

Developing a Phenotypic Assay of HIV Drug Susceptibility in Africa

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Aims and Objectives

Antiretroviral therapy (ART) to treat HIV/AIDS in the developing world, including in Sub-Saharan Africa, is following a public health approach as advocated by the World Health Organisation. In this setting the close lab monitoring used in more developed countries, is not economically possible. Patients are monitored clinically, for example the development of AIDS like symptoms influences whether their prescription is changed. The evolution of HIV in patients receiving ART without monitoring is not well understood and the natural susceptibility of HIV from African patients has not been fully determined.

This small grant has allowed the transfer of reagents and a few preliminary experiments to study the characteristics of HIV from patients to be studied at the Uganda Virus Research Institute (UVRI) in Entebbe, Uganda.

Our previous work has demonstrated that natural variation in HIV can alter drug susceptibility^{1,2}. Molecular modelling methods, as used by Professor Peter Coveney, will be used to study possible mechanisms for this variation.

Preliminary Results

A proof of principle experiment has demonstrated that there is suitable lab infrastructure and equipment in Uganda for the project. Some preliminary results from a few Ugandan samples are shown in Fig 1. Lopinavir is an HIV protease inhibitor used in second line ART in Uganda.

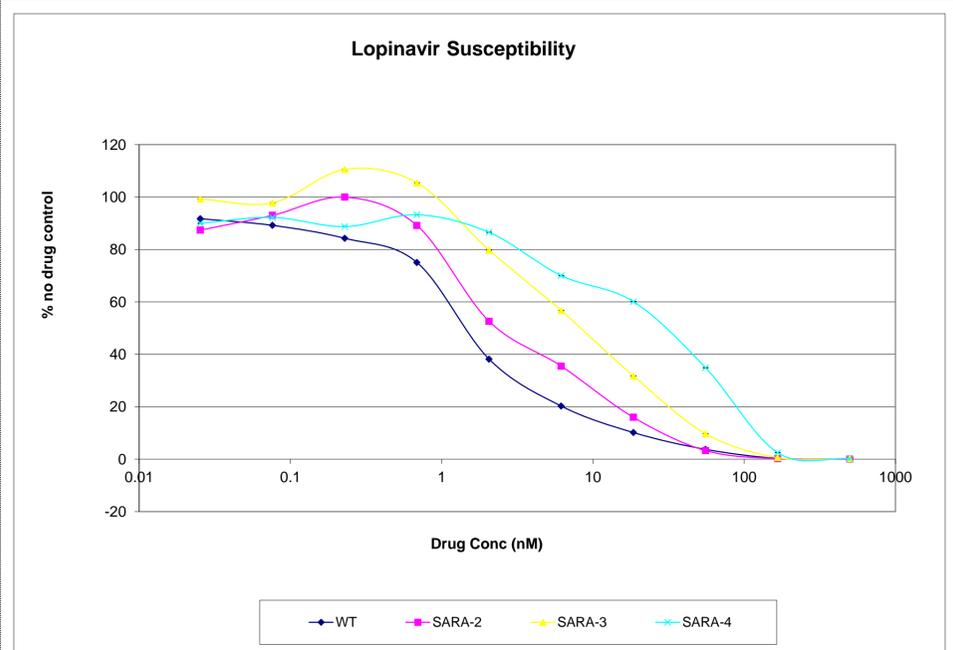


Fig 1: Lopinavir susceptibility curve. WT: Wild Type standard HIV strain. SARA-2 -3 and -4 are three HIV strains from Ugandan patients with out any known resistance mutations.

This graph shows that increasing the drug concentration reduces the amount of infectious virus. Low levels of the drug at the left of the graph shows near 100% infectivity. As the drug concentration increases (moving to the right of the graph) the infectivity reduces. All three Ugandan viruses need more drug than the standard “wild type” strain to reduce the infectivity to the same level (the curves are shifted to the right). Virus SARA-4 needs about 20 times more drug, despite not having any known resistance mutations.

Conclusions

- The HIV phenotypic assay has been successfully transferred.
- Preliminary results suggest some Ugandan viruses have reduced susceptibility to Lopinavir.

1: Gupta *et al* 2010 AIDS **24**: 1651-5;
2: Parry *et al* 2011 Antimicrob Agents Chemother. **55**: 1106-13