Scientists obtain clearer view of how eye lens proteins are sorted

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New research reveals how proteins that are critical for the transparency of the eye lens are properly sorted and localized in membrane bilayers. The study, published by Cell Press in the November 3rd issue of *Biophysical Journal,* analyzes how interactions between lipid and protein molecules can selectively concentrate proteins in certain regions of the cell membrane.

All cells are surrounded by a dynamic semi-permeable structure called the plasma membrane. Cell plasma membranes are made of a thin bilayer of lipids interspersed with a diverse complement of proteins. Research has shown that the lipids and proteins are not randomly distributed across the plasma membrane. Instead, functional microdomains or "rafts" are enriched for certain lipids and proteins. Although raft sequestration of many classes of lipids and proteins has been extensively studied, mechanisms for sorting proteins that span the membrane to form channels are not as well understood.

Dr. Thomas J.McIntosh from the Department of Cell Biology at Duke University Medical Center and his colleagues were interested in examining whether the plasma membrane distribution of the major eye lens channel proteins depends on how they are sorted between raft and non-raft microdomains. "We already knew that lens cell plasma membranes contain high concentrations of the raft lipids cholesterol and sphingomyelin, and that rafts form in lens membranes," says Dr. McIntosh. "In addition, we knew that lens channel proteins, connexins and aquaporin, are preferentially located in different regions of lens cell

plasma membranes."

Using both detergent extraction and confocal microscopy to analyze reconstituted membranes, the researchers discovered that lens connexins were primarily located in non-raft domains. In contrast, the microdomain location of aquaporin depended on its aggregation status, which was controlled by the protein: lipid ration in the membrane. Specifically, under conditions where aquaporin molecules are known to cluster together (homo-oligomerize), aquaporin was enriched in non-raft domains.

"Our observation that sequestration of aquaporin into raft microdomains was markedly increased under conditions where homo-oligomerization was observed supports the theory that protein clustering might modify microdomain sorting," offers Dr. McIntosh. "Taken together, our data suggest that protein-lipid interactions, as modified by aquaporin homo-oligomerization, can be a key factor in the sorting of proteins in lens cell membranes."

Source: Cell Press (news : web)