Researchers find molecular mechanisms within fetal lungs that initiate labor

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Researchers at UT Southwestern Medical Center have identified two proteins in a fetus' lungs responsible for initiating the labor process, providing potential new targets for preventing preterm birth.

Previous studies have suggested that signals from the fetus initiate the birth process, but the precise molecular mechanisms that lead to labor remained unclear. UT Southwestern biochemists studying mouse models found that the two proteins - steroid receptor coactivators 1 and 2 (SRC-1 and SRC-2) - control genes for pulmonary surfactant components that promote the initiation of labor. Surfactant is a substance released from the fetus' lungs just prior to birth that is essential for normal breathing outside the womb.

"Our study provides compelling evidence that the fetus regulates the timing of its birth, and that this control occurs after these two gene regulatory proteins - SRC-1 and SRC-2 - increase the production of surfactant components, surfactant protein A and platelet activating factor," said senior author Dr. Carole Mendelson, Professor of Biochemistry, and Obstetrics and Gynecology at UT Southwestern.

"By understanding the factors and pathways that initiate normal-term labor at 40 weeks, we can gain more insight into how to prevent preterm labor," said Dr. Mendelson, Director of the North Texas March of Dimes Birth Defects Center at UT Southwestern.

Each year about one in every nine infants in the United States is born preterm (before 37 weeks), according to the Centers for Disease Control and Prevention. Premature birth can cause brain hemorrhage and respiratory distress for babies, as well as long-term conditions such as cerebral palsy, chronic lung disease, and impaired vision.

The study, which appears in the *Journal of Clinical Investigation*, was supported by the National Institutes of Health and a Prematurity Research Initiative grant from the March of Dimes Foundation.

UT Southwestern researchers found that the proteins SRC-1 and SRC-2 activate genes inside the fetus' lungs near full term, resulting in an increased production of surfactant components, surfactant protein A (SP-A), and platelet-activating factor (PAF). Both SP-A and PAF are then secreted by the fetus' lungs into the amniotic fluid, leading to an inflammatory response in the mother's uterus that initiates labor.

The current study showed that a deficiency of both SRC-1 and SRC-2 inside the fetus' lungs drastically decreased the production of SP-A and PAF, causing a one- to two-day labor delay in mouse models, comparable to a three- to four-week labor delay in women.

Researchers further found that injecting either SP-A or PAF into the amniotic fluid of the deficient mice allowed the mothers to deliver on time. Together, the findings further define the underlying molecular mechanisms by which fetuses control the timing of birth.

Future research will include defining how fetal signals are transmitted to the mother's uterus, and relating these findings to the causes of preterm labor.

Provided by UT Southwestern Medical Center