Researchers aim to discover the unknown causes of premature birth

July 18 2013

This is Connor, born prematurely at 34 weeks' gestation, spent seven days in the Intensive Care Nursery at DHMC. Credit: none

Researchers from Dartmouth's Institute for Quantitative Biomedical Sciences (iQBS), the Center for Integrative Biomedical Sciences, and the Center for Genomic Medicine at the Geisel School of Medicine are studying the unknown causes of premature birth, as part of a $10 million March of Dimes grant awarded to a research collaborative of seven U.S. universities and medical centers. The collaborative will collectively study the evolution and biology of human pregnancy, how progesterone impacts pregnancy maintenance and preterm birth (defined as birth

before 37 weeks' gestation), the sociobiology of racial disparities in preterm birth, and the genetics of unique human populations. The Dartmouth team, led by professor Scott Williams and colleagues Jason Moore and Christopher Amos, is examining diverse world populations that have higher and lower levels of premature birth.

Scott Williams, PhD, Professor of Genetics at the Geisel School of Medicine, and Founder and Director of the Center for Integrative Biomedical Sciences in iQBS, says that, "Approximately 50% of preterm birth has no clear medical cause, and evidence strongly suggests that genetic factors contribute to some of these cases. In this work, we are trying to understand how genetic variation impacts the biological processes that underlie preterm birth."

Premature birth is the leading cause of newborn death and disease. In New Hampshire and Vermont, one of every 17 babies is born prematurely, or more than 1,000 babies per year in the region. Researchers don't know why preterm birth happens in roughly 10% of pregnancies in Caucasian women nationwide, but in about 20% of pregnancies of African-American women. They also don't understand why recently there has been a large increase in preterm birth rates, especially at 34-36 weeks, according to Dr. Williams. "This creates enormous health care costs, because much of childhood disease is due to short gestational age," he says. Babies who survive a premature birth may suffer "permanent vision and breathing problems, cerebral palsy, and learning disabilities," according to the March of Dimes.

Emily R. Baker, MD, Professor of Obstetrics and Gynecology and Radiology at Geisel, Director of the Maternal-Fetal Medicine Division and Vice-Chair for Obstetrics in the Department of Obstetrics and Gynecology at Dartmouth-Hitchcock Medical Center (DHMC), says, "We are pleased that Dartmouth investigators are part of this important new initiative to investigate the etiology of prematurity. As a tertiary-

care academic medical center with an active high-risk pregnancy service, we have front-line experience with the potentially devastating effects of premature birth."

William H. Edwards, MD, is Professor of Pediatrics at Geisel and Vice Chair of Pediatrics and Neonatology Section Chief at DHMC. He spent over 30 years as chief of the medical center's Intensive Care Nursery (ICN), and "quite literally cared for thousands of premature babies." Dr. Edwards says, "It is a sad fact that the U.S. prematurity rate has not decreased over the three decades in which I've been a neonatologist. We have made tremendous advances in caring for babies born early, with better survival rates and long-term outcomes. We have made very little progress in preventing prematurity. This research project has the promise to uncover some of the underlying factors in this multifactorial healthcare problem. Better understanding carries hope that effective strategies for prevention can be discovered."

Marlene B. Goldman, ScD, Professor of Obstetrics and Gynecology and Community and Family Medicine at Geisel, Vice-Chair for Research, and Director of the Division of Clinical Research in the DHMC Department of Obstetrics and Gynecology, states, "I think that the multi-project approach is particularly impressive given the likely complicated and multifactorial origins of this maternal-fetal condition."

In this large, collaborative effort, researchers with diverse backgrounds will exchange information and "create hypotheses to identify the many underlying causes of preterm birth, and translate new knowledge into new approaches to the prevention of premature birth." The collaborative includes medical schools and hospitals at Case Western Reserve University, Dartmouth College, Ohio State University, the University of Cincinnati, the University of Iowa, Vanderbilt University, and Washington University. The grant was developed in close consultation with March of Dimes leadership, who sought good science and "out of

the box" ideas, Dr. Williams says. "They asked, 'can we generate research teams that can take the research in new directions that may have a high payoff?'" Dr. Williams and colleagues aim to investigate new ways to filter and re-analyze genetic data to provide novel information and findings that were previously "tossed out" or missed.

Dr. Williams has studied the role that genetics plays in preterm birth and disparities among populations for almost ten years, and has shown that there may be population-specific risks. In the current program, his efforts will refocus on using the known differences in preterm birth rates across populations to help define genetic risks that might otherwise be missed with standard analytical approaches. This approach explicitly incorporates evolutionary processes that may have been critical in causing these prevalence differences.

"Understanding the biological processes of preterm birth will give us potential targets for further study," says Dr. Williams. "We can use genetics to identify biological pathways and learn what environmental factors we can address—including risks such as drinking or smoking. We can't change genes, but we can change behavior."

"Using genetics to prevent preterm birth may be a long-term goal," Dr. Williams adds. "However, as an example, people with the gene that causes sickle cell anemia are living longer, in part due to an understanding of the genetic processes that cause sickle cell anemia. Management of many medical conditions is getting better, and knowing what genes underlie the biology will help us better manage more conditions."

Jason H. Moore, PhD, Third Century Professor, Professor of Genetics and Community and Family Medicine at Geisel, Director of the iQBS, and Associate Director for Bioinformatics at Norris Cotton Cancer Center, says, "Preterm birth can be devastating for families. The

interdisciplinary approach employed by this team has tremendous potential for revealing some of the important risk factors. This project serves as a model for the future of biomedical research."

Provided by The Geisel School of Medicine at Dartmouth