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UT Southwestern researchers find process of cervical ripening differs between term and preterm birth

DALLAS – June 21, 2011 – Cervical ripening that instigates preterm labor is distinct from what happens at the onset of normal term labor, researchers at UT Southwestern Medical Center have found.

The findings challenge the conventional premise that premature cervical ripening and remodeling is likely just an accelerated version of the term labor process, and that normal term ripening is caused primarily by activation of inflammatory responses.

Cervical remodeling is the process by which the cervix is transformed to open sufficiently during the birth process.

“Premature cervical remodeling can occur by more than one mechanism and is not necessarily an acceleration of the physiologic process in term labor. Depending on the cause of preterm birth, that mechanism can vary,” said Dr. Mala Mahendroo, associate professor of obstetrics and gynecology and the Cecil H. and Ida Green Center for Reproductive Biology Sciences at UT Southwestern, and senior author of the study published in a recent issue of *Endocrinology*.

The study has been selected by the Faculty of 1000 – an international group of more than 10,000 leading scientists and researchers – to be in its top 2 percent of published articles in biology and medicine.

Previous studies suggest that in term or preterm labor, white blood cells influx into the cervix and release enzymes that break down tissue support and remodel the cervix, allowing a baby to pass through the birth canal. That’s only half-right, researchers in this investigation report.

“The immune system or inflammatory response is sufficient to cause cervical ripening, but it’s not absolutely necessary for it to happen,” said Dr. Brenda Timmons, research scientist in obstetrics and gynecology and co-lead author of the study.

Nearly 13 percent of all births in the U.S. are preterm. Premature infants can suffer respiratory distress, intraventricular hemorrhage and even cerebral palsy. Identified risk factors for preterm birth include smoking, alcohol consumption, advanced maternal age, genetics, cervical insufficiency, previous preterm birth and infection.

“In about half of all preterm births, the cause is unknown. It’s critical to determine the multiple causes of preterm birth so that effective therapies can be developed for each kind,” said Dr. Roxane

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Holt, a maternal-fetal medicine fellow and co-lead author of the study.

“When patients present in preterm labor, we don’t have a lot of therapy to stop the labor,” she said.

UT Southwestern researchers compared preterm birth models in mice. They injected lipopolysaccharide (LPS) to promote infection-like conditions and an inflammatory response in one model. In the other, they administered mifepristone (RU486) to simulate the withdrawal of the gestation-supporting hormone progesterone, which normally takes place at the end of a pregnancy.

Researchers report that cervical changes in inflammation-induced conditions are caused by an influx of white blood cells and an increased expression of pro-inflammatory markers with no increase in the expression of genes induced in term ripening. Preterm ripening induced by progesterone withdrawal results from the combined activation of processes that occur during term ripening and shortly postpartum.

“These findings, if translatable in women, suggest one therapy may not be effective for all preterm births, and that early identification of the cause of prematurity is necessary to determine the correct therapy,” Dr. Mahendroo said.

Also participating in the study from the Department of Obstetrics and Gynecology were Dr. Yucel Akgul, a postdoctoral fellow, and Meredith Akins, a graduate student.

The research was supported by grants from the National Institutes of Health.

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