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INVESTIGATING THE ROLE OF NS2B DYNAMICS IN DENGUE VIRUS NS3 PROTEASE FUNCTION

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The proteins of the dengue virus are expressed as a single polyprotein, which is then processed proteolytically into individual functional fragments by proteases from both the host and the virus itself. The viral protease is the N-terminal domain of the non-structural protein 3 (NS3pro) and is an attractive target for drug-based therapeutic intervention. NS3pro by itself is expressed in the inclusion bodies and requires a 47-residue hydrophilic region of the non-structural protein 2B (NS2B) for its correct folding and enzymatic activity. As NS2B is flexible and dynamic, existing crystal structures are unable to give a complete picture of the NS2B-NS3pro complex for drug development. A method inspired by a recent paper was used for the partial isotopic labelling of the NS2B-NS3pro complex, which simplifies the multidimensional spectra obtained through nuclear magnetic

resonance (NMR) experiments. We aim to find out how the dynamics of NS2B contributes towards the proteolytic activity of the dengue virus NS3pro, through various NMR dynamics experiments. Relaxation dispersion data reveal that the C-terminal portion of NS2B unfolds itself around 4% of the time. Mutants of NS2B were generated to explore how both the dynamics and protease activity change with the mutations.

Biography

Kenneth Lee is currently doing his PhD in the Department of Biological Sciences, of the National University of Singapore. He is expecting to complete his PhD in 2018.

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