Improving birth outcomes one amino acid at a time

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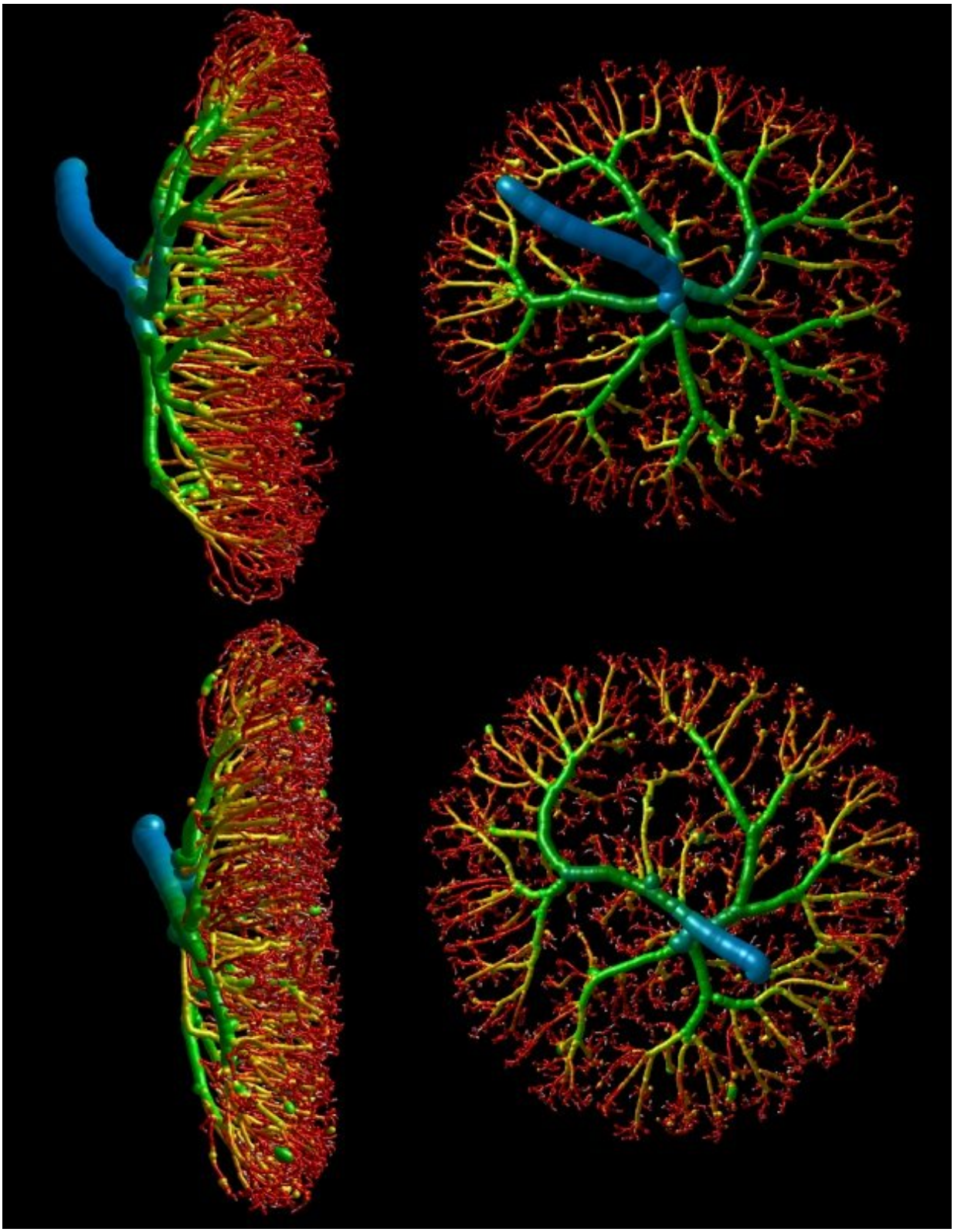

CT images of blood vessel formation in the placentas of malaria-infected mice

who receive either non-treated water (top image) or L-arginine supplemented drinking water (bottom inage). L-arginine supplementation increases the number of small vessels (those coloured in red) in placentas from malaria-infected litters, improving blood vessel development, blood flow and healthy birth outcomes. Credit: Courtesy of Chloe R. McDonald, Lindsay S. Cahill, Lisa M. Gazdzinski, John G. Sled and Kevin C. Kain.

A simple dietary supplement (L-arginine) was found to improve birth outcomes, paving the way for future clinical trials to test this inexpensive and safe intervention.

In their paper entitled, "Malaria in pregnancy alters L-arginine bioavailability and placental vascular development," *Science Translational Medicine*, 7 March 2018, Toronto General Research Institute (TGRI) and University of Toronto researchers report that Malawian women with malaria in pregnancy had altered levels of L-arginine which were associated with poor birth outcomes. L-arginine is an amino acid that improves blood flow and circulation and that humans get from their diet, including eggs, meat and dairy.

In an experimental model of malaria in pregnancy, supplementing the diet of pregnant mice with L-arginine increased blood vessel development in the placenta and reduced low birth weight/preterm birth and stillbirth.

Preterm birth and stillbirth are leading causes of childhood death accounting for an estimated 2 million deaths per year; however there are few safe and effective interventions. Globally many of these poor birth outcomes are associated with maternal infections such as malaria.

Led by Dr. Chloe McDonald and Dr. Kevin Kain at the Toronto General

Hospital Research Institute, University Health Network (UHN), the scientists show that supplementing the diet with L-arginine prevented malaria from depleting the L-arginine-nitric oxide (NO) pathway.

In the body, L-arginine is converted into nitric oxide, which is critical for normal placental blood vessel development and healthy birth outcomes. By the time a woman delivers, there are 250 kilometres of blood vessels in the placenta, which provide essential oxygen and nutrients to the rapidly growing baby.

"Our work shows that L-arginine is a critical component in regulating a key pathway that promotes blood vessel development in the placenta. Infections such as malaria can impair that pathway, restricting placental vascular development. Ultimately this can result in poor birth outcomes which can have long-term effects on babies who survive, including impaired brain and behavioural development," says Dr. McDonald, adding that research on safe, effective ways of promoting healthy birth outcomes are urgently needed.

Dr. Kain notes that the L-arginine-(NO) biosynthetic pathway identified in this research may be a common pathway underlying other conditions linked to poor birth outcomes, be they in low or high-income countries such as Canada.

"Our findings have broad implications not only for malaria in pregnancy (125 million pregnancies at risk each year), but also for other globally important causes of adverse birth outcomes such as preeclampsia," says Dr. Kain, who is also Science Director, Tropical Disease Unit at the Toronto General Hospital, UHN.

Since L-arginine can be given to women as a simple, safe, and inexpensive food supplement, (in peanuts, for example) in pregnancy, Dr. Kain and Dr. McDonald are now planning human clinical trials to

assess its impact on human birth outcomes.

Provided by University Health Network