Poster H-89

Conservation and Correlation Analyses of the V3 Sequences of HIV-1 Envelope Proteins

Authors:
Shuo L. Lin (*Wyeth Vaccines Research*)
Robert Zagursky (*Wyeth Vaccines Research*)

Short Abstract: A large collection of HIV-1 gp120 V3 loop sequences was analyzed by a variety of computational methods to reveal patterns of genetic conservation and correlation. These patterns were related to viral phenotypes and to the interactions between gp120 and host molecules.

Long Abstract:
Human immunodeficiency virus-1 (HIV-1) displays a variety of phenotypes with regard to syncytium induction, chemokine receptor usage, and sensitivity to antibody neutralization. Strong evidence exits suggesting an association between these phenotypes and the sequence variation of the V3 loop on the viral surface envelope glycoprotein (gp120). However, the pattern of association is far from simple, and it is mixed with those arising from various genetic phenomena such as virus subtype, epidemic history, and patient-dependent mutations. Despite the intricacy, definitive patterns and methods to detect them are continuously being proposed. They continue to be refined and applied to the rapidly growing HIV-1 sequence data. In this study, we employed a number of approaches to analyze thousands of V3 sequences currently collected in the HIV Sequence Database (http://hiv-web.lanl.gov). By pairwise comparison, we identified isolates suggestive of different mechanisms of sequence conservation, such as regional epidemic and functional restriction. By site-wise conservation measures, we found both agreement and deviation from certain promising pattern proposals. By measures of site covariance, we identified sites that were likely to co-evolve to preserve functionality. We mapped these sites onto the three-dimensional gp120 structure with intact V3 loop, recently solved by X-ray crystallography, to uncover possible effect of their variation to the structure of gp120 and its interactions with host molecules.