

## **"Chemical relic" offers clue to origin of life on earth**

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Media Contact: Warren R. Froelich, (619) 534-8564, Janet Howard, (619) 534-7572

"CHEMICAL RELIC" OFFERS CLUE TO ORIGIN OF LIFE ON EARTH

A chemical relic now found only in a few viruses and single-cell marine organisms may represent a missing link between two genetic worlds that could help explain the origin of life on Earth.

In an article published in today's issue of Science, two chemists from the University of California, San Diego describe how this chemical relic could have formed a bridge linking the prebiotic era and "RNA world" to the world as we know it today, based on DNA and proteins.

"This finding suggests that the 'RNA world' may have been far more diverse and active than previously thought," said Stanley Miller, a professor of chemistry and biochemistry at UCSD who co-authored the new research with Michael P. Robertson, a research fellow at UCSD.

In modern cells, RNA (ribonucleic acid) is a close cousin of DNA (deoxyribonucleic acid), acting as a messenger responsible for carrying out the instructions of DNA for building proteins that run the cell's day-to-day operations.

In the RNA world, a term coined by Nobel laureate Walter Gilbert, RNA not only would store genetic information as is now done by DNA, but it also would act as a biochemical catalyst, the role now played by proteins.

Critics, however, questioned the validity of this theory, arguing that RNA--as we know it today--is far too limited as a catalyst compared to proteins. As a result, many turned away from the RNA world theory.

The research of Miller and Robertson could bring them back.

"The catalytic shortcomings of RNA can be overcome with simple modifications that would have been unavoidable under primitive Earth conditions," Miller said.

By recreating certain conditions thought to exist on primitive Earth 3.7 billion years ago, the UCSD researchers produced a chemical reaction between uracil--one of four nucleic acid bases found in RNA--and formaldehyde, a simple molecule thought to have been abundant on prebiotic Earth.

The result was a molecule called hydroxymethyluracil (HMU), a chemical found today only in some viruses and dinoflagellates, small single cell organisms found in the sea that multiply so rapidly they form "poisonous tides" or "red tides."

Importantly, HMU can be further modified to form what chemists call a "functional group" or "reactive site," allowing it to do the work of an enzyme.

"By putting these functional groups on RNA, the molecules are ready to carry out all the chemistry that's done by proteins now," said Miller. "That's what we think."

As proof, the chemists reacted HMU with several simple molecules thought to be present in the prebiotic soup of early Earth such as hydrogen cyanide, glycine, methylamine, hydrogen sulfide, ammonia, and others.

All reacted well under these conditions, and formed compounds that contained the functional groups of 13 amino acids that make up proteins. The results offer a potential explanation for the selection of the 20 amino acids found in today's proteins.

"If the first biochemical reactions, using modified RNA catalysts, were dependent on particular functional groups to catalyze the reaction, then the proteins that eventually replaced the RNA catalysts would also require the same functional groups," Miller said.

"The modified uracils, therefore, would also allow a smoother transition from the RNA world to the protein world," he said. "They are the missing link between the RNA world and the DNA-protein world."

As a next step, the researchers plan to further explore the catalytic activity of the modified bases.

"We'd like to see if we could catalyze a wider range of reactions than RNA is capable of now with these extra functional groups," said Robertson.

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