Neuroscience Center of Excellence

Chancellor's Award Lecturer in Neuroscience

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Crosstalk Between The Acetylcholine Receptor And Its Lipid Environment: From Molecule to Cell.

The nicotinic acetylcholine receptor (AChR) is the prototype ligand-gated ion channel, and its function is dependent on its lipid environment. In our laboratory efforts are devoted to understanding the structural-functional crosstalk between the AChR and its lipid microenvironment at the cellular and molecular levels. The former is studied using clonal cell lines deficient in specific lipid biosynthetic steps and by pharmacological inhibition of lipid biosynthesis in normal cells, in combination with live imaging and high resolution non-linear fluorescence microscopies. The influence of canonical domain-resident lipids like cholesterol and sphingolipids (SL) on AChR cellular distribution, assembly, internalization, and trafficking to and organization at the plasma membrane are being investigated in normal and lipid-deficient, temperature-sensitive clonal cell lines. The efficiency of the AChR assembly process, its export at the early secretory pathway, trafficking to the cell membrane, and stability at the cell surface all appear to be modulated by lipid.

At the molecular level, we study AChR-lipid interactions using fluorescence, NMR and ESR spectroscopies in combination with molecular dynamics simulations of the whole AChR transmembrane region (TM) or isolated TM peptides thereof. Recent molecular dynamics calculations of the entire TM region provide clues as to how the motion of M4's, the lipid-contacting outermost ring, can convey information on the innermost (M2) channel-lining region of the AChR and thus explain the modulation of AChR channel kinetics by the lipid microenvironment.

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