

Enigmas concerning sterols and their surrogates in eukaryotic cell membranes

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A large fraction of eukaryotes and bacteria respectively possess sterols and hopanoids, which function as potent stabilizers of cell membranes. Sterols are also associated with fluidity and permeability of eukaryotic cell membranes, and are key to fundamental eukaryotic-specific cellular processes such as phagocytosis. Several steps of *de novo* sterol biosynthesis require molecular oxygen. For example, the epoxidation of squalene is the first oxygen-dependent step in the sterol pathway; the epoxidized squalene is then cyclized to either lanosterol or cycloartenol by the enzyme oxidosqualene cyclase. In contrast, prokaryotic hopanoid biosynthesis does not require molecular oxygen as a substrate, and the squalene is directly cyclized by the enzyme squalene-hopene cyclase.

Until now, it was unclear how bacterivorous unicellular eukaryotes that are abundant in anoxic or low oxygen environments could carry out phagocytosis. These eukaryotes cannot obtain sterols from food bacteria as the latter generally lack them and sterols cannot be synthesized *de novo* in the absence of molecular oxygen. We have previously provided evidence that the molecule tetrahymanol is synthesized by some anaerobic/microaerophilic eukaryotes and possibly functions as an analogue of sterols in these organisms. Nevertheless, neither sterol, nor tetrahymanol, nor their related molecule has been found in the other anaerobic/microaerophilic eukaryotes, and so it is still enigmatic how these organisms maintain their fluid and permeable membrane system specific to eukaryotes.

One more area of confusion is regarding sterols in bivalves with chemosynthetic bacteria inhabiting areas of deep-sea hydrothermal vents and methane seeps, such as *Calyptogena* spp. and *Bathymodiolus* spp. In general, bivalves cannot synthesize sterols *de novo* and it is necessary for them to obtain these molecules from small eukaryotic prey. On the other hand, *Calyptogena* spp. and *Bathymodiolus* spp. mainly or exclusively acquire nutrients produced by their bacterial symbionts, rather than from eukaryotes rich in sterols. Nevertheless, these "chemosynthetic bivalves" contain sterols. More curiously, *Calyptogena* spp. have intermediate metabolites of phytosterols (24-methylenecycloartanol, cycloeucalenol, and obtusifoliol), while *Bathymodiolus* spp. have high amounts of cholesterol typical of animals. Little attention has been given to how chemosynthetic bivalves produce or acquire these kinds of sterols.

In my talk, I will discuss potentially controversial topics regarding sterols and their surrogates in eukaryotic cell membranes, which do not appear in biochemical and geochemical textbooks.

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