

Probing an evolutionary bifurcation to host shut-off

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To infect its host, influenza A virus (IAV) critically depends on its ability to shut-off host cell gene expression. When infected, host cells activate defence-gene transcription whose protein-products interfere with viral propagation and induce an anti-viral state in neighbouring cells. A major contributor to IAV-induced host-cell shut-off is the non-structural protein 1 (NS1), which interferes both with gene activation and mRNA 3' end cleavage. The latter inhibits mRNA polyadenylation and nuclear export of cellular mRNAs thereby effectively preventing translation of newly induced genes, including those required to warn bystander cells. How - when host shut-off is active - can infected cells signal to bystander cells? We have identified a set of transcripts that escape host shut-off, some of which encode secreted messengers with the potential to establish the innate immune response to IAV infection.

NS1-mediated shut-off through disrupted transcription termination is well-characterised in human adapted strains but is absent in most studied zoonotic strains. Conversely, during adaptation of the zoonotic A/California/07/2009(H1N1) (pdmH1N1) to the human population, NS1 gained the ability to interfere with cellular transcription termination. How - if not through NS1-action - is host shut-off achieved in zoonotic IAV strains? We will present a hitherto unidentified mechanism of host shut-off that appears to be active in a range of zoonotic strains of the H5N1 clade 2.3.4.4.b.

Keywords

host shut-off, host pathogen interaction, host adaptation, mechanisms of gene expression control, innate immunity, bystander versus infected cells.

Professional status of the speaker

Senior Scientist

Junior scientist status

No, I am not a junior scientist.

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