

Chapter 14

Evolutionary Aside 14.1--DNA Replication

All three domains of life use DNA as genetic material and replicate this DNA using DNA-dependent DNA polymerases. All of these enzymes are incapable of initiating synthesis *de novo*, they all require a free 3' OH to extend. The reason for this requirement is not known; there is no obvious chemical need for it, and RNA polymerases are capable of *de novo* initiation. An obvious consequence of this is the need for priming of DNA synthesis. Four mechanisms are known: the use of a protein, the use of a tRNA, using a nick to create a free 3' end, and a dedicated primase enzyme. All three domains use a dedicated primase, but, based on molecular analysis, there actually appear to be two types: bacterial, and eukaryotic/archaeal.

Even more interesting, molecular analysis shows that the actual replication polymerases of bacteria and of archaea/eukaryotes do not seem to be related. A detailed analysis of all known polymerases indicates that they fall into six families designated A, B, C, D, X, and Y. The main replication polymerases in eukaryotic and archaeal cells fall into the B class; those for the bacterial Pol III falls into class C.

These two lines of evidence have led to the hypothesis that DNA replication evolved twice. The most obvious alternative hypothesis is that major parts of the replication apparatus have been replaced in one lineage. The hypothesis of a universal common ancestor (LUCA for last universal common ancestor) for all three domains seems to argue against two origins for replication unless such a replacement occurred. Another suggestion has been that LUCA did not have a DNA-only genome, but rather a hybrid RNA/DNA system. At this point these hypotheses cannot be tested, but as more genomes are sequenced, creative ways of testing them may be designed.