Renal macrophages observed playing crucial role in preventing kidney stones

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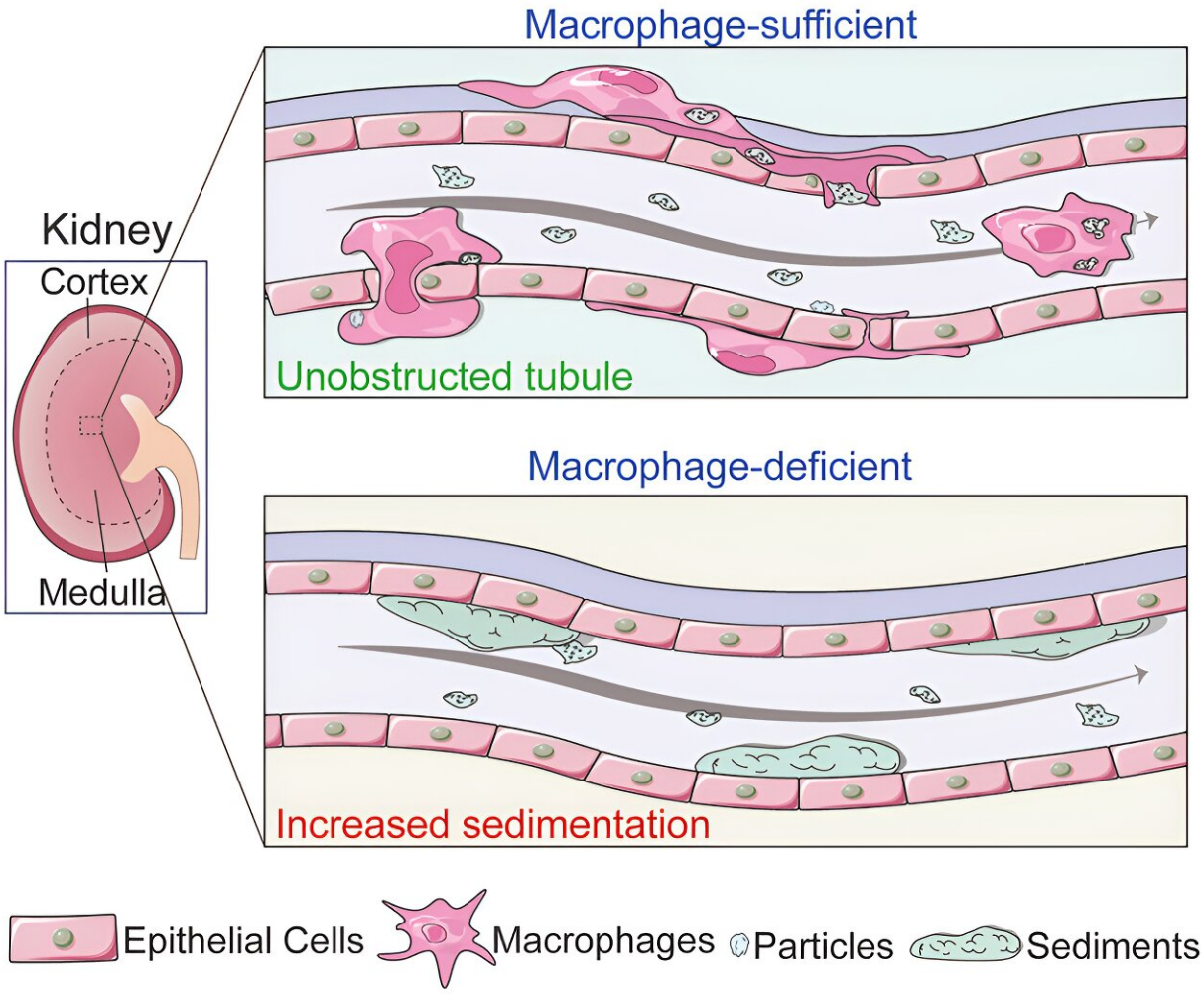

Graphical abstract. Credit: *Immunity* (2023). DOI: 10.1016/j.immuni.2023.12.003

Researchers at Zhejiang University School of Medicine, China, have investigated how the body's innate immune system of renal macrophages works to prevent kidney stones. In a paper, "Renal macrophages monitor and remove particles from urine to prevent tubule obstruction," published in *Immunity*, the authors detail their findings of mechanistic actions and strategic positioning of macrophages to surveil epithelial cells and intratubular environments.

When urine passes through the tubular system of the kidneys, it generates various microscopic sediment particles, including mineral crystals, from the concentrated urine. Pathological conditions can lead to the presence of proteins and inflammatory cells. These particles can become lodged in the tubules, blocking urine flow and causing renal dysfunction.

The researchers observed renal macrophages adjacent to the tubules in real-time, using high-resolution microscopy, live recordings and two-photon microscopy techniques. They were able to record macrophages extending transepithelial protrusions and interacting with intratubular particles, as well as their migration to assist in the excretion of urine particles.

These techniques captured the association of macrophages with particles in urine and demonstrated the role of macrophages in particle removal. Renal macrophages located near medullary tubules display specific behaviors, extending transepithelial protrusions and constantly sampling urine contents.

The macrophages were then seen to migrate and surround intratubular particles, aiding in their removal from the tubular system. Mice were injected with fluorescent inert latex beads into the kidney, and within 12 hours, free beads were almost absent from the lumen of the collecting ducts.

To confirm the role of the macrophages, the latex bead experiment was repeated with mice lacking renal macrophages. Macrophage-depleted mice showed increased retention of the fluorescent beads even after 36 hours despite the more prolonged exposure to natural urine flushing.

This result suggests that normal urine flushing alone could not efficiently remove big particles in the renal tubule system without the macrophage pre-disposal assistance.

The findings suggest potential therapeutic implications for kidney stones (nephrolithiasis or renal calculi) and for developing kidney-specific drug delivery methods based on these distinctive macrophage features.

More information: Jian He et al, Renal macrophages monitor and remove particles from urine to prevent tubule obstruction, *Immunity* (2023). DOI: 10.1016/j.immuni.2023.12.003