PREMATURITY RESEARCH CENTERS

FALL 2019
Welcome to the Fall Prematurity Research Centers Update

One of the defining tenets of the March of Dimes Prematurity Research Centers has been our insistence on a transdisciplinary approach to our research. We learned very early in this journey that prematurity was too big and too complex a phenomenon to be unraveled by a solitary researcher in a lab funded by traditional grants and stipends. We needed to throw out a much broader net, provide a financial commitment commensurate with the severity of the problem, and integrate approaches and disciplines no one had ever thought to apply to prematurity research. This PRC update illustrates the power of working together in this way.

In this issue you’ll learn about computer scientists working with molecular biologists, sociologists supplying insights to geneticists (and vice versa), and neonatologists and epidemiologists each illuminating the work of all the others. This kind of collaboration might never have happened without the framework and support the PRCs provide, and experts whose insights have informed the discoveries we’ve made so far would have been lost in the silos of thought traditional scientific inquiry typically creates.

But not here. And not now. At March of Dimes, we are proud to share the progress our brilliant scientists, clinicians, researchers and experts of every stripe have made since we instituted the Prematurity Research Centers just eight short years ago. As always, that progress would not have been possible without your generous commitment and steadfast support for which we are inexpressibly grateful. We’re proud of what we’ve done here, and how we’ve done it. And even more so to be able to share it with you, who have made it all possible.

STACEY D. STEWART
PRESIDENT AND CEO
MARCH OF DIMES
One would think that all women who start a pregnancy doing the “right things” would have an equally good chance of having a healthy, full-term baby. But that is not the case. African American women in the United States, regardless of their education, have worse birth outcomes by a large margin than white women, Hispanic women and other minority groups combined. Differences in genes are not enough to account for the gap in preterm birth rates. Among Black women, country of origin matters—Black women born in Africa who deliver babies here do not share the high rates of premature birth of their American-born Black counterparts. Therefore, we must address other factors to understand the discrepancy. A transdisciplinary research team at the March of Dimes Prematurity Research Center at the University of Pennsylvania is doing just that, with a new big data study called the GeoBirth initiative, the largest ever fielded to answer this critically important public health question.

GeoBirth uses a large electronic record health data repository to identify all premature births. Each one is then reviewed and cataloged by a team of research coordinators at Penn Medicine to determine if the premature birth was spontaneous or due to a medical condition. The team then overlays environmental data across metropolitan Philadelphia to identify contributors to specific conditions that lead to premature birth. To address this health inequity, it’s critical to understand both individual patient-level interventions and the population-based public health policies to change it.

Dr. Heather Burris, a neonatologist at University of Pennsylvania, heads the GeoBirth initiative. Her mother was a nurse, and her father was also a neonatologist. “While I was in college, I remember going to a seminar my father gave demonstrating prematurity was not evenly distributed across populations,” she said. “So it was a combination of recognizing the value of being a neonatologist, and having the opportunity to study this major health inequity that has motivated much of my career. I feel grateful that I ended up on this path.” Births at Penn Medicine that contribute data to GeoBirth account for half of all births in Philadelphia. The team geocodes every patient in order to identify hot spots where women have an increased incidence of adverse pregnancy outcomes and then correlates hot spots with publicly available data on environmental exposures in those same neighborhoods. Comparing neighborhoods with high rates of premature birth to otherwise similar neighborhoods with lower rates allows researchers to collect and analyze various biomarkers in smaller, targeted cohorts for a variety of exposures. This, in turn, could lead to novel ways to enroll patients in therapeutic trials in order to help those who are most at risk. It’s a step toward what Burris calls “precision public health.”

GeoBirth includes the type of transdisciplinary work that all our PRCs have become known for. Burris’ colleague, Allan Just, at Mt. Sinai Hospital in New York, is an air pollution modeler whose one-by-one kilometer daily reading of air pollutants links to Burris’ Geo Birth data to assign daily exposures to each participant. They work with Jane Clougherty, an environmental epidemiologist at Drexel’s Dornsife School of Public Health, whose career is devoted to understanding how stress affects susceptibility to physical pollutants. This work is complemented by that of Dr. Michal Elovitz, our PRC theme leader, who contributes translational science and maintains the research infrastructure.

GeoBirth will help identify the specific environmental exposures that adversely affect a woman’s chance at having a healthy birth outcome. And by partnering with investigators who are developing novel therapeutics that make a difference among women with that set of environmental exposures, we’ll begin to give every mom an equal chance of having a healthy baby.
BIG DATA, BIG INSIGHTS

To understand any human disease, you have to be able to map its complexity. Premature birth just happens to be an extreme case.

Premature birth is a collection of imbalances, inflammations, conditions, disorders and diseases that lead to different pathways by which a mom can give birth prematurely. Understanding the impact of each as well as their various combinations demands integrating monumental amounts of data that span the basics, like age, demographics and family history to the truly mysterious like genetic predisposition and the composition of the mother’s microbiome.

All of this valuable and relevant information is becoming increasingly available, but that doesn’t mean it’s automatically going to yield insights. The challenge for big data science is integrating the different types of data from different sources to provide a deeper understanding of the mystery of premature birth and how to treat it. That’s becoming possible thanks to Dr. Tony Capra an Associate Professor of Biological Sciences at Vanderbilt University, part of March of Dimes Ohio Collaborative Prematurity Research Center.

Dr. Capra, whose lifelong fascination with evolution and genetics lead him to study preterm birth, is leading the effort to use BioVU, Vanderbilt’s huge “biobank” of patient DNA linked to electronic health records. His research involves pulling together a rich characterization of the treatment history of millions of patients at Vanderbilt and integrating this with DNA samples from more than 250,000 people, along with lab tests, ultrasounds, and all the other data present in health records. Building on this resource, he’s using machine learning techniques to detect patterns that are predictive of pregnancy outcomes. “We have some very promising preliminary results; if we look at everything we know about a mom six months into her pregnancy, we can predict reasonably well whether she’s likely to deliver prematurely,” said Professor Capra. “Now, our main goal is to improve the accuracy of these predictions, determine how our algorithms can help us understand which attributes really increase risk, and ultimately use their predictions to give better treatments.”

Within the Ohio Collaborative and across the other PRCs, scientists are sharing their results with Professor Capra. For example, Dr. Lou Muglia and Dr. Ge Zhang at Cincinnati Children’s Hospital have contributed their mapping of the genetics of prematurity and how those genetic variations relate to premature birth risk. Researchers at the Stanford PRC and Marina Sirota’s team at UCSF will also look at whether the approaches being built in BioVU generalize to their databank.

Simply put, a challenge as difficult and important as premature birth requires diverse perspectives and expertise that no one individual or lab is able to supply. That’s why Capra works with statistical geneticists, computer scientists, molecular biologists and even evolutionary biologists to provide context for why premature birth happens in the first place. All these perspectives are critical to a holistic solution to this problem.

Professor Capra’s research contributes to the goal of ending premature birth by someday enabling clinicians to identify moms early in their pregnancies at high risk for giving birth prematurely, and then to suggest interventions personalized to the patient.

The hope is that we can make good predictions a month or two into a pregnancy, to see the warning signs and to take the proper steps to make sure a mom doesn’t give birth prematurely.

The hope is that we can make good predictions a month or two into a pregnancy, to see the warning signs and to take the proper steps to make sure a mom doesn’t give birth prematurely. “We’re not making full use of all the data and information available to us, so there’s more we can do today. But this isn’t a situation where we have to collect more data to make an impact,” said Capra.

“We just need the resources, like those provided by March of Dimes, to extract the insights from the data we already have and then communicate those insights in a way that influences care. Essentially, we want to treat premature birth before there is a premature birth.”

PROFESSOR TONY CAPRA, Ph.D.
VANDERBILT UNIVERSITY
GARY SHAW, DrPH
NICU Nurses Professor
Professor (Research), by Courtesy of Health Research and Policy (Epidemiology) and of (Obstetrics and Gynecology) Maternal Fetal Medicine
Stanford University School of Medicine
Looking at the statistics underlying 1.5 million births over a 20-year period can tell you a lot. We now know conclusively that short intervals between births, in particular, less than 6 months, increase the risk of adverse birth outcomes. Paramount among those risks is premature birth. But most instructive about this landmark study is what it doesn’t explain. Namely, that shorter birth intervals is not the reason for the racial disparities in premature birth, which shows black women are up to 50 percent more likely to give birth prematurely than their white counterparts.

The good news is that this study helped eliminate one of the variables in the complex matrix of possible causes of racial disparities in premature birth. While shorter intervals between pregnancies increase the risks of premature birth as well as some birth defects, we don’t know why. One hypothesis is that the mother’s nutritional status is somewhat depleted, but this idea hasn’t been fully explored. Other theories have also been eliminated. We know it’s not about the genetic difference between the races, although we have identified genes that seem to be triggers for either turning on or off signals implicated in both precipitating and preventing premature birth. And some areas of inquiry, such as epigenetics and the microbiome, are showing great promise.

This study was conducted at March of Dimes Prematurity Research Center at Stanford University by Professor Gary Shaw, an epidemiologist and co-principal investigator, and his team. That team represents researchers investigating the causes of premature birth and clinicians and scientists looking for ways to translate what we know into interventions that will help prevent premature birth. One very important intervention is birth-spacing counseling to help women plan their pregnancies with more time in between.

The transdisciplinary research approach at Stanford has brought together talented and innovative individuals at the top of their various disciplines, who worked in their own domains and weren’t focused on premature birth at all. With March of Dimes funding we can bring those people together to share their findings about the different biologics, genetic vulnerabilities, exposure profiles and even sociology types that women have in their environments. And point to what’s needed next to unravel the enigma of premature birth.

“If we’re going to make a dent in the population burden of spontaneous premature birth, we’ve got to understand what’s contributing to this elevated risk for African-Americans.”

GARY SHAW, DrPH
STANFORD UNIVERSITY

“The next place that we’re going with interpregnancy interval is to try to understand what the microbiome looks like in these shortened intervals between the end of one pregnancy and the start of the next. Another area we’re going look at is what’s known as the epigenome to understand how our genetic structure alters itself under different environmental influences. It’s a real privilege to be an epidemiologist working on this here at this time because I think we have the opportunity to make some real headway.”

It’s important for us to understand how to make populations at risk less vulnerable to things like premature birth and birth defects. And when we can do that, we’ll understand how to give every child the best possible start.

MISTY GOOD, MD, MS
Assistant Professor of Pediatrics
Co-Program Director, Neonatal-Perinatal Medicine Fellowship
Washington University School of Medicine
Department of Pediatrics
Division of Newborn Medicine
St. Louis Children’s Hospital
Basil O’Connor Award Grantee
March of Dimes
NO ONE KNOWS WHAT CAUSES THIS. YET.

Of all the possible consequences of premature birth perhaps none is more devastating than this one, which strikes without warning and in many cases is fatal.

Necrotizing enterocolitis (NEC) is a disease that can strike any newborn, but is most common in premature babies. And the smaller and earlier the baby is born, the higher the risk for NEC. It can show up without warning, and in 30 percent of the cases, results in death. Even though theories abound, no one knows what causes NEC or how to prevent it. March of Dimes–funded researchers like Dr. Misty Good are working to change that.

“I always wanted to be a pediatrician and care for children as they grew. As an intern on my NICU rotation, I loved taking care of babies from their birthday in the delivery room to graduating and thriving outside of the NICU. I thought that was really special,” said Dr. Good, a neonatologist at Washington University in St. Louis. “During my neonatology fellowship, I encountered several babies who would succumb to NEC, a deadly consequence of premature birth. I felt horrible because there’s nothing that could’ve been done to save them.”

“When it became time to conduct a research project to become a board-certified neonatologist, I knew I wanted to study NEC, and I’ve since dedicated my career to studying this devastating disease.”

MISTY GOOD, MD, MS
WASHINGTON UNIVERSITY

NEC is devastating because it can’t be predicted, there are no biomarkers for an accurate diagnosis and it comes out of nowhere. It most commonly affects fragile premature babies who have already overcome so many challenges in the NICU. They can be thriving and growing, when then suddenly, they present with a bloody stool. That’s one of the first clues that the baby’s intestines are inflamed and treatment must begin immediately. Typically, feedings are stopped, antibiotics are administered and sometimes that helps. In severe cases, the babies are rushed into surgery to remove parts of their intestines that have died as a result of the overwhelming inflammation. If this treatment fails, death comes quickly, within 6 to 24 hours of onset, taking 20-30 percent of the babies that have NEC, and as high as 50 percent for severe cases. The disease kills hundreds of babies a year in the U.S. alone.

One preventative measure seems to be breast milk, but not all moms who’ve given birth prematurely are able to provide it. We know breast milk is protective, but it doesn’t protect all babies and we are trying to understand why. That’s the mystery Dr. Good and her team at the Washington University School of Medicine in St. Louis are working on. Specifically, what ingredients in breast milk can provide protection against this disease and what nutritional factors present in breast milk can enhance the baby’s gut immune system. With this information, we can develop a nutritional therapy or additive to supplement their milk or develop a drug to enhance their intestinal immunity.

Dr. Good collaborates closely with specialists from other disciplines. Pediatric surgeons, for instance, supply pieces of inflamed bowel for further study in the laboratory. Dietitians in the NICU consult on how to feed the baby as safe as possible, while maximizing their growth. Lactation consultants work with moms to provide breast milk and enhance their production if possible. This collaboration even takes place before the babies are born, by working closely with maternal fetal medicine specialists who together, we provide counseling and support for at-risk moms to ensure they know that maximizing the length of pregnancy is the safest way to give birth to a healthy baby.

Dr. Good appreciates the impact that the March of Dimes’ effort to eradicate premature birth can have on her work. “If premature birth didn’t exist, I wouldn’t need to study NEC because 90 percent of the babies that get this disease are premature.” said Dr. Good. “That’s the biggest contribution March of Dimes can make. In the meantime, I’ll keep dedicating my career to saving the babies from NEC.” And there’s a lot more work to be done.

Washington University in St. Louis
School of Medicine
WE’RE FACING AN URGENT HEALTH CRISIS:
Premature birth has many possible causes and implications for moms and babies, and our Premature Research Centers are addressing the following:

• In this country 1 in 10 babies is born prematurely each year.

• Worldwide 15 million babies are born prematurely each year.

• Premature birth and its complications are the largest contributors to infant death in the United States and globally.

• More than 380,000 babies are born prematurely in the U.S. each year.

• In addition to the human toll, the societal cost of premature birth is more than $26 billion per year.

• Women of color are up to 50 percent more likely to give birth prematurely and their children can face a 130 percent higher infant death rate.

• In this country black women have maternal death rates over three times higher than women of other ethnicities.

• More than 20 percent of premature babies are born to black women—that’s 1 in 5 babies.

• Employers pay 12 times as much in health care costs for premature/low birthweight babies compared to babies born without these complications.

Each PRC is charged with exploring a different transdisciplinary research target that is likely to be crucial to the prevention of premature birth. The six March of Dimes Prematurity Research Centers are: Stanford University, the Ohio Collaborative, Washington University in St. Louis, the University of Pennsylvania, UChicago-Northwestern-Duke, and Imperial College London, in the UK.

DONATE TODAY

For more information on how you can be a part of this effort, please contact:

David “D.J.” Hampton II
Senior Vice President & Chief Development Officer
914-997-4492

March of Dimes
1550 Crystal Drive
Suite 1330
Arlington, VA  22202

philanthropy@marchofdimes.org

MARCHOFDIMES.ORG