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Using Bioinformatics to Answer Fundamental Questions in Microbiology : From Simple Peptides to Multicomponent Metabolons

Milton H. Saier, Jr.

Division of Biological Sciences University of California, San Diego La Jolla, CA 92093-0116

Integral membrane transport proteins have arisen by intragenic duplication, triplication and quadruplication events, in which the numbers of transmembrane -helical hydrophobic segments (TMSs) have increased. Using such pathways, genes encoding oligomeric peptide channels fused to give rise to protein channels, and specific amino acid substitutions subsequently allowed protein channels to evolve into carriers. These events occurred repeatedly during evolutionary history giving rise to many independently arising families oftransporters. The appearance of primary active transporters and group translocators resulted from the superimposition of energy-coupling proteins onto carriers. Such events permitted the creation of much greater concentration gradients than were possible if generated only by secondary carriers. Group translocation allowed the direct coupling of transport to metabolism.

Transport proteins, diffusible in the plane of the membrane, may be responsive to the presence of substrates which bind and induce transporter self-association. Conformational changes may promote association with dissimilar but functionally related proteins. Permeases of the bacterial phosphotransferase system provide examples of nucleating membrane proteins that first assemble their energy-coupling constituents and then promote formation of multicomponent glycolytic metabolons. The presence of physically associated enzymes of a pathway allows efficient substrate processing to yield energy-rich end products of metabolism. In the caseof glycolytic metabolons, this end product, phosphoenolpyruvate, is a master connector, feeding into new pathways, but also initiating a new round of glycolytic substrate metabolism. It thus completes the glycolytic cycle.