The Early Evolution of Lipid Membranes

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A seemingly profound difference in the composition of bacterial and archaeal cell membranes has confounded researchers for some time, suggesting that the last common ancestor of all living beings may have lacked a lipid membrane. However, recent results from David Moreira and colleagues indicate the enzymes that synthesize the components of archaeal and bacterial membranes descended from ancient protein families, providing insight into a long-standing question in biology.

Darwin's seminal idea that evolution proceeds through common descent with modification led him to think that, ultimately, all living beings share a unique common ancestor from which they all derive. Accordingly, the comparison of the characteristics of contemporary species should allow inferring those of ancestral species. In that way, characteristics shared by a group of species are supposed to have already been present in their last common ancestor (e.g., the presence of a vertebral column in the last common ancestor of all vertebrates). This simple approach can be applied to try to reconstruct the portrait of very ancient organisms, including the last common ancestor of all living beings: the cenancestor (also known as LUCA, the last universal common ancestor). Thus, a number of characteristics that are shared by all living species, such as the genetic code or the synthesis of proteins by ribosomes, were most likely already present in the cenancestor. Likewise, since all contemporary living beings are composed of the same structural units – cells – it seems logical to imagine that the cenancestor was also a cell.

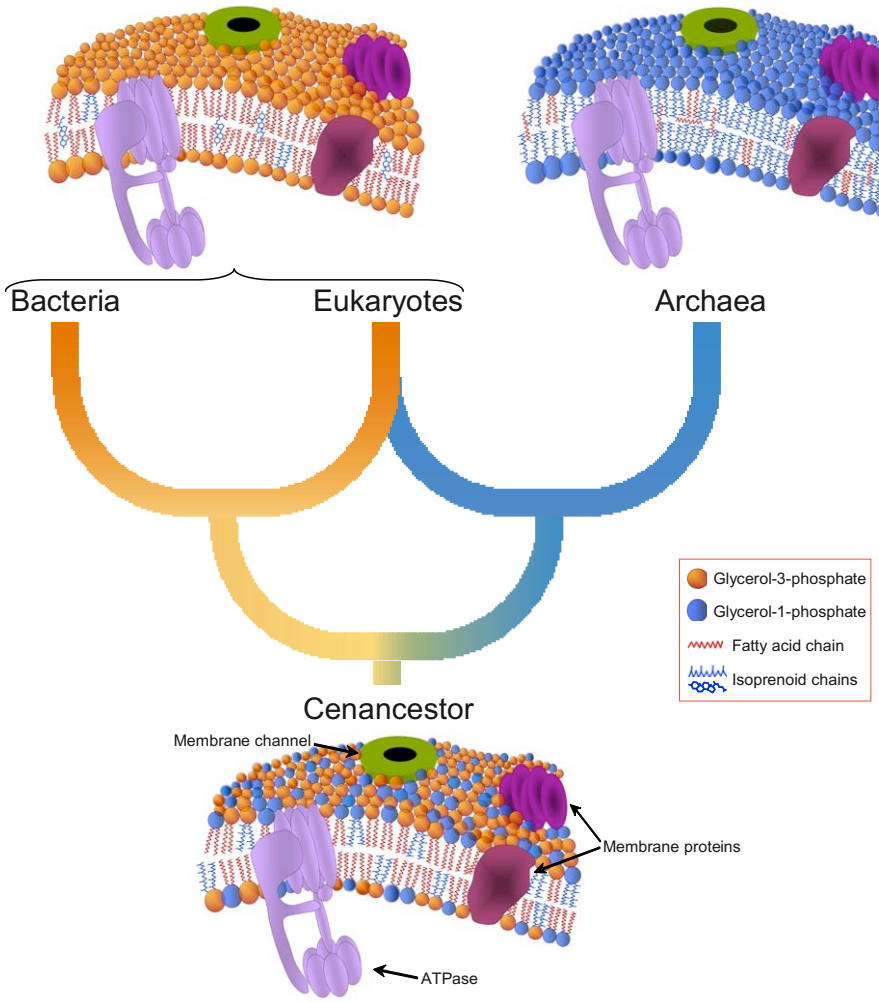

Figure 1. Characteristics of present-day bacterial, eukaryotic and archaeal cell membranes and of those of the last common ancestor of all living beings, the cenancestor, inferred by phylogenomic analysis. Bacteria and eukaryotes share the same type of cell membranes, probably because eukaryotes inherited them from bacteria. The membrane of the cenancestor had mixed characteristics that subsequently specialized during the evolution of the bacterial and archaeal lineages.

One of the most conspicuous characteristics of cells is that they are bounded by a membrane composed of lipids (more precisely, of complex amphiphilic molecules called phospholipids). The membrane serves as a physical barrier to maintain the cell's integrity. It has also selective permeability, often thanks to the insertion of specific channel proteins which allow the exchange of a variety of molecules with the surrounding environment. This selective permeability allows the establishment of an electrochemical gradient across it, which is essential for the cell's bioenergetics. Such a gradient allows one of the best conserved transmembrane proteins in the three domains of life (Bacteria, Archaea and Eucarya), ATPase, to synthesize ATP, the cell energy currency. The level of conservation of these features in contemporary cells

strongly supports that they are ancient, likely dating back to the time of the cenancestor. The cenancestor would have already been endowed with a lipid membrane and an ATPase able to utilize an electrochemical gradient.

However, the situation is not so simple. The first biochemical studies of membrane lipids in a large diversity of archaeal species in the last decades showed that they differ significantly from those of bacteria. In fact, all archaea have membrane lipids made up of glycerol-1-phosphate linked to two chains, most often isoprenoid chains, whereas membrane lipids in all bacteria and eukaryotes contain glycerol-3-phosphate, usually linked to two chains of fatty acids. The subsequent discovery that the enzymes involved in the synthesis of bacterial and archaeal lipids appeared not to be homologous (i.e. they did not apparently derive from the same ancestral enzymes) was unexpected and cast doubts on the idea that the cenancestor had a lipid membrane. Indeed, to explain the absence of homology between bacterial and archaeal enzymes, several authors hypothesized that lipid membranes appeared independently in ancestral bacteria and archaea only when the different enzymes required for their synthesis evolved in these organisms. In these evolutionary scenarios, the cenancestor would have been devoid of a lipid membrane. Whereas Koga stated that this meant that the cenancestor was not a cell but a collection of molecules thriving on pyrite surfaces, Russell and Martin proposed that it had membrane-like boundaries, though they were not made of lipids but of minerals precipitating in a hydrothermal chimney. These are interesting ideas that, if confirmed, would have a profound impact in our vision of the evolution of early life on our planet.

The encapsulation of a genetic system was certainly a decisive step in the origin of life. It was necessary to allow natural selection, which acts upon individual entities that have to maintain a certain stability of their individualized genomes over generations to achieve the degree of sophistication that the cenancestor most likely had (for example, comparative genomics studies suggest that it had a genome with several hundred different genes). All this is difficult to reconcile with the hypotheses of an acellular cenancestor or of a cenancestor with mineral boundaries. The first does not provide the necessary individualization of different entities for natural selection to act upon them whereas the second requires that all the evolution from prebiotic chemistry to the cenancestor and the differentiation of archaea and bacteria takes place in a same hydrothermal chimney, something difficult to envisage given the short lifetimes of these geological structures (no more than a few hundred years). So, how to explain the differences in contemporary archaeal and bacterial membranes and the requirement of a membrane in the cenancestor?

Recent phylogenomic studies may provide the answer. Phylogenomics studies the evolutionary history of genes taking advantage of the increasing number of complete genome sequences from a wide variety of organisms. This approach has revealed that the different components of present-day membrane phospholipids are probably much more ancient than previously thought: all of them were likely present in the

cenancestor. This includes enzymes belonging to two dehydrogenase superfamilies that may have been able to synthesize a mix of glycerol-1-phosphate and glycerol-3-phosphate, a pathway to synthesize isoprenoid chains and, likely, also a pathway to synthesize fatty acid chains. In addition, the enzymes necessary to link together these different components appear also to be very ancient. Therefore, it is plausible that the cenancestor could synthesize membrane phospholipids with the same components as those found in contemporary cells. The subsequent evolution of bacteria and archaea was accompanied by the specialization of their membranes, with a choice of one of the enzymes responsible of the synthesis of glycerol-phosphate (glycerol-1-phosphate in archaea versus glycerol-3-phosphate in bacteria) and a preference for isoprenoids as lateral chains in archaea and of fatty acids in bacteria (Figure 1). The reasons for this differentiation remain unknown. They may have been purely accidental or related to selective pressures linked to, for example, the adaptation to high temperature environments by the ancestors of archaea.

From an origin-of-life perspective, these discoveries strengthen the importance of lipid membranes in early evolutionary times. Several research groups working on prebiotic chemistry have convincingly shown that amphiphilic molecules able to form vesicles with interesting permeability properties were common on early Earth. Therefore, it is tempting to propose that there was a continuity from early prebiotic times up to the cenancestor in the use of those molecules to build compartments that defined different individuals upon which natural selection operated. At the beginning, those molecules would have been of abiotic origin (e.g., long chain carboxylic acids and alcohols) and later replaced by phospholipids synthesized by enzymes when the first cells evolved. The convergence of bottom-up approaches starting from prebiotic chemistry and top-down approaches based of comparative genomic and phylogenomic studies will certainly help to better understand that transition.

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