# Ion channel properties of the E5 Protein of Human Papillomavirus – A Molecular Dynamics Simulation Study

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Human papillomaviruses (HPV) infect mucosal and cutaneous epithelial cells leading to precancerous lesions. The HPV genome encodes three oncoproteins: E5, E6 and E7 from which E5 is the least understood. E5 of HPV type16, which is one of the "high risk" types of HPV strains, is an 83 amino acid membrane protein, with three hydrophobic transmembrane domains (TMDs). It is experimentally found that E5 forms hexamers and renders membranes permeable to ions. Computational modeling is used to obtain structural and functional features of this protein.

The three TMDs of E5 are identified using secondary structure prediction programs and assembled into a monomer using a series of protocols of a 2D docking approach. In a consequent step, loops linking the three helices are added using the program Loopy. Finally six monomers are assembled into a hexameric bundle. The bundle with TMD2 lining the pore remains intact allowing water filled pocket formation around C-terminal hydrophilic residues during entire 100 ns MD simulations.

With TMD2s facing the pore, ion channel activity possible. The number of Cl-ions passing through the pore is higher than that of the Na-ions when simulating at various voltages. The potential of mean force (PMF) calculations support the notion that E5 forms a pore with low selectivity. Full correlation analysis (FCA) reveals asymmetric dynamics of the TMDs.