

The Structure of the Influenza A Virus Genome

Content

The IAV genome consists of eight single-stranded viral RNA (vRNA) segments contained in separate viral ribonucleoprotein complexes (vRNPs) that are packaged together into a single virus particle. The structure of the vRNA is believed to play a role in assembling the different vRNPs into budding virions and in directing reassortment between established human influenza viruses and influenza viruses harboured in the animal reservoir. Reassortment can lead to the emergence of novel influenza strains to which there is little pre-existing immunity in the human population. While previous studies have revealed the overall organisation of the proteins within vRNPs, characterisation of vRNA structure using conventional structural methods is hampered by limited resolution and an inability to resolve dynamic components.

We have employed multiple high-throughput sequencing approaches to generate the first global high-resolution structure of the IAV genome. We find that different IAV genome segments acquire distinct RNA conformations and form both intra- and inter-segment RNA interactions inside influenza virions. We demonstrate that this extensive network of RNA-RNA interactions is required for the assembly of the viral RNA genome and virus replication. We then used our detailed map of IAV genome structure to provide the first direct evidence for how inter-segment RNA interactions drive vRNP co-segregation during reassortment between different IAV strains. This work is a roadmap both for the development of antivirals targeting key RNA interactions and for the creation of a framework to 'risk assess' reassortment potential to better predict the emergence of new pandemic influenza strains.

Choose primary session

Visualising Flu

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Viral Replication

Contribution Type : Oral presentation