Pregnancy places high demands on a woman’s bioenergetics, the human body’s system for energy conversion and consumption. But if for some reason the critical organs of gestation—the placenta, uterus, and cervix—are deprived of this much-needed chemical energy, many suspect it could be a major contributor to preterm birth.

This is a key premise of Theme One at the March of Dimes Prematurity Research Center at the University of Pennsylvania/Children’s Hospital of Philadelphia. A major part of the theme’s research will focus on mitochondria, which have been called the body’s “cellular power plants” and are found in every cell of the human body.

The hypothesis that will be tested in Theme 1 is that the deficits in the capacity of reproductive tissues to maintain bioenergetic and metabolic stability during the course of pregnancy are a significant cause of preterm birth.

“What’s amazing is that nobody has done any research on this that we are aware of,” adds Dr. Simmons. “This is exciting, pioneering work that is encouraged by the March of Dimes because research over the last 30 years has yielded such little progress in reducing preterm birth.”

**FOCUS OF THEME ONE**

To test the theme’s hypothesis, Dr. Simmons’ team will perform a complementary series of multifaceted investigations to test whether relevant reproductive tissues from mouse models and humans with preterm birth show mitochondrial dysfunction. And if so, what causes damage to mitochondria and how does it then impact pregnancy.

Theme One is linked to the studies of the microbiome and the cervix conducted by Dr. Elovitz’s team in Theme Two. “Bacteria in a microbiome affect how nutrients are metabolized,” says Dr. Simmons. “A byproduct of abnormal bacteria is inflammation and other abnormalities, including creating metabolites that might impair mitochondrial function.”

**GENES AND EPIGENETICS**

Theme One will also study how genetics or alterations in gene expression result in preterm birth. The mitochondria have their own set of genes which impact mitochondrial function. But are there certain mutations or genetic variants that may contribute to mitochondrial dysfunction leading to preterm birth? This question will also be addressed in Theme One by Drs. Neal Sondheimer and Sarah Tishkoff.

A new and growing field of inquiry is epigenetics, which is the study of how a person’s DNA is regulated by methylation. Methylation is a process that typically silences genes so they are not expressed. In effect, it turns off certain sections of the genetic code.

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Mitochondria disturbance has been implicated in several human diseases, including abnormal cardiac function and Type 2 diabetes, and they may play a role in the aging process. “Mitochondria regulate the most basic and critical functions of the cell,” says Rebecca Simmons, M.D., professor of pediatrics at the University of Pennsylvania and Co-Project Leader of Theme One. “We suspect that if you analyze placenta cell functions, for instance, and find the mitochondria are not working properly, then it’s likely the placenta will be unable to adequately support the fetus and deliver the right nutrients for development,” says Dr. Simmons.

This theme will attempt to understand why abnormalities in mitochondria, also known as “cellular power plants,” in the cells of the placenta and maternal reproductive tissues may be contributors to preterm birth.
A number of recent studies have supported the hypothesis that pregnancy-related risk factors can cause epigenetic modifications of the DNA, which may influence the risk of preterm birth.

HOPE TO ACHIEVE

Dr. Simmons’ team will seek to identify abnormalities in mitochondria function and mitochondrial DNA that contribute to preterm birth and ultimately hope this will lead to new ways to prevent preterm birth.

THEME 1 LEADERS

Rebecca A. Simmons, M.D.
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Pennsylvania, and the Children’s
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For more information on how you can be a part of this effort please contact: 914.997.4492

MARCHOFDIMES.ORG

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. The University of Pennsylvania has unique strengths in researching abnormalities in mitochondria, cervical remodeling and placental dysfunction.