The magnesium transporter A, is dependent on cardiolipin and selectively sensitive to free magnesium

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Abstract

Three classes of Magnesium transporters have been identified in Bacteria and Archaea; CorA, MgtE and MgtA/MgtB (Groisman et al., 2013). CorA and MgtE are constitutively expressed. CorA and MgtE are both magnesium efflux transporter. Influx is believed to mediated by MgtA The magnesium transporter A (MgtA) is a specialized P-type ATPase, that import Mg^{2+} into the cytoplasm. In both *Salmonella typhimurium* and *Escherichia coli*, the virulence determining two-component system PhoQ/PhoP regulates the transcription of the *mgtA* gene by sensing Mg^{2+} concentrations in the periplasm, along with low pH and the presence of cationic peptides. This study demonstrates, for the first time, that MgtA is highly depended on anionic phospholipids and in particular, cardiolipin, the in vitro kinetic experiments performed on detergent solubilized MgtA suggest that cardiolipin act as a magnesium chaperone. We further show that MgtA is highly sensitive to free Mg^{2+} (Mg^{2+}_{free}) levels in the solution. MgtA is activated when the Mg^{2+}_{free} concentration is reduced below 10 μM and is strongly inhibited above 1 mM, indicating that Mg^{2+}_{free} acts as product inhibitor. Furthermore, colocalization studies confirm that MgtA is found in the cardiolipin lipid rafts in the membrane. Combined, our findings indicate that MgtA may act as a sensor as well as a transporter of Mg^{2+} (Subramani et al., 2016). With the present functional data, we now hypothesize that regulation of ion transport in the MgtA might be fundamentally equivalent to that of the Na^{+}/K^{+} -ATPase. The discovery that MgtA acts as a receptor in addition to being an ion transporter, is a major breakthrough. It is still a controversial subject whether the Na^{+}/K^{+} ATPase might act as receptor as the receptor binding site or the mode of signaling through the tyrosine-protein kinase Src still needs to be verified (Liang et al., 2007;Tian et al., 2006;Wu et al., 2013).

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