Researchers Discover Remnant of an Ancient 'RNA World'

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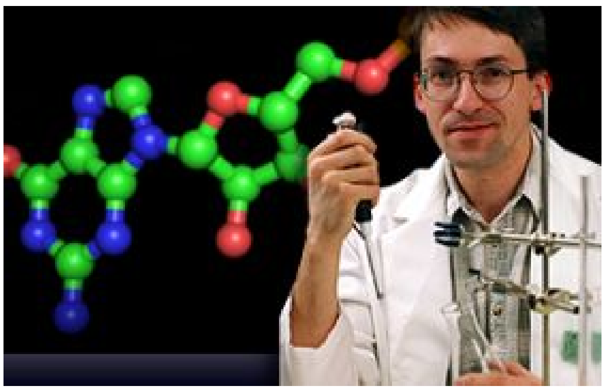

Ronald Breaker and the chemical structure of cyclic di-GMP.

(PhysOrg.com) -- Some bacterial cells can swim, morph into new forms and even become dangerously virulent - all without initial involvement of DNA. Yale University researchers describe Friday in the journal *Science* how bacteria accomplish this amazing feat - and in doing so provide a glimpse of what the earliest forms of life on Earth may have looked like.

To initiate many important functions, bacteria sometimes depend entirely upon ancient forms of RNA, once viewed simply as the chemical intermediary between DNA's instruction manual and the creation of proteins, said Ronald Breaker, the Henry Ford II Professor of Molecular, Cellular and Developmental Biology at Yale and senior author of the study.

Proteins carry out almost all of life's cellular functions today, but many scientists like Breaker believe this was not always the case and have found many examples in which RNA plays a surprisingly large role in regulating cellular activity. The Science study illustrates that - in bacteria, at least - proteins are not always necessary to spur a host of fundamental cellular changes, a process Breaker believes was common on Earth some 4 billion years ago, well before DNA existed.

"How could RNA trigger changes in ancient cells without all the proteins present in modern cells? Well, in this case, no proteins, no problem," said Breaker, who is also a Howard Hughes Medical Institute investigator.

Breaker's lab solved a decades-old mystery by describing how tiny circular RNA molecules called cyclic di-GMP are able to turn genes on and off. This process determines whether the bacterium swims or stays stationary, and whether it remains solitary or joins with other bacteria to form organic masses called biofilms. For example, in Vibrio cholerae, the bacterium that causes cholera, cyclic di-GMP turns off production of a protein the bacterium needs to attach to human intestines.

The tiny RNA molecule, comprised of only two nucleotides, activates a larger RNA structure called a riboswitch. Breaker's lab discovered riboswitches in bacteria six years ago and has since shown that they can regulate a surprising amount of biological activity. Riboswitches, located within single strands of messenger RNA that transmit a copy of DNA's genetic instructions, can independently "decide" which genes in the cell to activate, an ability once thought to rest exclusively with proteins.

Breaker had chemically created riboswitches in his own lab and - given their efficiency at regulating gene expressions - predicted such RNA structures would be found in nature. Since 2002, almost 20 classes of riboswitches, including the one described in today's paper, have been discovered, mostly hidden in non-gene-coding regions on DNA.

"We predicted that there would be an ancient 'RNA city' out there in the jungle, and we went out and found it," Breaker said.

Bacterial use of RNA to trigger major changes without the involvement of proteins resolves one of the questions about the origin of life: If proteins are needed to carry out life's functions and DNA is needed to make proteins, how did DNA arise?

The answer is what Breaker and other researchers call the RNA World. They believe that billions of years ago, single strands of nucleotides that comprise RNA were the first forms of life and carried out some of the complicated cellular functions now done by proteins. The riboswitches are highly conserved in bacteria, illustrating their importance and ancient ancestry, Breaker said.

Understanding how these RNA mechanisms work could lead to medical treatments as well, Breaker noted. For instance, a molecule that mimics cyclic di-GMP could be used to disable or disarm bacterial infections such as cholera, he said.

Provided by Yale University

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