Life Studies in Clay

Exploring physical-chemical mechanisms for how it all began.

Researchers have identified conditions that possibly led to the development of living cells on Earth, though they are quick to note it isn't the definitive word on the origins of life. HHMI investigator Jack W. Szostak and colleagues Martin M. Hanczyc and Shelly M. Fujikawa at Massachusetts General Hospital discovered that montmorillonite, a type of absorbent clay, could have catalyzed the assembly of tiny fatty acid particles, called micelles, into sacs that ultimately evolved into the first living cells.

Under simulated conditions in the laboratory, the researchers also demonstrated that such sacs, known as vesicles, could be induced to grow in size and to split into separate vesicles. They reported their studies in the October 24, 2003, issue of *Science*.

Szostak and his colleagues were prompted to perform their experiments by other scientists' discovery that montmorillonite could catalyze the chemical reactions needed to construct RNA from building blocks called nucleotides. If the clay could also foster the formation of vesicles, they thought, it would not be inconceivable that clay particles with RNA on their surface could end up inside such vesicles. And if that were true, the resulting conditions might be amenable to self-replication.

The researchers knew that micelles are stable under conditions of basic pH but spontaneously assemble into vesicles when exposed to more acidic conditions, though the process takes some time. "We reasoned that if the right kind of mineral surface was present, this lag phase would be eliminated," says Szostak. Indeed, he and his colleagues found that adding small quantities of the clay to micelles greatly accelerated the initial rate of vesicle formation. They also discovered that many other substances with negatively charged surfaces catalyzed formation of vesicles as well.

When the researchers loaded montmorillonite particles with fluorescently labeled RNA and then added them to micelles, they were able to detect the RNA-loaded particles inside the resulting vesicles. Going a step further, they showed that when they encapsulated labeled RNA alone inside vesicles, it did not leak out.

"Thus, we have demonstrated that not only can clay and other mineral surfaces accelerate vesicle assembly, but assuming that the clay ends up inside at least some of the time, this provides a pathway by which RNA could get into vesicles," Szostak says.

However, Szostak notes, even primitive, nonliving cell-like structures need a mechanism to grow and divide. So the scientists explored the behavior of vesicles to which micelles were slowly added. Using tracking dyes and quantitative methods, they confirmed that the added micelles were, in fact, being incorporated into preformed vesicles and increasing in size, rather than congregating and forming new vesicles.

"After we showed that efficient growth was possible, the next problem was how to complete the cycle by persuading these vesicles to divide," Szostak recalls. The scientists discovered that if they extruded larger dye-containing vesicles through small-pore filters, the result was a proliferation of smaller vesicles that still contained dye.

They aren't sure exactly how the proliferation occurs, though they are developing different models to explain the process. "The important thing is that it all works. You end up with small vesicles in which the contents have stayed mostly inside," says Szostak. "This is important if the process is to be vaguely analogous to biological cell division. Now that we have proof of principle that growth and division are possible in a purely physical-chemical system, we are trying to get this cycle to function in a way that is more natural," he says.

Meanwhile, the investigators are keeping their findings in perspective. "We are not claiming that this is how life started," Szostak maintains. "We *are* saying that we have demonstrated growth and division without any biochemical machinery. If we can now demonstrate more natural ways in which this might have happened, it may begin to give us clues about how life could have actually gotten started on the primitive Earth."

In addition, he suggests, further research should aim to demonstrate that the formation of RNA—or a related polymer molecule—could take place concurrently with vesicle replication. "If we could demonstrate both processes under arbitrary laboratory conditions," says Szostak, "we could begin to make them work under more natural conditions."

—DENNIS MEREDITH

Jack Szostak looks for clues about how life could have started on primitive Earth.

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