Scientists find evidence for alternate theory of how life arose

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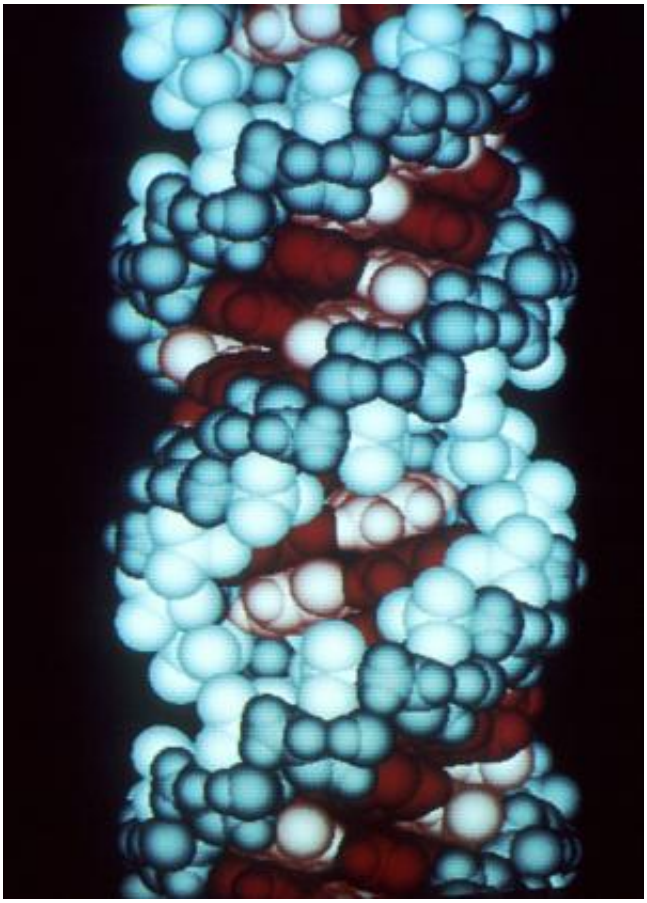

This is a computer graphic of an RNA molecule. Credit: Richard Feldmann/Wikipedia

A new study led by scientists at The Scripps Research Institute (TSRI) offers a twist on a popular theory for how life on Earth began about four

billion years ago.

The study questions the "RNA world" hypothesis, a theory for how RNA molecules evolved to create proteins and DNA. Instead, the new research offers evidence for a world where RNA and DNA evolved simultaneously.

"Even if you believe in a RNA-only world, you have to believe in something that existed with RNA to help it move forward," said Ramanarayanan Krishnamurthy, associate professor of chemistry at TSRI and senior author of the new study. "Why not think of RNA and DNA rising together, rather than trying to convert RNA to DNA by means of some fantastic chemistry at a prebiotic stage?"

The study was published recently in the journal *Angewandte Chemie*.

A Look Back in Time

Researchers have explored the RNA world hypothesis for more than 30 years. The idea behind this theory is that a series of chemical reactions led to the formation of self-replicating RNA molecules. RNA then evolved to create proteins and enzymes that resembled early versions of what makes up life today. Eventually, these enzymes helped RNA produce DNA, which led to complex organisms.

On the surface, RNA and DNA molecules look similar, with DNA forming a ladder-like structure (with nucleobase pairs as the rungs and sugar molecule backbones as the sides) and RNA forming what looks like just one side of a ladder.

If the RNA world theory is accurate, some researchers believe there would have been many cases where RNA nucleotides were mixed with DNA backbones, creating "heterogeneous" strands. If stable, these

blended "chimeras" would have been an intermediate step in the transition to DNA.

Problems with Instability

However, the new study shows a significant loss of stability when RNA and DNA share the same backbone. The chimeras do not stay together as well as pure RNA or pure DNA, which would compromise their ability to hold genetic information and replicate.

"We were surprised to see a very deep drop in what we would call the 'thermal stability,'" said Krishnamurthy, who in addition to his position at TSRI has joint appointments with the National Science Foundation (NSF)-National Aeronautics and Space Administration (NASA) Center for Chemical Evolution and the Simons Collaboration on the Origins of Life. This instability appeared to be due to a difference in the DNA sugar molecule structure versus the RNA sugar molecule.

The finding supported previous research from Nobel laureate and Harvard University Chemistry and Chemical Biology Professor Jack Szostak that showed a loss of (nucleotide-binding aptamer) function when RNA mixed with DNA.

Because of this instability, chimeras in the RNA world would have likely died off in favor of more stable RNA molecules. This reflects what scientists see in cells today: If RNA nucleobases mistakenly join a DNA strand, sophisticated enzymes will rush to fix the mistake. Evolution has led to a system that favors more stable, "homogeneous" molecules.

These sophisticated enzymes were probably not around at the time of RNA and DNA's early evolution, so these substitutions may have had a crippling effect on the molecules' ability to replicate and function. "The transition from RNA to DNA would not have been easy without

mechanisms to keep them separate," said Krishnamurthy.

Considering a Second Theory

This realization led the scientists to consider an alternate theory: RNA and DNA may have arisen in tandem.

Krishnamurthy emphasized that his lab is not the first to propose this theory, but the findings on chimeric instability give scientists new evidence to consider.

If the two evolved at the same time, DNA could have established its own homogeneous system early on. RNA could have still evolved to produce DNA, but that may have occurred after it first met DNA and got to know its raw materials.

Krishnamurthy added that scientists will never know exactly how life began (barring the invention of a time machine), but by considering circumstances of early evolution, scientists can gain insights into the fundamentals of biology.

In addition to Krishnamurthy, authors of the study "RNA-DNA Chimeras in the Context of an RNA-world Transition to an RNA/DNA-world," were Jesse V. Gavette (first author) and Matthias Stoop of TSRI and the NSF-NASA Center for Chemical Evolution; and Nicholas V. Hud of the Georgia Institute of Technology and the NSF-NASA Center for Chemical Evolution.

More information: Jesse V. Gavette et al. RNA-DNA Chimeras in the Context of an RNA World Transition to an RNA/DNA World, *Angewandte Chemie International Edition* (2016). DOI: 10.1002/anie.201607919

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