Evolving an Epidemic: Optimizing Sialic Acid Receptor Configurations to Increase the Binding Affinity of Avian Influenza H5N1 to Human Cell Glycoproteins

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Avian influenza, or bird flu, has been present since the early 20th century, with the first outbreak recorded in Scotland in 1959. Notable outbreaks occurred in the late 1990s and early 2000s, notably involving the H5N1 strain, which gained global attention due to its severe impact on poultry and occasional transmission to humans, resulting in fatalities. The virus targets specific receptors on host epithelial cells: sialic acid alpha 2,3 (SA a2,3) receptors, preferentially bound by avian influenza viruses, and sialic acid alpha 2,6 (SA a2,6) receptors, primary targets for human influenza viruses. Understanding receptor specificity helps explain the limited human-to-human transmission of avian influenza viruses, as they are adapted to target avian receptors. This project aims to investigate the potential alteration of receptor specificity by optimizing the configuration of sialic acid receptors. Utilizing GNINA software on Colaboratory, we will dock both of the SA a2,3 and SA a2,6 receptors with the virus's hemagglutinin protein to predict optimal configurations and affinities. After analyzing the results of the docking, we can gain a better understanding of the changes that are needed in the position and the geometry of the sialic acid receptors to not only increase its affinity to SA a2,3 (which it already naturally binds to) or increasing its affinity to SA a2,6 (which would overcome the receptor specificity). In either case, this could lead to the ability for the virus to spread from human to human and yield a possible epidemic. Our research endeavors to illuminate how altering receptors can increase affinity between viruses and human cell glycoproteins, furthering efforts to develop drugs and vaccines combating viral infections and diseases.