## The Virus-Host Interaction

Virus-host interactions are the drivers of all outcomes of an infection and can occur in the host at numerous levels; the cell, the individual and also the entire community, helping to drive evolution. The host is an extremely hostile environment, which must be overcome by viruses in order to transmit and persist. Interactions occur during every stage of the viral life cycle, from the first point of contact with a cell to when the virus leaves the cell. Recognition of a virus triggers a cascade of responses resulting in the production of interferon, which is the first line of defence for host cells. The release of interferon is comparable to the rallying of troops, sent out to protect neighbouring settlements from attack. The surrounding cells put up their shields and enter an antiviral state preventing further spread of the invading virus. In this essay I shall focus upon the virus-host interactions arising at the entry of viruses into host cells and the subsequent strategies cells have developed to prevent this invasion. I shall also discuss how these interactions affect the host on a larger scale leading to the evolution of defence mechanisms, and how viruses have helped to shape this process.

The consequences of an interaction between a virus and its host partially depend upon the host proteins that the virus comes into contact with. There are host proteins called restriction factors which function to block viral replication, while others called host dependency factors are required by viruses to complete their replication cycles. The host has a plethora of these restriction factors which are germ line encoded and are capable of signalling to the innate immune system. These factors appear in many different parts of the cell to block specific stages of the virus life or explore that aid to block viral fusion. Fusion and entry into cells are an essential part of the virus life cycle, without which a virus cannot replicate its genome and transmit to other cells. Therefore this is a logical stage for host cells to restrict.

Host-cell bird og is etween the virus and a cell, leading to subsequent nrst point of mere t fusion and entry. Different viruses have different cell tropisms depending upon their viral glycoproteins (gp) and the host membrane proteins that these gp's recognise. E.g. HIV-1 utilises two viral gp's on its envelope; gp120 and gp41. Gp120 has a binding site which recognises the host receptor CD4, which is present on a number of host immune cells including CD4 T cells, macrophages and dendritic cells. This is the first interaction occurring between the virus and the host, and it defines the cellular tropism of HIV-1. The entry of HIV-1 into cells also requires a co-receptor, either CXCR4 or CCR5. This extra level of interaction further defines cellular tropism of the virus. The binding of gp120 induces a conformational shift, resulting in the exposure of the hydrophobic terminus of gp41. Gp41 is a fusion protein. All enveloped viruses must undergo virus-cell fusion into order to enter a cell, whether at the cell membrane or at the endosome membrane. Fusion is a tricky process of merging two separate plasma membranes into one. HIV-1 gp41 has two heptad repeat regions, HR1 and HR2, which have repeating amino acids sequences (Furuta et al., 1998). These sequences interact with each other causing the formation of a trimeric hairpin motif (prehairpin intermediate) which is inserted into the host membrane. This allows the host and viral membranes to be brought into close proximity with each other, referred to as apposition. This conversion of the fusion peptide into an embedded hairpin is a common feature of all enveloped viruses despite the diversity of their fusion peptides, and is triggered by either receptor binding, e.g. HIV-1, or a low pH, e.g. Influenza A virus.