

Helping preterm infants grow bigger kidneys would prevent kidney disease later in life

May 21 2018



Credit: CC0 Public Domain

Nephrons are the microscopic blood-filtering units inside our kidneys that convert waste products into urine, regulate our electrolyte levels and our blood pressure.

Most of us are born with about 1 million nephrons, all of which form in the womb between weeks 25 to 36 of gestation. Unfortunately, the [nephron](#) formation process can be interrupted when babies are born preterm, which places them at higher risk of developing [kidney](#) disease later in life.

Now a study led by scientists at Cincinnati Children's reveals one mechanism involved in regulating when nephron formation ends. The discovery, based on mouse models, suggests that intervention during pregnancy or after preterm birth could extend nephron development. If translated to clinical practice years from now, the result could be reduced need for kidney transplants and fewer deaths from kidney disease.

Findings were posted online today in the journal *PNAS*.

The paper is the latest advance by scientists at Cincinnati Children's who are trying to reduce preterm birth by addressing environmental factors, understanding genetic drivers, and exploring the mechanisms that regulate complications.

"All the nephrons you or I have were generated while we were in our mother's uterus. Prematurity terminates this process too early. As a result, adults that were born prematurely are at high risk for hypertension, heart disease and end stage renal disease," says Raphael Kopan, Ph.D., Director of the Division of Developmental Biology at Cincinnati Children's, and senior author of today's study.

"The question we tried to address is how we generate the specific number of nephrons we have as adults, and how can we increase this number in [premature babies](#)."

Can a closing window of development be propped

open?

By studying how mice control their nephron numbers, the researchers discovered that a protein called hamartin plays a central role in shutting down the nephron formation process.

Until now, this protein was known primarily as a factor involved in tuberous sclerosis complex, a rare genetic disease that causes benign tumors to grow in the brain, kidneys, heart, and other organs. In this study, when mice were bred to produce reduced amounts of hamartin, their kidneys developed 25 percent more nephrons than a control group.

However, when bred to produce no hamartin at all, the mice developed fatal kidney defects. These results were seen in mice with two different genetic backgrounds, suggesting that hamartin function did not depend upon the method the research team used to reduce its level.

"This study provides important new information that will improve outcomes for all babies born prematurely," says Louis Muglia, MD, Ph.D., Co-Director of the Perinatal Institute at Cincinnati Children's and Director of the Center for Prevention of Preterm Birth. "Optimizing pregnancy outcomes is a central focus shared by the basic scientists and clinicians in the Perinatal Institute, and this work reflects that shared commitment."

More study needed before people can benefit

From affected families to society at large, the health impact of preterm birth remains a major concern.

Overall, about one in 10 infants are born prematurely (before 37 weeks) in the U.S. That's about 387,000 births a year, according to the U.S.

Centers for Disease Control and Prevention. Of those, nearly 109,000 are considered "early" preterm births (before 34 weeks). This group faces the highest risk of complications from interrupted kidney development.

As they grow up, many of those babies join the ranks of more than 8 million Americans affected by chronic [kidney disease](#), including more than 100,000 who begin dialysis each year while awaiting a kidney transplant.

At first glance, today's findings suggest that the hamartin protein would be a prime target for a medication to protect kidney development. However, in people, directly reducing hamartin production would likely cause tuberous sclerosis.

"We have discovered the tip of the iceberg," Kopan says. "We are hoping that the mechanism hamartin acts through to regulate nephron numbers will contain druggable targets."

If a safe drug can be developed, treatment would need to be provided shortly after a preterm infant is delivered.

"We never make another nephron after we are 36 weeks old," Kopan says. "It would be necessary to target at-risk premature babies to try to prolong their nephron-generating window."

So far, no diagnostic test exists that can determine if a developing fetus or newborn preterm baby has a nephron shortage. But several research groups around the world are studying how to use MRI scans to measure nephron supply. That work currently is focused on adults, but if proven safe, will eventually become applicable in newborns.

Science builds upon cradle Cincinnati work

Today's study is one of many efforts underway at Cincinnati Children's to address the problem of prematurity. Cincinnati Children's is a leading partner in Cradle Cincinnati, a community-wide collaboration to reduce high rates of preterm birth and infant mortality in Hamilton County.

The organization has already helped reduce infant deaths through initiatives to manage factors that contribute to [preterm birth](#), such as promoting smoking cessation, waiting at least a year between pregnancies, and safe sleep practices.

Until recently, not much was known about how genetic factors might play a role in premature birth. In a breakthrough study last year, scientists here collaborated with the company 23andMe in a large-scale genetic study. They discovered six genomic locations that show strong potential to affect birth timing.

It remains to be seen how that discovery will lead to improved treatments. But together with Cradle Cincinnati's programs and today's study, research is helping identify ways to reduce some of the problems associated with premature [birth](#), Muglia says.

More information: Oded Volovelsky et al., "Hamartin regulates cessation of mouse nephrogenesis independently of Mtor," *PNAS* (2018). www.pnas.org/cgi/doi/10.1073/pnas.1712955115

Provided by Cincinnati Children's Hospital Medical Center

Citation: Helping preterm infants grow bigger kidneys would prevent kidney disease later in life (2018, May 21) retrieved 26 April 2024 from <https://medicalxpress.com/news/2018-05-preterm-infants-bigger-kidneys-kidney.html>

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.