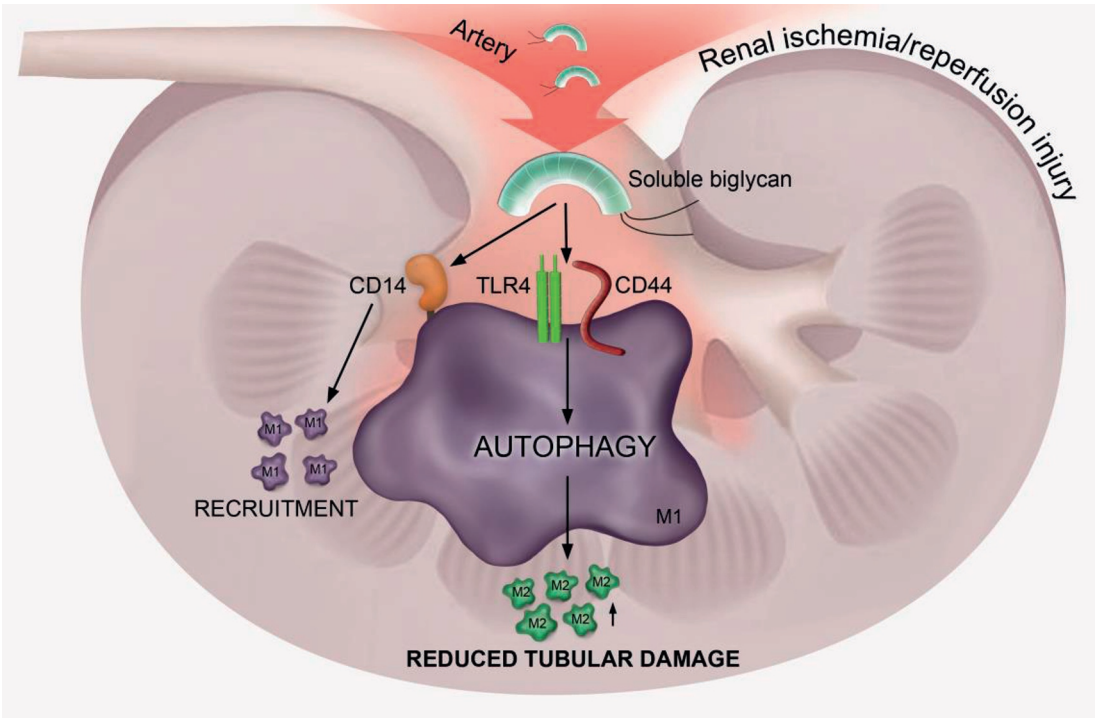

Figure 1. Schematic of biglycan/CD44-evoked renal macrophage autophagy to ameliorate kidney inflammation and damage. Figure kindly provided by Chiara Poluzzi.