

Targeting viral membrane proteins *in silico*.

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Abstract

Many viral membrane proteins interact with membrane proteins of the host to steer the cell for a successful mass production of novel virions. The viral proteins rely on selective interactions of their transmembrane domains (TMDs) with those of the host protein. An understanding of the modalities of recognizing the proper host target, on the revers, can be turned against the virus.

Getting insights into the specificity of binding, the interaction of oncoprotein E5 of human papillomavirus-16 (HPV-16), an 83 amino acid membrane protein containing 3 TMDs, with a peptide corresponding to the fourth TMD (TMD4) of the 16 kDa subunit of the ATP6V0C is investigated as an example. HPV-16 is the major cause of cervical cancer diagnosed today. E5 is a membrane protein which is expressed at an early (hence the letter E) stage of the infectivity cycle when the virus turns the cell malignant. The protein interacts with a series of host factors but has also been identified experimentally to allow channel activity when most likely in a hexameric assembled form [1]. Computational modeling suggests a weak selectivity of the channel [2]. Docking approaches as well as coarse grained molecular dynamics (CGMD) simulations of the peptides within a hydrated lipid membrane specify the mode of binding of TMD4 with either E5 protein or its individual TMDs [3]. From potential of mean force calculations (PMF) and statistical analysis enthalpy and entropy contributions are attributed of TMD4 binding to TMD3 and TMD2 of E5, respectively.

Publications

1. Fischer WB, Li L-H, Mahato DR, Wang Y-T, Chen C-P (2014) Viral channel proteins in intracellular protein - protein communication: Vpu of HIV-1, E5 of HPV16 and p7 of HCV. *Biochim. Biophys. Acta* 1838:1113-1121
2. Mahato DR, Fischer WB (2016) Weak selectivity predicted for modeled bundles of the viral channel forming protein E5 of human papillomavirus-16. *J. Phys. Chem. B* 120:13076-13085
3. Fischer WB, Kalita MM, Heermann D (2016) Viral Channel forming proteins - how to assemble and depolarize lipid membranes in silico. *Biochim. Biophys. Acta* 1858:1710-1721



Biography

Dr. Wolfgang Fischer is Professor at the Institute of Biophotonics, School of Biomedical Science and Engineering, National Yang-Ming University, Taipei, Taiwan (www.ym.edu.tw/~wfischer/). He has obtained his PhD in Chemistry at Heidelberg University, Germany, working in the field of vibrational spectroscopy in 1991. After years in the US (Boston University, postdoctoral fellow working on bacteriorhodopsin using vibrational spectroscopy), Germany (TU-Dresden, Analytical Chemistry, working on ion channels as potential biosensors), UK (Oxford University as EU Marie Curie Research Fellow and later as Lecturer working on viral ion channels using bilayer recordings and molecular dynamics simulations) he moved to Taiwan. The field of research is on biophysical aspects describing dynamics and energetic of protein-protein interactions (PPIs) of membrane proteins. The focus is on the development of computational platform technologies to support drug discovery and design as well as materials sciences.

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