NANYANG TECHNOLOGICAL UNIVERSITY

School of Biological Sciences

Research Theme: **Virology**

Research Project Title: **Signalling pathways that mediate respiratory syncytial virus morphogenesis**

Principal Investigator/Supervisor: **A/Prof Richard Sugrue**

Co-supervisor/ Collaborator(s) (if any): NA

Project Description

a) Background

The mature respiratory syncytial virus (RSV) particles form at the cell surface with a filamentous morphology and are referred to as virus filaments. The involvement of lipid-raft microdomains and F-actin in RSV morphogenesis has been demonstrated, and we have demonstrated an the F-actin dependent intercellular transmission involving hydroxymethylglutaryl coenzyme A reductase (HMGCR) activity. HMGCR is a key regulatory enzyme in cholesterol biosynthetic pathway and its enzyme activity can be specifically inhibited using statin-based drugs. Lovastatin treatment inhibited virus filament formation and virus transmission (, suggesting that this is a viable antivirus strategy, but this inhibitory effect was not directly due to impaired cholesterol biosynthesis. Our studies have suggested that the drug acts by inhibiting the F-actin remodeling that is essential for RSV morphogenesis. This project will establish the signaling networks involved in RSV assembly and elucidate the mechanism of action of anti-viral of lovastatin.

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2. Ravi LI, Liang L, Wong PS, Brown G, Tan BH, **Sugrue RJ**. (2013) Increased hydroxymethylglutaryl coenzyme A reductase activity during respiratory syncytial virus infection mediates actin dependent inter-cellular virus transmission. Antiviral Res. 2013 Aug 28;100(1):259-268.

3. . Radhakrishnan A, Yeo D, Brown G, Myaing MZ, Iyer LR, Fleck R, Tan BH, Aitken J, Sanmun D, Tang K, Yarwood A, Brink J, **Sugrue RJ**. (2010). Protein analysis of purified respiratory syncytial virus particles reveals an important role for heat shock protein 90 in virus particle assembly. Mol Cell Proteomics. 9(9):1829-48.

4. Jeffree, CJ; Brown, G; Aitken, J; Yeo Su-Yin, D; Tan BH and **Sugrue RJ**. (2007). Ultrastructural analysis of the interaction between F-actin and respiratory syncytial virus during virus assembly. Virology

b) Proposed work

Cell biology, biochemistry and basic virology methods will be employed

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