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Developing a Molecular Biology for Alternative Biopolymers in Early Evolution

E. Biondi[1,2], Z. Yang[1], L. Zhang[3], S. Dasgupta[4], J. A. Piccirilli[4], N. A. Leal[2] and S. A. Benner[1,2,*].

[1]Foundation for Applied Molecular Evolution, 13709 Progress Blvd., Alachua FL, 32615, [2]Firebird Biomolecular Sciences LLC, Alachua FL, [3]University of Florida, Gainesville FL, [4]University of Chicago, Chicago IL.

* sbenner@ffame.org

One of the more discussed hypotheses for the origin of life is the "RNA first" model. This model postulates that organic molecular systems first gained access to Darwinism through a spontaneous prebiotic formation of RNA molecules that were able to generate replicates, with imperfections, where the imperfections were themselves replicable.

Unfortunately, decades of *in-vitro* evolution attempts at reproducing the events that would have led to such a replicase delivered few, if impressive, results, most of which are highly derived RNA ligases. The fact that it is so difficult to reproduce an RNA species central to the "RNA first" hypothesis suggests that we might be missing something. Thus, many laboratories have sought alternative biopolymers that are both prebiotically accessible, and that also support Darwinism as well or better than standard RNA, managing the rather low intrinsic catalytic ability of RNA as it is today found in terran biology, and the frequently reproduced experimental observation that it is easier to get nucleic acid molecules that catalyze the destruction of RNAs than nucleic acids that catalyze its synthesis.

Here, we report experimental results with such nucleic acid-like biopolymers made from six different building blocks (Artificially Expanded Genetic Alphabet, or AEGIS). These additional nucleotides carry functionality that chemical theory suggests might assist in binding and catalysis, perhaps even catalysis for the synthesis of RNA.

We will describe the development and applications of a molecular biology for this artificial genetic system, including pipelines to synthesize its nucleoside triphosphates and phosphoramidites, procedures to synthesize a oligonucleotides, enzymes that copy the alternative genetic system, and procedures that place the expanded, richer, genetic system under Darwinian selection pressure in the laboratory, with downstream sequencing and analysis to assess the sequelae of laboratory Darwinism.

These results have led to several discoveries. First, additional building blocks appeared to allow the system to adopt macro conformations different from, and additional to, those accessible with standard four letter nucleic acids. Further, it appears that the added information density by added letters provides options for the system to access specific binding confirmations. Further, although quantitative comparison is difficult, preliminary data suggests that the added functionality also allows the system to get tighter and more specific interactions between evolvable biopolymers and a target as it serves both genetic and phenotypic roles.