



BIOLOGY COLLOQUIUM

Friday, 24 Mar 2017 | 4pm | DBS Conference Room 1

Hosted by A/P Ganesh Anand

Understanding the Neurovirulence of Enterovirus 71

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Enterovirus 71 (EV71) is a non-enveloped, positive-stranded RNA virus that causes Hand, Foot and Mouth Disease, and that is regarded as the most important neurotropic virus worldwide. Although the route of EV71 neuroinvasion remains debatable, current studies support the retrograde axonal transport as a major route of EV71 to reach the central nervous system (CNS), whereby the virus infects motorneurons at the neuromuscular junctions and employs a retrograde axonal transport mechanism to eventually reach the brain. Here we report a novel in vitro model of EV71 infection using NSC-34 motor neuron cell line to investigate the intrinsic neurovirulence potential of EV71. NSC-34 cells exhibit high morphological and physiological resemblance to neurons at neuromuscular junctions, thus suggesting that they may represent a relevant in vitro model to study EV71 neurovirulence. Our work indicates that NSC-34 cells are permissive to EV71 infection with production of infectious viral particles in the culture supernatant. However, unlike in muscle RD cells, EV71-infected NSC-34 cells did not display cytopathic effect and did not undergo apoptosis, suggesting a non-lytic virus release process. In addition, up-regulation of autophagic markers was observed in EV71-infected NSC-34 cells, which may suggest the ability of EV71 to hijack the autophagic pathway for its exit, similar to what has been previously described with poliovirus. Finally, the ability of EV71 to infect productively NSC-34 cells correlated with its ability to invade the CNS in vivo, supporting the relevance of NSC-34 cells to study the intrinsic neurovirulence of EV71 strains.

As the mechanisms of EV71 neuroinvasion remains unclear, study of EV71 infection cycle in this novel in vitro model may provide further understanding of viral pathogenesis in the CNS.

