New insights on kidney disease in African Americans could lead to therapies

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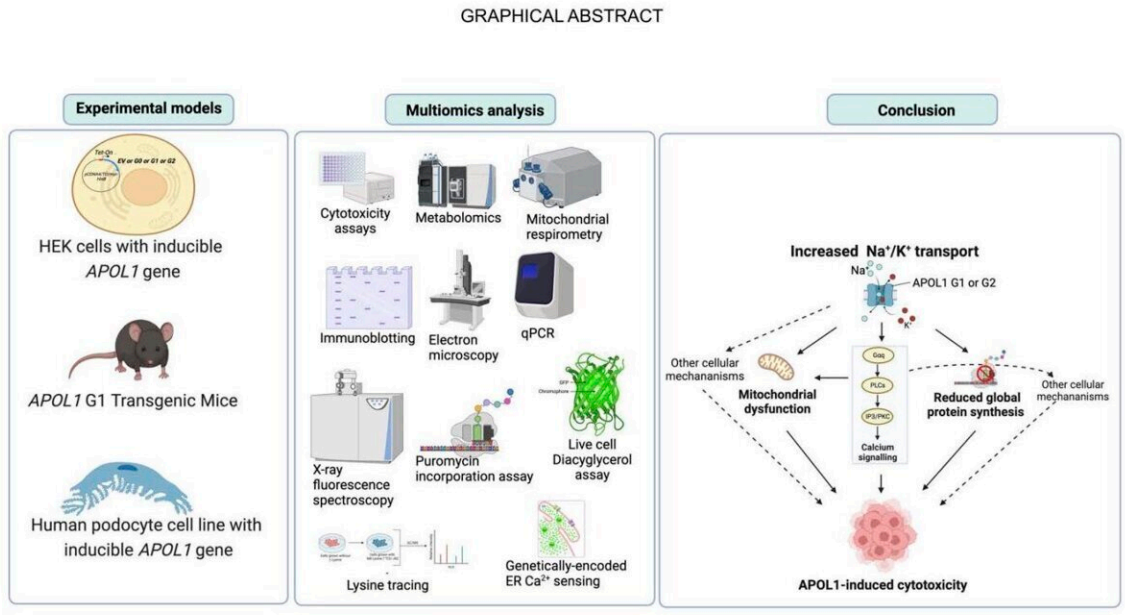

Credit: *Journal of Clinical Investigation* (2024). DOI: 10.1172/JCI172262

In a finding that could help reduce the racial disparity in kidney disease, Duke Health researchers have detailed how two common gene variants among African Americans can cause kidney failure.

The finding, reported in the *Journal of Clinical Investigation*, could point to new treatment approaches and advance investigational therapies that

block the gene.

"African Americans develop end stage kidney disease at four times the rate of white Americans and represent more than 30% of people on dialysis," said lead author Opeyemi Olabisi, M.D., Ph.D., associate professor in the Department of Medicine at Duke University School of Medicine.

"For more than a decade, we have known that two APOL1 gene variants account for much of the excess risk of non-diabetic kidney failure in African Americans, but we have only a limited understanding of how these variants work. Our study provides that insight."

Two variants in the APOL1 gene—G1 and G2—are known risk factors for kidney disease. These variants arose 5,000 years ago among people in West Africa to provide immunity against African sleeping sickness.

Today, 13% of African Americans carry these two APOL1 gene variants. Approximately 20% of them will develop kidney disease in their lifetime, making APOL1 the most common genetic driver of racial kidney health disparity in the U.S.

Using mice and human cell lines, Olabisi and colleagues found that the APOL1 G1 causes kidney disease by increasing the flow of sodium into and potassium out of a type of cell in the kidney called the podocyte, which forms a protective barrier in the kidney.

This increased flow of sodium and potassium triggers a series of events that damage the kidney. The researchers were able to reduce that damage using an investigational molecule that blocks the function of the APOL1 protein.

"Insights from this work support ongoing therapeutic strategies testing

this APOL1 blocker," Olabisi said. "Additional cellular mechanisms that we've identified could also be explored as new therapeutic targets to treat APOL1-mediated kidney disease, with the hope of reducing the high burden of kidney disease in African Americans."

More information: Somenath Datta et al, APOL1-mediated monovalent cation transport contributes to APOL1-mediated podocytopathy in kidney disease, *Journal of Clinical Investigation* (2024). DOI: 10.1172/JCI172262

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