Nature Reviews Nephrology **10**, 242 (2014); published online 18 March 2014; doi:10.1038/nrneph.2014.46

STONES

CSF-1 SUPPRESSES CRYSTAL FORMATION

Renal crystal formation is suppressed by macrophage colony-stimulating factor 1 (CSF-1) in a process involving polarization of the macrophage phenotype, according to findings published by researchers at Nagoya City University Graduate School of Medical Sciences, Japan.

In their previous work, the team demonstrated a correlation between migration of macrophages—which can be classically activated (proinflammatory, M1) or alternatively activated (reparative, M2)—to renal tubular cells and the formation of calcium oxalate crystals. Although M2 macrophages are known to promote repair and regeneration of renal tissue, whether these cells also had a role in suppressing renal crystal formation was not known. Accordingly, the researchers investigated the role of these cells in renal crystal formation during hyperoxaluria, using an animal model of kidney stone formation—CSF-1-deficient mice, which contain an inactivating point mutation in *Csf1*.

3D computed tomography revealed markedly increased deposition of calcium oxalate crystals in the kidneys of homozygous CSF-1-deficient mice in comparison with kidneys of heterozygous CSF-1-deficient and wild-type mice. Conversely, administration of recombinant human CSF-1 suppressed renal crystal formation in mice of all genotypes. Macrophage population analysis revealed a significant reduction in the M2 macrophage population in homozygous CSF-1-deficient mice compared with wild-type mice. Re-establishing this cell population in homozygous CSF-1-deficient mice by transfusion of bone marrow-derived M2 macrophages effectively suppressed renal crystal formation. Further, these M2 macrophages displayed greater ability to eliminate calcium oxalate crystals in *in vitro* phagocytosis assays than either M1 macrophages or renal tubular cells. Overall, the findings suggest that M2 macrophages are able to suppress renal crystal formation and this process is induced by CSF-1.

"Control of macrophage polarization is a key defense mechanism that protects the kidney against deposition of calcium oxalate crystals," states researcher Kazumi Taguchi. He continues, "Our findings suggest a possible route to develop novel treatments for patients with kidney stones."

David Holmes

Original article Taguchi, K. *et al*. Colony-stimulating factor-1 signaling suppresses renal crystal formation. *J. Am. Soc. Nephrol*. doi:10.1681/ASN.2013060675