

**POSTER 6****DC-SIGN DETERMINANTS NECESSARY FOR HIV-1 AND DENGUE VIRUS INTERACTIONS**

Nancy P.Y. Chung<sup>1</sup>, Jaideep M. Karamchandani<sup>1</sup>, Thomas D. Martin<sup>1</sup>, Ted Pierson<sup>2</sup>, and Vineet N. KewalRamani<sup>1</sup>

<sup>1</sup>HIV Drug Resistance Program, NCI, Frederick, MD; <sup>2</sup>Laboratory of Viral Diseases, NIAID, Bethesda, MD

Dendritic cell-specific ICAM-3-grabbing nonintegrin (DC-SIGN) is a 44 kD C-type lectin that is expressed as a tetramer on the surface of myeloid-lineage DCs, activated B cells, and macrophages subsets. DC-SIGN interacts with a number of pathogens including HIV, SIV, CMV, Ebola virus, and dengue virus as an attachment receptor facilitating *cis*- or *trans*- infection. Prior studies demonstrated that human Raji B cells expressing DC-SIGN efficiently capture and transmit HIV to susceptible target cells. However, liver/lung/ lymph node-specific ICAM-3-grabbing nonintegrin (L-SIGN), a DC-SIGN related molecule with 77% amino acid identity, is less effective in virus binding and transmission. To understand the molecular differences between DC-SIGN and L-SIGN in HIV transmission efficiency, Raji lines expressing DC-SIGN/L-SIGN chimeras with different domain compositions were made. Chimera analysis revealed that replacement of the DC-SIGN carbohydrate recognition domain (CRD) with the L-SIGN CRD was sufficient to impair virus binding and transmission. By contrast, virus binding was observed in L-SIGN chimeras containing the DC-SIGN CRD. We further analyzed the contribution of DC-SIGN-specific residues within the CRD and observed residues 253 to 288 to be necessary for virus binding and transmission. Mutagenesis of this proximal region revealed that DC-SIGN W258 was required for virus transmission. Consistent with HIV transmission requirements, DC-SIGN mutants W258K/A also impaired dengue virus infection. By contrast, these DC-SIGN mutants were capable of ICAM-3 binding. Based on the crystal structural of the DC-SIGN CRD, W258 is distal from the carbohydrate recognition and calcium binding sites, which are critical for ligand binding and specificity, but may affect overall conformation or interactions between CRD tetramers. Further studies are underway to identify residues within the DC-SIGN CRD that interact with W258 and influence glycoprotein selectivity.