Overview/Abstract

No woman should die from cervical cancer, a disease that is highly preventable if detected and treated at an early stage. Yet, it remains one of the leading causes of cancer-related mortality in women worldwide [1].

Cervical cancer is caused by a persistent infection with high-risk human papillomaviruses (hrHPVs) [2]. HPV infection is the most common sexually transmitted infection and more than 80% of sexually active women will contract HPV at least once in their lifetime. Although most HPV infections of the cervix are benign and resolve spontaneously, persistent infections with hrHPVs result in precancerous lesions and cancer [2]. Regular screening is the most effective strategy to prevent cervical cancer [3, 4]. However, one in four women do not participate in regular screenings in the US [5].

The standard approach to cervical screening is a multistep process that includes: 1) collection of cervical specimens by a gynecologist, and cytology test (Pap test); 2) confirmatory diagnosis of women with a positive Pap test by colposcopy and biopsy; and 3) treatment. This approach requires multiple visits and skilled health care professionals at each step. Consequently, many patients are lost to follow-up and remain untreated. Alternatively, the screen and treat approach enables women to be screened and treated during the same visit without confirmatory diagnosis. Newer screening methods suitable for use in all settings such as the HPV DNA test and visual inspection with acetic acid (VIA) are used. This single-visit process reduces patient attrition and obviates the need for trained personnel. However, it results in unnecessary treatments as most HPV-positive women have benign infections and will not develop cervical cancer (**Fig. 1**).

Current screening methods have drawbacks. They are either expensive, invasive or anxiogenic. Crucially, they cannot provide any clues on whether the infection will progress to cervical pre-cancer or cancer. This results in overdiagnosis and overtreatment of women with HPV positive test results, which causes further anxiety for patients and an unnecessarily high burden on healthcare systems. There is an urgent need for optimal screening strategies that will allow efficient risk-stratification of HPV-positive women.

Our goal is to develop a test that will identify women that have an HPV infection that is progressing to cervical pre-cancer or cancer. We will develop a low-cost but high-end diagnostic test that combines cutting-edge microfluidics and molecular assays. We will tackle this challenge by combining 1) our innovative digital thermoplastic platform with 2) isothermal amplification assays for HPV E6/E7 mRNA trancripts**.** Our portable and handheld testing device will allow at home testing and at point of care. It will establish a framework for healthcare providers to effectively triage high-risk individuals for treatment while avoiding unnecessary follow-ups and invasive procedures for low-risk patients. Our innovative approach represents a paradigm shift in cervical cancer testing by switching from screening to detecting cancer (**Fig. 1**).

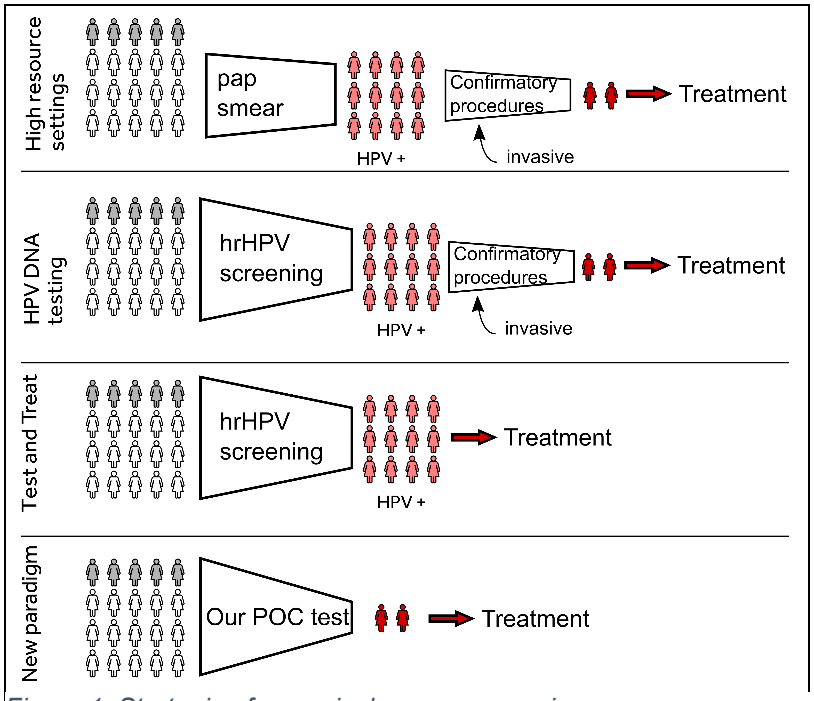

Figure 1. Strategies for cervical cancer screening.

The goal of this seed grant is to generate preliminary data that will de-risk the project and convince NIH reviewers to fund it. In this seed grant, we will develop a digital HPV16 E6/E7 mRNA assay and demonstrate that we can translate our assay for point-of-care testing.