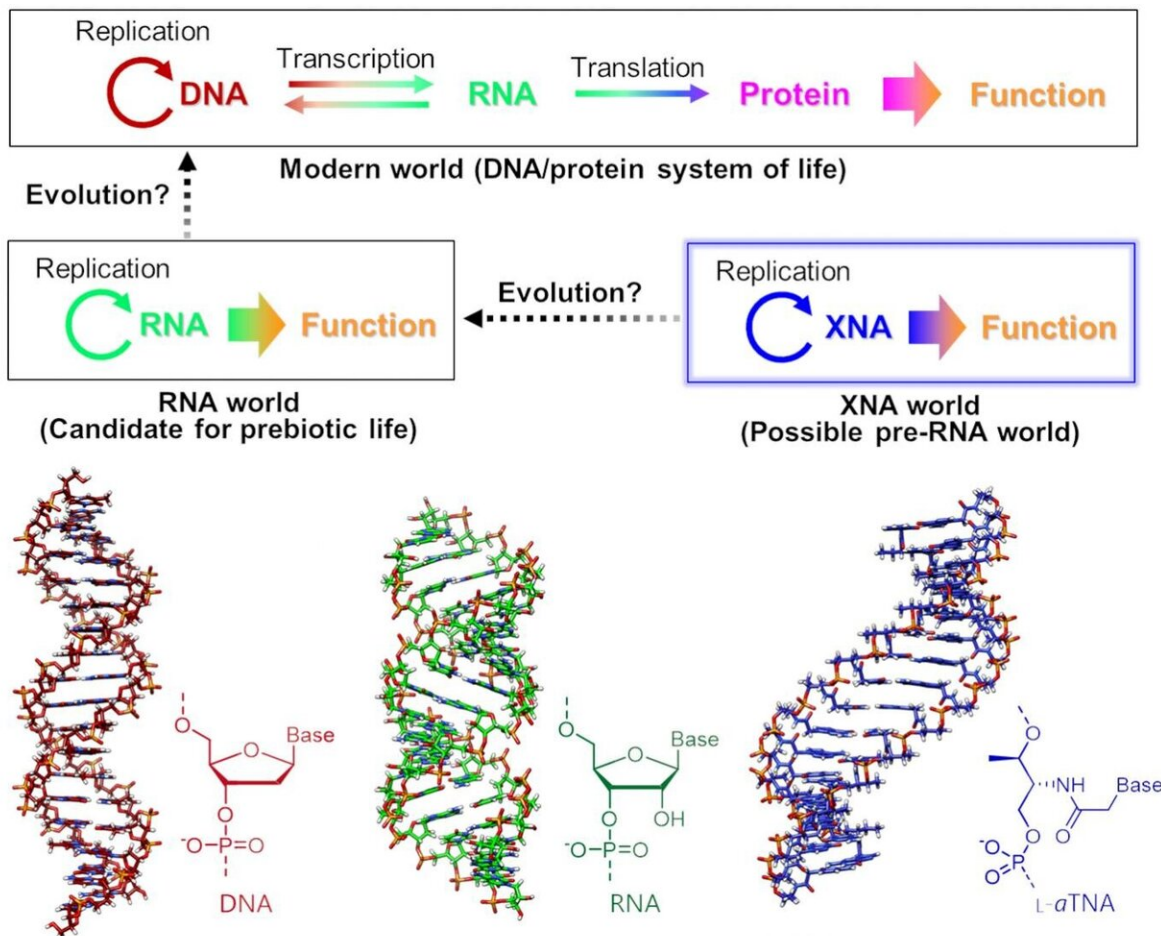


Origins of life could have started with DNA-like XNAs

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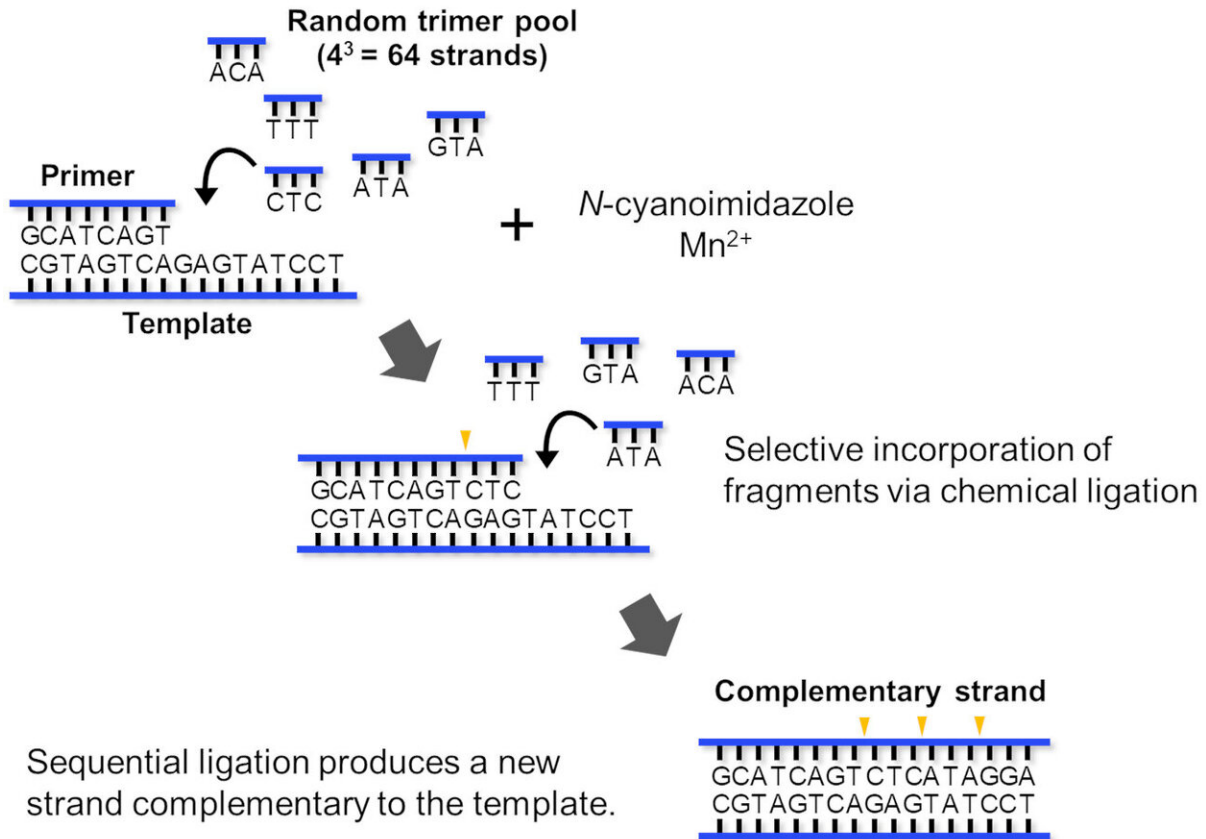
Some scientists think that XNA evolved into RNA, which then evolved into DNA, forming the very beginnings of life. Credit: Keiji Murayama

Nagoya University scientists in Japan have demonstrated how DNA-like molecules could have come together as a precursor to the origins of life. The findings, published in the journal *Nature Communications*, not only suggest how life might have begun, but also have implications for the development of artificial life and biotechnology applications.

"The RNA world is widely thought to be a stage in the origin of life," says Nagoya University biomolecular engineer Keiji Murayama. "Before this stage, the pre-RNA world may have been based on molecules called xeno [nucleic acids](#) (XNAs). Unlike RNA, however, XNA replication probably didn't require enzymes. We were able to synthesize an XNA without enzymes, strongly supporting the hypothesis that an XNA world might have existed before the RNA world."

XNAs are formed of chains of linked nucleotides, similar to DNA and RNA but with a different sugar backbone. XNAs can carry genetic code very stably because the human body can't break them down. Some researchers have reported that XNAs containing specific sequences can act as enzymes and bind to proteins. This makes XNAs exciting in the field of synthetic genetics, with potential biotechnology and molecular medicine applications.

Murayama, Hiroyuki Asanuma and colleagues wanted to find out if conditions likely present on early Earth could have led to XNA chain formation. They synthesized fragments of *acyclic* (non-circular) L-threoninol nucleic acid (L-*a*TNA), a molecule that is thought to have existed before RNA came to be. They also made a longer L-*a*TNA with a nucleobase sequence that complemented the sequences of the fragments, similar to how DNA strands match up.



Murayama and his colleagues showed that L-aTNA fragments could interlink on complementary L-aTNA, RNA and DNA templates without the need for enzymes. Credit: Keiji Murayama

When placed together in a [test tube](#) under controlled temperature, the shorter L-aTNA fragments came together and linked up with each other on the longer L-aTNA template. Critically, this happened in the presence of a compound, called N-cyanoimidazole, and a metal ion, like manganese, both of which were possibly present in early Earth. The fragments interlinked when a phosphate at the end of one chemically attached to a hydroxyl group at the end of its neighbor, without the help of an enzyme.

"To the best of our knowledge, this is the first demonstration of template-driven, enzyme-free extension of *acyclic* XNA from a random fragment pool, generating phosphodiester bonding," says Murayama.

The team also demonstrated that L-*a*TNA fragments could interlink on DNA and RNA templates. This suggests that [genetic code](#) could be transferred from DNA and RNA onto L-*a*TNA and vice versa.

"Our strategy is an attractive system for experimenting with the construction of artificial life and the development of highly functional biological tools composed of *acyclic* XNA," says Murayama. "The data also indicate that L-*a*TNA could have been an RNA precursor."

The team plans to continue their investigations to clarify whether L-*a*TNA could have been synthesized in early Earth 'pre-life' conditions and to examine their potential for developing advanced biological tools.

More information: Keiji Murayama et al, Nonenzymatic polymerase-like template-directed synthesis of acyclic l-threoninol nucleic acid, *Nature Communications* (2021). [DOI: 10.1038/s41467-021-21128-0](https://doi.org/10.1038/s41467-021-21128-0)

Provided by Nagoya University

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