

World's first artificial enzymes created using synthetic biology

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A team of researchers have created the world's first enzymes made from artificial genetic material.

The research is published in the journal *Nature* and promises to offer new insights into the origins of life, as well as providing a potential starting point for an entirely new generation of drugs and diagnostics.

In addition, the authors speculate that the study increases the range of planets that could potentially host life.

The findings build on previous work in which the scientists, from the MRC Laboratory of Molecular Biology in Cambridge and the University of Cambridge, created synthetic molecules called 'XNAs'.

These are entirely artificial genetic systems that can store and pass on genetic information in a manner similar to DNA.

The synthetic enzymes, which are made from molecules that do not occur anywhere in nature, are capable of triggering chemical reactions in the lab.

All life on earth depends on the chemical transformations that enable cellular function and the performance of basic tasks, from digesting food to making DNA.

These are powered by naturally-occurring enzymes which operate as catalysts, kick-starting the process and enabling such reactions to happen at the necessary rate.

For the first time, however, the research shows that these natural biomolecules may not be the only option, and that artificial enzymes could also be used to power the reactions that enable life to occur.

Using these XNAs as building blocks, the new research involved the creation of so-called 'XNAzymes'. Like naturally occurring enzymes, these are capable of powering simple biochemical reactions.

Dr Alex Taylor, a post-doctoral researcher at St John's College, University of Cambridge, who is based at the MRC Laboratory and was the study's lead author, said: "The chemical building blocks that we used in this study are not naturally-occurring on Earth, and must be synthesized in the lab. This research shows us that our assumptions about what is required for biological processes - the 'secret of life' - may need some further revision. The results imply that our chemistry, of DNA, RNA and proteins, may not be special and that there may be a vast range of alternative chemistries that could make life possible."

Our cells contains thousands of different enzymes, many of which are proteins.

In addition, however, nucleic acids - DNA and its close chemical cousin, RNA - can also form enzymes.

The ribosome, the molecular machine which manufactures proteins within all cells, is an RNA enzyme.

Life itself is widely thought to have begun with the emergence of a self-copying RNA enzyme.

Dr Philipp Holliger, from the MRC Laboratory of Molecular Biology, said, "Until recently it was thought that DNA and RNA were the only molecules that could store genetic information and, together with proteins, the only biomolecules able to form enzymes."

He stated, "Our work suggests that, in principle, there are a number of possible alternatives to nature's molecules that will support the catalytic processes required for life. Life's 'choice' of RNA and DNA may just be an accident of prehistoric chemistry."

"The creation of synthetic DNA, and now enzymes, from building blocks that don't exist in nature also raises the possibility that if there is life on other planets it may have sprung up from an entirely different set of molecules, and widens the possible number of planets that might be able to host life," he further added.

The group's previous study, carried out in 2012, showed that six alternative molecules, called XNAs, could store genetic information and evolve through natural selection.

Expanding on that principle, the new research identified, for the first time, four different types of synthetic catalyst formed from these entirely unnatural building blocks.

These XNAzymes are capable of catalyzing simple reactions, like cutting and joining strands of RNA in a test tube.

One of the XNAzymes can even join strands together, which represents one of the first steps towards creating a living system.

Because their XNAzymes are much more stable than naturally occurring enzymes, the scientists believe that they could be particularly useful in developing new therapies for a range of diseases, including cancers and viral infections, which exploit the body's natural processes.

Dr Holliger added, "Our XNAs are chemically extremely robust and, because they do not occur in nature, they are not recognized by the body's natural degrading enzymes. This might make them an attractive candidate for long-lasting treatments that can disrupt disease-related RNAs."

Prof. Patrick Maxwell, chair of the MRC's Molecular and Cellular Medicine Board and Regius Professor of Physic at the University of Cambridge, said, "Synthetic biology is delivering some truly amazing advances that promise to change the way we understand and treat disease. The UK excels in this field, and this latest advance offers the tantalizing prospect of using designer biological parts as a starting point for an entirely new class of therapies and diagnostic tools that are more effective and have a longer shelf-life."

Funders of the research included the MRC, European Science Foundation and the Biotechnology and Biological Sciences Research Council.