SIGNIFICANCE STATEMENT

Tamm–Horsfall protein (THP), also known as uromodulin, is a protein uniquely expressed by the kidney and secreted into the urine and, to a lesser extent, in the kidney interstitium and serum. It is unclear if THP exerts an immunomodulatory role on kidney resident phagocytic cells. This paper uncovers a previously unknown role of THP in regulating the number, activity, and plasticity of kidney mononuclear phagocytic cells in the kidney in the normal physiologic state and after AKI induced using an ischemia-reperfusion model. Added to its effect on the epithelium and granulopoiesis, this new immunomodulatory role could explain the protection conferred by THP during AKI, and lay the foundation for modulating THP or its targets, as a therapy for AKI.