Origin of life: the search for the first genetic material

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How did life originate on Earth? Until now, there have only been theories to answer this question. One of the fundamental steps leading to living organisms is the development of molecules that can replicate and multiply themselves—the first genetic material. A team led by Ramanarayanan Krishnamurthy and Albert Eschenmoser at The Scripps Research Institute in La Jolla, California, is researching how this molecule might have looked.

Our own genetic material is DNA. Its backbone is made of sugar and phosphate building blocks. Like a strand of pearls, the four "letters" of the genetic code are arranged along this backbone. Two complementary strands of DNA form a double helix because the purine bases adenine (A) and guanine (G) form specific pairs with the pyrimidine bases thymine (T) and cytosine (C), attaching to each other through two or three docking sites.

This type of structure could also be the basis for the first genetic material. However, it is doubtful that its backbone consisted of sugar and phosphate; it may have consisted of peptide-like building blocks. Amino acids, from which peptides are made, were already present in the "primordial soup". However, the bases may also have looked different in their primitive form.

To find the right track in searching for the origins of life, the team is trying to put together groups of potential building blocks from which primitive molecular information transmitters could have been made. The researchers have taken a pragmatic approach to their experiments. Compounds that they test do not need to fulfill specific chemical criteria; instead, they must pass their "genetic information" on to subsequent generations just as simply as the genetic molecules we know today—and their formation must have been possible under prebiotic conditions.

Experiments with molecules related to the usual pyrimidine bases (pyrimidine is a six-membered aromatic ring containing four carbon and two nitrogen atoms), among others, seemed a good place to start. The team thus tried compounds with a triazine core (a six-membered aromatic ring made of three carbon and three nitrogen atoms) or aminopyridine core (which has an additional nitrogen- and hydrogen-containing side group). Imitating the structures of the normal bases, the researchers equipped these with different arrangements of nitrogen- and hydrogen- and/or oxygen-containing side groups.

Unlike the usual bases, these components can easily be attached to many different types of backbone, for example, a backbone made of dipeptides or other peptide-like molecules. In this way, the researchers did indeed obtain molecules that could form specific base pairs not only with each other, but also with complementary RNA and DNA strands. Interestingly, only one sufficiently strong pair was formed within both the triazine and aminopyridine families; however, for a four-letter system analogous to the ACGT code, two such strongly binding pairs are necessary.

"Our results indicate that the structure of the bases, rather than the structure of the backbone, was the critical factor in the development of our modern genetic material," says Krishnamurthy. Many chain molecules are able to adopt a suitable spatial structure, but only a few bases can enter into the necessary specific pairing. In this, our alternative bases are clearly inferior to the usual Watson–Crick bases. "Based on our observations, we are beginning to understand why the natural bases are optimal with regard to the function they perform."

Citation: Ramanarayanan Krishnamurthy et al., Mapping the Landscape of Potentially Primordial Informational Oligomers: Oligodipeptides and Oligodipeptoids Tagged with Triazines as Recognition Elements / Mapping the Landscape of Potentially Primordial Informational Oligomers: Oligodipeptides Tagged with 2,4-Disubstituted 5-Aminopyrimidines as Recognition Elements, *Angewandte Chemie International Edition*, doi: 10.1002/anie.200603207

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