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CHARACTERIZING TINY RESIDENTS OF THE LIPID BILAYER

Within the dynamic lipid bilayer that makes up cell membranes, specific groups of lipids band together to form ordered domains called lipid rafts. Now Frederick A. Heberle, John Katsaras, and colleagues have measured particularly tiny rafts—known as nanoscopic domains—that are too small to study with optical microscopy (DOI: 10.1021/ja3113615).

Lipid rafts can "float" within the relatively disordered cell membrane and are involved in transferring signals across it. Scientists have visualized micrometer-scale rafts with optical microscopy but have not been able to directly observe rafts smaller than 100 nm in diameter.

Here, the researchers study a model membrane system using small-angle neutron scattering to find that the lipid composition of the bilayer influences the lateral size of these domains. Domain size increases with a greater degree of acyl chain unsaturation. Additionally, the size of domains is correlated with the mismatch in thicknesses between coexisting ordered and disordered liquid phases.

By providing the best characterization yet of these tiny rafts, this study advances our understanding of how the composition of lipid bilayers regulates their physical organization and ultimately aids the critical process of signal transduction across a cell membrane. **Deirdre Lockwood**

A RECEPTIVE STRATEGY FOR GLYCOLIPID RECEPTOR DISCOVERY

Chi-Huey Wong and co-workers identify and characterize a receptor for a glycolipid called stage-specific embryonic antigen-4 (SSEA-4) whose expression is correlated with the metastasis of some malignant tumors (DOI: 10.1021/ja312210c). Glycolipids—biomolecules composed of a carbohydrate group attached to a lipid molecule—reside in cell membranes, where they are involved in numerous important processes such as cell adhesion, growth, and signaling events. The inherent structural complexity of these compounds has hindered detailed characterization of their biological activity.

Using a technology called magnetic bead affinity capture, the authors create magnetic beads decorated with the SSEA-4 structure and use them to capture any proteins present in breast cancer cells that bind to the glycolipid. They discover that a protein called FKBP4 binds to SSEA-4. They then add FKBP4 to microarrays comprising various glycans and identify specific carbohydrate structures recognized by the receptor.

When FKBP4, which mediates cellular processes including protein folding, trafficking, and immunoregulation, is inhibited, cell surface expression of SSEA-4 is likewise inhibited. The authors speculate that "the down-regulated expression of SSEA-4 ... could be linked to the suppression of malignant processes of cancers." Additionally, this high-throughput screening strategy can be generalized to the study of other important glycolipids. **Eva J. Gordon, Ph.D.**

DECIPHERING A KANOSAMINE CLUSTER

David Palmer and co-workers use a wide range of chemical tools to show that a group of three enzymes in the bacterium *Bacillus subtilis* synthesizes a monosaccharide antibiotic called kanosamine, a related but simpler product than was previously thought (DOI: 10.1021/ja4010255). This work provides a clear mechanism for identifying new enzymatic function, particularly in cases in which the product of the reaction cannot be isolated.

As part of their detective work to characterize the gene cluster, or operon, the researchers compare the amino acid sequences of each enzyme to those of enzymes whose functions are known, allowing them to hone in on their likely activities. They also clone each enzyme so that they can examine its activity outside the bacterial host.

A force driving expanded understanding of these biosynthetic pathways is the search for molecules that have therapeutic value—possibly antibiotic or anticancer activity—in humans. As part of their normal biological function, bacteria may synthesize complex biomolecules, many of which possess a desirable biological activity. The process described here can serve as a model, applied to deciphering which clusters of genes within a bacteria are responsible for the synthesis of compounds with potential medicinal uses. **Eva J. Gordon, Ph.D.**

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