SEMINAR

Department of Biological Sciences

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Hosted by Dr Lu Gan

Structural Studies of HIV-1 Neutralization by Broadly Neutralizing Antibodies

Reza Khayat

Research Associate at The Scripps Research Institute

The HIV envelope glycoprotein (Env) is composed of three copies of the gp120/gp41 heterodimer. Env is necessary for gaining HIV entry into the cell, and is the sole known target of neutralizing antibodies by the immune system. The Env glycans, being extensive and variable, act as the shield by which HIV evades the humoral immune response. However, the recently identified potent and broadly neutralizing antibodies PGT128 and PG9 directly interact with the Env glycan shield to neutralize HIV. Moreover, both antibodies interact with the variable regions of gp120 (regions exhibiting greatest sequence diversity among HIV isolates). To better understand how these antibodies interact with the Env glycan shield and the highly variable regions to neutralize HIV, we used a combination of biochemistry, X-ray crystallography, and electron microscopy. The biochemical studies provide the potency and specificity of the antibodies, the crystallographic studies produce an atomic description of the interaction between each antibody and portions of the gp120 monomer, and the electron microscopy studies place these interactions in the context of a complete Env trimer and potentially the virus.

About the speaker

I started my scientific career by obtaining a Bachelor of Science in Chemistry from University of California, Irvine. Then I moved to New York city where as a doctoral student of Liang Tong at Columbia University I used a combination of X-ray crystallography, biophysics and biochemistry to study the mechanism by which the Human Cytomegalovirus (HCMV, a herpesvirus) protease is regulated, as well as carry out structure activity relationship studies for inhibitor design against this protease. HCMV infects 40% of the adult population worldwide and can be life-threatening for immuno-compromised individuals. This protease is crucial for the life cycle of HCMV and is therefore an excellent target for therapeutic design.

Then I moved back to California where I combined electron microscopy with X-ray crystallography in the laboratory of Jack Johnson at The Scripps Research Institute to study the architecture, assembly, and life-cycle of non-enveloped viruses such as the archaeal Sulfolobus Turreted Icosahedral Virus, Flock house virus, and porcine circovirus 2. I then moved to the laboratory of Ian Wilson where I implemented a high-throughput platform for electron microscopy to study how the humoral immune system neutralizes enveloped viruses such as HIV and influenza for structure-assisted vaccine design.

My talk will encompass two recent publications in the laboratory of Ian Wilson where I studied the neutralization of HIV by infected individuals. These individuals do not exhibit symptoms of acquired immune deficiency syndrome (AIDS).