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VASCULAR DISEASE

Clearing the pipes via angiophagy

In 2010, Jaime Grutzendler and colleagues reported that cerebral microvascular clots could be cleared by a hitherto unknown mechanism. They showed that endothelial membrane projections enveloped the emboli and translocated them into the perivascular parenchyma through an opening in the endothelial barrier, clearing the obstruction and re-establishing blood flow. Grutzendler and his team now report that this process—which they have named 'angiophagy'— also occurs in other organs, including the kidney. These results could have implications for the treatment of patients with spontaneous and iatrogenic renal emboli.

Using a combination of high-resolution two-photon *in vivo* imaging in live mice, and confocal microscopy and electron microscopy on fixed tissue samples, the researchers introduced labelled fibrin and cholesterol emboli into various organs and studied the occurrence and timing of angiophagy. "We found that microvessels in the murine kidneys removed vascular obstructions by angiophagy, as we had described in the brain," explains Grutzendler. The extravasation of the emboli from the renal microvasculature occurred at a rate comparable to that in the brain and heart. They also demonstrated that angiophagy occurs in the human eye, supporting the hypothesis that this is a universal process.

"Interestingly, in the kidneys, extravasated emboli were translocated across the endothelium and the adjacent epithelia—into the renal tubules," says Grutzendler. The implication? The kidneys might be able to permanently expel microemboli from the body in the urine, a novel mechanism for clot removal, although this still needs to be demonstrated.

Angiophagy is seemingly beneficial as it removes emboli that have failed haemodynamic and fibrinolytic clearance, but the process might also sequester emboli from clearing agents, such as endogenous tissue plasminogen activator (tPA) and therapeutic exogenous tPA. "These dual actions of angiophagy are important because future treatments that inhibit early embolus envelopment could enhance fibrinolytic clearance of emboli and improve blood flow in renal vessels, particularly in cases of massive emboli generation, such as after aortic manipulation," explains Grutzendler. However, the 'debris' from such a process could lead to microemboli accumulation in small vessels over time, necessitating the promotion of angiophagy to clear the blockages. Understanding this delicate balance will be of extreme importance should angiophagy have a clinical role in treating renal vascular conditions.

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Original article Grutzendler, J. *et al.* Angiophagy prevents early embolus washout but recanalizes microvessels through embolus extravasation. *Sci. Transl. Med.* doi:101126/scitranslmed.3006585

Further reading Lam, C. K. *et al.* Embolus extravasation is an alternative mechanism for cerebral microvascular recanalization. *Nature*, **465**, 478–482 (2010)