Background: Preeclampsia is a pregnancy complication that develops in women during pregnancy and can result in serious or fatal complications for both mother and unborn child. Irregular formation of blood vessels in the placenta leads to preeclampsia, which is characterized by hypertension and damage to the organs in the mother’s body. The early symptoms of preeclampsia include hypertension and increased proteinuria or excess protein in the urine of a pregnant woman. Because of the subtlety of these symptoms, women are often unaware of their complication unless they receive routine prenatal care or their undiagnosed preeclampsia develops into a more severe and often life-threatening complication. In low and middle-income countries like Uganda, the average woman attends one prenatal care visit when she first realizes she is pregnant and does not return to receive health care until it is time for her to give birth or she is experiencing severe health problems.

Proposed Innovation: Our the team is developing a urine-based point-of-care early diagnostic test strip which expecting mothers can use at home to self-screen for preeclampsia so they know when to seek medical care. Without routine prenatal care screenings, knowing when complications are developing and when it becomes critical to seeking medical care is essential to the reducing the detrimental impacts of preeclampsia and eclampsia, and saving thousands of mothers and babies from preventable harm.

Urine Strip: Early indicators for developing preeclampsia include dramatically increased levels of the biomarkers activin A and inhibin A in a woman’s urine. The self-diagnostic tool will be a urine strip created by adapting lateral flow immunoassay technology to detect dangerous levels of these biomarkers in the urine of pregnant women. The test will inform the woman if she is developing preeclampsia and needs to seek medical care before her symptoms become severe and endanger the life of her and her unborn child.

Development Plan: Our 1-year goal is to develop a functioning prototype that can detect dangerous levels of the biomarkers activin A and inhibin A from a urine sample. This will be done with two parallel parts:
1) A small-scale clinical study at Mulago National Referral Hospital in Kampala, Uganda
2) Prototype development at BioMedomics in Durham, NC, USA.

Clinical Study
The first goal of this study is to verify the increase in biomarker levels as suggested by the literature holds true for our study population in Sub-Saharan Africa. The second goal is to quantify the levels of activin A and inhibin A to determine a cutoff value for the levels of biomarkers that indicate a normal pregnancy and the levels of biomarkers that indicate preeclampsia. This information will be used to determine what concentration of activin A and inhibin A the urine test strip needs to detect so a woman can determine whether she is at risk of developing preeclampsia.

The clinical study has received IRB approval from Makerere University School of Biomedical Sciences and administrative clearance from Mulago National Referral Hospital in Kampala. Patients will be enrolled and urine samples collected in the department of obstetrics and gynecology at Mulago. The laboratory analysis will be completed using standard ELISA test kits in the immunology facilities at Makerere University. This study is a case-control study that will be run in two parts based on funding availability. The first part will be a pilot study to enroll 20 case-control pairs and establish all clinical workflow logistics. The second part will be a full study enrolling 80 more case-control pairs in order to achieve statistical significance.

Urine samples will be collected from women enrolled in the study and analyzed using standard ELISA kits for activin A and inhibin A in the immunology lab at Makerere University. To analyze the data we will first create a descriptive table that stratifies the variables across different variables based on the demographic information collected from the women, including but not limited to: age, comorbidities, and place of residence. The independent variable of normal and preeclamptic pregnancy status will be compared using standard chi-square tests and the dependent continuous outcome levels of the biomarkers will be summarized and compared using a Chi square test.

Prototype Development
While the team in Uganda is conducting the clinical study, the team at Duke will be developing a prototype in the lab. The prototype will be an adaptation of existing lateral flow assay (LFA) technology, which is a commonly used test for rapid diagnostics.

For the preeclampsia diagnostic test, two test lines will be used – one to detect activin A and one to detect inhibin A. To create the test strip, conjugated gold nanoparticles will be used as receptors. The components will be sprayed onto a cellulose membrane and allowed to dry. After the strips have been assembled, the effectiveness of the strip to detect different levels of proteins will be verified. Once the full clinical study has been completed, the prototype can be tuned to detect the specific levels of activin A and inhibin A indicated by the study.