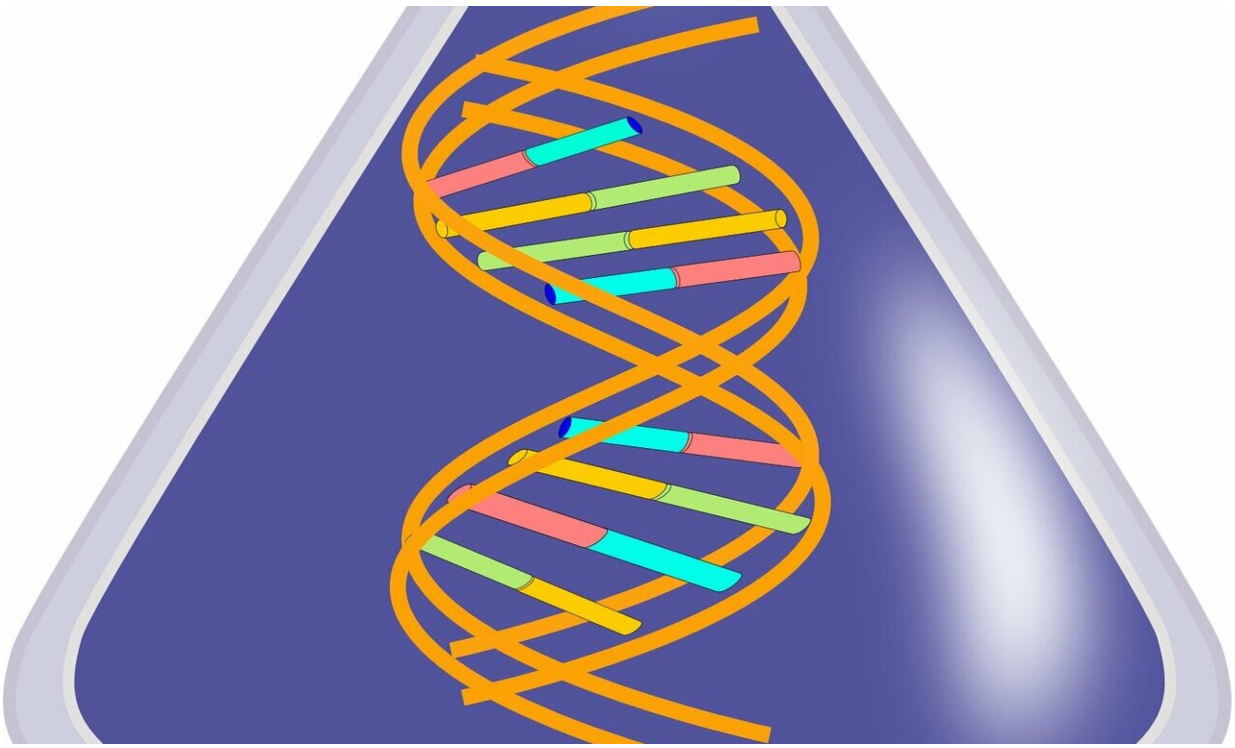
Discovery boosts theory that life on Earth arose from RNA-DNA mix

December 28 2020



Credit: CC0 Public Domain

Chemists at Scripps Research have made a discovery that supports a surprising new view of how life originated on our planet.

In a study published in the chemistry journal *Angewandte Chemie*, they demonstrated that a simple compound called diamidophosphate (DAP), which was plausibly present on Earth before life arose, could have chemically knitted together tiny DNA building blocks called deoxynucleosides into strands of primordial DNA.

The finding is the latest in a series of discoveries, over the past several years, pointing to the possibility that DNA and its close chemical cousin RNA arose together as products of similar chemical reactions, and that the first self-replicating molecules—the first life forms on Earth—were mixes of the two.

The discovery may also lead to new practical applications in chemistry and biology, but its main significance is that it addresses the age-old question of how life on Earth first arose. In particular, it paves the way for more extensive studies of how self-replicating DNA-RNA mixes could have evolved and spread on the primordial Earth and ultimately seeded the more mature biology of modern organisms.

"This finding is an important step toward the development of a detailed chemical model of how the first life forms originated on Earth," says study senior author Ramanarayanan Krishnamurthy, Ph.D., associate professor of chemistry at Scripps Research.

The finding also nudges the field of origin-of-life chemistry away from the hypothesis that has dominated it in recent decades: The "RNA World" hypothesis posits that the first replicators were RNA-based, and that DNA arose only later as a product of RNA life forms.

Is RNA too sticky?

Krishnamurthy and others have doubted the RNA World hypothesis in part because RNA molecules may simply have been too "sticky" to serve as the first self-replicators.

A strand of RNA can attract other individual RNA building blocks, which stick to it to form a sort of mirror-image strand—each building block in the new strand binding to its complementary building block on the original, "template" strand. If the new strand can detach from the template strand, and, by the same process, start templating other new strands, then it has achieved the feat of self-replication that underlies life.

But while RNA strands may be good at templating complementary strands, they are not so good at separating from these strands. Modern organisms make enzymes that can force twinned strands of RNA—or DNA—to go their separate ways, thus enabling replication, but it is unclear how this could have been done in a world where enzymes didn't yet exist.

A chimeric workaround

Krishnamurthy and colleagues have shown in recent studies that "chimeric" molecular strands that are part DNA and part RNA may have been able to get around this problem, because they can template complementary strands in a less-sticky way that permits them to separate relatively easily.

The chemists also have shown in widely cited papers in the past few years that the simple ribonucleoside and deoxynucleoside building blocks, of RNA and DNA respectively, could have arisen under very similar chemical conditions on the early Earth.

Moreover, in 2017 they reported that the organic compound DAP could have played the crucial role of modifying ribonucleosides and stringing them together into the first RNA strands. The new study shows that DAP under similar conditions could have done the same for DNA.

"We found, to our surprise, that using DAP to react with deoxynucleosides works better when the deoxynucleosides are not all the same but are instead mixes of different DNA 'letters' such as A and T, or G and C, like real DNA," says first author Eddy Jiménez, Ph.D., a postdoctoral research associate in the Krishnamurthy lab.

"Now that we understand better how a primordial chemistry could have made the first RNAs and DNAs, we can start using it on mixes of ribonucleoside and deoxynucleoside building blocks to see what chimeric molecules are formed—and whether they can self-replicate and evolve," Krishnamurthy says.

He notes that the work may also have broad practical applications. The artificial synthesis of DNA and RNA—for example in the "PCR" technique that underlies COVID-19 tests—amounts to a vast global business, but depends on enzymes that are relatively fragile and thus have many limitations. Robust, enzyme-free chemical methods for making DNA and RNA may end up being more attractive in many contexts, Krishnamurthy says.

More information: Ramanarayanan Krishnamurthy et al, Prebiotic Phosphorylation and Concomitant Oligomerization of Deoxynucleosides to form DNA, *Angewandte Chemie International Edition* (2020). DOI: 10.1002/anie.202015910

Provided by The Scripps Research Institute