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Improved lipid nanodiscs for studies of membrane proteins

Researchers at Stanford and their colleagues have developed compositions and methods for producing improved lipid nanodiscs that enable more effective studies of membrane proteins. Traditionally, scientists have studied proteins using x-ray crystallography. This is a tedious and challenging task, particularly for membrane proteins. Recently, cryo-EM methods have been developed to study integral membrane proteins. These methods do not require protein crystallization, but they do require the proteins to be removed from membranes, which can lead to denaturation. To reduce this challenge, lipid nanodiscs have been developed to hold the proteins together. These nanodiscs, however, have their own complications as they lack structural regularity, can lose co-factors, may require harmful detergent steps for formation, and formation may be time-sensitive. To overcome these limitations, the inventors have developed these compositions and methods to create simpler, more effective lipid nanodiscs. This technology provides for the use of poly (styrene-co-acrylic acid) (AASTY) copolymers to effectively make regularly sized lipid nanodiscs by incubating the polymer with lipid bilayers, including living cell membranes. This technology reduces the challenges associated with studying membrane proteins as it enables them to be studied in their native conformation.

Stage of research
Proof-of-concept studies have shown great promise. Additional development is ongoing.

Applications

- Research tool- facilitates the study of membrane proteins
- Drug development- solubilize hydrophobic drugs in aqueous solvents
- Dermal drug delivery

Advantages

- More effective than existing methods
- Enables challenging proteins to be more easily studied
- Facilitates the structural characterization of membrane protein-lipid interactions
    - Consistently solubilizes membrane proteins together with their native lipids
    - Allows membrane proteins to be studied in their native conformations
- Better control of monomer sequence to enable better structural regularity
- Higher protein stability
- Nanodiscs can be easily manufactured with existing equipment

Patents

- Published Application: WO2020257637

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