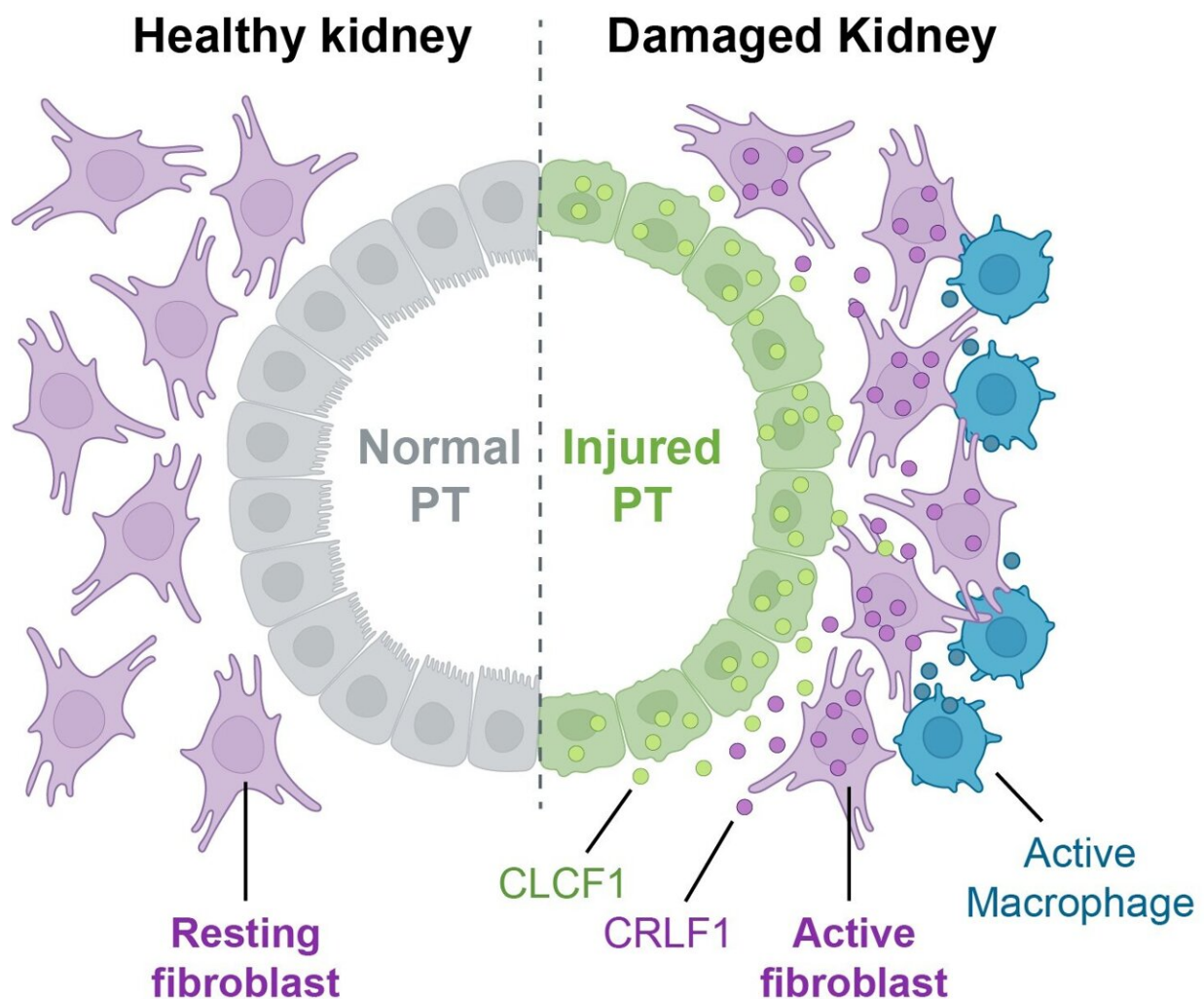


# New study shows cells get involved in unhealthy relationships after acute kidney injury in mice

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Following acute kidney injury, damaged cells interact within disease-promoting microenvironments, a process that may lead to chronic kidney disease. Credit:

Michal Polonsky

A study [published](#) in *Nature Communications* provides new insight into how damaged cells interact within disease-promoting microenvironments following acute kidney injury, or AKI. With limited treatment options, AKI frequently progresses to chronic kidney disease (CKD), which affects more than 1 in 7 U.S. adults—an estimated 37 million people.

The new findings may contribute to future efforts to prevent CKD, which can lead to [kidney failure](#).

The study brought together scientists from Andy McMahon's lab at USC and Long Cai's lab at Caltech.

In the study, co-first authors Michal Polonsky from Caltech and Louisa Gerhardt from USC leveraged a cutting-edge tool, called seqFISH, developed in the Cai laboratory. With this tool, researchers can gather information about [genetic activity](#) and study cellular interactions in intact kidney tissue in mice with AKI. This allowed the scientists to analyze the precise expression of over 1,000 genes in the injured kidney tissue, identify microenvironments associated with injury, and predict [cellular interactions](#) associated with the progression to CKD.

"Dr. Cai's seqFISH technology provides unprecedented insight into the cellular interplay in the kidney following injury," said McMahon, who is the W.M. Keck Provost and University Professor of Stem Cell Biology and Regenerative Medicine at USC and will join the faculty of Caltech in October. "A better understanding of kidney injury is needed to identify targets for preventing the progression to [chronic kidney disease](#)

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Cai, who is a Professor of Biology and Biological Engineering, added, "We're thrilled that our technology has enabled a deeper understanding of kidney injury and disease. This study exemplifies the importance of cross-institutional and cross-disciplinary collaborations to advance biomedical research."

In the kidney's outermost layer, the scientists identified a likely pathological microenvironment, which they dubbed "ME-5." This microenvironment contains a type of kidney cell particularly vulnerable to injury, known as a proximal tubule cell or PT.

In ME-5, injured PTs and neighboring connective tissue cells, known as fibroblasts, exchange signals that could drive injury progression. Key signals involved the genes *Clcf1* and *Crfl1*, which encode proteins that can promote inflammation and fibrosis, or scarring. Additional signals detected in ME-5 could contribute to recruitment of immune cells, thereby further contributing to the development of inflammation, fibrosis and other pathological changes.

The scientists also identified another important injury-associated microenvironment, which they named "ME-16," featuring aggregations of various immune cell types called tertiary lymphoid structures that are known to contribute to chronic inflammation. Rather than being confined to a specific region of the kidney, ME-16 was distributed throughout the injured organ.

To share their discoveries, the team constructed a comprehensive map of cellular, molecular, and structural changes following AKI, which refines our understanding of the transition to CKD. This map is [publicly available](#).

Additional co-authors are Kari Koppitch from USC; Jina Yun, Katsuya Lex Colón, Henry Amrhein, Matt Thomson, and Barbara Wold from

Caltech; and Shiwei Zheng and Guo-Cheng Yuan from the Icahn School of Medicine at Mount Sinai.

**More information:** Spatial transcriptomics defines injury specific microenvironments and cellular interactions in kidney regeneration and disease, *Nature Communications* (2024). [DOI: 10.1038/s41467-024-51186-z](https://doi.org/10.1038/s41467-024-51186-z)

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