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The first fruits of an HTP membrane platform: crystal structure of the CorA Mg^{2+} transporter

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Membrane proteins constitute 30% of prokaryotic and eukaryotic genomes but comprise a small fraction of the entries in protein structural databases. A number of features of membrane proteins render them challenging targets for the structural biologist, among which the most important is the difficulty in obtaining sufficient quantities of purified protein. We have developed robust procedures to express and purify large numbers of prokaryotic membrane proteins. Using a set of standard conditions, expression can be detected in the membrane fraction for approximately 30% of cloned targets. To date, over 30 membrane proteins have been purified in quantities sufficient for structural studies, typically in just two chromatographic steps. Theses include several transporters/channels, sensor kinases, and rhomboid intramembrane proteases. Using this system, we have recently crystallized and solved the structure of the CorA magnesium transporter, the primary Mg^{2+} uptake system of most prokaryotes. Crystal structures of the full-length *Thermotoga maritima* CorA in an apparent closed state and its isolated cytoplasmic domain were determined at 3.9Å and 1.85Å resolution respectively. Our HTP strategy for membrane proteins, and the first structure from this effort, will be discussed.