PREGNANCY AFFECTS ALMOST ALL TISSUES IN A MOTHER’S BODY. UNDERSTANDING HOW PREGNANCY INDUCED CHANGES WORK ACROSS MULTIPLE TISSUES CAN OPEN EXCITING NEW WAYS TO UNRAVEL BIRTH TIMING?

“Everybody knows how to get pregnant; but nobody knows how pregnancy works,” said Dr. Sing Sing Way, Theme 2 Co-leader at March of Dimes’ Ohio Collaborative Prematurity Research Center. “It’s funny because it’s true, and gets at the heart of why pregnancy research is so complicated. Pregnancy has so many moving parts and those parts all interact with one another in intricate and complex ways. As a result, we don’t yet really understand why things go smoothly, let alone why they go wrong.”

There’s another reason why we don’t yet understand pregnancy and pregnancy complications. Traditionally, scientists have studied it through the lens they’ve specialized in. For example, we know hormonal changes have to occur during pregnancy, and people have studied that. We know anatomical changes have to occur in the uterus, so people have studied that. Immunological shifts also have to occur in the mother so she doesn’t reject the baby, which is genetically foreign, so people have studied that.

Until the advent of the transdisciplinary research pioneered by March of Dimes Prematurity Research Centers, scientists, researchers and doctors essentially worked in their own scientific silos without a forum for integrating their work across disciplines. But pregnancy is complicated, with changes across a mother’s multiple tissues and cell types. That’s why the Ohio Collaborative’s new Theme 2 is so important. For perhaps the first time, this Theme will explore the inter-relationship between two of the most important and powerful systems at work during pregnancy—the hormonal and the immunological—to understand with how they work together to determine gestational length and birth timing.

A great deal of study on the endocrine system has focused on progesterone because of its central role in reproduction. Progesterone is released by the ovaries and makes it possible for a fertilized egg to implant itself in the mother’s uterus. It suppresses ovulation for the duration of the pregnancy, and it drives anatomical changes in both the uterus, allowing it to accommodate the fetus, and the breast ducts, preparing them for breastfeeding immediately following birth. But how progesterone affects immune cells, and particularly the immune cells that protect the baby from attack and rejection by mother’s immune system has not been examined.

There is certainly plenty of evidence to support this innovative line of inquiry. Women who suffer from autoimmune diseases such as rheumatoid arthritis or multiple sclerosis report that their symptoms almost uniformly get better during pregnancy. Although the immune cells involved in autoimmunity and protecting the baby from rejection are not the same, if progesterone lessens the severity of autoimmune diseases, it’s very likely that it can also affect the function of other immune cells that allow the mother to tolerate the developing fetus.

“Our preliminary findings show that one of the key immune cells essential to healthy pregnancy contain a lot of progesterone receptors and respond to progesterone stimulation in a petri dish. So, understanding how progesterone works on this particular protective immune cell subset in the context of pregnancy is vital to our understanding how pregnancy works, and by extension, reasons for pregnancy complications,” said Dr. Way. “If we’re successful in showing the connection between these two systems, then I think we can develop innovate new hormone based and immunological based therapeutic strategies.”

The team assembled at the Ohio Collaborative is typically diverse, pulling in research teams from Case Western Reserve University, Cincinnati Children’s Hospital, faculty from Ohio State University and clinicians from Nationwide Children’s Hospital. Dr. Way was trained as an infectious disease pediatrician, and his expertise is understanding
Moms and babies in the U.S. are facing an urgent health crisis:

- 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 in the U.S. 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.

Because premature birth has many possible causes, each PRC is charged with exploring a different transdisciplinary research target that is likely to be crucial to the prevention of premature birth. To accomplish its goal the Ohio Collaborative has developed five interrelated theme areas, each bringing together renowned thinkers, researchers, physicians and top academics to focus on key aspects of the underlying causes of preterm birth.

Why the mother’s immune system responds to the baby as a foreign body. Joining him are Professor Sam Mesiano, Co-lead and Ph.D., with expertise in progesterone and progesterone receptor signaling, and Drs. Irina and Catalin Buhimschi, both expert in human pregnancy and its complications.

“One of the benefits of being a part of the March of Dimes Prematurity Research Center is that scientists who wouldn’t normally work together are able to collaborate and share their complementary expertise in new and exciting ways. From that perspective, we are grateful to March of Dimes for providing this extraordinary opportunity to expand the scope of research into the human pregnancy and the causes of preterm birth,” said Professor Mesiano.

**THEME 2 LEADERS**

**Sam Mesiano, PhD.**
William H. Weir, Professor of Reproductive Biology, Department of Reproductive Biology, Case Western Reserve University; Vice Chair for Research and Research Division Director, Department of Obstetrics and Gynecology, University Hospitals of Cleveland

**Sing Sing Way, MD, PhD.**
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For more information on how you can be a part of this effort, please contact:

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