



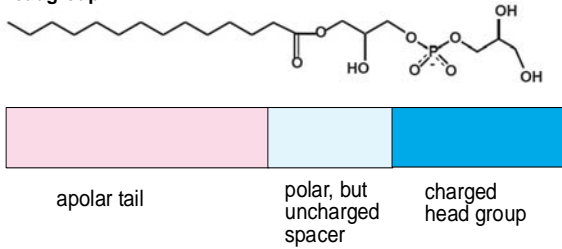
On the Virtues of Lyso-Phospholipids



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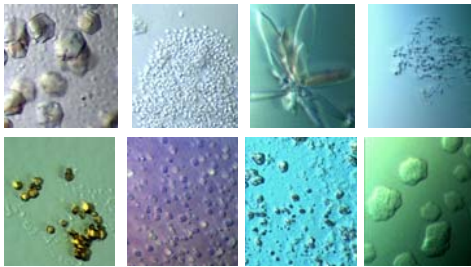
The lyso-phospholipids (e.g., LMPG—below) are unusual among commercially available detergents in that they have a polar, but uncharged spacer between the non-polar tail and a charged headgroup.



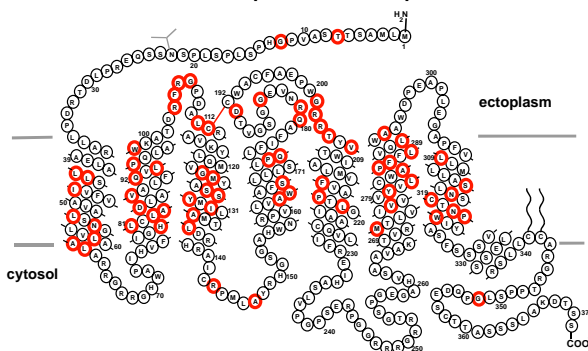
In the case of the diacylglycerol kinase, the lysolipids are among the few detergents that can sustain native-like catalytic activity for this enzyme (homotrimer with 3 TM helices per subunit).

Lyso-phospholipids have been reported to be effective at solubilizing difficult membrane proteins such as GPCRs and the CFTR channel in a manner that retains native function.

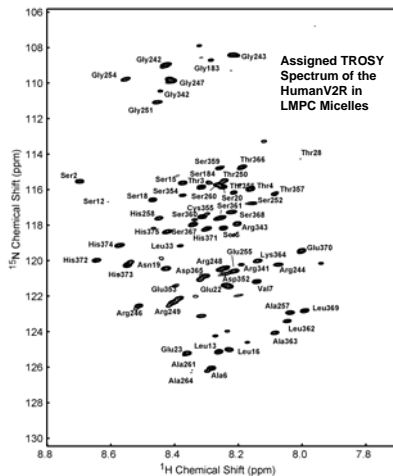
Shown below are NMR spectra and crystals of the vasopressin V2 receptor obtained using LMPG as the detergent component.



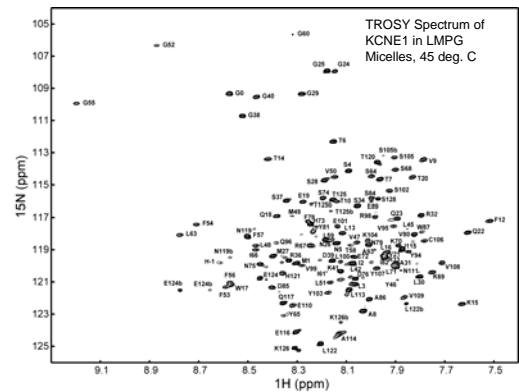
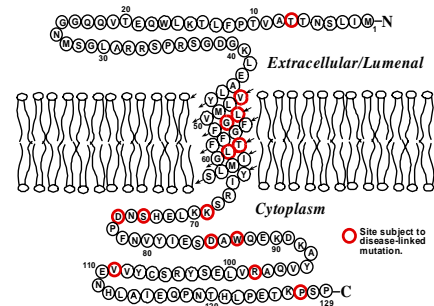
Human Vasopressin V2 Receptor



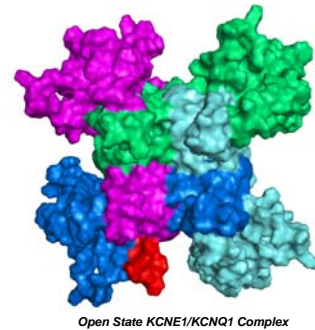
○ Sites for which mutations result in diabetes insipidus



For 3 out of 5 of the integral membrane proteins being studied by solution NMR in the Sanders lab, lysolipids yield the best spectrum. Shown below is the NMR spectrum of KCNE1, a protein that regulates voltage-gated potassium channels.



The structure of KCNE1 in LMPG micelles was determined using NMR. Shown below the experimental KCNE1 structure (TM domain only shown) which has been ROSETTA-docked into a homology model for the KCNQ1 channel.



Shown below are whole cell oocyte KCNQ1 potassium channel currents measured after injecting oocytes with micellar solutions of purified KCNE1. The lysolipids yielded native-like KCNE1 regulation of KCNQ1, while DPC and SDS did not.

