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Scientists discover critical molecular biomarkers of preeclampsia

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Credit: Tel Aviv University

Preeclampsia, a sudden pregnancy complication that can interfere with the blood flow to the placenta and possibly to the fetus, can lead to low birth weight, prematurity and even death. It is also a leading cause of maternal mortality in the US. A new Tel Aviv University study identifies novel molecular biomarkers of preeclampsia, signaling the potential for an early diagnostic blood test.

Research for the study was led by Dr. Noam Shomron and Prof. Moshe Hod and conducted by Liron Yoffe and other lab members, all affiliated with TAU's Sackler School of Medicine, and in collaboration with Prof. Kypros Nicolaides of King's College, London. The conclusions were

published in the journal *Scientific Reports*.

"Up to eight percent of pregnant women may contract preeclampsia during their second or third trimester," Dr. Shomron says. "This is a serious disease that endangers the health, sometimes even the lives, of the mother and the fetus. We don't know what causes it, but preeclampsia, if caught in time, has a simple and proven remedy: low doses of aspirin administered from the 16th week until the end of pregnancy."

Turning to genetics

Until now, medical practitioners have assessed a woman's risk of preeclampsia by referring to previous pregnancies, blood pressure levels and other general symptoms. "But we sought a definitive biomarker that appears in a patient's blood as early as the first trimester, before any symptoms appear," Dr, Shomron explains. "Our findings form the basis for a simple blood test that would predict preeclampsia and, in turn, allow doctors to provide treatment that would prevent the very onset of the disease."

Over the course of six years, the researchers examined the blood samples from thousands of pregnant women in their first trimester from clinics in the UK. The team then narrowed their focused to 75 specific blood samples: 35 taken from women who eventually contracted preeclampsia, and 40 taken from those who completed their pregnancies in full health.

The researchers extracted the RNA molecules (snippets of molecular information present in human cells) from the plasma of the samples and sequenced these using Next Generation Sequencing (NGS). The scientists discovered the new biomarkers by analyzing the data using computational methods that included statistical analyses and machine learning algorithms.

"We identified 25 small RNA molecules that were differentially expressed between the preeclampsia and the control groups. Based on those RNA molecules, we then developed a model for the classification of preeclampsia samples," says Liron Yoffe. "These findings indicate the predictive value of circulating small RNA molecules in the first trimester, and lay the foundation for producing a novel early non-invasive diagnostic tool for preeclampsia, which could reduce the life-threatening risk for both the mother and fetus."

Early diagnosis leads to early prevention

According to Prof. Moshe Hod, the new research follows a global trend, which "seeks to establish pregnancy tests in the first trimester, as opposed to today, when most tests are performed in the third trimester."

Prof. Hod, the President of the European Association of Perinatal Medicine and Chairman of The International Federation of Obstetrics and Gynecology (FIGO) Committee that deals with maternal and offspring health, is leading a global effort to develop new diagnostic techniques to improve prediction and prevention of complications like gestational diabetes, preeclampsia and preterm birth in the first trimester of pregnancy.

"Early testing or prediction will allow doctors to safeguard the health of mother and fetus alike. It will also facilitate, if necessary, early preventive interventions to improve maternal and offspring's outcome," concludes Prof. Hod.

"The samples recently collected from other countries—Italy, Spain, Russia, and in particular Israel—will be used to apply our findings collectively to patients from around the world," adds Dr. Shomron.

More information: Liron Yoffe et al, Early Detection of Preeclampsia

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Using Circulating Small non-coding RNA, *Scientific Reports* (2018).
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