

Hemagglutinin in Action

Hemagglutinin is a deadly molecular machine that targets and attacks cells. This occurs in several steps. First, the three binding sites at the top of the spike bind to sugars on cellular proteins, shown in green at the top left (PDB entry 1hge ②). Then, the whole virus is carried inside the cell into the endosome and the cell adds acid, which normally digests the stuff inside the endosome. But in the case of the virus, the acidic environment serves to arm the attack mechanism. In acid, hemagglutinin unfolds and then refolds into an entirely different shape. The portions shown in orange and red are normally folded against the protein, but in acid, they pop out and point upward, as shown in the center illustration (PDB entries 1htm ②, 1ibn ② and 2vir ③). The red portion, termed the fusion peptide, has a strong affinity for membranes, so it inserts into the cell membrane and locks the virus to the cell. Then, as shown on the left (PDB entry 1qu1 ②), the yellow portions zip up the side of the protein, pulling the two membranes close together. Finally, the new conformation of hemagglutinin somehow causes the two membranes to fuse—that part is still not well understood—and the viral RNA flows into the cell, starting the process of infection.

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