

Lipid-like Phosphocholine Detergents

Summary:

Commercially available single-chain phosphocholine (Fos) detergents are usually very efficient at solubilizing biological membranes but are often quite harsh that they denature proteins. We synthesized a class of lipid-like Fos detergents (Figure 1), hoping to bridge the structural differences between phospholipids and the commercially available Fos-detergents and to generate less denaturing molecules that retains their ability to solubilize membranes. In collaboration with the Wüthrich laboratory at TSRI, we found that Fos-detergents were superior than all other classes tested in refolding OmpX and that the single chain Fos-detergents are more effective than the double chain analogues (including DHPC). We selected the best performing detergents in the sample preparation for further NMR analysis using microprobe technology. This approach has led to the most recent success of finding new detergents that yielded high quality spectrum of OmpX. Additionally, in collaboration with the Stout laboratory at TSRI and using FOS-138, we have had recent success in crystallizing a membrane protein which we had previously had difficulties in generating.

Avilability:

Please contact Professor Qinghai Zhang (<u>Qinghai@scripps.edu</u>) or Professor Ray Stevens (<u>stevens@scripps.edu</u>) if you have questions or comments regarding the availability and use of these compounds.

References:

Q. Zhang, R. Horst, M. Geralt, X. Ma, W. X. Hong, M. G. Finn, R. C. Stevens and K. Wuthrich (2008) Microscale NMR screening of new detergents for membrane protein structural biology J Am Chem Soc 130: 7357-63 ; Determine the structure of the st

R. Horst, A. L. Horwich, K. Wüthrich (2011) Translational diffusion of macromolecular assemblies measured using transverse relaxation-optimized PFG-NMR. J Am Chem Soc. 2011 Sep 16. [Epub ahead of print] Publiced.



Figure 1 Chemical structure of the newly synthesized detergents categorized by the type of spacer groups between the phosphocholine head and alkyl tail. (a) Branched alkyl chain-containing detergents (12), (b) Ester bond linkages,(12), (c) Amide bond linkage (8), (d) Miscellaneous (including ethylene oxide-linked phosphocholine detergents (10). Detergents examined by NMR are shown in blue and red, with the latter exhibiting the best performance.







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