BIOCHEMISTRY SEMINAR

Decoding Channel Selectivity through Membrane Protein Design

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Abstract: Membrane channels and transporters enable the selective movement of ions and water, critical for cellular function. However, the molecular mechanisms underlying proton, water, and ion selectivity remain unclear. Using de novo protein design, we systematically investigate the determinants of selective transport by engineering membrane channels with defined structural and chemical features. Herein, we describe the design of functional proton, water, and ion channels to elucidate mechanisms of selective transport.

For proton selectivity, we test how protein and water dynamics dictate selectivity through the design of functional proton channels with tunable hydrogen-bonding networks. For water selectivity, we probe whether proton exclusion is determined by the pore electrostatic or dielectric environment. For ion selectivity, we assess the interplay of coordination chemistry and pore geometry by designing helical bundles with tunable binding sites, enabling us to dissect the fundamental principles of ion discrimination.

This work provides a mechanistic framework for selective transport, advancing our understanding of natural channels while enabling the design of biomimetic membranes with tailored transport properties for biotechnological and therapeutic applications.

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