

SIGNIFICANCE STATEMENT

The countercurrent multiplication mechanism in the kidney medulla underlies the exquisite regulation of urine concentration and facilitates water and electrolyte excretion to maintain fluid homeostasis. The medullary interstitium is, therefore, an important site where interstitial fluid accumulates and is returned to the systemic circulation. We discovered that the ascending vasa recta (AVRs) are specialized hybrid vessels, having properties of both blood and lymphatic vessels. Attenuation of angiopoietin/Tie2 signaling specifically leads to loss of the AVR, causing dilution and increased output of urine, and the formation of interstitial cysts in the medulla. Our findings provide formal genetic proof that the AVR with its novel lymphatic-like features is key for fluid drainage in the medulla, a region devoid of classic lymphatic vasculature.