



## A Synthetic DNA Built from Eight Building Blocks

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**Alachua, FL** – Life may be defined as a self-sustaining chemical system capable of Darwinian evolution. On Earth, humans use DNA to evolve, transferring information stored in its four building blocks first to RNA, and then to proteins. DNA and RNA are "universal" among known life forms on Earth. But are they truly *universal*, in life throughout the cosmos?

An article published today in *Science* magazine suggests not. It reports a new kind of DNA, not from nature, but made in the lab by synthetic biologists. That new DNA doubles the four building blocks in natural DNA, making an 8-letter synthetic genetic system, called "hachimoji" DNA (from the Japanese "hachi" meaning "eight", and "moji" meaning "letter", as in "e-moji").

Hachimoji DNA can do everything that DNA does to support life. It pairs predictably, and rules predict its stability. Hachimoji DNA can be copied to make hachimoji RNA, able to direct protein synthesis. Hachimoji RNA can have a selectable phenotype, in this article, a green-fluorescent glow. Information storage, transmission, and selectable phenotype are three requirements of evolution.

But there is a fourth: Structural regularity. "In 1942, Schrödinger predicted that no matter what genetic polymer life uses, its informational building blocks must all have the same shape and size," said Steven Benner, who led the team that created hachimoji DNA. Hachimoji meets this prediction. "Crystal structures of three different hachimoji DNA double helices reveal sequence-specific properties while retaining the essential features of natural DNA," said Millie Georgiadis, whose team at the Indiana University School of Medicine provided the crystal structures of hachimoji DNA.

"This study reminds us of how much we have yet to learn about DNA and RNA", said Jack Szostak, 2009 Nobel Laureate in Medicine, whose own research concerns RNA and the origin of life. Szostak was not involved in this study. That learning comes by studying hachimoji DNA. "Careful analysis of the shape, size, and structural regularity in hachimoji DNA shows the importance of hydrogen

bonding and charge in evolvable informational molecules", remarked John Santa Lucia, whose team at DNA Software calculated the rules for hachimoji stability.

But could hachimoji DNA have arisen on other planets? "We do not suggest that this eight-letter alphabet arose prebiotically, any more than we think that DNA-RNA-protein arose together," remarked Andrew Ellington, who provided enzymes that make hachimoji RNA. "However, we can imagine parallel processes. On Earth, life struggled first to improve RNA, modifying its building blocks. Some of these modifications survive today. However, terran biology eventually took a different route, inventing proteins. On Vulcan, life may have continued to improve its RNA without inventing proteins, maybe to give an 8-letter system that this work shows is possible."

Last year, Chris McKay of NASA Ames asked Breakthrough Foundation panelists where they expected to first find alien life. While Europa, Mars, Titan, and Enceladus were all discussed, Benner suggested that it might come first from a lab on Earth. "However, it is wrong to say that hachimoji DNA is alien life," Benner cautions. "For that, the system also must be self-sustaining." Hachimoji DNA requires a steady supply of lab-created building blocks and proteins from an attentive scientist. As none of these are available outside, hachimoji DNA can go nowhere if it escapes the laboratory.

Hachimoji DNA also has many applications. These include improved diagnostics, alternatives to silicon for information storage, proteins with extra amino acids, and new kinds of drugs. Firebird Biomolecular Sciences, which provided the synthetic material, commercializes these. "Parts of this new DNA are already in products to diagnose disease and monitor the environment for disease-causing viruses," said Mark Poritz, who directs product development at Firebird. "It is exciting whenever basic science can impact people's health, as this work can."

Paper cited: Hoshika, S, Leal NA, et al. Hachimoji DNA and RNA: A genetic system with eight building blocks. *Science*. February 22, 2019

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**Figure.** Crystal structure of a double helix built from eight hachimoji building blocks, G (green), A (red), C (dark blue), T (yellow), B (cyan), S (pink), P (purple), and Z (orange). The first four building blocks are found in human DNA; the last four are synthetic, and possibly present in alien life. Each strand of the double helix has the sequence CTTAPCBTASGZTAAG. Notable is the geometric regularity of the pairs, a regularity that is needed for evolution.



### **About Templeton World Charity Foundation**

Based in Nassau, the Bahamas, the Templeton World Charity Foundation aims to provide scientific breakthroughs and practical tools relating to the search for meaning, purpose, and truth. The Foundation works with top institutions, thought leaders, and innovators from around the globe to support projects of the highest caliber and communicate the results of these projects to a wide audience. Since 2013 the Foundation has invested more than \$20 million in new research through its Power of Information Initiative. The purpose of the Initiative is to explore scientifically and philosophically the concept of information and its utility for understanding a wide variety of physical and biological processes.

### **About DNA Software**

DNA Software, Inc. provides accurate and comprehensive software tools for assay development and nucleic acid research. Unique among software companies, DNA Software also conducts original "wet" laboratory research. Thus, the company's software programs are based on advanced algorithms and models driven by a large database of thousands of diverse, wet lab-derived, experimental results. DNA Software offers contract research, custom software development, commercial web applications, and scientific consulting for nucleic acid research. The company licenses packaged software tools that help scientists quickly and accurately develop new assays, diagnostics, and therapeutics. The company has recently expanded its original DNA and RNA-based, molecular biology solutions to include modified nucleotides, oligonucleotide kinetics, structural biology and, of course, hachimoji DNA.

### **About Firebird Biomolecular Sciences LLC**

Firebird Biomolecular Sciences LLC is a biotechnology company specializing in the manufacture and sale of innovative nucleic acid reagents, enzymes that manage them, and integrated systems that use them, for DNA synthesis, DNA sequence analysis, diagnostics, laboratory research, and therapeutics. These include building blocks for hachimoji DNA, both separately and in applications. For more information please visit [www.firebirdbio.com](http://www.firebirdbio.com).