



**PROFESSOR CLIVE GRAY**

**HIV-SPECIFIC CELLULAR THERAPY WITH PRIMED DENDRITIC CELLS AND ALLOGENEIC HIV SPECIFIC HLA MATCHED CYTOTOXIC T-LYMPHOCYTES**

**JAMES GEAR FELLOW: 1995**

Clive Gray was awarded the James Gear Fellowship in 1995, just after being awarded his PhD from the University of the Witwatersrand in 1994. He used his award to fund his post-doctoral fellowship at Stanford University, Center for AIDS Research (CFAR) with Dr Thomas Merigan. He spent the next 28 months performing HIV immunology research in the CFAR group. He was the first to describe the plasticity of the immune system in HIV infected adults and their ability to restore immunity in response to antiretrovirals (1998). Thereafter, he showed that when antigen is suppressed, the requirement for antigen-specific T cells diminishes, and that antigen (i.e. HIV) drives the immune response (1999). These are facts about HIV that are taken for granted today, but were novel and unknown at the time. In 1998, he returned to South Africa and to what was then the National Institute for Virology, NIV (today, the National Institute for Communicable Diseases, NICD). He formed an HIV immunology research group at the NIV and developed a dynamic team that went on to discover that there is a hierarchy of antigen recognition by T cells in HIV infected hosts, where if Gag is recognized first, the host can control virus and if Nef is recognized first, there is no viral control (2004). Prof Gray describe the early T cell response in acute HIV infection in African persons (2009) and was the first to describe the kinetics of anti-Gag CD4 and CD8 responses using polychromatic flow cytometry (2012). In 2011, Gray moved to Cape Town and became the Chair of the Division on Immunology at the University of Cape Town. Here, he strove to address gaps in the immunology curriculum and research at UCT to include translational science. At UCT, he began his second research group and began studying paediatric and reproductive immunology, both under-researched despite the large maternal and infant morbidity and mortality in Africa. He was the first to describe the risk of maternal vascular malperfusion in the placenta (2021), and that maternal

immune imbalance in HIV infected pregnant women is reflected in the placenta despite an absence of vertical transmission (2021). Events during pregnancy lead to altered immunity in infants born to mothers with HIV. Gray, using deep phenotyping and polychromatic flow cytometry, defined the ontogeny of T cell subsets in HIV exposed uninfected and HIV unexposed uninfected infants over the first 9 months of life (2021).

After a very successful decade as Chair of Immunology at UCT, he took early retirement (and is now Emeritus Professor) and moved to Stellenbosch University where he has started a reproductive immunology laboratory: the Reproductive Immunology Research Consortium in Africa (RIRCA). He is full Professor in the Division of Immunology in the Biomedical Research Institute. His current research group (being the third he has formed), is focusing on how alterations in the balance of T cells and macrophages in the placenta from pregnant people living with HIV cause adverse birth outcomes and poor infant health in the first 1000 days of life.

Not long after arriving at Stanford University, courtesy of the James Gear Fellowship, Gray decided to dedicate the remainder of his professional career to bettering basic and applied immunology in South Africa through research, teaching and training. He noted the lack of immunology training in Southern Africa and beyond and began a concerted effort to train South African scientists in flow cytometry and other techniques. His efforts to train South African immunologists have extended way beyond training of individuals. In 2005, Prof Gray founded Immunopaedia (<https://www.immunopaedia.org.za/>), which was funded through his International Leadership Award, a competitively funded award from the Elizabeth Glaser Pediatric AIDS Foundation. Immunopaedia is an innovative immunology learning tool for clinicians and basic science students that is kept up to date and heavily utilised by scientists all over the globe. Immunopaedia was awarded the SPORE prize in 2010 for innovation in on-line learning. In its almost 20 years of use, Immunopaedia is used on all continents and is also the official learning site for the International Union of Immunology Societies (IUIS). The site is used to train young junior scientists on immunology and since 2007, he has trained approximately 1200 students/early career immunologists in Africa, Latin America and India. To this end, Prof Gray started an Ambassador programme in 2016 of young investigators around the globe who use Immunopaedia as a way of connecting emerging scientists with common interests. After starting RIRCA at Stellenbosch University, Prof Gray initiated a reproductive immunology training programme: TIGRIS (Next Generation training in HIV research: Immunity in the first 1000 days in mother-infant dyads), funded by the US National Institutes of Health, with the plan to train 100 scientists in reproductive immunology over the next 5 years. Gray has funding for his research from the National Institutes of Health (R01, R21, D71), Canadian Institute of Health Research, European Commission, SAMRC, PRF and NRF. He has mentored/supervised multiple

MSc, PhD, PDF's and early career scientists over the past 25 years and has published widely (over 120 papers).

His time at Stanford University established Gray's ability to network and collaborate with the World's leading virologists and immunologists. He was the first to apply MHC tetramer analysis to humans and to identify how driving HIV to undetectable levels impacted on host immunity. These formative years shaped his scientific and teaching abilities and one of the most valuable lessons: to come up with new ideas, to implement them, to produce new knowledge and at the same time train the next generation of scientists.