

New study could lead to preeclampsia prevention

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Dr. Stella Goulopoulou, a postdoctoral fellow in the Medical College of Georgia Department of Physiology at GHSU, has received a \$25,000 Vision Grant from the Preeclampsia Foundation. Credit: By Phil Jones, Georgia Health Sciences University Photographer

Excessive turnover of cells in the placenta may trigger an unnatural increase in blood pressure that puts mother and baby at risk, researchers say.

It's called preeclampsia, a condition that can develop after the 20th week of pregnancy, prompting an unhealthy increase in the mother's blood pressure that can result in <u>premature delivery</u>. Georgia Health Sciences



University researchers want to know if dead placental cells in some cases produce an exaggerated immune response that constricts blood vessels and raises blood pressure.

"During pregnancy, there is a natural turnover of trophoblasts – the main cell type in the placenta," said Dr. Stella Goulopoulou, a <u>postdoctoral fellow</u> in the Medical College of Georgia Department of Physiology at GHSU. "In pregnancies with preeclampsia, we see exaggerated rates of <u>cell death</u> compared to normal pregnancies."

When those cells die, they can release their mitochondria, or powerhouse, which then binds to a key receptor, Toll-like receptor 9, and causes an <u>inflammatory response</u>. Previous research has linked mitochondria released by damaged or <u>dead cells</u> to inflammatory responses associated with <u>sepsis</u> and <u>heart failure</u>.

"Blood vessels, like other tissues, have receptors that respond to mitochondrial DNA and other components of the mitochondria," Goulopoulou said. "DNA from the mitochondria can specifically activate Toll-like receptor 9, which is present in blood vessels. In our experiments, we found that activating Toll-like receptor 9 causes the blood vessels to constrict more than normal."

Goulopoulou has received a \$25,000 Vision Grant from the Preeclampsia Foundation to study whether that is behind the generalized global inflammation and if that ultimately impairs the growing baby's supply of nutrients and oxygen. Vision Grants provide initial funding for novel lines of research to encourage young investigators to study causes and treatments of preeclampsia.

"The placenta is a dynamic tissue," she said. "We think it is the source of the mitochondria implicated in preeclampsia because it is the only tissue that undergoes such cell turnover during pregnancy. It also goes away, in



most cases, when the <u>placenta</u> and baby are delivered."

Preeclampsia is characterized by high blood pressure, protein in the urine – a sign the kidneys are stressed - and restricted growth of the fetus. It can also cause long-term damage to the mother's blood vessels, kidneys and liver. The condition causes approximately 76,000 maternal and half a million infant deaths worldwide each year. The symptoms—headaches, nausea, swelling, aches—can be indistinguishable from those of ordinary pregnancy, which can complicate diagnosis. Risk factors include first pregnancy, multiple fetuses, obesity, maternal age greater than 35 and a maternal history of diabetes, high blood pressure or kidney disease. Researchers suspect many different causes for the condition, and although mild cases may be treated with dietary modifications, bed rest and blood pressure medication, birth is the only cure, Goulopoulou said.

Goulopoulou is looking for a molecular explanation for what triggers Toll-like receptor 9 to signal the body's inflammatory response, leading to vessel constriction. "When vessels in the uterus constrict, it inhibits blood flow, oxygen and nutrient supply to the baby," she said. "So, increased uterine constriction could be responsible for restricting the baby's growth." Women with preeclampsia often have underweight and underdeveloped babies.

By injecting <u>mitochondria</u> from placental cells into pregnant rats, Goulopoulou expects to see an inflammatory response and symptoms of preeclampsia. She will also measure the levels of mitochondrial DNA in the circulation of women with preeclampsia.

"One of the main objectives of this study is to discover why and how activation of Toll-like receptor 9 by mitochondrial DNA causes abnormal function of the <u>blood vessels</u>," she said. "If it is determined that this receptor is responsible, it could be a valid therapeutic target."



Provided by Georgia Health Sciences University

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