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DISSERTATION TITLE:	*Biochemical characterization and crystallization of the magnesium transporting P-type ATPase MgtA*

Avhandlingen omfatter den første detaljerte biokjemiske beskrivelsen av det bakterielle membranproteinet Magnesiumtransporter A (MgtA). Studiet har vist at lipider er helt avgjørende for proteinets følsomhet for magnesium (Mg2+). MgtA ble i tillegg krystallisert for å muliggjøre fremtidige strukturstudier.

The thesis describes the first detailed biochemical characterization of the bacterial membrane protein, the magnesium transporter A (MgtA). This study revealed the unique lipid requirement of the protein and its sensitivity for magnesium ion. In addition, the protein was crystallized to facilitate future structural studies.

Magnesium (Mg^{2+}) is the most abundant divalent cation in living cells and plays many important roles in the functioning of living cell. The ion is required for metabolic pathways that produce the energy currency of the cell, ATP and maintains the structure of many macromolecules like cell membrane, ribosomes and DNA. Mg^{2+} also plays an important role in the photosynthesis of plants. Mg^{2+} deficiency affects organisms in all three domain of life. In humans Mg^{2+} deficiency can cause muscle spasms, abnormal heart rhythms and seizures, while in plants the leaves turn yellow leading to death. Researchers observed that Mg^{2+} depletion affected cell division and growth rate of bacteria. Thus, all organisms have systems to maintain the physiological Mg^{2+} levels. Such systems are well studied in microorganism like bacteria. They have three classes of Mg^{2+} transporting proteins. One of the classes includes a P-type ATPase called magnesium transporter A (MgtA). It is produced by bacteria only when the Mg^{2+} level of both its surrounding environment and cytoplasm decreases below a threshold level. Research over the past two decades has led to the identification and detailed characterization of signal transduction system that activate the expression of MgtA. However, the mechanisms by which MgtA transports Mg^{2+} ions into the cells and the factors that activate or affect its transport activity remained unknown.

The studies reported in this thesis describe the first functional analysis of purified *Escherichia coli* MgtA. We discovered that MgtA requires anionic phospholipid cardiolipin for its activity and is able to function even in the presence of trace amount of Mg^{2+}. We also found that the protein activity decreases above the physiological Mg^{2+} levels of *E. coli*. These findings lead us to propose that the cytoplasmic Mg^{2+} concentration of the bacteria might directly regulate the MgtA activity. Further, MgtA was crystallized in the presence of lipids and Mg^{2+} which will help future investigations on the mechanism of Mg^{2+} by MgtA.