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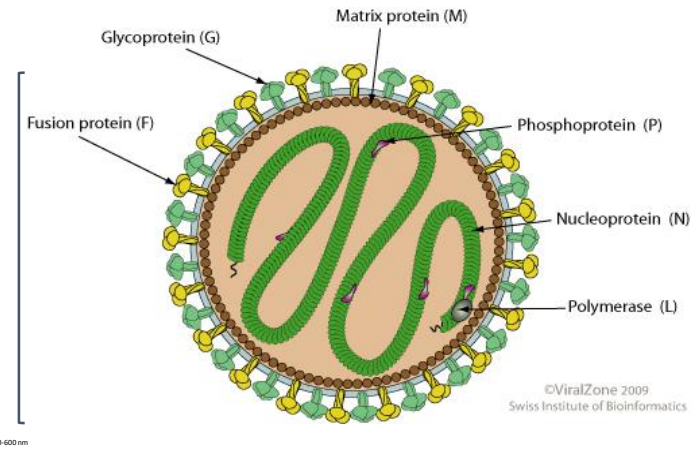

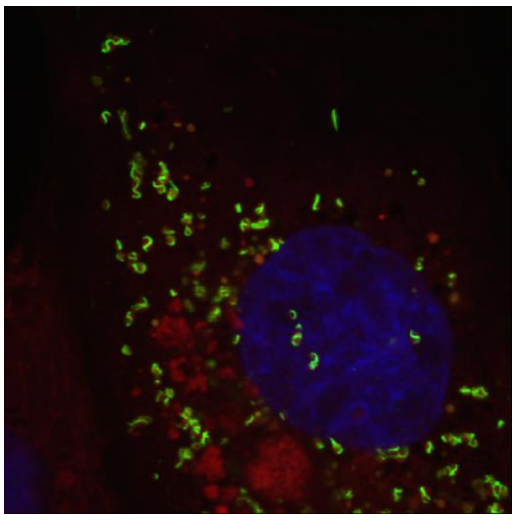

BATS, HUMANS and NIPAH VIRUSES

The World Health Organisation has included henipaviruses in a list of nine select agents with the potential to cause a public health emergency and for which there is an urgent need for accelerated R&D attention. Nipah (NiV) and Hendra (HeV) viruses are immediately relevant for Australian health and biosafety. These highly pathogenic viruses can be transmitted from animals to humans, through contaminated food/biological fluids and from human to human.

The reservoir of NiV and HeV was found to be pteropid fruit bats (flying foxes) based on serological evidence and virus isolation. For HeV, flying foxes have a seroprevalence of 73%, an impressive number suggesting an endemic infection of the bat population throughout Australia and near major cities. Surprisingly, although bats are carriers of NiV and HeV and excrete active viruses in their urine, faeces and saliva, they show little signs of illness themselves.

Our laboratory is developing a combination of comparative virology and comparative immunology to discover

(1) which protein interactions are important for immunomodulatory effects and determination of the virulence of NiV
(2) why bats are resistant to these viruses that are highly pathogenic to humans. Bats are unique animals with very different metabolism and unusually long lifespan, and their innate immunity is radically different from ours.

We use single-molecule techniques and protein-protein interactions assays to study protein binding and protein self-association. We will build on our previous studies and focus specifically on the concept of polymerisation-driven amplification of signalling in innate immunity. Human and bat proteins have interesting differences in protein sequence, and we have already found that MAVS and MyD88 have a dramatic increased propensity to polymerise compared to their human orthologs; this suggests that bats have evolved to hyper-activate pathways to resist interference by viruses. **We propose two projects for 6-months to 1-year internships:**

Project 1- comparative virology: interaction of henipaviruses with innate immunity proteins
We will study the binding of the viral proteins M and P (C/V/W) to the components of the major human innate immune signalling pathways, focussing on the disruption of large signalling platforms.

Project 2- comparative immunology: proteins of the innate immunity of humans and bats
Here, we will discover whether the equivalent bat proteins have dampened/enhanced ability to form self-assemblies and understand molecular origins of our weakness and bat resistance to viruses.

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