Exploring the molecular inter-relationship of SRPK1 and SRSFs during Human Rhinovirus (HRV)-infection and their subsequent effects on viral replication

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Introduction

- Human rhinoviruses (HRV A, B, C) are causative agents of more than half of upper respiratory tract infections globally[1].
- Infections in immunocompetent individuals are self-limiting, but can lead to major respiratory complications in immunocompromised groups such as pre-school children and the elderly[1].
- A link between HRV infection in pre-school children and asthma development in adulthood has been proposed[2].
- The precise molecular mechanisms underlying this pathophysiology remain elusive, as does the aetiology of the enhanced disease severity in HRV-C infections.

Objective

To explore whether HRV alters splicing regulatory factors (SRSFs) and their regulatory kinase (SRPK1) and any downstream effects on viral replication and respiratory epithelial cell function.

Discussion

- In vivo data indicated differential expression of SRPK1 in HRV-C infected children. There were correlations between SRPK1 gene expression and several SRSFs genes.
- Treatment with the kinase inhibitor SRPIN340 and RNA-interference can reduce the activity and protein expression levels of SRPK1 in the epithelial cell lines HeLa Ohio and A549.
- Preliminary studies show altered SRPK1 and SRSF levels following HRV16 infection in A549 cells.

Future directions

- Compare and contrast HRV-A and HRV-C effects on SP proteins levels and localisation.
- Translate observed effects in 3D cultures of differentiated primary respiratory epithelial cells.
- Determine effect of SRPK1 inhibition/knock-down on viral replication.
- Determine specific splicing events affected along with their roles in epithelium integrity and antiviral immune response via RNA sequencing.

References