

**Dr. Graeme Jacobs, Life Sciences, Postdoctoral research scientist, Stellenbosch University, Private Bag X1, Matieland, 7602, Stellenbosch, South Africa**

## **Current NRF-Funded Project**

### **Short Title**

Tracking the molecular epidemiology and resistance patterns of HIV-1 in South Africa

### **Abstract**

HIV/AIDS is a major health problem in South Africa. There are an estimated 5.6 million people living with HIV/AIDS in the country. However, only 1.8 million people are receiving antiretroviral therapy (ART), with many more eligible. This is the highest number of people in a single country receiving long term ART. The genetic diversity of HIV-1 is dynamic as a result of the high evolutionary rate of the virus. In South Africa, HIV-1 subtype C predominates, spreading mainly via heterosexual transmission. In recent years we have detected more Circulating Recombinant Forms (CRFs) and Unique Recombinant Forms (URFs) in our study cohorts. This could be as a result of the changing epidemic in South Africa and warrants further investigation. The majority of research has been focused on clinical samples from the Western Cape, Mpumalanga, Gauteng and Kwazulu-Natal. Very little is known about the HIV-1 molecular epidemiology of HIV-1 in the rest of South Africa. Viral diversity clearly influences diagnostic assays and vaccine design strategies. It is still unclear what effects HIV-1 genetic diversity will have on the overall success rate of ART. Our research efforts will aim to track the inter and intra patient molecular epidemiology of HIV-1 in South Africa through modern genotyping methods. We will also investigate the resistance patterns of HIV-1 in our cohorts using the most recent available techniques. With more people having access to ART and genotyping testing, it will become crucial to identify the viral strains circulating in the country and within the various communities. By studying the viral sequences with phylogenetic and bioinformatics tools we may also be able to identify HIV-1 transmission patterns. This will help us identify target populations where intervention and treatment programs are most needed. The research will make a significant contribution towards understanding the spread of HIV-1 in South Africa.

### **Problem statement**

Southern Africa is in the grip of the most devastating HIV/AIDS epidemic in the world. According the latest UNAIDS and WHO estimates roughly one-third of the people living with HIV/AIDS in the world resides in the Southern African region. In South Africa an estimated 5.6 million people are currently infected with the virus, with an additional 280,000 dying each year from HIV/AIDS related diseases, such as HIV-associated malignancies. Although HIV-1 infection in South Africa has stabilized in recent years, an estimated 850 new infections still occur each day.

Thus, HIV-1 is a major health problem in South Africa with an average prevalence rate of 29.1% in pregnant women. High and unequal variations of prevalence are seen between the provinces of South Africa, with the Western Cape having the lowest prevalence (16.1%) and Kwazulu-Natal the highest (38.7%). One of the major features of HIV-1 is the extreme genetic diversity of the virus, which may impact on diagnostic assays, antiretroviral treatment (ART), prevention strategies and vaccine development. HIV-1 is constantly evolving, which leads to changing epidemics. HIV-1 subtype C is responsible for the majority of HIV-1 infections in the country, with other subtypes being detected sporadically. During the last 3 years we have identified an unusually large number of unique recombinant forms (URFs) of HIV-1 in three different provinces in South Africa (Western Cape, Mpumalanga and Gauteng). This may indicate a change in the dynamics of the predominant subtype C epidemic in South Africa. This phenomenon will be thoroughly investigated during this study.

Highly active antiretroviral therapy (HAART) has been shown to be very effective in improving the quality of life as well as the life span of individuals living with HIV/AIDS. In South Africa the national ART rollout program started in 2004. There are currently 1.8 million people receiving ART in the country - this is the largest number of people on ART in any one country in the world. In first world countries a baseline genotyping assay is considered essential for each HIV patient before the initiation of ART. This allows for the tracking of virus evolution and has led to an understanding of virological failure in individual patients receiving ART. This will be difficult to achieve in South Africa as the cost and logistics involved in managing so many patients on ART are far greater than anywhere else in the world. However, with more people having access to ART and genotyping testing, it will become crucial to identify the viral strains circulating in the country and within the

various communities. It will also be important to identify the most common viral resistance mutations impacting the success of ART. Therefore, this study will firstly identify the HIV-1 genotype within our cohorts and secondly identify the resistance mutations most commonly found in patients receiving ART. By studying the viral sequences of patients we can understand how the virus is evolving. This allows us to identify transmission clusters within our cohorts and communities and will help identify target populations where intervention and treatment programs are most needed.