Researchers find that the amino acid arginine may have played a more important role in the chemical origins of life

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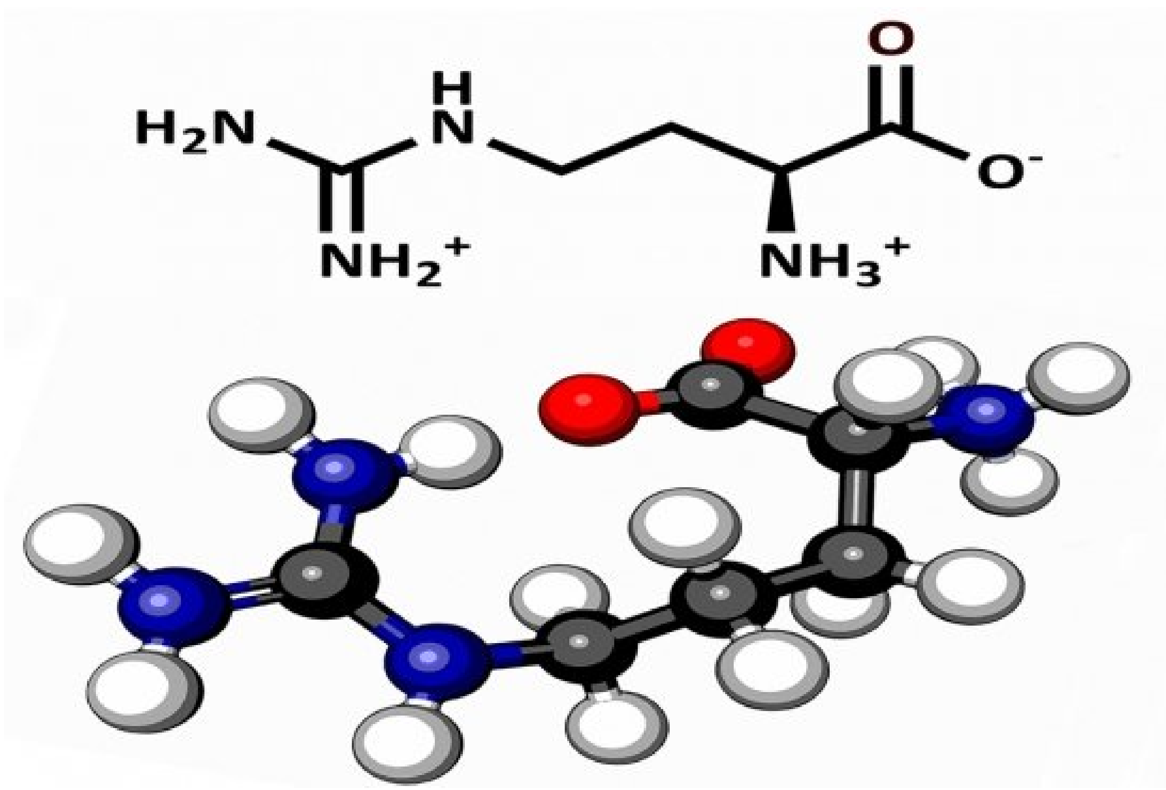

Credit: University of California - Santa Barbara

Life as we know it originated roughly 3.5 to 4 billion years ago in the form of a prebiotic ("before life") soup of organic molecules that somehow began to replicate themselves and pass along a genetic formula. Or so goes the thinking behind the RNA World, one of the most robust hypotheses of the origin of life.

Researchers at UC Santa Barbara have now found evidence that the amino acid arginine (or its prebiotic world equivalent) may have been a more important ingredient in this soup than previously thought.

"People tend to think of arginine as not being prebiotic," said Irene Chen, a biophysicist whose research focuses on the chemical origins of life. "They tend to think of the simpler amino acids as being plausible, such as glycine and alanine." Arginine, by contrast, is relatively more complex, and was therefore thought to have entered the game at a later stage.

Primordial Earth, according to the RNA World theory, had the conditions to host several types of biomolecules, including nucleic acids (which become genetic material), amino acids (which eventually link to form the proteins that are responsible for structure and function of cells) and lipids (which store energy and protect cells). Under what circumstances and how these biomolecules worked together is a source of ongoing investigation for researchers of the origins of life.

For their investigation, the UCSB scientists analyzed a dataset of in vitro evolved complexes of proteins and aptamers (short RNA and DNA molecules that bind to specific target proteins).

"We were looking at the interface for which properties favored binding," said Celia Blanco, a postdoctoral researcher in the Chen Lab, and lead author of a paper that appears in the journal *Current Biology*. In vitro evolution was an important factor when selecting these evolutionarily independent complexes, she pointed out, to avoid the confounding effects resulting from biological evolution and to closely mimic the conditions of a prebiotic world.

"There are so many constraints in biology," said Chen, who also is a medical doctor. "Biologically evolved protein-DNA or protein-RNA interactions have to work inside a cell; that's not exactly going to be the case for the origins of life."

What the researchers found was that arginine was a player in many of the chemical interactions between proteins and aptamers.

"Of course, we expected it to be very important for electrostatic interactions because it's positively charged," Chen said, "but it was also the dominant amino acid for hydrophobic interactions, stacking interactions and these other different modes of interacting that other amino acids are more known for." To a lesser degree, lysine (another positively charged amino acid) also played significant roles in these interactions.

Among other reasons, arginine may have been overlooked because it is a relatively more difficult amino acid to synthesize.

"Usually people base the consensus of what is prebiotic and what is not on experiments," Blanco said. "And using what people believe are prebiotic conditions, arginine and lysine seem to be difficult to either synthesize or detect." But just because something such as arginine hasn't been produced in the laboratory experiments conducted so far, Blanco continued, doesn't mean it wasn't there.

The researchers are careful to point out that although the amino acid we call arginine was found to be important in the aptamer-protein binding interactions they examined, billions of years ago the biomolecule may not necessarily have been today's arginine but perhaps a positively charged primordial equivalent.

This development sheds more light on what might have been the ideal conditions for the rise of life. There are a variety of hypotheses—from comets to hydrothermal vents to other environments—that may have been favorable for the eventual evolution of cells, as well as several landmark experiments that bolster the RNA World idea.

"If we had found that glycine was really important for RNA-protein interactions—and glycine is everywhere—then that would not have been helpful for determining plausible conditions," said Chen. "But finding that arginine was important constrains the type of scenarios that could have given rise to the genetic code."

More information: Celia Blanco et al. Analysis of Evolutionarily Independent Protein-RNA Complexes Yields a Criterion to Evaluate the Relevance of Prebiotic Scenarios, *Current Biology* (2018). DOI: 10.1016/j.cub.2018.01.014

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