

Microsymposium

MS16.O06

Broad Neutralization of Viral Pathogens

I. Wilson¹

¹*The Scripps Research Institute, Department of Integrative Structural and Computational Biology, La Jolla, USA*

Influenza, Hepatitis C, and HIV-1 continue to constitute significant threats to global health. We have structurally and functionally characterized several potent, broadly neutralizing antibodies (bnAbs) against HIV-1, influenza and hepatitis C viruses. The surface antigens of these viruses are the main target of neutralizing antibodies. However, most antibodies are strain-specific and protect only against highly related strains within the same subtype. Recently, a number of antibodies have been identified that are much broader and neutralize across multiple subtypes and types of these viruses through binding to functionally conserved sites, such as the receptor binding site or the fusion domain. For example, co-crystal structures of bnAbs with influenza hemagglutinin (HA) identified highly conserved sites in the fusion domain (stem) and in the receptor binding site (head) as target for broad neutralization[1]. HCV is also genetically diverse, but some antibodies have potent neutralizing activity across most genotypes of the virus. One family of these antibodies targets a conserved antigenic site on the HCV E2 envelope glycoprotein that overlaps with the CD81 receptor-binding site[2]. For HIV-1, structural and functional characterization of different families of bnAbs have led to identification of novel epitopes on HIV-1 Env, many of which involve glycans. These glycan-dependent Abs have unique features that enable them to penetrate the glycan shield and bind complex epitopes that consist of sugars and underlying protein segments on gp120 on HIV-1 Env. Recent x-ray[3] and EM structures of a soluble form of HIV-1 Env have revealed that the epitopes are more extensive and complex than previously appreciated. This structural information is now being used to aid in structure-assisted vaccine design for HIV-1, HCV and for a more universal flu vaccine. IAW is supported by NIH grants AI100663, AI082362, AI84817, AI099275 and GM094586 and the Crucell Vaccine Institute.

[1] N. S. Laursen, I. A. Wilson, *Antiviral Res.*, 2013, 98, 476-83, [2] L. Kong, E. Giang, T. Nievesma, et al., *Science*, 2013, 342, 1090-4, [3] J. P. Julien, A. Cupo, D. Sok, et al., *Science*, 2013, 342, 1477-83

Keywords: antibody, influenza, HIV