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Using three-dimensional imaging to study how kidney lymphatic vessels develop

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Kidney development is a complex process, involving the interaction of a variety of cell types which establish the function of the mature organ. One cell receiving relatively little attention is the lymphatic cell, which assemble into vessels to help clear dying cells, tissue fluid and toxins from organs. Kidney lymphatics are difficult to study owing to limitations in imaging technology, and so little is known about how lymphatics form or what role they play in the developing kidney.

We overcame these limitations by developing a technique for wholemount immunolabelling, optical clearing and 3D imaging of mouse and human embryonic kidneys down to the resolution of a single cell. Computational techniques were then used to segment and generate 3D lymphatic models and quantify the dynamics of lymphatic growth during kidney development.

We found that lymphatics first emerged as a ring-like cellular plexus in the hilum of the developing mouse kidney at embryonic day (E)14.5. As the mouse kidney matures through to E18.5, the lymphatics develop into lumenised network of vessels, wrap around the base of the nascent renal pelvis and branch towards the cortex alongside renal arterioles. We also found a population of cellular clusters expressing lymphatic markers growing adjacent to the lymphatic network, proliferating and increasing in number as kidney development progressed. Analysis of human embryonic kidneys between 10 and 12 post-conceptional weeks revealed an analogous appearance of both lymphatic vessels and clusters.

In summary, we implement a strategy for 3D imaging to reveal the dynamics and spatial relationships of lymphatics in the developing kidney. The lymphatic cell clusters in both mouse and human kidneys may represent an evolutionarily conserved lymphatic progenitor, as has recently been described in other organs.