



SCIENCE FOR THE BENEFIT OF HUMANITY

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# A Novel Method for the Production of Nanoscale Membrane Particles

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### Technology Summary

There are currently considerable research efforts on membrane-associated proteins in both academic and commercial settings. Academic researchers are intrigued by questions of ligand activation, assembly, multimerization, etc. Many companies view these proteins as potential drug targets as they can be accessed from outside of the cell. At the same time, these membrane proteins can be very difficult to study due to *in-vitro* solubility and stability issues.

Apolipoproteins are called “protein detergents” because their properties permit the solubilization of functional membrane-associated proteins into nanoscale lipid bilayers. Our scientists have engineered a truncated and tagged variant of an apolipoprotein from zebrafish (*Danio rerio*), which self-assembles with phospholipids to form a nanosized disc-shaped bilayer, that they have termed Nanoscale Apolipoprotein Bound Bilayers (NABBs). They have also demonstrated rapid and stable reconstitution of transmembrane proteins into the NABBs without compromising the function of the proteins and lending native-like stability.

### Advantage

- The NABBs are easy to prepare in a scalable manner, including on a large scale (grams).
- The NABBs provide a native-like, membrane-mimetic system for the membrane protein of interest resulting in long-term stability of the protein, compared to commonly used detergents.
- The planar geometry of the NABB allows access to both sides of the bilayer, thus addressing both the extracellular and cytoplasmic regions of the proteins that typically carry out different functions.

### Area of Application

- NABBs are ideal platforms to study transmembrane receptors, viral membrane protein or ion channels by structural studies (X-ray crystallography, EM imaging, NMR), and conventional assays.
- High-throughput screening (HTS) or high-content screening (HCS) of compound libraries.
- Drug discovery, including lead molecule discovery/generation and optimization.
- Discovery and validation of drug targets in membrane proteins such as GPCRs.
- Membrane protein microarrays, proteomics and protein purification.
- Drug delivery platform for hydrophobic drugs due to solubility rendered by the NABB lipid core.
- Research tools for functional studies of membrane proteins and *in vitro* assay development.
- Detergent adjunct for solubilizing and capturing membrane proteins from cells into NABBs.

### Stage of Development

- Our scientists have successfully and stably incorporated functional bovine rhodopsin into the NABBs.

### Inventors

- Dr. Thomas Sakmar, Dr. Thomas Huber, and Sourabh Banerjee

### Patent Information & References

- U.S. Patent 8,999,320 and other patent applications are pending.
- Banerjee, *et al.* 2008. *J. Mol. Biol.* DOI: 10.1016/j.jmb.2008.01.066