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RESEARCH NEWS

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Battle of the Bubbles May Have Sparked Evolution

The first survival-of-the-fittest competition was likely a physical duel between fatty bubbles stuffed with genetic material, researchers from the Howard Hughes Medical Institute are proposing. The scientists suggest that genetic material that replicated quickly may have been all the bubbles needed to edge out their competitors and begin evolving into more sophisticated cells.

This possibility, revealed by laboratory experiments with artificial fatty acid sacs, contrasts sharply with a current theory of the earliest evolution of cells, which suggests that cellular evolution was driven by primordial genetic machinery that actively synthesized cell membranes or otherwise influenced cell stability or division.

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The researchers, led by Howard Hughes Medical Institute investigator Jack W. Szostak, published their findings in the September 3, 2004, issue of the journal *Science* . Szostak and first author Irene Chen, both from Massachusetts General Hospital and Harvard Medical School, collaborated on the studies with Richard Roberts of the California Institute of Technology.

Cells are basically sacs encapsulated by bilayered membranes of fatty acids and other lipids, plus proteins. A central question in evolution is how simple versions of these cells, or vesicles, first arose and began the competitive process that drove the evolution of life.

“Most of the previous thinking about how cells grew and evolved was based on the idea of the initial evolution of structural RNAs or ribozymes—enzymes that could synthesize membrane molecules,” said Szostak. The ribozymes might have made more membrane material while the structural RNAs might have formed a cytoskeleton that influenced stability, shape, growth or division, he said.

However, Szostak and his colleagues theorized that a far simpler physical process might explain why cells would compete with one another for the materials necessary to expand their size.

“We proposed that the genetic material could drive the growth of cells just by virtue of being there,” he said. “As the RNA exerts an osmotic pressure on the inside of these little membrane vesicles, this internal pressure puts a tension on the membrane, which tries to expand. We proposed that it could do so through the spontaneous transfer of material from other vesicles nearby that have less internal pressure because they have less genetic material inside.”

In order to test their theory, the researchers first constructed simple model “protocells,” in which they filled fatty-acid vesicles with either a sucrose solution or the same solvent without sucrose. The sucrose solution created a greater osmotic pressure inside the vesicles than the solvent alone. The membranes of the simple vesicles were not as sophisticated as the membranes of today's living cells, said Szostak. However, they closely resembled the kinds of primordial vesicles that might have existed at the beginning of evolution.

When the scientists mixed the two vesicles, they observed that the ones with sucrose - in which there was greater membrane tension - did, indeed, grow by drawing membrane material from those without sucrose.

“Once we had some understanding that this process worked, we moved on to more interesting versions, in which we loaded the vesicles with genetic molecules,” said Szostak. The researchers conducted the same competition tests using vesicles loaded with the basic molecular building blocks of genetic material, called nucleotides. Next, they used RNA segments, and finally a large, natural RNA molecule. In all cases, they saw that the vesicles swollen with genetic material grew, while those with no genetic material shrank.

It is important to note, said Szostak, the concentrations of genetic material that his group used were comparable to those found in living cells.

“In contrast to the earlier idea that Darwinian competition at the cellular level had to wait until the evolution of lipid-synthesizing ribozymes or structural RNAs, our results show that all you would need is to have the RNA replicating,” said Szostak. “The cells that had RNA that replicated better—and ended up with more RNA inside—would grow faster. So, there is a direct coupling between how well the RNA replicates and how quickly the cell can grow. It's just based on a physical principle and would emerge spontaneously,” he said.

According to Szostak, the next step in the research will depend on another major effort under way in his laboratory to create artificial, replicating RNA molecules.

“If we can get self-replicating RNAs, then we can put them into these simple membrane compartments and hope to actually see this competitive process of growth that we are hypothesizing,” he said.