Virus Entry

Inhibition of Influenza Virus Activity using multivalent Particles
(BA, MA thesis)

Influenza virus infection starts with binding of the virion to the target membrane of the host cell (Fig. 1a). During this first step the viral glycoprotein hemagglutinin (HA) binds to sialic acid (SA) sugars on the surface of the host cell. The virus enters the cell by receptor mediated endocytosis. The endosomal maturation leads to an acidification of the lumen which induces a large scale conformational change of the HA. This consequently leads to fusion of the viral membrane with the endosomal membrane and to the release of viral content. In frame of the project we investigate the effect of synthetic multivalent inhibitors (Fig. 2b) on the different stages of influenza infection. Furthermore we want to gain insights into the molecular functioning of multivalency.

Projects:
1. Study of the lateral mobility and diffusion rate of HA trimers after heterologous expression in mammalian cells. Effect of the inhibitors on the mobility and trimerization of HA using confocal microscopy of fluorescently labelled HA.
2. Evaluating the specificity of the inhibitors. Vesicular stomatitis virus (VSV) and Sendai Virus invade their host cells via similar mechanisms to influenza virus. The aim of this project is to study the effect of the inhibitors on binding, fusion and infection of VSV and Sendai Virus.

Methods: Fluorescence Spectroscopy / Microscopy, FACS, Virus- / Cell culture, heterologous expression

![Fig.1: (a) Replication cycle of an Influenza Virus (b) Model of the synthetic inhibitor. The molecule exposes multiple copies of the natural HA ligand sialic acid (SA)](image)

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