# Crystal structure of the MgtE $Mg^{2+}$ transporter

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The magnesium ion, $Mg^{2+}$, is one of the most abundant divalent cations in biological systems and is vital for all living organisms. $Mg^{2+}$ has the largest hydrated radius among all cations, while its ionic radius is the smallest. It remains obscure how $Mg^{2+}$ transporters selectively recognize and dehydrate the large, fully-hydrated $Mg^{2+}$ cation for its transport.

The MgtE family of $Mg^{2+}$ transporters is ubiquitously distributed in all three kingdoms, and human homologues were functionally characterized and suggested to be involved in magnesium homeostasis However, the MgtE transporters have not been thoroughly characterized, and it is even not clear whether MgtE works as a channel or an active transporter.

We determined the crystal structure of the full-length *Thermus thermophilus* MgtE at 3.5 Å resolution. The transporter adopts a homodimeric architecture, consisting of the C-terminal five transmembrane (TM) domain, and the N-terminal cytosolic domains, composed of the superhelical N domain and the following typical duplicated cystathionine-β-synthase domains, which reportedly plays a regulatory function in other transporter proteins, e.g. human chloride channels and the osmoregulated ABC transporter. A solvent-accessible pore nearly traverses the TM domains, with one potential $Mg^{2+}$ bound to the conserved Asp residues within the pore, which might be related to the ion selectivity by MgtE. The TM5 helices from both subunits close the pore through interactions with the “connecting helices”, which connect the cytosolic and TM domains. Four putative $Mg^{2+}$ ions are bound at the interface between the connecting helix and the other domains, which may lock the closed conformation of the pore. A structural comparison of the $Mg^{2+}$-bound and $Mg^{2+}$-free cytosolic domains showed the $Mg^{2+}$-dependent movement of the connecting helices, which might reorganize the TM helices to open the pore. These findings suggest a $Mg^{2+}$ homeostasis mechanism, in which the cytosolic domains regulate the gating of the pore by sensing the intracellular $Mg^{2+}$ concentration.