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Gating Control; Mechanism of Magnesium Transporter MgtE

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The MgtE family of Mg^{2+} transporters is ubiquitously distributed in all three domains, and human homologues SLC41 have been functionally characterized and suggested to be involved in magnesium homeostasis. However, the MgtE transporters have not been thoroughly characterized. We determined the crystal structures of the full-length *Thermus thermophilus* MgtE at 3.5 Å resolution and the cytosolic domain in the presence and absence of Mg^{2+} at 2.3 Å and 3.9 Å resolutions, respectively. 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 tandemly-repeated cystathionine-β-synthase (CBS) domains. A solvent-accessible pore nearly traverses the TM domains, with one potential Mg^{2+} bound to the conserved Asp432 within the pore. The TM5 helices from both subunits close the pore through interactions with the connecting helices, which connect the CBS and TM domains. Number of Mg^{2+} are bound at the interface between the connecting helices and the other domains, which may lock the closed conformation of the pore. A structural comparison of the two states of the 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 homeostasis mechanism, in which Mg^{2+} bound between cytosolic domains regulate Mg^{2+} flux by sensing the intracellular Mg^{2+} concentration. Our recent MD simulation as well as genetic and biochemical experiments has provided a clue to answer to whether this presumed regulation mechanism actually controls the gating of the ion channel.

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