Blood mutations increase risk for acute kidney injury, says study

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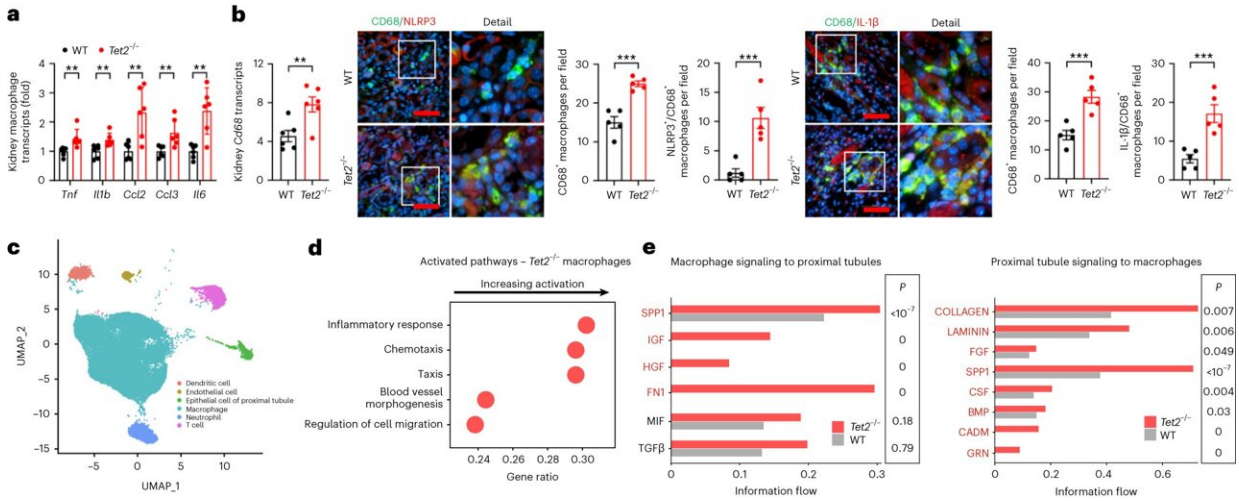


Tet2-deficient macrophages are hyperinflammatory in early ischemic kidney injury. Credit: *Nature Medicine* (2024). DOI: 10.1038/s41591-024-02854-6

A U.S.-Canadian research collaboration led by Vanderbilt University Medical Center has identified common, age-associated changes in the blood as a risk factor for acute kidney injury (AKI), which occurs in more than 1 in 5 hospitalized adults worldwide.

This discovery, reported in the journal *Nature Medicine*, could open the door to new, more effective treatments for AKI and a way to prevent its progression to end-stage renal disease requiring kidney dialysis.

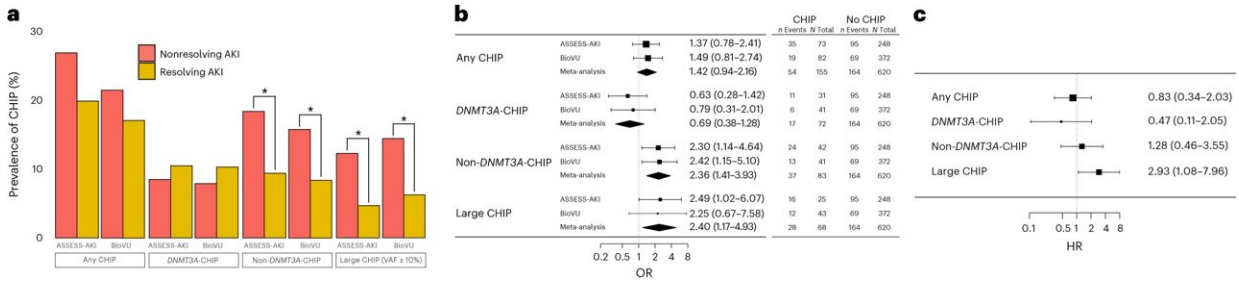
The focus of this investigation was clonal hematopoiesis of indeterminate potential (CHIP), somatic (noninherited) mutations in blood stem cells that can trigger explosive, clonal expansions of abnormal cells.

CHIP, which affects 10–20% of people ages 65 and older, is associated with an estimated 40% greater risk of death from cardiovascular, lung and liver disease, and other inflammatory conditions. This age group is also especially vulnerable to AKI.

"In addition to known causes for AKI, identification of an association with CHIP provides new insight into the increased risk and underlying mechanisms for the development of AKI among the older population," said Raymond Harris, MD, co-corresponding author of the paper with Alexander Bick, MD, Ph.D.

"We commonly think about how a chronic inflammation caused by CHIP can cause chronic diseases, but I was quite surprised at the effect CHIP had on an acute inflammation," Bick added.

Bick, an assistant professor of Medicine in the Division of Genetic Medicine, has pioneered methods for determining the presence of CHIP and the mechanisms by which it leads to disease.



CHIP is associated with impaired recovery from AKI in the ASSESS-AKI and

BioVU cohorts. a, Prevalence of CHIP among individuals with a resolving AKI pattern in ASSESS-AKI (n = 191) and BioVU (n = 88) compared to a nonresolving AKI pattern (n = 130 for ASSESS-AKI and n = 366 for BioVU), as defined by Bhatraju et al. b, Odds of nonresolving AKI pattern according to CHIP status, adjusted for age, sex, baseline creatinine, AKI stage, smoking status, ethnicity and history of diabetes, hypertension and cardiovascular disease. c, Risk of significant kidney function impairment (primary study composite outcome of ESKD or eGFR decline by ≥50%) over 5 years of follow-up among ASSESS-AKI participants with baseline AKI according to CHIP status, adjusted for age, sex, baseline creatinine, AKI stage, smoking status, ethnicity and history of diabetes, hypertension and cardiovascular disease. *P

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