Abstract No. dutz590

Structure Determination of a CLC Chloride Channel

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Beamline(s): X25

Introduction: Important physiological processes like the maintenance of the resting potential, osmotic control, and epithelial flux are linked to the movement of chloride ions through biological membranes. The permeation of chloride through the impermeable membrane is selectively catalyzed by ion channel proteins of the CLC family [1]. Members of the CLC channel family are ubiquitously expressed in prokaryotic and eukaryotic cells and their sequence is conserved from bacteria through mammals [2]. In order to understand the structural basis for chloride selectivity we are attempting to solve the structure of a bacterial CLC channel by S-ray crystallography. As in the case of eukaryotic channels, the prokaryotic channels are homo-dimeric proteins [3]. The monomers are 370 to 450 residues long and consist of 8-12 putative transmembrane helicies.

Results: We have cloned and over-expressed CLC channels from various bacterial organisms. In a large number of crystallization experiments we were able to identify different crystal forms. Since CLC crystals diffract X-rays only weakly the bright beam of X-25 is crucial for us to collect data. Several visits at BNL during the last year were used for evaluation and data collection on different crystal forms. The best crystal form allowed us to collect data at 3Å resolution at X25 during the last cycle. In an attempt to solve the structure by MIR/AS methods we are continuing to collect data of various heavy metal derivatives. The usage of X25 will hopefully enable us to solve the first structure of this important novel class of ion channels.

Acknowledgments: The CLC project is supported by NIH grant 4700 and by the Howard Hughes Medical Institute.

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