MOLECULAR REPLICATION

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ABSTRACT. The replication of DNA is the process by means of which genetic information is passed from one generation to the next in all living organisms. It is widely believed that a similar process must have become important early in the development of life on the Earth, either before or at the same time as the evolution of protein synthesis. The evolution of any life-form based on familiar chemistry would seem to require the early appearance of some type of residue-by-residue replication, although it might be very different in detail from the one we know.

If one wishes to study this problem experimentally, one is almost forced to start with the components of nucleic acids, nucleotides or deoxynucleotides, for a number of reasons. First, we do not know any other system that has a high probability of working. Second, the starting materials are readily available as biochemicals - the precursors of other hypothetical replicating systems could only be obtained by laborious synthesis. Third, enzymatic methods greatly simplify the analysis of natural oligonucleotide products, and are not available for the products of novel "replication" reactions. The study of an alternative replicating system would be fascinating, but very difficult.

For many years we have been studying one particular aspect of molecular replication - the template-directed non-enzymatic synthesis of an oligonucleotide that is complementary to the template. We would like to be able to take a complicated sequence such as ACUGCCGUUAU. for example, and cause this sequence to direct the synthesis of its complement AUAACGGCAGU (note chain reversal). If we could carry out this reaction and then use the product to direct the synthesis of a second molecule of the original template (by the same rules), we would be able to bring about molecular replication.

We have had considerable success, but are far from achieving molecular replication. We can use sequences of Cs to bring about synthesis of the corresponding sequences of Gs. C_7 for example will direct the synthesis of G_7. In special cases we can "transmit" sequence information. We can use CCGCC, for example, to direct the synthesis of GGCGG in 20% yield. However, much further work is needed before we can

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bring about molecular replication in the test-tube, without the help of enzymes.

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