



Title of PhD project	Development of novel approaches for HIV drug resistance detection using nanopore sequencing technology	
Supervisor	Dr Damien Tully	LSHTM
Co-Supervisor	Dr Deogratius Ssemwanga	LSHTM
Co-Supervisor	Professor Pontiano Kaleebu	LSHTM
Brief description of project	<p>Antimicrobial resistance (AMR) is one of the greatest global health challenges. AMR can evolve in all groups of pathogens including viruses. Over the past decade, the world has witnessed an unprecedented increase in the use of antiretroviral therapy (ART) which has saved the lives of millions of people living with HIV/AIDS. Concurrent with the increased use of treatment has been the emergence of HIV drug resistance. This global rise in resistance to crucial HIV drugs has a significant clinical impact and threatens the significant progress that has been made in suppressing HIV. In Africa, this threat is particularly acute where several countries have reported levels of HIV resistance exceeding 10% to the standard first-line therapy.</p> <p>The advent of portable sequencing technology means viral genomic sequencing is now positioned to exert a greater public health impact to the upsurge in resistance. This project aims to develop a nanopore sequencing-based pipeline for HIV resistance genotyping. The student will optimize, evaluate, and validate the sequencing method using spiked plasma samples followed by a clinical evaluation from HIV-infected patients with known levels of drug-resistance. Lastly, it is proposed that the student will develop an open-source data processing and analysis pipeline for reporting HIV drug resistance. It is envisaged that this pipeline will support public health decisions and aid clinicians and laboratories in interpreting genotypic resistance. Taken together, this project will serve as the underlying basis for exploring how rapid viral sequencing can be best used in the future towards integration into local public health surveillance to decrease the incidence of drug resistance and onwards transmission.</p>	

	The student will benefit from a highly multidisciplinary supervisory team and will spend time at the MRC Uganda unit. This work is innovative, implements genome sequencing technologies and big data bioinformatics. This project is expected to yield scientific publications and deliver novel tools to support public health surveillance of drug resistance.
Skills we expect a student to develop/acquire whilst pursuing this project	The student will greatly benefit from expertise, networks and opportunities at both locations. This is a multidisciplinary project and the student will develop core skills in genomic sequencing, bioinformatics, phylogenetics, epidemiology and public health.
Particular <u>prior</u> educational requirements for a student undertaking this project	Students would benefit from some experience and prior skills in bioinformatics and/or laboratory skills. Students should demonstrate an interest and aptitude in the area of infectious disease and sequencing. Prior knowledge of HIV is also desirable.
Project key words	HIV Drug resistance Genomics Public Health Molecular epidemiology Evolution
Possible under 1+4 route? Master's options identified.	Yes LSHTM - MSc Control of Infectious Diseases LSHTM - MSc Epidemiology
MRC Core Skills developed through this project	Quantitative skills Interdisciplinary skills
MRC LID themes	Global Health Infectious Disease
Further reading	Rates of HIV-1 virological suppression and patterns of acquired drug resistance among fisherfolk on first-line antiretroviral therapy in Uganda Rapid metagenomic identification of viral pathogens in clinical samples by real-time nanopore sequencing analysis Towards a genomics-informed, real-time, global pathogen surveillance system