subunit. However, it does not appear that the majority of mutations that confer resistance to nucleoside analogues act through the p51 subunit. If the p51 subunit has some sort of dNTP binding site, it plays no major role in polymerization or resistance to nucleoside inhibitors.

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The helix from which the arch was made

During the familiar process of bacterial replication, an essential 5′ nuclease activity is carried out by the N-terminal portion of DNA polymerases. The N-terminal 5′ nuclease domain of *Taq* polymerase was shown last year to be made up of a β-sheet core flanked on two sides by α-helices, forming a deep active-site cleft (Kim *et al.*, *Nature* **376**, 612–616). The floor of the cleft is lined with highly conserved Asp and Glu residues that ligate three metal ions, two of which are likely to participate in catalysis. But due to the occasional vicissitudes of crystallography, ~30% of the 5′ exonuclease domain of *Taq* was disordered.

The missing portion of a 5′ exonuclease has now been filled in by a newly reported structure (T A. Ceska, J.R. Sayers, G. Stier and D. Suck, *Nature*, **in the press**). The 5′ nuclease in phage T5 is encoded by a separate gene from the polymerase, but its structure (left) shows many conserved features with the N-terminal domain of *Taq*: a β-sheet core (green) is flanked by two assemblies of helices (red), and although the proposed active-site region is rather shallower than that described for *Taq*, conserved carboxylates ligate metal ions (only two, shown as silver balls). The new information added by this structure is shown in purple. The long, purple helix 4 forms an arch in concert with red helix 5. Four positively charged residues line the arch on one side; the other side is lined with Phe residues. A hole in a protein such as that formed formed by the arch demands to be filled, and the authors have obliged: DNA is proposed to lie across the 'front' of the protein (as viewed in the picture), with a 5′ single strand threaded, twisting through the arch at the 'back', its backbone interacting with the positively charged helix 4 residues, and the bases perhaps interacting with the Phe residues on helix 5. The region near where the single strand joins the double would then lie approximately between the catalytically important metal ions at the base of the arch. This model also helps explain the endonuclease activity sometimes seen with this enzyme, which could cut at the root of a single strand threaded through the arch. **AF**