BIOL 647 Structure-Function of Membrane Proteins; Syllabus:

Topics of Lectures/Discussions

The general theme of the course is to describe and discuss the current state of knowledge of the structures of membrane proteins, application to their role in maintaining cell and organelle function and energy level, and the consequences for disease of changes in structure that result in failures of function. The conceptual approach to the subject involves a combination of biochemistry and biophysics.

I. Lipid Environment. Lipid environment; intra-protein lipids, hydrophobicity scales, *in vitro* and *in vivo*, hydrophobic mismatch; lipid phase transitions, fluidity, rafts; role of cholesterol. Lipid, protein diffusion, measurement by spectroscopies (e. g., epr, fluorescence; fluorescence resonance energy transfer (FRET); lateral pressure in membranes from lipids leading to crystallization by lipoid cubic phase.

II. Architecture of Membrane Proteins. α-helical and β-barrel (gram-negative bacterial outer membrane) structures; role of intra-protein lipid, analysis by mass spectroscopy; rules for membrane protein topology; e.g., the *cis*-positive rule; topology dependence on lipid (e. g., PE).

III. Structure Determination. Properties of detergents; extraction and purification of integral membrane proteins; the detergent problem. Crystallization: (i) use of antibodies to improve crystallization; (ii) in detergent; (iii) lipid cubic phase; (iv) bicelles. Cryo- Electron Microscopy; mass spectroscopy; lipid-protein interactions.

IV. Biogenesis

(**a**) Sec-dependent & Sec-independent; the translocon; (b) Refolding/insertion of outer membrane proteins.

V. Structure-Function; Altered Function and Disease

A) α-Helical proteins; hetero-oligomeric complexes. (**a**) Energy transduction, transduction of H+, Na+ electrochemical potential: (i) respiratory, photosynthetic hetero-oligomeric electron transport complexes; H^+-, Na^+-ATPase, ATP synthase; (ii) active transport; symporters and anti-porters; lactose symporter, sodium-proton antiporter; ABC transporters; bacterial homologues of eukaryotic proteins; "alternating access."

c) Signal transduction – GPCRs; drug binding; physiological functions. d) Ion channels; K^+, Cl^-, H^+; lipid interactions. (**A.1**) **Consequences for Disease**: (i) Brain mitochondrial dysfunction; role of membrane proteins; (ii) cystic fibrosis trans-membrane regulator (CFTR); (iii) Autophagy: altered structures of membrane proteins. (iv) influenza virus. (**B**) β-barrel bacterial Omps; OmpF, nutrient receptors; LamB; Fe siderophores, Tol, Ton proteins; parasitization of nutrient receptors by phages and colicins; (**B.1**) **Consequences for Disease**: *Neisseria*; *Yersinia*; folate receptor, cancer.

(VI) Reading, references, grades: (1) Notes on **Blackboard**; (**2)** Luckey, M. 2014**.** *Membrane Structural Biology,* Cambridge Univ. Press, Life Sci. Lib; article**s** in literature**; (5) Grades**: (**a**) Homework (problems most weeks), 30%; Midterm (1 hr), 30 %; Final Exam (2 hr), 40%.