and deformation modes of the prismatic architected materials.

One of the appealing aspects of Overvelde and colleagues' algorithm is that it describes architected materials defined by simple structural and physical rules: the entire deformable architecture is made up of a single type of cell. The idea of using tessellated and repeated cell components resonates with the design principles of origami and of modular robots.

The controllability of the architected materials could be increased by introducing 'lockable' joints that can be made either rigid or flexible, rather than using passive elastic hinges as in the current work. The authors manually handled their prototypes to demonstrate the deformation modes (see Supplementary Information for the paper[1]), but the size and direction of the applied loading stresses are constrained by the flexibility of the hinges. Having actively lockable joints could further validate the effects of reconfigurable modes under various loadings. It would also allow the robotics community to discover origami platforms that have controllable degrees of freedom dictated only by the geometric constraints of a repeating cell module.

Building interactive, versatile hardware that has a high degree of freedom and mobility remains a key design challenge for many automated instruments and robots. Overvelde *et al.* introduce a robust strategy for designing reconfigurable modes for architected materials. Potentially, many more designs for architected materials will be made possible by using different assemblies of convex polyhedra. The authors' algorithm might well translate into strategies for designing automated systems, including diverse origami robotic systems. ■

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MICROBIOLOGY

Mind the gaps in cellular evolution

Eukaryotic cells, with complex features such as membrane-bound nuclei, evolved from prokaryotic cells that lack these components. A newly identified prokaryotic group reveals intermediate steps in eukaryotic-cell evolution. SEE ARTICLE P.353

JAMES O. MCINERNEY & MARY J. O'CONNELL

Eukaryotic cells contain membrane-bound organelles such as a nucleus, and complex cellular components, including protein-based transport systems that move molecules around the cell. About 1.8 billion years ago[1], eukaryotic cells arose from cells that lack these features, known as prokaryotic cells. However, there are gaps in the cellular family tree, specifically between prokaryotes and eukaryotes. There is limited evidence for how some eukaryote-specific features arose in the evolution of eukaryotic cells. On page 353, Zaremba-Niedzwiedzka *et al.*[2] identify a superphylum branch of the prokaryotic family tree that contains some genes previously thought to be eukaryote-specific.

On the basis of their gene content and aspects of their cellular physiology, prokaryotes are classified into two domains: Bacteria and Archaea. Their commmon ancestor is known as the 'last universal common ancestor'. Eukaryotes are thought to be derived from a merger that occurred when an archaeal cell engulfed a bacterial cell related to modern alphaproteobacteria[3]. It has been proposed[4] that, within these early eukaryotic cells, the internalized proteobacterium eventually evolved to form the membrane-bound organelles known as mitochondria that provide energy for the cell. However, early events in eukaryotic evolution have remained poorly understood. Few species have been identified whose genome content could provide insight into steps in the transition between prokaryotic and eukaryotic cells.

Until now, the archaea that have been identified as the most closely related ancestors of eukaryotic cells come from the group known as Lokiarchaeota[5]; these were identified by genome sequencing of organisms found in deep-sea sediments. Lokiarchaeota contain features that were previously thought to be eukaryote-specific, including several genes distantly related to those involved in eukaryotic protein transport. However, to understand the transition from prokaryotic to eukaryotic cellular life, a more complete picture is needed of the genes present in the archaeal cells that gave rise to eukaryotes.

DNA encoding 16S ribosomal RNA sequences is often used to determine the genetic relationships (phylogeny) between species. Twenty-five years ago, a study[6] of such DNA, obtained from seawater organisms, revealed the presence of archaeal groups related only distantly to the known archaea cultured in laboratories. This work hinted that cultured prokaryotes capture just a small fraction of global prokaryotic diversity. Zaremba-Niedzwiedzka *et al.* also investigated samples of underwater organisms, and their results reveal that major groups of life can still be discovered.

The authors obtained samples of aquatic sediments from seven locations worldwide. They extracted short fragments of DNA, representing a mixture of the species present, and sequenced more than 644 billion nucleotides. The short fragments of sequence were assembled into longer pieces, and sequences containing at least six genes from an evolutionarily conserved ribosomal-protein gene cluster were identified. These were analysed to determine the taxonomic relationships of the sampled genomes. The researchers identified the sequences that were most similar to the previously sequenced Lokiarchaeota[5] and Thorarchaeota[7] (another archaeal species related to eukaryotes).

Zaremba-Niedzwiedzka *et al.* used a statistical method[8] to classify the ribosomal sequences on the basis of similarities in the patterns of nucleotides used. From this analysis, they identified a superphylum of Archaea containing four major lineages of genetic material: Lokiarchaeota, Thorarchaeota and the newly found groupings of Odinarchaeota and Heimdallarchaeota. The authors named this superphylum Asgard. The exact family-tree relationships between the groupings within the Asgard superphylum are difficult to ascertain, because of statistical uncertainty in the phylogenetic trees that were constructed. But the analyses support the existence of the superphylum as a whole.

The position of the Asgard group in the family tree of cellular life suggests that its members form the closest known archaeal sister lineage to eukaryotes (Fig. 1). This finding is consistent with the view[3] that the

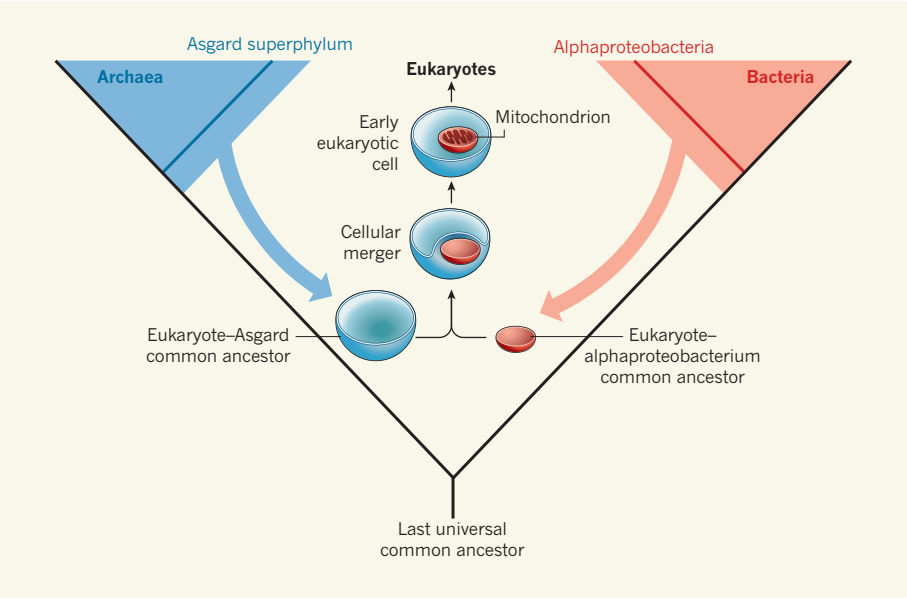

Figure 1 | A family tree of cellular life forms. The last universal common ancestor evolved to give rise to cells in the domains of Archaea and Bacteria, also known as prokaryotic cells. Eukaryotic cells have complex cellular features such as membrane-bound mitochondrial organelles and evolved from prokaryotic cells lacking these features. Eukaryotic cells are thought to have arisen when an archaeal cell merged with a type of bacterial prokaryotic cell related to modern-day alphaproteobacteria[3]. However, many aspects of the early evolution of eukaryotic cells remain unknown, such as how eukaryote-specific features might have arisen. Zaremba-Niedzwiedzka *et al.*[2] analysed genomic sequences from deep-sea organisms and identified a superphylum of Archaea that they named the Asgard group. Their genetic analysis placed this group near to the eukaryotic cell lineage. Members of this superphylum contain versions of genes previously thought to have been eukaryote-specific.

three-domains hypothesis, which suggests that eukaryotes arose independently of bacterial or archaeal diversification, has fallen. The work by Zaremba-Niedzwiedzka *et al.* adds to the body of evidence that eukaryotes arose through a merger of cells from within Archaea and Bacteria.

In the newly discovered Asgard archaeal groups, the authors found several eukaryotic-like genes that function in protein transport, signalling and protein degradation and that were previously reported to be present in Lokiarchaeota[5]. Their work also reveals expanded repertoires of these genes. The Asgard members are certainly not eukaryotes. However, they harbour types of gene that, until now, were thought only to have originated early in eukaryotic evolution. This research therefore pushes back the origins of parts of some cellular machinery.

Of particular interest in the Asgard group are the genes that relate to the cytoskeleton: a framework of structural proteins that gives a cell its shape and helps to organize its internal structure. Tubulin protein can form filaments that are key components of the cytoskeleton and are essential for eukaryotic cell division. The presence of tubulin in Archaea has previously been reported[9]. However, Zaremba-Niedzwiedzka *et al.* identified tubulin in Odinarchaeota that is closer in sequence to eukaryotic tubulin. They also found sequences encoding other cytoskeletal components, as well as sequences relating to the protein complex ARP2/3, which regulates the cytoskeleton. The sequences identified do not represent the blueprint for a complete eukaryotic cytoskeletal complex, but the authors indicate that these cellular machines, previously thought to be specific to eukaryotes, might instead have archaeal origins.

Asgard sequences also contain components of DNA-processing machinery that were previously thought to be exclusively eukaryotic. These include versions of the ε subunit of DNA polymerase enzymes. In eukaryotes, this polymerase subunit contains three domains. In the Asgard group, however, it contains two and is missing the evolutionarily conserved domain of unknown function.

Another surprising discovery was that versions of genes encoding eukaryotic membrane-trafficking proteins are found in the Asgard superphylum. In eukaryotes, such proteins are involved in moving proteins around the cell, between membrane-bound organelles known as the endoplasmic reticulum and the Golgi complex. But the small size of prokaryotic cells suggests that such intracellular trafficking mechanisms might not be necessary. Given the absence of organelles such as the endoplasmic reticulum and Golgi complex, it is unclear how these genes might function in Archaea. Of course, shared sequence similarity does not guarantee evolutionarily conserved function. The most recent common cellular ancestor of Asgard and eukaryotic cells existed 1.8 billion years ago[3], so these

genes have evolved independently over a total of 3.6 billion years, a time span that could have allowed many functional differences to arise in the encoded proteins.

The distribution of genes formerly thought to be eukaryote-specific is patchy in the Asgard superphylum, and no individual archaeal group seems to have a full set of such genes. So, although eukaryotes usually need all these genes together, the members of the Asgard group do not. Members of the Asgard superphylum have not yet been observed through the microscope, nor has their laboratory culture been reported. Therefore, many key details about their ecology, evolution and cell biology remain to be described. Further investigation of this superphylum might shed more light on the early origins of eukaryotic cells. ■

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VIROLOGY

Ins and outs of picornaviruses

Competition between the phospholipase enzyme PLA2G16 and the protein galectin-8 determines whether the RNA-based genomes of picornaviruses can be effectively delivered into host cells. SEE LETTER P.412

KEVIN L. MCKNIGHT & STANLEY M. LEMON

Picornaviruses cause a broad range of human and animal diseases, including polio, hepatitis A, and foot and mouth disease. The RNA-based genomes of this large and diverse family are packaged into protein shells called capsids, but the viruses lack the surrounding, lipid-containing membrane envelope present in many other types of virus. Whereas influenza and HIV infect hosts by fusing their envelopes with the host-cell membrane, it is unclear how picornaviruses safely deliver their RNA cargo to the interior of cells. Staring *et al.*[1] shine light on this process on page 412, identifying two host proteins that have opposing roles in picornaviral entry.

Different picornaviruses attach to the host cell by interacting with different receptor proteins on the cell membrane. But it seems likely that the mechanism by which RNA subsequently enters the cell is shared. Previous studies[2] with various picornaviruses show that a small membrane region pinches off around the virus to form a vesicle called an endosome just below the cell surface. Interactions with the receptor protein then trigger a rearrangement of capsid proteins, with hydrophobic internal domains flipping to the exterior of the capsid and puncturing the endosome membrane, creating a pore through which the viral RNA gains entry to the cell cytoplasm[3]. Once inside the cell, the RNA is translated into proteins by the host cell's ribosome machinery. These proteins then coordinate the formation of membranous structures in the cytoplasm called replication factories, in which the viral genome is amplified.

What factors mediate the transition of RNA in a capsid from the endosome into the host cytoplasm? Staring and colleagues discovered that the host protein PLA2G16 is essential for poliovirus entry, acting at a previously unknown step between pore formation and translation of viral RNA. Cells in which the *PLA2G16* gene was deleted were resistant to virus infection, and mice lacking the gene were protected from a dose of a virus that would normally be lethal. This is a surprising role for PLA2G16, which is a phospholipid-modifying enzyme previously identified in completely different roles — as a tumour suppressor and a major regulator of lipid breakdown in fat[4,5].

To better understand the mechanism by which PLA2G16 acts, the authors established a clever 'counter screen', introducing random genetic mutations into *PLA2G16*-deficient cells and searching for those that restore the ability of poliovirus to infect the cells. This screen revealed many mutations in genes related to autophagy — a cellular process in which unwanted cytoplasmic components are engulfed in vesicles called autophagosomes and degraded. In particular, Staring *et al.* identified a mutation in a gene that encodes the protein galectin-8.

The galectin family binds β-galactoside ligands on glycoproteins and glycolipids[5], which are typically located on the extracellular side of the cell membrane and so are arrayed on the interior surface of the endosome membrane after it pinches off into the cell. As such, galectins can sense endosomal-membrane damage — their ligands become accessible only after membrane rupture by bacteria or viruses[6]. Galectins then recruit proteins that initiate autophagy to selectively target the intruder[7].

Staring *et al.* tagged galectin-8 with green fluorescent protein (GFP), and studied its location in cells infected with poliovirus. Clusters of GFP-tagged galectin-8 formed rapidly when cells were exposed to the virus, and in some cases these puncta were found alongside viral RNA at the presumed sites of pore formation. The authors also found that GFP-tagged PLA2G16 was recruited to sites of poliovirus-induced membrane rupture, independent of galectin-8. Deletion of *PLA2G16* enhanced the proportion of galectin-8 puncta that co-localized with viral RNA. Together, these data suggest that PLA2G16 facilitates RNA displacement from the pore, somehow protecting it from galectin-8-mediated autophagy (Fig. 1). Consistent with this model, deletion of the gene *ATG7*, which encodes a core component of autophagy, also restored the ability of poliovirus to infect *PLA2G16*-deficient cells.

Autophagy is already known[8] to have key roles in picornaviral infections. After initial infection, proteins from some picornaviruses seem to promote the formation of autophagosome-like membranes that are co-opted to build replication factories[9]. At the other end of the life cycle, the new virus may be shed from the cell in autophagous microvesicles[10]. Staring and colleagues' work suggests a third point of engagement between viruses and this host pathway — galectin-8 senses dangerous pore formation and responds by activating autophagy.

Other players are unquestionably involved in this pathway. For instance, the enzyme TRIM16 and the autophagy machinery proteins ULK1 and ATG16L1 are essential for responses to bacterial membrane rupture that are mediated by another member of the galectin family[7], galectin-3. Interestingly, mutation