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Structural genomics of integral membrane proteins - Past successes and future directions

Brian Kloss
New York Structural Biology, USA

Approximately one-third of all human genes, as well as genes from most other organisms, across all kingdoms of life - encode integral membrane proteins. Nonetheless, the number of integral membrane protein structures solved lags far behind the number of those solved for their soluble counterparts, due primarily to the difficulty of recombinant expression and the instability of membrane proteins once they are detergent-extracted from the lipid bilayer. Over the past 10-20 years, the number of integral membrane protein structures solved, primarily by x-ray crystallography, has increased significantly and structural genomics approaches have played a considerable role in this progress. More recently, advances in cryo-electron microscopy techniques have permitted structures of integral membrane proteins to be determined at resolutions comparable to that of x-ray crystallography, but requiring much smaller quantities of protein. Concurrently, detergents that improve the stability of integral membrane proteins and purification techniques that allow proteins to be extracted and purified in their native lipid environment have also been developed, allowing structural studies of integral membrane proteins to move forward at an exceedingly rapid pace. I will summarize our past integral membrane protein structural biology efforts that employed structural genomics approaches and high-throughput techniques and describe our plans for future structural studies that will continue to make use genomics-based methods, as well as more recently available reagents, techniques and technologies.

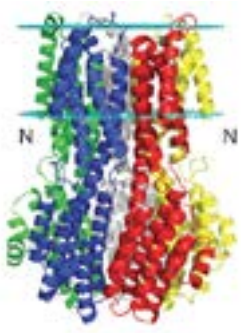

Figure1: *Ribbon diagram showing the structure of the homologue of the human calcium-activated chloride channel bestrophin from Klebsiella pneumoniae.*

Biography

Brian Kloss began his research career as a graduate student in the Laboratory of Carter Bancroft at the Mount Sinai School of Medicine, studying the transcriptional regulation of the pituitary-specific prolactin and growth hormone genes. He went on to do a Postdoc with Michael Young at Rockefeller University, studying the genetic control of circadian rhythms in *Drosophila melanogaster*. Afterwards, he spent almost six years at a biotech startup, helping to develop a cell-based assay for the screening of ligands of GPCRs. For the past ten years, he has been a part of the protein production facility of the Center on Membrane Protein Production and Analysis (COMPPÅ), located at the New York Structural Biology Center. There, he has led a small group focused on the identification, cloning and expression screening of integral membrane proteins of prokaryotic origin, mainly for structural studies.

bkloss@nysbc.org

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