SIgN Immunology Seminar



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Structural and biochemical characterisation of the interaction between alphavirus protein nsP3 and the host stress granule protein G3BP

Host
Dr Lisa Ng
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Date
Thursday
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Time
11am – 12pm

Venue
SIgN Seminar Room
Immunos Building
Level 4
Biopolis

Stress granules (SGs) are dynamic aggregates of proteins and translationally silenced mRNA that form in cells upon various stress conditions, including virus infection. The Ras-GAP SH3 domain–binding proteins (G3BP) are essential regulators of SG formation. Many viruses including chikungunya virus (CHIKV) block SG induction by targeting G3BP. We recently demonstrated that the G3BP-binding motif in the nonstructural protein nsP3 of Semliki Forest virus (SFV) and CHIKV consist of two FGDF motifs, in which both phenylalanine and the glycine residue are essential for binding. In addition, we showed that binding of the cellular protein USP10 and also the herpes simplex virus protein ICP8 to G3BP are also mediated by FGDF motifs. Overexpression of WT nsP3 but not mutants lacking the FGDF motifs blocks SG assembly. We also present a three-dimensional crystal structure of the G3BP NTF2-like domain bound to an FGDF-containing peptide, likely representing a binding mode shared by many proteins to target G3BP. The FGDF-mediated G3BP binding represents an attractive target for therapeutic interventions against a range of diverse viral infections.