

CFAR International

Project Staff: Jeff Martin, Diane Havlir, David Bangsberg, Steven Deeks, Allison Ellman, Richard Clark

Project Description: With the prevalence of HIV infection among young adults varying between 10% and 40% in individual countries, sub-Saharan Africa is the site of the most compelling public health crisis of our generation. Because the definitive solutions to this problem--potent preventive and curative interventions--are not in hand nor on the foreseeable horizon, continued investment is needed in understanding the natural history of infection in this region and the response to currently available therapeutic agents. In particular, because widespread availability of antiretroviral therapy is likely to occur in the next five years, it is essential to establish an infrastructure to evaluate the effects of these agents.

While the research questions for sub-Saharan Africa are numerous, the critical niche that the UCSF/GIVI Center for AIDS Research can uniquely fill is the same one it does in the US. That is, while many groups will be focusing on, for example, issues pertaining to the optimal systems for delivery of antiretroviral therapy in Africa, there exists an urgent need for high-quality research aimed at understanding the clinical, virologic, and immunologic outcomes once individuals are treated, and the mechanistic determinants of these outcomes. Given the many differences in biologic and sociocultural factors that exist in resource-limited versus resource-privileged regions (e.g., host genomic diversity, viral diversity, socio-economic barriers to adherence, endemic co-infections), there is ample reason to believe that treatment outcomes could vary from what has been observed in the US. Just as has been the case in the U.S., we believe that the strength of the UCSF/GIVI CFAR--a strong cadre of laboratory-based investigators who collaborate closely with clinical and behavioral scientists and epidemiologists to address translational questions of immediate clinical relevance--should be emphasized as the CFAR initiates its international work. Therefore, we have chosen to focus on a requisite first step in the conduct of translational research, the assembly of a cohort of well-characterized, longitudinally followed HIV-infected individuals. Because of a long-standing relationship between UCSF and the Makerere School of Medicine and the more recent coalescence of interest in Uganda by UCSF researchers, we have chosen to pursue this work in Uganda.

The long-term objective is to assemble a freestanding cohort of HIV-infected adults who are identified prior to their need for therapy (i.e. asymptomatic and CD4 + T-cell count 250 to 500 cells/mm³) and who are then followed as they progress to require therapy, and after they commence therapy. By selecting persons prior to initiation of therapy, we would have the opportunity to investigate the determinants of both untreated natural disease progression and disease course after therapy. In particular, an ample period of observation prior to initiation of therapy will allow for investigation of how pre-therapy parameters (e.g., T-cell activation) impact the response to treatment. Every other year the cohort would be supplemented by new recruitment in order to evaluate temporal epidemic trends and to have a continual stream of subjects at early stages of follow-up for the application of recently developed translational measurements.