

POSTER 1

IDENTIFICATION OF RESIDUES WITHIN THE L-SIGN CARBOHYDRATE RECOGNITION DOMAIN (CRD) THAT INTERACT WITH WEST NILE VIRUS

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The C-type lectins DC-SIGN and L-SIGN are tetrameric type II integral membrane proteins, which serve as attachment receptors for a variety of enveloped viruses including retroviruses (HIV and SIV), flaviviruses (West Nile virus, Dengue virus, and hepatitis C virus), and the SARS-Coronavirus. Prior studies have shown WNV preferentially infects cells expressing L-SIGN but not DC-SIGN. Given their similarity in structure, chimeras between DC-SIGN and L-SIGN were made and expressed in Raji cells to study the differences in receptor usage by WNV. Chimera analysis revealed that replacement of the L-SIGN CRD with the DC-SIGN CRD was sufficient to prevent WNV infection. We further analyzed the contribution of L-SIGN-specific residues within the CRD and observed that residues 265 to 300 in the N-terminal CRD segment and residues 338-399 in the C-terminal CRD segment were required for infection. Point mutational analysis in both the N-terminal and C-terminal CRD segment demonstrated that H267 and N379 were required for WNV infection. Interestingly, introduction of the P255H mutation in DC-SIGN and a C-terminal L-SIGN CRD subdomain supported WNV infection. Based on the crystal structure of L-SIGN CRD, H267 is located at the junction between the neck and CRD domain. It is conceivable that mutating H267 in L-SIGN may alter the trajectory of CRD and the overall stability of tetramer on the cell surface, resulting in impaired WNV interaction. Further characterization of these structural determinants will provide insights on the design of inhibitors to block WNV infection with C-type lectins.