Mechanism of ATP-dependent gating in CFTR channels

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Cystic Fibrosis Transmembrane conductance Regulator (CFTR) is a small conductance, PKA-regulated, ATP-dependent anion channel known to be the only one member of the ATP Binding Cassette (ABC) transporter superfamily which functions as an ion channel. CFTR channel is very valuable to study because it is a useful model protein for the research of ABC transporters beside being a product of the Cystic Fibrosis gene.

Since CFTR was cloned in 1989, a number of biochemical and electrophysiological functional studies had been performed to elucidate the mechanism of the ATP-dependent gating. In the middle of the first decade in 21st century, the atomic structures of several ABC transporters were solved. These crystal structures suggested that two Nucleotide Binding Domains might form a dimer with sandwiching two ATP molecules in the dimer interface. Employing this NBD dimerization idea, we could explain a lot of single channel gating data by reproducing them on the computer simulation. Now the latest gating model involves seven states with a loose coupling between the ATP binding-hydrolysis-release cycle in NBD and the pore gating cycle. Also recent advances in the single molecule biophysics are going to enable us to shoot movies of single molecules in action.