UT SOUTHWESTERN MEDICAL CENTER NEWS

Media Contact: Erin Prather Stafford
214-648-3404
erin.pratherstafford@utsouthwestern.edu

# Estrogen activates critical lung genes to improve lung function following preterm birth, UT Southwestern researchers find

DALLAS – March 12, 2009 – Estrogen may be a new postnatal therapy to improve lung function and other outcomes in preterm infants, researchers at UT Southwestern Medical Center have found in an animal study.

"Ironically, a hormone that has received great attention as a potential means to optimize the health of older women may be a beneficial treatment for humans during the earliest stages of life," said Dr. Philip Shaul, professor of pediatrics at UT Southwestern and the study's senior author.

The study, conducted in preterm primates, appears in the March issue of the *American Journal of Respiratory and Critical Care Medicine*. The study was performed at the Southwest Foundation for Biomedical Research Primate Center in San Antonio as part of a National Institutes of Health-funded consortium investigating causes and treatments for bronchopulmonary dysplasia (BPD), a devastating primary complication of premature birth that develops in the preterm lung following ventilation and oxygen support.

Sufficient production of nitric oxide in fetal and newborn lungs is necessary for the lungs to develop and function properly. During the latter part of pregnancy the placenta produces large amounts of estrogen that enters the fetal circulation. Another spike of estrogen occurs during labor. In prior studies in cultured cells the investigators found that estrogen activates the genes in lung cells encoding nitric oxide synthases, enzymes that produce nitric oxide. That research suggested treatment with the hormone may achieve the same results in the intact lung. Premature infants – nearly 50,000 are born in the U.S. each year – miss out on this exposure to estrogen in the womb and, as a consequence, may experience respiratory problems because they lack nitric oxide.

Dr. Shaul and his colleagues found that administering estrogen to premature primates accomplished several things.

First, the treated animals had greater abundance of nitric oxide synthases in their lungs, resulting in markedly enhanced lung function and a significantly reduced need for ventilation support. This represents an important step in lessening the lung injury that causes BPD in humans, Dr. Shaul said. It also prevented low blood pressure, which is a common problem in preterm infants.

(MORE)

Estrogen also caused the closure of the ductus arteriosus, a shunt that connects the pulmonary artery to the aorta during the primates' fetal development to allow blood flow to bypass the fetus' fluid-filled lungs. In the case of full-term infants, the ductus arteriosus normally closes at the time of birth once breathing is established. In premature infants, however, it frequently fails to close resulting in further impairment in lung and heart function.

"With just one therapeutic intervention multiple benefits occurred in the lungs and the circulation," Dr. Shaul said. "Estrogen-based therapies to prevent BPD and other complications of prematurity should be further developed, and it is our hope to begin clinical trials in the near future."

Dr. Shaul said that future studies also would need to evaluate other potential targets of estrogen in the lung in addition to nitric oxide synthases and possible effects of postnatal estrogen treatment on nonpulmonary development, including those related to the later reproductive health of the child.

Other UT Southwestern researchers involved in the study were the lead author Dr. Donald McCurnin, professor of pediatrics and medical director of the neonatal intensive care unit at Children's Medical Center Dallas; Dr. Brigham Willis, a former assistant professor of pediatrics; and Ivan Yuhanna, senior research associate in pediatrics.

Also participating were researchers from UT Health Science Center at San Antonio; the Southwest Foundation for Biomedical Research; Washington University School of Medicine; National Jewish Medical and Research Center, the University of Utah School of Medicine, the University of California, San Francisco, School of Medicine; SRI International, the University of Rochester School of Medicine and Dentistry; and Vanderbilt University School of Medicine.

Visit www.utsouthwestern.org/pediatrics to learn more about UT Southwestern's clinical services in pediatrics.

###