Projekt 3 (P3): Biophysical Characterization of putative amphipathic helixes in Dengue Virus proteins NS4A and NS5

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Summary

Dengue virus (DENV) infection is a growing public health problem with more than one-third of the world population at risk. DENV is a mosquito-transmitted virus that causes dengue fever, dengue hemorrhagic fever and dengue shock syndrome. There is no vaccine available for DENV and no specific treatment for dengue fever. DENV is believed to replicate its RNA genome in association with modified intracellular membranes. To better understand how the replication complex components anchor to the intracellular membranes we focus on the DENV non-structural proteins 4A (NS4A) and 5 (NS5), which shows stretches of conserved putative amphipathic helices (AH). Mutations inside these putative AHs negatively affect viral replication. AHs are known to be involved in membrane binding, membrane remodeling and protein-protein interactions. The project focuses on the characterization of the structure and function of these putative AHs, by using biophysical techniques like circular dichroism spectroscopy (CD), surface plasmon resonance (SPR) and nuclear magnetic resonance (NMR) spectroscopy both in absence and in presence of membrane mimicking detergent micelles or nanodiscs.