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Order in the chaos of a cell membrane: Crystalline areas form in model membranes based on previously unknown mechanism

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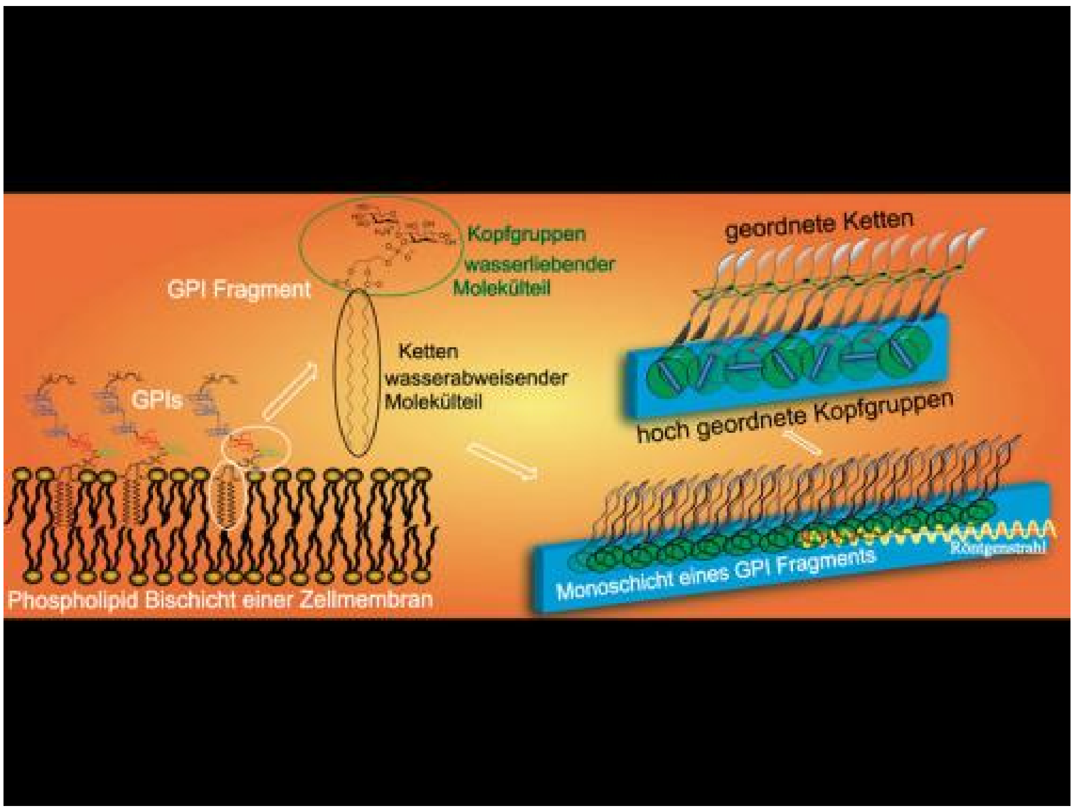

Model of a cell membrane with embedded glycolipids, or more precisely glycosylphosphatidylinositols, GPIs (left), and the formation of a molecular lattice in a monolayer at the water-air boundary (right). Credit: MPI of Colloids and Interfaces

(Phys.org)—An explanation has been proposed for the way in which ordered structures arise in cell membranes. Scientists from the Max Planck Institute of Colloids and Interfaces in Potsdam have discovered how complex compounds of sugar and lipids – known as glycolipids – order themselves in cell membranes into rafts, namely small, highly organised domains. The arrangement of glycolipids on the surface of plant and animal cell membranes regulates numerous cellular processes. If errors occur in this process, diseases like PNH and BSE can arise.

Lipids, i.e. fats and fat-like substances, arise all over the human body. They are the body's most important energy storage system and are crucial structural components of cell membranes. Compounds formed from complex sugar components and fats are known as glycolipids. Those are vital communicators found in the membranes of every human cell, and constantly exchange information about the type and state of the cell. Numerous metabolic processes depend on glycolipids and their recognition. Even the immune system identifies and combats many pathogens using certain sugar structures located on the surface of the pathogen cells.

Glycosylphosphatidylinositols (GPIs) belong to the group of natural glycolipids. They are found on the surface of plant and animal cell membranes, where they appear either as free molecules or as membrane anchors for various proteins. The arrangement in clusters and their preference for denser and, in part, highly-organised micro-domains in the membrane are seen as essential for the effective functioning of a cell. These minuscule clusters are extremely important for the regulation of many cellular processes, and their malfunction can have very serious consequences. For example, it has been proven that the accumulation, missing or alteration of GPI-anchored molecules can trigger the development of serious diseases like BSE and paroxysmal nocturnal hemoglobinuria (PNH). Scientists at the Max Planck Institute of Colloids and Interfaces in Golm near Potsdam have gained new insight into how GPIs structure themselves in membranes.

Crystalline lipid areas never previously observed in membranes

It was assumed up to now that the arrangement of the GPIs in clusters and rafts was determined by the water-repelling section of the glycolipids embedded in the cell membrane. The chemical structure of the hydrophobic ends is actually responsible for strong interactions with similarly rigid neighbouring molecules. If the number of the molecules that interact with each other is big enough, rigid and partly organised domains may arise like icebergs on the surface of the ocean.

Cristina Stefaniu and her colleagues have now discovered that, in addition to the hydrophobic ends, the large GPI head groups, which contain sugar, mainly contribute to the formation of the rafts. This means that the hydrophylic part of the molecule is able to build strong interactions with the neighbouring GPI molecules. This part of the molecule is located precisely on the boundary between the membrane surface and the liquid medium. "The interactions between neighbouring GPI molecules result in the formation of crystalline orders that have not previously been observed for other membrane lipids", says Cristina Stefaniu.

Hydrogen bonds connect the hydrophylic head groups

The scientists reached this new conclusion about the order in membranes by studying a model molecule. This is a GPI fragment that was synthesised by the groups headed by Peter Seeberger and Daniel Varón Silva and that imitates the behaviour of entire GPIs. It forms a very thin film, just one molecule thick, on the surface of the water. This so-called monolayer is the simplified model of a half cell membrane which the researchers analysed using synchrotron x-ray scattering. "Surprisingly, the highly ordered structure in the GPI monolayer is predominantly determined by the bulky hydrophilic head groups that connect through hydrogen bonds", says Stefaniu. A hydrogen bond is a relatively weak chemical bond and usually links two molecules through the bonding of a hydrogen atom from one molecule with an oxygen or nitrogen atom from the other molecule. Thus the monolayers of the GPI fragment are characterised by both the order of the hydrophilic lipid chains and the crystalline arrangement of the GPI head groups.

"The molecular lattices observed here have not yet been described for lipid monolayers," says Cristina Stefaniu. "A similar order forms in lipid bilayers if they are stored at temperatures close to zero degrees Celsius." The strong interactions between the head groups can only be disrupted and the molecular lattice destroyed through the addition of a highly concentrated urea solution, which breaks the hydrogen bonds, eliminates the strong interactions of the head groups and destroys the molecular lattice. In addition, the scientists proved that ordered clusters can arise in mixtures of the GPI fragment with typical membrane lipids, which only form unordered films. Thus, the GPIs are able to generate order in the chaos of a membrane. This special skill could be very important for the GPI interactions in real cell membranes.

More information: Stefaniu, C. et al. Subgel Phase Structure in Monolayers of Glycosylphosphatidylinositol Glycolipids, *Angewandte Chemie International Edition*. 14 December 2012; doi: 10.1002/anie.201205825

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