

The DNA polymerase gene from the hyperthermophilic marine archaebacterium, *Pyrococcus furiosus*, shows sequence homology with α-like DNA polymerases

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Recent studies in the evolutionary relationships of life on this planet have placed the root of the universal tree between eubacteria (or Bacteria) on the one hand and archaebacteria (or Archaea) and eukaryotes (or Eucarya) on the other (1, 2). The latter two Urkingdoms are therefore thought to have a common ancestor. Support for such a conclusion comes from molecular comparisons of rRNAs, tRNAs, RNA polymerases and elongation factors (3,4). Of significance is the fact that the most ancient phenotype of the archaebacterial-eukaryotic lineage is also the most thermophilic. Thus, the extremely thermophilic archaebacteria (5) are considered to have a life strategy closely related to the ancestor of all extant life. To date sequence information has been limited to one hyperthermophilic enzyme, and this was not analyzed in phylogenetic terms (6). In this communication, we describe the first amino acid sequence information from an archaebacterial DNA polymerase gene and its striking homology to α-like DNA polymerases.

DNA polymerases are ideal for evolutionary analyses as close structural and functional relationships have already been demonstrated between the enzymes from phylogenetically diverse sources and conserved regions have been described (7, 8). We have recently cloned the gene encoding a high fidelity DNA polymerase from the hyperthermophilic archaebacterium, *Pyrococcus furiosus* (*Pfu*) (9–11) and report here on the implications of its amino acid sequence.

Figure 1 shows that the deduced amino acid sequence of *Pfu* DNA polymerase has considerable homology (37 of 57 residues) with highly conserved regions in α-like DNA polymerases (7, 12, 14). In addition to α-human DNA polymerase, this group also contains α-yeast, δ-yeast, and REV3 cellular eukaryotic DNA polymerases. In contrast, the homology between *Pfu* and Pol1-like DNA polymerases in the same regions is considerably less (20 of 57 conserved residues). Along with *E. coli* DNA polymerase 1, the Pol1-like polymerase group contains *Thermus aquaticus* (*Taq*), T7, T5, *Streptococcus pneumoniae* (*Spn*) pol1 and SPO2 procaryotic and bacteriophage DNA polymerases. Interestingly, α-like DNA polymerases exihibit 24 of 57 conserved residues with Pol1-like DNA polymerases within the same regions. Since present day eubacterial and eukaryotic DNA polymerases are thought to have evolved from a common ancestral 'Klenow-like' core, the sequence homology of *Pfu* DNA polymerase not only supports the archaebacterial-eukaryotic relationship, it may more closely resemble the ancestral form of the eukaryotic polymerase enzyme.

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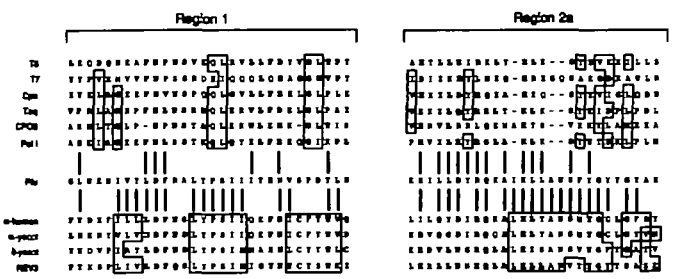

Figure 1. Alignment of amino acid residues from *Pfu*, Pol1-like and α-like DNA polymerases in the highly conserved regions 1 and 2a. Bold lefters indicate consensus amino acids considered conserved among all DNA polymerase groups; boxed-in letters indicate consensus amino acids within the Pol1-like and α-like groups (figure adopted from Blanco,L., Blasco,M. and Salas,M. (1991) *Gene* **100**, 27–38).