

LEMELSON-MIT



Mira Moufarrej
Stanford University

\$15,000 “Cure it!” Lemelson-MIT Student Prize Graduate Winner

Liquid biopsy tests to monitor prenatal health and identify high risk pregnancies, and a pipeline for high volume, customized pipetting in small labs

The Challenge: Pregnancy and childbirth can present risks to both mothers and babies worldwide, even in wealthy countries. Mothers can suffer pregnancy-related health conditions that may be life-threatening, or experience preterm birth, which can be detrimental to the development and well-being of the newborn. Preterm birth is the leading cause of infant death and one in ten babies worldwide is born preterm.¹ Preterm babies who survive are likely to be underdeveloped and require hospitalization in a neonatal intensive care unit (NICU). NICU care is not always available in small communities, and when it is available, it is expensive, costing an average of \$65,000 per person for the full care needed, and sometimes as much as \$4 million.² These costs fall to hospitals, insurance companies, and families who often spend thousands of dollars in deductibles. From a medical standpoint, preterm babies who survive are at high risk for a wide variety of health conditions throughout their lives, including cerebral palsy, asthma, attention deficit disorder, and learning disorders.

Pregnancy-related health conditions such as preeclampsia, a medical syndrome characterized by dangerously high blood pressure and signs of multi-organ damage, affect 1 in 25 expectant mothers in the U.S.³ and worldwide.⁴ According to the CDC, 60% of maternal deaths are preventable and often linked to undiagnosed pregnancy complications such as preeclampsia. Preeclampsia also results in an increased risk of cardiovascular problems for the mother and health issues for the baby, particularly if they are preterm. Preeclampsia disproportionately affects Black mothers in the U.S.,⁵ including Serena Williams and Beyoncé, who both suffered from the syndrome. In conjunction with already existing inequities in access to healthcare for women of color, preeclampsia can leave Black mothers especially vulnerable to catastrophic, medical outcomes.

Ultrasound, the primary method of prenatal monitoring and evaluation, cannot predict preterm birth or preeclampsia, so there is currently no way for medical professionals to know whether to intervene with

¹ World Health Organization 2018. <https://www.who.int/news-room/fact-sheets/detail/preterm-birth>.

² New York Times 2020. <https://www.nytimes.com/2020/02/11/parenting/nicu-costs.html>.

³ Center for Disease Control and Prevention 2020. <https://www.cdc.gov/bloodpressure/pregnancy.htm>.

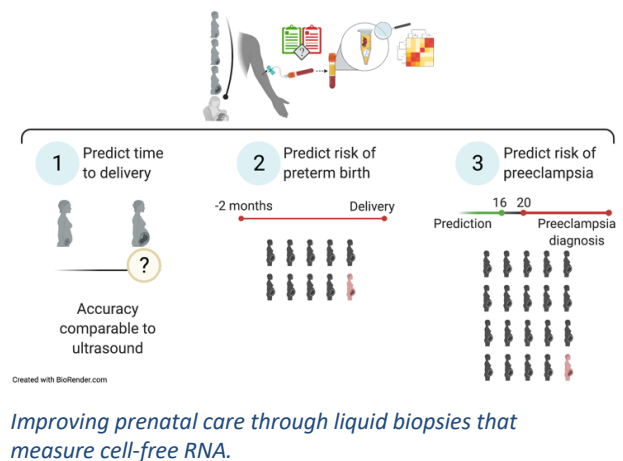
⁴ Abalos et al 2013. <https://pubmed.ncbi.nlm.nih.gov/23746796/>.

⁵ HCUP report 2017. <https://hcup-us.ahrq.gov/reports/statbriefs/sb222-Preeclampsia-Eclampsia-Delivery-Trends.jsp>.

possible treatments in a timely manner. According to Dr. Michael Elovitz, Director of the Maternal and Child Health Research Center at the University of Pennsylvania, doctors “just guess” which babies may arrive preterm. Although tests exist to triage mothers at risk for preeclampsia in the third trimester, no test exists to predict its onset. Preeclampsia’s early symptoms can also be vague and easily mistaken for normal pregnancy symptoms (e.g., headaches, dizziness, nausea), and the condition often goes underdiagnosed.

The Solutions: Mira’s primary invention is a new kind of non-invasive prenatal testing (NIPT). She developed a set of blood tests that dramatically improve the current standard in medical care to predict pregnancy-related complications, including preterm birth and preeclampsia. They work by taking a routine blood sample from the expectant mother and measuring a specific portion of the blood in the plasma, called cell-free messenger RNA, to provide early detection for these two dangerous conditions.

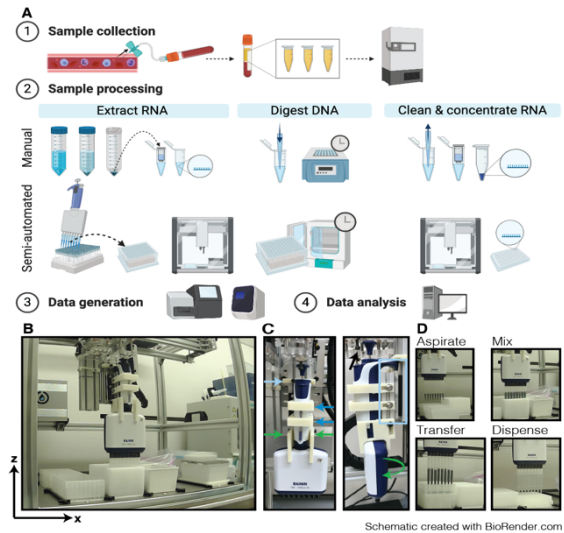
RNA is a messenger molecule that changes over time and under different conditions. During pregnancy it encodes messages, which can be measured in blood, that communicate what building blocks are needed to create the baby. Because RNA changes over time, it can provide information regarding how the pregnancy is progressing. The blood sample only needs to be taken from the mother, yet cell-free messenger RNA will glean information about both baby and mother.



Mira’s blood tests can be conducted in an outpatient setting. For both tests, prediction is sensitive and specific, meaning that the blood test accurately identifies when the condition is present (sensitive), and it does not erroneously predict the condition when it is not present (specific). The test for preterm birth can predict preterm birth two months ahead of time, with 80% sensitivity and 83% specificity. This predictive ability has been shown in mothers at risk for preterm birth, and studies are currently underway to confirm it in a broad range of mothers. The new RNA blood test for preeclampsia can predict the development of the medical condition in the first trimester, rather than the third trimester. In a proof-of-concept study this test has near perfect sensitivity and 88% specificity.

These two blood tests could change the standard of prenatal care by predicting risk earlier. Knowing they are at risk for preterm birth, families could identify the closest NICU facility in advance. If doctors are aware of the risk for preeclampsia earlier, they can work to prevent it by intervening with low-risk medications (for example, low-dose aspirin). Armed with objective data, pregnant mothers can ensure that their symptoms are addressed. This increased understanding of what is happening during pregnancy may also help scientists develop new medications to further manage complications. These tests also have the potential to save families, hospitals, and insurance companies millions of dollars.

Mira's secondary invention is a research pipeline that allows for semi-automated high volume, low cost, customized pipetting in small labs. It was used in her research while developing the preeclampsia test. Though large-scale labs have already moved to fully-automated robotic pipetting, small labs (such as some in academia) cannot afford the high cost of automated solutions (\$20K-\$100K) and have stuck to manual pipetting, which can be prone to human error. The semi-automated pipeline that Mira invented extracts RNA 12-fold faster, reduces costs by 3-fold and reduces biohazardous waste by 4-fold. Mira was able to process nearly 700 samples in 6 days, compared to the several months it would have taken manually.



An inexpensive semi-automated sample processing pipeline for cell-free RNA.

Commercialization: The market for non-invasive prenatal tests is \$3 billion and growing 17% annually.⁶ While most prenatal tests cost \$800-\$3,000 each (billed to insurance), Mira's diagnostic blood tests to predict preterm birth and preeclampsia are expected to cost less than \$100 each. Mira and her team expect that insurance companies will readily cover the costs of these tests, both because of the high societal and medical costs associated with these conditions and because there is already an established billing code for processing.

The technology for the blood test that predicts preterm birth is patented and has been licensed to Mirvie, a startup built around this technology under the guidance of Mira and her doctoral advisor at Stanford. A patent application for the technology for the blood test that predicts preeclampsia has been filed and will be licensed soon as well.

Mira's secondary invention of the semi-automated research pipeline would democratize large-scale research by allowing for large-scale sample processing within small research labs. She has shared this work in the public domain, including computer code and parts designs for 3D printing.

⁶ Fortune Business Insights. <https://www.fortunebusinessinsights.com/industry-reports/non-invasive-prenatal-testing-market-100998>.