

SFB
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Protonation Dynamics
in Protein Function

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Freie Universität Berlin

via WebEx

➤ Colloquium

➤ Prof. Thomas E. DeCoursey

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Proton Selective Conduction Through hHV1, the Human Voltage-gated Proton Channel

In order to function effectively, proton channels must be extremely selective for protons, because protons are present in biological solutions at concentrations 10^6 lower than other cations. The strategies used by the human voltage-gated proton channel (hHV1) to achieve perfect proton selectivity will be discussed. The unique chemical properties of protons, compared with other cations, are crucial determinants of the selective conduction mechanism. One crucial feature is a specific Aspartate112 in the middle of the S1 helix. This location is not exclusive - the Aspartate can be shifted one helical turn to position 116; however no function was detected at other locations. The selectivity filter consists of this Aspartate interacting with an Arginine from the S4 helix. This 'salt-bridge' motif also occurs in several other proteins that contains critical proton conduction pathways. As important as proton selective conduction through open channels is the prevention of conduction when the channel is closed. Four hydrophobic amino acids in a plane near the center of the membrane form a 'hydrophobic gasket' that prevents proton leak.

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