Poster Presentation

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Small angle X-ray scattering studies of flaviviral NS3

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Dengue virus is an arthropod-borne flavivirus which consists of four antigenically distinct serotypes (DENV 1-DENV 4). Infections by the dengue virus cause dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS). These diseases have emerged as a global concern for human health and are most prevalent in tropical and subtropical regions. The Dengue virus genome is an 11 kb positive-strand RNA. It comprises of a single open reading frame that encodes a single polyprotein. This polyprotein is co-translationally and post-translationally processed by the host cell and viral proteases into three structural (capsid, membrane and envelope) and seven nonstructural proteins (NS1, NS2A, NS2B, NS3, NS4A, NS4B and NS5). NS3 plays an important role in polyprotein processing and viral replication and hence is considered a target for the development of antiviral inhibitors [1]. It is a two domain protein connected via a linker. The N-terminal domain is a serine protease while the C-terminal domain possesses RNA helicase, nucleoside and RNA triphosphatase activities. Small angle X-ray scattering of the NS3 from DENV-2 reveal the protein to be extended and flexible in solution. The importance of the linker residues in flexibility and domain-domain arrangement was shown by the compactness of the individual protease and helicase domains [2]. Swapping of the 174PPAVP179 linker stretch of the related hepatitis C virus (HCV) NS3 into DENV-2 NS3 did not alter the elongated shape of the engineered mutant [2]. For the first time SAXS studies of NS3 of Zika virus (ZIKV) were performed, demonstrating that the protein is elongated and flexible in solution. The comparison of ZIKV NS3 and -NS5 solution data with the related DENV nonstructural proteins shed light into the similarities and diversities of these classes of enzymes. Furthermore, enzymatic studies unravel the interaction and effects of resveratrol- and quercetin-binding in ZIKV NS3 [3].

[1] Xu, T. et al. (2005). J. Virol. 79(16), 10278-88.
[2] Pan, A. et al. (2017) Acta Crystallogr. D. Manuscript submitted.
[3] Saw, W.G. et al. (2017). Antiviral Res. 141, 73-90.

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