BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Gray, Clive Maurice

eRA COMMONS USER NAME (credential, e.g., agency login): CLIVEGRAY

POSITION TITLE: Professor of Immunology in Molecular Biology and Human Genetics

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of Western England, UK	BSc (Hons)	11/1984	Applied Biology
University of the Witwatersrand, South Africa	MSc	12/1987	Immunology
University of the Witwatersrand, South Africa	PhD	12/1994	Immunology
Stanford University, Center for AIDS Research, USA	Postdoctoral	04/1998	HIV Immunology

A. Personal Statement

I have been involved in HIV-1 related research since 1995, and in 1996 I took up a post-doctoral fellowship at the Center for AIDS Research, Stanford University Medical Center. Here, I began to use polychromatic flow cytometry along with MHC tetramer staining. I was one of the first to describe restoration of immunity in HIV infected individuals receiving highly active antiretroviral therapy (HAART). My work provided one of the first insights into *ex vivo* antigen-specific CD8+ T cell dynamics. When I returned to South Africa, I built up an internationally recognized immunology laboratory from scratch at the National Institute for Communicable Diseases (NICD) which also became the only regional T cell end-point lab of the HIV Vaccine Trials Network (HVTN) outside of the US under my leadership. My research interests focused on immunopathogenesis of HIV and what constitutes survival and differentiation of antigen-specific memory T cells. I led a team to identify T cell responses to HIV in early/acute infection and showed that a less differentiated memory CD8 response correlated with low levels of *in vivo* HIV replication. I led the immunology of the South African AIDS Vaccine Initiative (SAAVI) and was part of the SAAVI development team for the DNA and MVA candidate vaccines that were later put into clinical trials. I played a leading laboratory role in the HVTN and in the Centre of the AIDS Programme of Research in South Africa (CAPRISA), where I was responsible for building up cellular HIV immunology in South Africa. On moving to the University of Cape Town (UCT), I started a research group to investigate the characteristics and functional capacity of T cells and other cell types in HIV exposed, uninfected newborn infants. This has great relevance for understanding abnormalities in immune regulatory networks and will provide clues to understanding susceptibility to HIV infection and in devising new treatments that can reduce the morbidities found in this vulnerable infant population. Over the last 5 years, I have been involved in understanding the human placenta and the impact of maternal HIV infection on cells at the feto-maternal interface. I have now established the Reproductive Immunology Research Consortium in Africa at Stellenbosch University (SU) and I will use my immunology research and teaching expertise to consolidate reproductive immunology.

Ongoing and recently completed projects that I would like to highlight include:
R21 HD103498-01
Chakraborty/Gray (PIs)
07/01/2020-06/30/2022
Mechanisms by which trophoblasts recruit T cells to the placental villi during maternal HIV and CMV co-infection.

R01HD102050-01
Gray/Jaspan (PIs)
04/03/2020 – 03/31/2025
Mechanisms leading to adverse birth outcomes in South African HIV-infected women.

U01AI131302-01
Gray/Jaspan/Blish (PIs)
03/11/2017 – 02/28/2022
Impact of HIV exposure, feeding status, and microbiome on immune ontogeny and vaccine responses in infants.

1R01HD080385-01 ML
Newell (PI). Role: co-investigator
2014-2020
ART and risk of preterm delivery in a rural high HIV prevalence area

R21HD083344-01
Gray/Jaspan (PIs)
2015-2018
Mechanisms of altered immune responses in HIV-exposed infants

Citations:

1. Ikumi NM, Pillay K, Tilburgs T, Malaba TR, Dzanibe S, Enninga EAL, Chakraborty R, Lamorde M, Myer L, Khoo S, Jaspan HB, **Gray CM**. T cell Homeostatic Imbalance in Placentae from Women with HIV in the absence of Vertical Transmission. J Infect Dis. 2021 Apr 21;. doi: 10.1093/infdis/jiab192. [Epub ahead of print] PubMed PMID: 33880544.
2. Ikumi NM, Malaba TR, Pillay K, Cohen MC, Madlala HP, Matjila M, Anumba D, Myer L, Newell ML, **Gray CM**. Differential impact of antiretroviral therapy initiated before or during pregnancy on placenta pathology in HIV-positive women. AIDS. 2021;35(5):717-726. doi: 10.1097/QAD.0000000000002824. PubMed PMID: 33724257.
3. Mdletshe N, Thobakgale C, Malaba TR, Madlala H, Myer L, Muema DM, Mogeni P, **Gray CM**, Altfeld M, Newell ML, Ndung'u T. Low immune activation in early pregnancy is associated with preterm but not small-for-gestational age delivery in HIV infected women initiating antiretroviral therapy in pregnancy: a PIMS case-control study in Cape Town, South Africa. Clin Infect Dis. 2021; doi: 10.1093/cid/ciab151. PubMed PMID: 33606024.
4. Kiravu A, Osawe S, Happel AU, Nundalall T, Wendoh J, Beer S, Dontsa N, Alinde OB, Mohammed S, Datong P, Cameron DW, Rosenthal K, Abimiku A, Jaspan HB, **Gray CM**. Bacille Calmette-Guérin Vaccine Strain Modulates the Ontogeny of Both Mycobacterial-Specific and Heterologous T Cell Immunity to Vaccination in Infants. Front Immunol. 2019;10:2307. doi: 10.3389/fimmu.2019.02307. eCollection 2019. PubMed PMID: 31649662; PubMed Central PMCID: PMC6793433.

B. Positions, Scientific Appointments, and Honors

Positions and Scientific Appointments

2021 - Present	Professor of Immunology in Molecular Biology and Human Genetics, Department of Biomedical Sciences, Stellenbosch University, Cape Town, South Africa
2021 - Present	Emeritus Professor of Immunology, University of Cape Town, South Africa
2011 - 2021	Wernher and Beit Chair, Professor and Head, Division of Immunology, University of Cape Town, South Africa
2003 - Present	Adjunct Professor, Department of Immunology, Duke University, North Carolina, USA
2016 - Present	Vice-Chair of the Education Committee, IUIS
2003 - 2010	Chief Specialist Scientist, National Institute for Communicable Diseases, Johannesburg, South Africa
1998 - 2003	Medical Natural Scientist, National Institute for Virology, Johannesburg, South Africa

2002 - 2010	Principal Investigator, NIH, HIV Vaccine Trials Network (HVTN) Regional Immunology Laboratory
2006 - 2011	Scientific Advisory Board, Biomarkers for Protective Immunity of TB in Africa, Grand Challenges in Global Health, GC6
2014 - 2017	President of the South African Immunology Society

Honors

2010	American Association of Immunologists: Science Prize for Online Resources in Education (SPORE), Science
2004	International Leadership Award, Elizabeth Glaser Pediatric AIDS Foundation
1999	Fogarty Fellowship, Fogarty AITRP, Columbia University
1995	James Gear Fellowship. Poliomyelitis Research Foundation, South Africa

C. Contributions to Science

1. My early publications focused on early and acute adult HIV infection and the polyfunctional nature of CD8+ T cells associated with low viral set-point. Due to the longitudinal nature of follow-up in our cohorts, we began to associate CD8+ T cell functional responses with viral load set point and disease progression. We showed that recognition of HIV-1, as measured by the IFNg ELISPOT assay, had no association with viral set point made at 12 months. However, polyfunctional CD8+ T cells and central memory cells could differentiate HIV-1 infected individuals with low set point, indicating that the quality and level of memory maturation is an important determinant of viral control.

a. Riou C, Burgers WA, Mlisana K, Koup RA, Roederer M, Abdool Karim SS, Williamson C, **Gray CM**. Differential impact of magnitude, polyfunctional capacity, and specificity of HIV-specific CD8+ T cell responses on HIV set point. J Virol 2014; 88(3): 1819-1824. PMID: 24227857; PMCID: PMC 3911608.
b. Chopera DR, Mlotshwa M, Woodman Z, Mlisana K, de Assis Rosa D, Martin DP, Abdool Karim S, **Gray CM**, Williamson C. Virological and immunological factors associated with HIV-1 differential disease progression in HLA-B 58:01-positive individuals. J Virol 2011; 85(14): 7070-7080. PMID: 21613398; PMCID PMC: 3126593.
c. **Gray CM**, Mlotshwa M, Riou C, Mathebula T, de Assis Rosa D, Mashishi T, Seoighe C, Ngandu N, van Loggerenberg F, Morris L, Mlisana K, Williamson C, Karim SA. HIV-specific IFN{gamma}-ELISPOT Responses targeting specific regions of the proteome during primary subtype C infection are poor predictors of the course of viraemia and set point. J Virol 2009; 83(1): 470-478. PMID: 18945774; PMCID 2612312.
d. Burgers WA, Riou, A, Mlotshwa M, Maenetje P, de Assis Rosa D, Brenchley J, Mlisana K, Douek DC, Koup R, Roederer M, de Bruyn G, Abdool Karim S, **Gray CM**. Association of HIV-specific and total memory phenotypes in subtype C HIV-1 Infection with viral set point. J Immunol 2009; 182:4751-4761. PMID:19342652; PMCID PMC 2792921.

2. Additionally, I investigated targeting conserved HIV-1 epitopes by T cells. Using the IFNg ELISPOT assay, we could identify conserved and dominant CTL epitopes and how these are associated with plasma viral load. This body of work contributes more directly to vaccine design, by identifying commonly targeted epitopes and identifying which ones are present across different clades and which are preferentially recognized.

a. Zembe L, Burgers WA, Jaspan HB, Bekker LG, Bredell H, Stevens G, Gilmour J, Cox JH, Fast P, Hayes P, Vardas E, Williamson C, **Gray CM**. Intra- and inter-clade cross-reactivity by HIV-1 Gag specific T-cells reveals exclusive and commonly targeted regions: implications for current vaccine trials. PLoS One 2011; 6(10): e26096. PMID: 22022524; PMCID: PMC 3192159.
b. Geldmacher C, **Gray C**, Nason M, Currier JR, Haule A, Njovu L, Geis S, Hoffmann O, Maboko L, Meyerhans A, Cox J, Hoelscher M. A high viral burden predicts the loss of CD8 T-cell responses specific for subdominant gag epitopes during chronic human immunodeficiency virus infection. J Virol 2007; 81(24): 13809-13815. PMID: 17898052 PMCID: PMC 2168820.
c. Masemola AM, Mashishi TN, Khoury G, Bredell H, Paximadis M, Mathebula T, Barkhan D, Puren A, Vardas E, Colvin M, Zijenah L. Katzenstein D, Musonda R, Allen S, Kumwenda N, Taha T, Gray G, McIntyre J, Karim SA, Sheppard HW, **Gray CM**. Novel and promiscuous CTL epitopes in conserved regions of Gag targeted by individuals with early subtype C HIV type 1 infection from southern Africa. J Immunol 2004; 173(7): 4607-4617. PMID:15383595.
d. Masemola A, Mashishi T, Khoury G, Mohube P, Mokgotho P, Vardas E, Colvin M, Zijenah L,

Katzenstein D, Musonda R, Allen S, Kumwenda N, Taha T, Gray G, McIntyre J, Karim SA, Sheppard HW, **Gray CM**. Hierarchical targeting of subtype C human immunodeficiency virus type 1 proteins by CD8+ T cells: correlation with viral load. J Virol 2004;78(7):3233-3243. PMID:15016844; PMCID: PMC 371059.

3. I am exploring different facets of infant and adolescent immunity that predispose individuals to HIV susceptibility at the cellular immune level. I am currently leading studies to investigate how maternal HIV exposure has an impact on different aspects of HIV exposed infant immunity.

a. Tchakoute CT, Sainani KL, Osawe S, Datong P, Kiravu A, Rosenthal KL, **Gray CM**, Cameron DW, Abimiku A, Jaspan HB; INFANT study team. Breastfeeding mitigates the effects of maternal HIV on infant infectious morbidity in the Option B+ era: A multicenter prospective cohort study. AIDS 2018 32(16):2383-2391. PMID: 30134300.
b. Tchakoute CT, Hesseling AC, Kidzeru EB, Gamieldien H, Passmore JS, Jones CE, **Gray CM**, Sodora DL, Jaspan HB. Delaying BCG vaccination until 8 weeks of age results in robust BCG-specific T cell responses in HIV-exposed infants. J Infect Dis 2014; 211(3):338-346. PMID: 25108027; PMCID: PMC 4318913.
c. Enninga EAL, Raber P, Quinton RA, Ruano R, Ikumi N, **Gray CM**, Johnson EL, Chakraborty R, Kerr SE. Maternal T Cells in the Human Placental Villi Support an Allograft Response during Noninfectious Villitis. J Immunol. 2020;204(11):2931-2939. doi: 10.4049/jimmunol.1901297. Epub 2020 Apr 22. PubMed PMID: 32321754; PubMed Central PMCID: PMC7307888.
d. Zulu MZ, Martinez FO, Gordon S, **Gray CM**. The Elusive role of Placental Macrophages: The Hofbauer Cell. J Innate Immun 2019; 11(6):447-456. PMID: 30970346; PMCID: PMC6758944.

4. Using these knowledge areas and devising training courses, I have gained a large body of expertise in holding workshops, immunology courses and devising on-line immunology materials for both Faculty and student learning.

a. Kabelitz D, Letarte M, **Gray CM**. Immunology Education Without Borders. Front Immunol. 2019;10:2012. doi: 10.3389/fimmu.2019.02012. eCollection 2019. PubMed PMID: 31555265; PubMed Central PMCID: PMC6724660.
b. Nemes E, Burgers WA, Riou C, Andersen-Nissen E, Ferrari G, **Gray CM**, Scriba T. Teaching advanced flow cytometry in Africa: 10 years of lessons learned. Cytometry A. 2016 Nov;89(11):971-974. doi: 10.1002/cyto.a.23015. PMID: 27870536; PMCID: PMC5326675.
c. **Gray CM**, Loubser S, Kriel C, Mercer M, Brookes, HJ. Immunology for Clinicians: A Trojan Horse Approach. Science 2010; 329:1613-1. DOI: 10.1126/science.1186963; PMID: 20929838.

Complete List of Published Work in MyBibliography:
https://www.ncbi.nlm.nih.gov/myncbi/clive.gray.1/bibliography/public/