Early study points to potential therapeutic avenue for a pair of rare pediatric diseases

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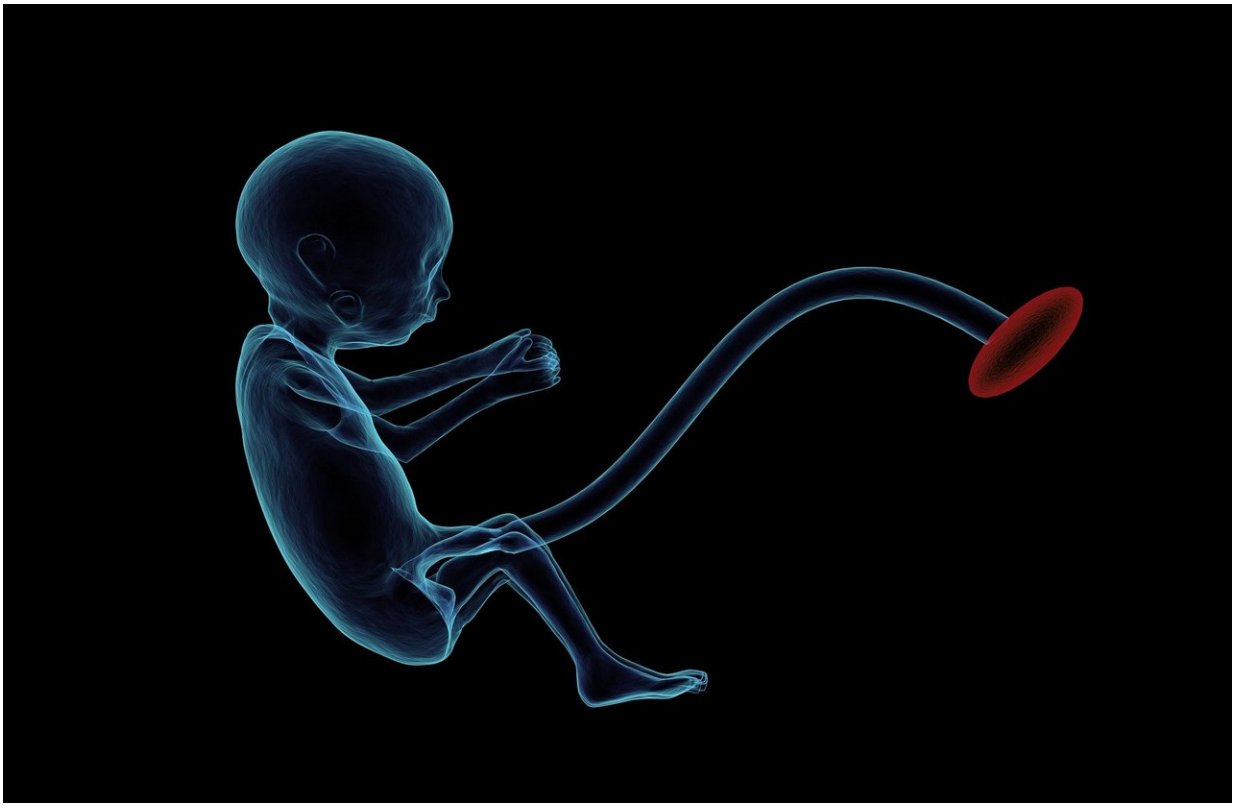

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Scientists have devised a new approach for detecting and potentially heading off the effects of two rare pediatric diseases before birth.

The study, performed in mouse models of the diseases and published

today in *Cell Reports*, represents an important step toward much-needed early interventions for Beckwith-Wiedemann syndrome and Silver-Russell syndrome.

Both diseases result in growth-related symptoms in children and often lead to additional problems later in life, such as increased cancer risk from Beckwith-Wiedemann syndrome and increased metabolic disease risk from Silver-Russell syndrome.

"Both of these diseases have lifelong consequences," said Piroska Szabó, Ph.D., an associate professor at Van Andel Institute and the study's corresponding author. "Our findings provide a critical foundation for additional studies that we hope will translate into new, life-changing prenatal detection and treatment methods. Our goal is for children to be born healthy."

Fetuses with Beckwith-Wiedemann syndrome experience too much growth during development while fetuses with Silver-Russell experience too little growth. Likewise, about one-third of Beckwith-Wiedemann cases and two-thirds of Silver-Russell cases may arise from having either too much or too little of a protein called IGF2, which plays a critical role in fetal growth and development.

Using models of the diseases, Szabó and colleagues were able to detect and measure IGF2 in amniotic fluid and correlate variations in IGF2 levels with Beckwith-Wiedemann and Silver-Russell syndromes, opening up new opportunities for early detection.

The researchers also were able to correct IGF2 levels in a genetic experiment, essentially reversing the fetal growth problems associated with both disease models. They found that treatment before birth with an FDA-approved cancer medication that targets IGF2 signaling normalized fetal growth in the Beckwith-Wiedemann model.

More research and clinical studies are needed before it is known whether the findings hold true in humans, Szabó cautioned. She hopes to find a clinical collaborator with whom to partner for future studies.

"There's a big gap between an experiment in the lab and implementation in the clinic," Szabó said. "However, our results are a vital step toward finding ways to identify and treat these syndromes before birth."

More information: Ji Liao et al. Prenatal correction of IGF2 to rescue the growth phenotypes in mouse models of Beckwith-Wiedemann and Silver-Russell syndromes. *Cell Reports* 2012.
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