Welcome to the Summer Prematurity Research Centers Update

We knew that solving the mystery of premature birth would be neither easy nor quick. Then again, from our founding work on the eradication of polio, March of Dimes has a legacy of taking on tough challenges. Prematurity certainly falls into that category.

One way we sustain our drive and energy is to constantly attract new, bright thinkers. This issue of our newsletter highlights the work of four young researchers who have found their passion in the study of premature birth. They’re excited to share how working at our centers across the country and across the world fuels that passion in ways they never expected.

These profiles illustrate how our transdisciplinary research approach allows us to explore the human birth experience in truly unique ways, immersed in perspectives that don’t often get shared in a traditional laboratory setting.

Some of our researchers are working at the molecular and cellular level, while others focus on the epidemiological scale, where insights are gained with big data analysis and software rather than a microscope. Experts from a diverse set of disciplines are able to mentor and teach each other in this way. They note the importance of this transdisciplinary influence and partnership, and are eager to pay the wisdom forward.

Your support makes our daily commitment to this inspiring work possible. For that, and for everything else your generosity fuels for moms and babies, we’re truly grateful. We hope you enjoy this opportunity to find out more.

STACEY D. STEWART
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MARCH OF DIMES
MIRA NOURA MOUFARREJ
Ph.D. Candidate, Bioengineering
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Before we’re born, an obstetrician checks that, as fetuses, we’re hitting all our developmental milestones. But the tools to understand what’s happening are limited. So far, the best tool has been the ultrasound, but it doesn’t predict the risk of premature delivery. That’s where March of Dimes comes in.

The work at our center at Stanford University focuses on understanding spontaneous preterm delivery from every conceivable angle to determine the causes and how to predict and stop it. As pregnancy progresses, certain telltale molecules are found in the mother’s blood in increasing amounts. The results of a pilot study show that by measuring these molecules at any given point, we can gain a snapshot about the progression of a pregnancy, indicating who will go on to deliver preterm. Researchers, like Mira Moufarrej, believe these predictive factors can help us understand what might be causing spontaneous premature birth and develop targeted therapies to prevent it.

“These molecules, and even combinations of molecules, signal something, and by looking at them from complementary perspectives, researchers are beginning to understand which are associated with predicting premature birth.”

MIRA NOURA MOUFARREJ
STANFORD UNIVERSITY

Moufarrej works in Dr. Stephen Quake’s lab, the epicenter of this groundbreaking research, where she’s investigating the actions of RNA molecules in a mother’s plasma. Like everyone in the PRC network, Moufarrej collaborates with other scientists, each of whom looks at a different type of molecule. These molecules, and even combinations of molecules, signal something, and by looking at them from complementary perspectives, researchers are beginning to understand which ones are associated with predicting premature birth. Being involved in this way has given Moufarrej a new appreciation of the benefits of transdisciplinary research.

“When I started at Stanford as a graduate student, I didn’t understand transdisciplinary research and how it could push forward certain research questions,” said Moufarrej. “But I quickly came to appreciate how someone who’s working on proteomics or the immune system would fit with what I was doing. The combination of those perspectives helps to get at the main question, which is how we can better enable an obstetrician or a neonatologist to provide the best standard of care in predicting and preventing premature birth.”

The transdisciplinary nature of the network also functions as a remarkably effective mentoring system. Dr. Stephen Quake is Moufarrej’s primary mentor as a graduate student, but she also benefits from the insights of Dr. David Stevenson, the Center’s principal investigator and a neonatologist, and Dr. Gary Shaw, an epidemiologist whose work with demographic data shows how premature birth directly affects people’s lives. These mentors, along with the dozens of other biologists, chemists, engineers and clinicians amplify her work with their various viewpoints.

Her experience has yielded a certain amount of wisdom she’s keen to pass on to young researchers coming up through the ranks. “Don’t be afraid of what you don’t know, but also don’t discount what you do know, and be confident in your ability to learn,” Moufarrej said. “The questions we’re trying to answer are difficult, and you’ll never know enough going in. But that should fill you with excitement because you’re breaking new ground.”
MOLLY STOUT, MD, M.S.C.I.
Associate Professor
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LEARNING WHY PREMATURE BIRTH HAPPENS

Every birth is unique. But understanding the different types of premature birth gets us closer to what causes them, and ultimately, their prevention.

We know what constitutes premature birth. But not all premature birth is alike. Understanding the various causes begins with looking into and categorizing the different ways moms give birth prematurely. And there's more than one way to do that.

Some investigators classify all premature birth together, regardless of the reason. Others classify it into different categories according to why mom delivered preterm. A premature birth at 28 weeks because of severe preeclampsia is put into a different category than spontaneous labor at 28 weeks. There's even data to suggest those babies may have different neonatal and, perhaps even, childhood outcomes.

There are also socio-demographic, ethnic and disease risk factors that must be considered. But they have one categorization in common: severity as determined by gestational age.

Making sense of this, at least from an epidemiological point of view, is Dr. Molly Stout, Chief of Maternal Fetal Medicine in OB/GYN and a researcher at our center at Washington University in St. Louis. Beyond statistics gathering, there are several reasons why her work is so important.

First, a woman who has a particular type of premature birth is at much higher risk for the same type of premature birth in her subsequent pregnancies, but also at risk for different causes of preterm delivery. And, clinical prediction of who will and who will not deliver preterm are still very limited. Second, Dr. Stout’s work ties directly into the various types of obstetric research being conducted at Washington University. These include basic science investigations into fundamental cellular processes, examinations of the electrical activity of contractions and how maternal cells guard against or work with certain types of bacteria. Third, her work represents the intersection of clinical epidemiology and basic science for findings that, in the lab, will uncover how and why different clinical treatments may affect patients differently. These fundamental lab investigations can help researchers and clinicians see different patient populations in a new light.

“Thanks to March of Dimes, I’m able to work with mechanical and optical engineers with subspecialties in imaging and image processing,” said Dr. Stout. “They’ve actually designed the instruments that take optical pictures of the cervix, but they also process the images to give us data that’s even more refined than a CT-scan or an MRI. Before we would’ve needed a biopsy. It’s incredibly valuable.”

Dr. Stout’s analyses of these images gives the research team unprecedented information about the underlying physiologic processes involved in various stages of pregnancy. But her multi-dimensional work also includes statistical modeling of microbial and viral communities in the vagina with Kristine Wylie, a Ph.D. virologist at the McDonnell Genome Institute. And she’s partnering with experts in mass spectroscopy and organic chemistry to work on the metabolism of synthetic progesterone. The work she’s pursuing makes her one of the center’s most promising young researchers.

“March of Dimes not only funds the Prematurity Research Center here, they also funded multiple pilot projects for me, and I’ve been lucky enough to work with this whole team who are thinking about prematurity in new ways,” Dr. Stout said. “In particular two of the mentors and collaborators, Dr. Methodius Tuuli and Dr. George Macones, have had an incredible impact. They’ve completely changed my career trajectory.”
MALKO ADAN, MSc
Senior Research Midwife
Department of Surgery and Cancer
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Imperial College London
IDENTIFYING TRENDS IN PREMATURE BIRTH

Analyzing big data has the potential to tell us more causes of premature birth—and where to concentrate our research to help eliminate it.

The research team at our center at Imperial College London, led by Professor Phillip Bennett, focuses on the role of bacteria in premature birth. More specifically, it’s concerned with how the relationships between bacteria and the body, along with inflammation, either raise or lower the risk of premature birth. A large component of the research is the ability to harness big data sets linked to the National Health Service in the UK. Mining that data helps us understand premature birth trends at a national level and how links to changing demographics, including ethnicity, age and causal factors might influence preterm risk.

For several years, March of Dimes has issued The Premature Birth Report Card, U.S.-based prematurity data that has shocked the medical community, raised awareness of this worldwide health crisis and galvanized us to find new ways to fight rising rates. Unfortunately, the same kind of report card has never existed in the UK, so the country’s researchers and scientists are unable to monitor national preterm rates. Thanks to funding from March of Dimes and researchers like Ph.D. candidate Malko Adan, that’s about to change.

Adan isn’t a scientist. She’s a senior research midwife who manages the preterm birth surveillance clinics at Imperial College Healthcare NHS Trust hospitals. With our transdisciplinary approach, she also works with scientists, bioinformatics specialists and clinicians to see that women get the best possible care during their pregnancy, and where possible, are able to contribute to world leading research.

In the UK midwives are integral in the care of moms and babies and also premature birth research. But what Adan is doing is unique. Thanks to records going back more than a hundred years, she’ll be able to investigate premature trends in the UK over a period of time, and for the first time perform follow-up research using the UK’s National Neonatal Research Database to track the progress of premature babies as they get older.

Her passion for finding the answers isn’t just professional; it’s personal, too. “Premature birth is something that I’ve come across in the course of my practice, obviously. But it’s also something that I’ve personally experienced,” said Adan. “That made me want to not just be a bystander. Being a midwife meant I had the opportunity to do the research to understand why this is happening. That seemed like a natural progression for me.”

The tradition of midwifery in the UK is rich in mentorship. When a midwife qualifies, and all through training, there’s a system of mentorship and support. Now in a position to be a mentor herself, Adan has advice for junior midwives and researchers coming into the program.

“I think the most important thing is for them to understand their experiences, who they are as a person and how that makes them unique, so their contribution and perspective will be unique,” she said. “Find something they’re passionate about and actively add their voice to that particular cause. Because I can almost guarantee that what they have to say will matter.”

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MALKO ADAN, MSc
IMPERIAL COLLEGE LONDON
MODELING HUMAN PREGNANCY

During pregnancy, cells from the mother and cells from her fetus communicate with each other. What we don’t know is how they tell each other it’s time to give birth.

The mystery of birth timing is clearly in our cells, but not apparent to providers or mothers (or any of us). One of our young researchers, Virginia Chu Cheung, is working to figure out exactly how cells from mom and her developing baby communicate with each other. And whether something in that interaction triggers birth timing. The goal is to build a model to understand how these cells interact because there’s no safe way to study this in vitro. If successful, this research could produce one of the most important models of human pregnancy ever created.

To build this model, blood cells are collected from moms who deliver at term as well as moms who deliver preterm. Those cells are then programmed into stem cells—the building blocks that can transform into any cell type. This gives the research team unlimited regeneration capacity, and the cells can be banked and studied longer. This research is being conducted and coordinated by Dr. John Kessler’s team at March of Dimes University of Chicago-Northwestern-Duke (uC-N-D) Prematurity Research Center.

Graduate student Cheung’s role is to develop an efficient method for differentiating these stem cells into cells of the endometrium, the mucus membrane lining the uterus. Using these cells as well as others, she’s developing a three-dimensional model of the maternal fetal interface to study how all these cell types communicate in at term and preterm pregnancies.

A unique aspect of this research is the collaboration with Dr. Vincent J. Lynch’s Genomics Lab at University of Chicago, now at University of Buffalo. Dr. Lynch’s background is in evolutionary biology, the discipline that studies which traits have been deemed successful by nature and which have not. Added to that is the fact that Dr. Kessler is a neurologist whose specialty is the study of stem cell biology in the nervous system, brain and spinal cord. Applying his expertise to seemingly unrelated endometrium and premature birth, Dr. Kessler brings a unique perspective to incorporate what we learn from evolution and apply that to the differentiation of stem cells to the cells that regulate human pregnancy. This approach has profoundly affected Cheung as a scientist and researcher in the field of premature birth.

“Being able to work with people studying the epigenetic and molecular signature of premature birth at the cellular level, as well as others working at the other PRCs in completely different areas, underscores the importance and magnitude of this effort.”

VIRGINIA CHU
NORTHWESTERN UNIVERSITY

“It’s impossible not to feel the support and motivation March of Dimes provides. It’s what encourages me to do good science, something every young researcher should aspire to.”

There’s currently no way to study the human maternal and fetal interface other than looking at the cellular interactions between a mom and her developing baby. The understanding we’ll gain from this work will allow us to develop and test new interventions and treatments before moving to clinical trials. If these new therapies work in our cellular models, we’ll know that they’ll be safe for moms and babies whose cells guided us to these solutions.
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:

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