Computational Prediction of Influenza Receptor Specificity

Robert J. Woods

Complex Carbohydrate Research Center, Department of Biochemistry and Molecular Biology, University of Georgia, Athens, GA 30602, USA

Email: rwoods@ccrc.uga.edu

Hemagglutinin (HA) mediates attachment to and entry of influenza virus into host cells by binding to sialic acid receptors at the cell surface. Human influenza viruses preferentially bind to sialic acid linked to galactose by alpha-2,6 linkages; the main type found on the epithelial cells of the human upper respiratory tract. Avian viruses tend to bind to alpha-2,3 linkages that are found predominantly on avian intestinal epithelium. All influenza A viruses that have infected mammals emerged as some point from avian species. Changes in the amino acid sequence of HA can alter the sialic acid specificity of influenza viruses, with the change of one or two amino acids being sufficient to change the receptor binding specificity and affect interspecies transmission barriers.

We report computational docking (using AutoDock) and Molecular Dynamics simulations (using the GLYCAM force field) [1] of human and avian receptor – HA complexes, based on structural data for the human 1934 H1 influenza strain. The theoretical methods correctly predict that this H1 hemagglutinin is selective for human alpha-2,6 linkages and provide insight into the origin of the affinity differences, but also indicate limitations of current simulational and docking methods.

1. Kirschner KN, Yongye AB, Tschampel SM, Daniels CR, Foley BL, and Woods RJ. GLYCAM06: A Generalizable Biomolecular Force Field. Carbohydrates. J Comput Chem 2007, Early View (DOI: 10.1002/jcc.20820).