Contribution ID: **19** Type: **Poster Presentations**

# Structural Studies on the Purified Cxcr4 Expressed by Cell-Free

*Tuesday, 17 November 2015 18:10 (2 minutes)*

Membrane proteins constitute up to 30% of the genome and have extremely important roles in many biological processes such as signal transduction, or the substrate transport energy production. Economically, existing drugs targeting GPCRs generate annually nearly $ 25 billion in the world economy. It is therefore essential to have a thorough understanding of their structures and their dynamics to understand their functions and / or their failures to develop new specific active molecules of these receptors.

CXCR4 is a membrane protein of the family of G-coupled receptors (GPCR) which we are using as a well-characterised model system for this project. CXCR4 is a chemokine receptor for the SDF-1 (CXCL12), which is involved in chemotaxis of lymphocytes. Additionally, CXCR4/SDF-1 is known to be important regulator of haematopoiesis, and deregulation of its function has been linked to carcinogenesis. Of most interest however, is the role of CXCR4 as a co-receptor required for HIV infection.

Recombinant GPCR proteins are typically extremely difficult to produce in cellular expression systems due to namely, poor yields, aggregation and misfolding. Using the cell free technology and the experience of Synthelis, we aim to remove these barriers. Using CXCR4 as our model, the first objective of the project is to obtain a proof of concept of the feasibility of effectively purifying GPCRs from proteoliposomes. Upon purification, CXCR4 shall be characterised both structurally and functionally using techniques available at Synthelis and ILL/ESRF. We shall for instance assess its binding to its native ligand, SDF-1. Additionally, with the expertise of the University of Witwatersrand (Johannesburg, South Africa), we also shall seek to demonstrate the binding of gp120 viral protein, and viral particles, to CXCR4. Ultimately, we wish to obtain structural insights of the protein using SANS/SAXS and potentially, X-ray crystallography. In parallel with the work on the CXCR4 model system other, but uncharacterised, proteins benefitting from the unique capabilities of cell-free expression will be studied.

**Primary author:** Mr JUGNARAIN, Vinesh (ESRF/ILL/SYNTHELIS/WITS/UJF)

**Co-authors:** Mr TILLIER, Bruno (SYNTHELIS); Mr MITCHELL, Edward (ESRF); Mrs PAPATHANASOPOULOS, Maria (WITS); Mr HAERTLEIN, Micheal (ILL); Mrs CORTES, Sandra (SYNTHELIS); Mr FORSYTH, Trevor (ILL)

**Presenter:** Mr JUGNARAIN, Vinesh (ESRF/ILL/SYNTHELIS/WITS/UJF)

**Session Classification:** Poster Session

**Track Classification:** Main