

# Development of a low-cost Anti-Retroviral Treatment Failure Detection System for HIV Positive Patients

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The treatment of the Human Immunodeficiency Virus strain HIV-1 requires close monitoring of patient viral load in order to verify successful inhibition and suppression of retroviral replication. The impact of HIV drug resistance (DR) following the initiation of first-line antiretroviral therapy (ART) is an emerging issue of critical importance to the success of HIV treatment in developing countries. Current antiretroviral treatment involves regular viral load testing, which costs roughly \$80,000 in laboratory equipment and \$65 per test. Although these price points are within reach in the United States and Western European nations, patients and hospitals in limited-resource settings oftentimes cannot afford such testing or lack personnel and equipment for proper sample preparation and analysis. Doctors must instead monitor hematological, immunological and clinical parameters that all too frequently are unable to demonstrate drug-resistance until the disease has progressed into its more developed form of AIDS.

In order to confront these challenges, the Engineering World Health chapter at UCSD has launched a project to design a cost-effective point-of-care solution to screen HIV patients for ART drug resistance, using a nucleic acid test proven to detect early onset of drug resistance, thus enabling hospitals and clinics in the developing world to better diagnose and appropriately treat their patients.

Working with clinicians and virologists at the UC San Diego School of Medicine, Engineering World Health at UCSD has begun work to design automated devices for viral RNA

extraction, polymerase chain reaction (PCR) DNA amplification, and gel electrophoresis as a precise method to monitor for virologic failure of antiretroviral therapy (ART) in resource-limited settings. To increase affordability of the viral load test, a prototype is being developed with a price-point goal of under \$2000 with the capability of performing a pooled-sample assay developed at UCSD to screen patients for treatment failure at a reduced cost.

The prototype design is comprised of three distinct stages. First, a microfluidics system is used to automate the viral RNA extraction process from human blood serum. This stage aims to employ a gravity-based flow system that can aseptically isolate RNA with an adherent filter mesh. Using a pinch valve-manifold system, the design hopes to limit the number of disposables per screening. Second, a thermo-electric cooler based thermocycler used to run PCR. Initial prototyping has made use of Peltier effect heating technology couple with a heat-sink-cooling fan interface. Able to run up to six samples simultaneously, this initial design aims to achieve ramp rates of 2.0°C/sec. The assay protocol requires precise denaturation, annealing, and elongation temperatures of 95°, 50°, and 72°C. The thermocycler interface will include a liquid crystal display with real time temperature monitoring and built in protocol to simplify user operation. Last, the design of a gel electrophoresis box and high-voltage power supply will be to fit to the needs of the previous stages in an effort to reduce costs.

The drug resistance-screening assay will provide either a positive or negative result depending on the presence or absence of viral RNA in the patient's blood. By pooling the blood samples of five patients together, the number of tests required is significantly reduced, as more than half of patients are likely to test negative. With initial prototype completion projected for mid-2013, Engineering World Health at UCSD plans to validate prototype accuracy against current manually performed pooling standards in order to work towards the future adoption of HIV drug resistance screening in the developing world.