Human kidney map charts our growing immune defense

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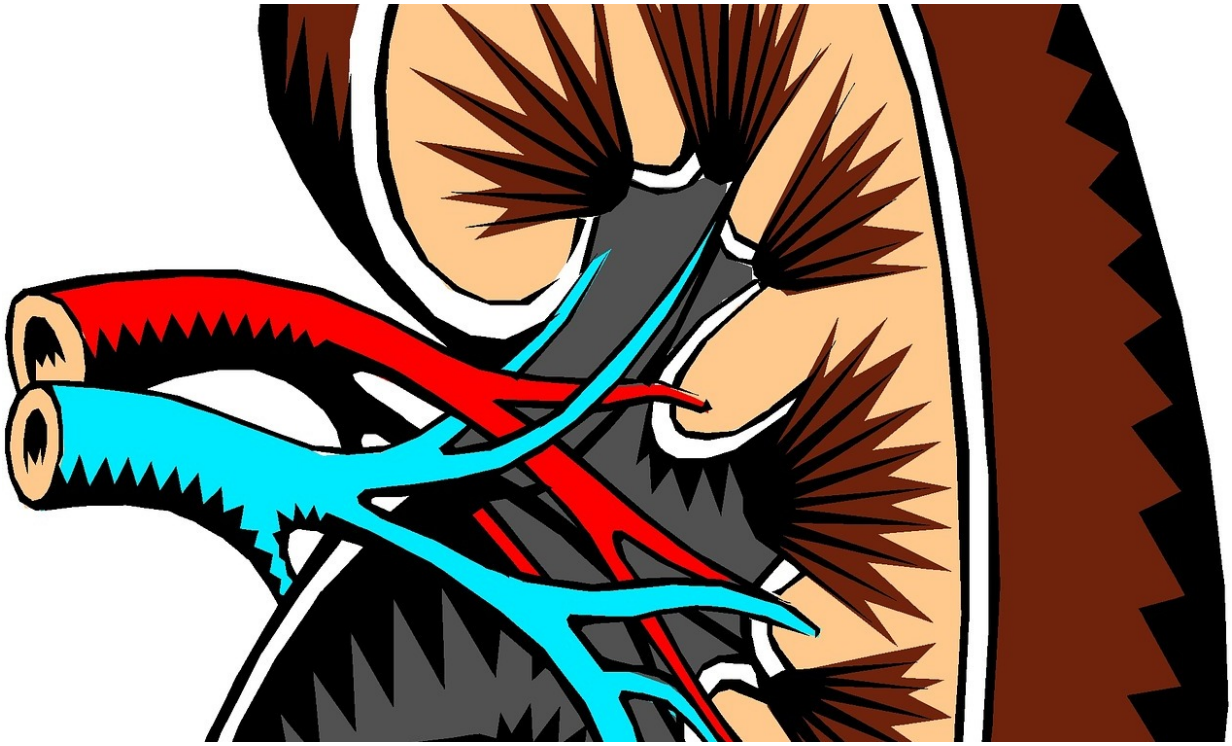

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The first cell atlas of the human kidney's immune system has been created after scientists mapped nearly 70,000 individual kidney cells from early life and adults. Researchers at the Wellcome Sanger Institute, University of Cambridge, Newcastle University and their collaborators have generated the atlas and used it to map the communities of immune

cells in the kidney. This shows for the first time how the immune system in our kidneys develops during early life in the womb, and strengthens after birth and as we mature into adults.

The results, published in *Science*, open the door to understanding how the kidney immune system works with important implications for tackling many types of kidney disease and transplant rejection.

The kidneys are two bean-shaped organs located below the rib cage that have an important role of filtering our blood. A pair of kidneys filter about half a cup of blood ever minute, removing waste and extra water which leaves the body as urine. They are critical in maintaining a healthy balance of water, salts and minerals in our blood, which enables our nerves, muscles and other tissues in the rest of the body to work properly.

When the kidneys are damaged and can't filter blood properly, they gradually lose function over time and patients develop chronic kidney disease. Chronic kidney disease affects more than 850 million people worldwide and is commonly caused by diabetes, high blood pressure and recurrent infection. Unfortunately, chronic kidney disease can progress to kidney failure, which without dialysis or a kidney transplant, is fatal. The immune system plays a critical role in responding to kidney tissue damage, but very little is known about how this works in human kidneys.

To understand the immune system in the kidneys, what happens when tissue damage or infections occur, how this can lead to chronic kidney disease, and why kidney transplants are rejected, researchers created the first map of the kidney immune system.

The team were able to chart which types of immune cells were present in particular zones of the kidney at different stages of life—from early life in the womb to adult life.

Professor Menna Clatworthy, co-lead author from the University of Cambridge Department of Medicine and Wellcome Sanger Institute, said: "The kidney cell atlas allows us to chart where different types of immune cells are located in different zones of the kidney. We highlighted a strong defence zone at the base of the kidney, near where urine leaves the kidney via the ureter, which fights against urinary tract infections. Understanding how different cell types in a healthy kidney protects us against disease is important for tackling the development of chronic kidney disease and identifying new treatments."

To create the kidney cell atlas during different development phases, researchers studied developmental§, child and adult kidney tissue. The team sequenced the activity of genes in 67,471 individual cells, using single-cell RNA sequencing, to pinpoint the types of immune cells present.

Scientists then mapped those cells over developmental time from early life to adult stage, and within the anatomical space of the kidney to understand how the kidney's immune system develops and is organised.

Researchers discovered that the very earliest cells that populate the developing kidney are macrophages—large white blood cells that eat bad bacteria and viruses—which remain in the kidney as we grow older. There were few active immune cells in the developing kidney, which aligns with the view that a developing baby is relatively sterile and only encounters bacteria during and after birth, prompting the immune system to develop as we grow.

Professor Muzlifah Haniffa, co-lead author from the Wellcome Sanger Institute, Newcastle University and Newcastle Hospitals NHS Foundation Trust, said: "We have created the first map showing how the immune system in the kidney develops in early life and how that changes as we mature into adults. We uncovered the very earliest cell types in the

developing kidney—these macrophages that live in the kidney throughout life are important for protecting us against infection."

Dr. Sam Behjati, co-lead author from the Wellcome Sanger Institute and University of Cambridge, said: "The kidney cell atlas provides a window to understand what happens in diseases in children, including childhood kidney cancers. The atlas will allow researchers to ask fundamental questions about disease, like why some patients respond to treatment and others do not."

Dr. Sarah Teichmann, co-lead author from the Wellcome Sanger Institute and University of Cambridge, and co-chair of the Human Cell Atlas initiative, said: "Mapping the human kidney brings us one step closer to producing the Human Cell Atlas—a Google map of the 37 trillion cells in the human body. We will discover new cell types and uncover how our cells change over time, learn how and why we age and what happens when we get a disease. The Human Cell Atlas will be a free online resource, for anyone to use."

More information: "Spatiotemporal immune zonation of the human kidney" *Science* (2019). science.sciencemag.org/cgi/doi … 1126/science.aat5031

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