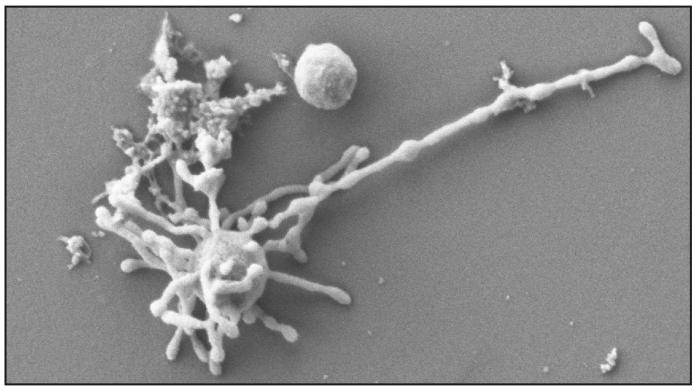
The search for your missing single-cell ancestor is heating up

Microbes that look like strange deep-sea creatures are turning out to be a missing link in the story of how we got here.

By Veronique Greenwood Updated April 18, 2023, 3:00 a.m.



An image from a scanning electron microscope shows archea cells with protusions that hint at an aspect of our deepest evolutionary history. ANDREAS KLINGL, LMU MUNICH

here's a mystery at the roots of the tree of life. There is a hole in the story.

You, the mushrooms in your lawn, and your golden retriever, as well as many other forms of life, are all eukaryotes, which means our cells have a nucleus.

That makes us unlike prokaryotes — more simple creatures like bacteria.

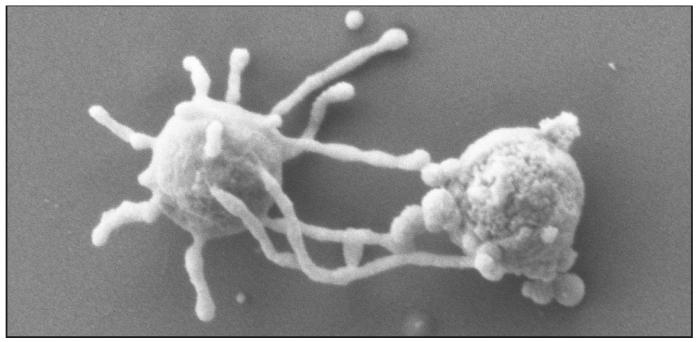
For us to be here today, some prokaryotic ancestor must have evolved a nucleus to store its DNA and adopted a system of small sacs, or organelles, in each cell. It must have absorbed a bacterium so long ago that the details are unknown and transformed it into our mitochondria, which are organelles that power our cells.

How that happened has long intrigued biologists. But information on what that ancestral cell looked like is hard to come by. When you build a family tree of all the creatures that scientists have studied, there is a huge gap between the bacteria and the rest of us. Buzz Baum, a professor of biology at University College London, imagines a game of survivorship played out over millennia, the sidelines littered with the losers. The half-formed versions of us are no longer here for scientists to study.

But 13 years ago, in deep-sea sediments north of Norway, scientists exploring near a hydrothermal vent found something that promises, at last, some answers. In that mud were archaea — single-celled organisms that look like bacteria. And in these particular archaea, the scientists later realized, were genes that had strong links to ours. They even had genes for a kind of actin, a protein that forms fibers within a eukaryotic cell and controls its shape. The Asgard archaea, as the scientists eventually called this group, look like they can help us understand what bridged the gap between prokaryotes and eukaryotes.

Since that initial discovery, scientists have been able to study the Asgards' genomes but not much more. To look at the creatures directly requires growing them in large numbers in the lab. This has proven very difficult — it took more than a decade for a team of Japanese researchers to grow one type from deep-sea sediments, and their numbers were too small for more than a few glimpses. In December, however, a team in Europe announced that at long last they had succeeded in growing enough Asgard archaea to make substantial observations. When they put fluid containing the microbes under an electron microscope, they beheld cells covered with limb-like protrusions, sometimes wound in an embrace with bacteria, other times frozen in place on their own.

This new ability to grow more Asgard archaea heralds a rush of future studies that will bring this lost cousin into focus — and perhaps reveal the origins of our own branch of life.



Another image from a scanning electron microscope of Asgard archea cells. ANDREAS KLINGL, LMU MUNICH

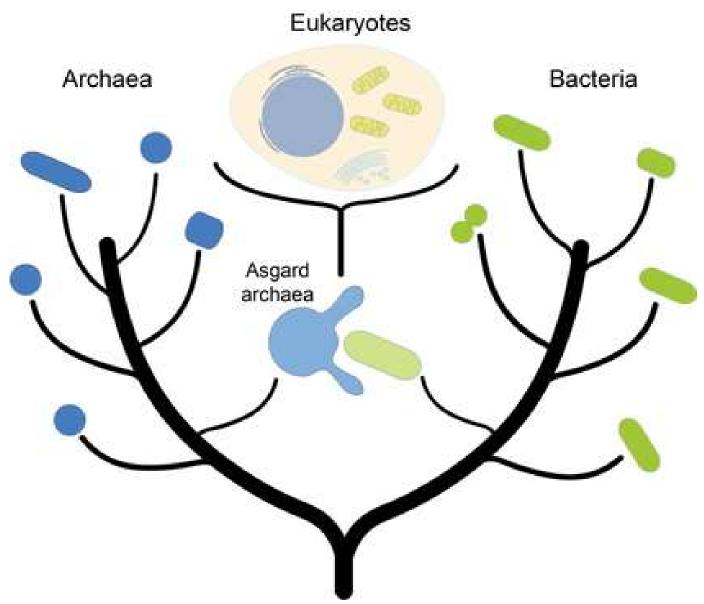
Hiding in plain sight

Incredibly, these missing links to the world before eukaryotic life have been living all around us all this time.

"When the Asgards were first discovered, we thought they were strange deep-sea creatures," recalls Toni Gabaldón, a geneticist at the Biomedical Research Institute and Barcelona Supercomputing Center in Spain. The suggestion that there might be more such organisms out there sent researchers looking for matches to the Asgard genomes in databases of genes sequenced from soil around the world. "They started to find them almost everywhere," Gabaldón says. "They are not very abundant, they are fragile — you don't see them because you don't look for them." This particular Asgard that is now being studied in more detail was plucked from a shallow canal on the coast of Slovenia by a team led by University of Vienna's Christa Schleper.

About 4 percent of the microbes that Schleper and her team found in the sediment from the Slovenian canal were this kind of Asgard. After they took the soil back to Vienna, a lengthy period followed, almost operatic in its highs and lows, in which Thiago Rodrigues-Oliveira, a post-doctoral researcher in Schleper's lab, treated the archaea with everything from antibiotics to Japanese powdered baby formula to try to get them to thrive. The cells grew, then stopped, then started again. When he

eventually discovered a technique that worked, says Schleper, it was almost more stressful than the failures: "Imagine you have struggled for years and then you see it's working! He had sleepless nights because he was so afraid that they would stop again."

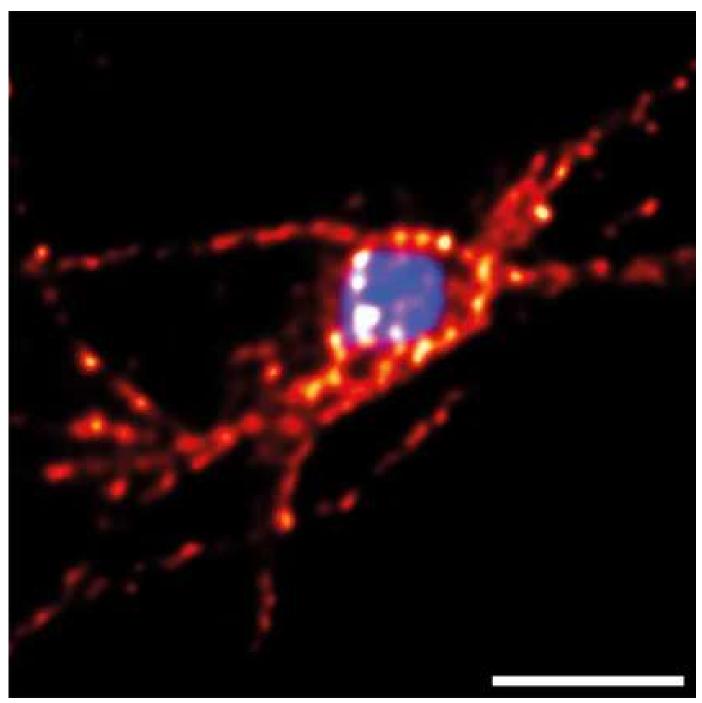


In this sketch of how evolutionary history appears to have transpired, eukaryotes (the category that includes us) arose after one of the Asgard archea incorporated a bacterium. COURTESY OF FLORIAN WOLLWEBER, ETH ZURICH

The cells were so fragile that they fell apart under the slightest touch. But the scientists have managed to take some images to look for evidence of actin-like fibers, which showed up as red strands spreading out across the cells. They also gently placed a sample of the culture on a metal grid and flash-froze it to look at in an electron microscope, a technique that would allow them to see at the cells' shapes.

These Asgards are tentacled, Medusa-like, their cells sprouting snaking protrusions. "The images are just incredibly beautiful," says Baum. Looking closer at the

membranes of the cells revealed that they are surpassingly strange. They are composed not of two layers of fat molecules, like our cells' membranes, nor a layer of fats and a layer of sturdy protein, like those of other archaea, but a single fat layer. That perhaps explains some of the cells' fragility.



Super-resolution fluorescence microscopy images of the actin-like fibers in Asgard archaea. This hints at a link to an ancestor of ours. FLORIAN WOLLWEBER, ETH ZURICH

Baum, who was not involved in the current study, has suspected for a while that the cells would have such tentacle-like shapes. Here's why: The mitochondria in our cells are the last visible fragment of a bacterium that formed a relationship with our ancestor. Some theories imagine our ancestor swallowing a bacterium whole and

figuring out how to make use of its abilities later on. In 2014, Baum and a colleague put <u>forth another idea</u>: It might have made more sense for the ancestral cell to form a partnership with a bacterium, perhaps encircling it gradually with long protrusions. Eventually, the bacterium and the creature embracing it found a way to become one.

Baum is quick to point out that his notion about the origin of mitochondria is still just a hypothesis: Whatever cell first acquired a mitochondrion lived more than a billion years ago, and it is not clear if the present form of these Asgards reflects that of their ancestor.

Reconstructing *that* organism would give us a clearer picture of our place in the tree of life. The swirl of new genetic information from the Asgards over the last few years shows that the lineage of eukaryotes — you, the mushrooms, the golden retriever, and much of everything else you see when you look around the natural world — turns out to be <u>a sister group to the Asgards</u>. So whatever ancestor the Asgards share with other archaea — that's our ancestor too.

There is something electrifying about looking at the tree of life from this new angle. There we are, sprouting up from among the archaea, side-by-side with the Asgards. Some of their strains bear the names of Norse gods, these tiny creatures that have been living alongside us, unnoticed, all these eons. What could be grander than the revelation that almost all the life we see around us descends from an ancestor shared by something so alien?

Veronique Greenwood is a science writer who contributes frequently to Ideas. Follow her on Twitter <u>@vero_greenwood</u>.

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