EMERGENCE OF BACKBONE HOMOGENEITY THROUGH HETEROGENEITY? J. V. Gavette[1] and R. Krishnamurthy[1], [1]The Scripps Research Institute, 10550 North Torrey Pines Road, La Jolla, CA 92037

Introduction: The widely accepted "RNA World" theory suggests that RNA pre-dated DNA as the dominant informational biopolymer,[1] but RNA suffers from an inability to self-assemble from its constituents. As a result many have postulated that RNA was in fact predated by a "simpler" dominant informational biopolymer that *was* capable of self-assembly under early Earth conditions.[2]

Numerous structures of the pre-RNA polymer(s), so-called XNAs, have been proposed and are typically modeled after DNA and RNA in that they are composed of non-covalent recognition elements, homogeneous structural backbones, and inter-monomer linkage moieties).[3] The proposed XNAs therefore maintain homogeneity at backbone level (utilize a conserved structural chemical entity) while allowing heterogeneity only at the recognition element level (use four different nucleobases). But, was this backbone homogeneity strictly conserved throughout the evolution of RNA from pre-RNA candidates?

We hypothesize that cross reactive monomers of the differing dominant biopolymers could have coexisted during the transitional periods between the pre-RNA era, the RNA World, and the current DNA World allowing the existence of hybrid biopolymers with heterogeneity in the backbone and recognition element (Figure 1). These hybrids could have facilitated the transfer of information and/or function between the homogeneous backbone systems. We are interested in exploring what effects a heterogeneous (mixed) backbone will have on informational biopolymers. This is achieved, initially, by studying the basic base-pairing properties of biopolymers with alternating (chimeric) backbone functionality.

We have focused on one XNA, specifically, an isomer of the glycerol nucleic acid backbone (isoGNA).[4] Part of this work will highlight the base-pairing properties of chimeric backbone oligomers containing combinations of RNA- and isoGNA-based moieties as possible prebiotic informational biopolymers. Preliminary results show that self-complementary chimeric RNA/isoGNA oligonucleotide sequences composed of adenosine-thymidine repeats exhibit greatly increased base-pairing properties compared to a similar all isoGNA-based system, and form secondary structures not observed in analogous RNA sequences.

We are also interested in comparing base-pairing properties of chimeric DNA/RNA oligonucleotide sequences. Since the "parent" biopolymers for these hybrids can be directly studied we are able to see how these mixed backbone systems could have eased the prebiotic transition from the RNA World to the DNA World.[5] Preliminary results from this study indicate that the DNA/RNA chimeric systems show base-pairing that is weaker than that found in the homo-DNA- or homo-RNA-based systems which could have implications for replication and information transfer in the enzyme-free environment of the RNA World.

References:

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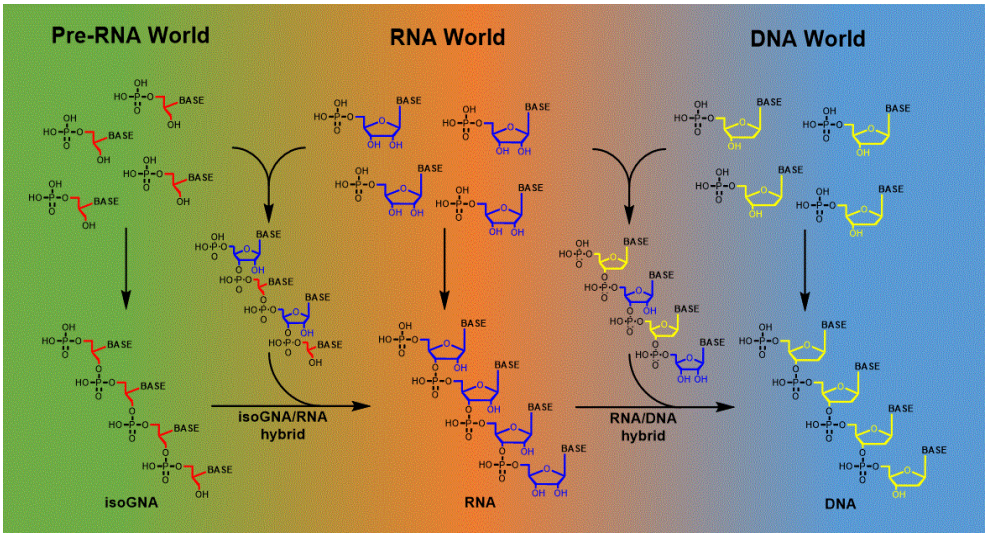

Figure 1 Proposed transition of Pre-RNA World to RNA World to DNA World via hybrid (chimeric) informational biopolymers.