Contribution ID: **7** Type: **Poster Presentations**

Mapping the Epitope: Defining the Structure of the Highly Immunogenic Env-CD4 Complex

Tuesday, 17 November 2015 18:24 (2 minutes)

The HPRU has focused on the development of an effective prophylactic HIV vaccine which utilizes a novel immunogen called gp120-2dCD4S60C that consists of a human two domain CD4 with a S60C mutation covalently bound to monomeric gp120. This covalent complex acts as a "super immunogen" in pre-clinical studies in rabbits, where it elicits potent and broadly protective neutralizing antibody responses against HIV-1 Tiers 1, 2, 3, HIV-2 and SIV pseudoviruses. Prior to initiating further preclinical development of the gp120-2dCD4S60C vaccine immunogen in rhesus macaques, it would be critical to characterize and define the structure of the immunogenic HIV-1 gp120-2dCD4S60C complex, and ultimately fine map the specificities of the potent, broadly neutralizing antibodies elicited by the gp120-2dCD4S60C complex in rabbits. The broad aim of this study is therefore to characterize the structure of gp120-2dCD4S60C as compared to gp120 bound to 2dCD4WT. Resolving the architecture of the immunogenic gp120-CD4S60C complex will ultimately be important for defining the structures of the exposed target epitopes of potent neutralizing antibody responses, as compared to those of native non-covalent complex formed with wild-type CD4. Both low-resolution (small-angle x-ray/neutron scattering – SAXS/SANS) and high-resolution (synchrotron X-ray crystallography) structural information will be obtained in collaboration with the Institut Laue-Langevin and European Synchrotron Radiation Facility (ILL-ESRF), both based in Grenoble, France. Only preliminary data has been gained thus far, but it will ultimately assist in gaining insights into the underlying mechanisms of the antiviral activity that will guide strategies for optimizing CD4-based immunogens that will likely provide protection from infection.

Primary author: Dr OWEN, Gavin (HIV Pathogenesis Research Unit, Department of Molecular Medicine and Haematology, University of the Witwatersrand)

Co-authors: Prof. PAPATHANASOPOULOS, Maria (University of the Witwatersrand); Dr KILLICK, Mark (HIV Pathogenesis Research Unit, Department of Molecular Medicine and Haematology, School of Pathology, Faculty of Health Science, University of the Witwatersrand); Dr HAERTLEIN, Michael (Institut Laue-Langevin, Partnership for Structural Biology); Dr CERUTTI, Nichole (HIV Pathogenesis Research Unit, Department of Molecular Medicine and Haematology, School of Pathology, Faculty of Health Science, University of the Witwatersrand); Prof. FORSYTH, Trevor (Keele University); Prof. MITCHELL, edward (ESRF)

Presenter: Dr OWEN, Gavin (HIV Pathogenesis Research Unit, Department of Molecular Medicine and Haematology, University of the Witwatersrand)

Session Classification: Poster Session

Track Classification: Main