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**Ternary Substrate Complex Structures of DNA Polymerase  $\beta$  with Mutagenic DNA Intermediates: Active Site Constraints for Mispair Extension.** Batra, V.K., Beard, W.A., Pedersen, L.C., Wilson, S.H., Laboratory of Structural Biology, National Inst. of Environmental Health Sciences, Research Triangle Park, NC.

DNA polymerases, including DNA polymerase  $\beta$  (Pol  $\beta$ ), occasionally insert the wrong (incorrect) nucleoside triphosphate (dNTP). For this base substitution error to become a mutation, the mispair must be extended. Earlier, we compared the extension efficiency of all 12 possible mispaired primer termini (Beard et al., 2004). Although the extension of terminal mispairs is kinetically challenging, transition intermediates were generally extended more easily than transversions. Mismatches at the primer terminus diminished correct nucleotide insertion efficiency without affecting DNA binding affinity. Here, we present ternary complex structures of Pol  $\beta$  with most of the mismatched primer termini and an incoming non-hydrolyzable dNTP analogue (dUMPNPP). These structures reveal that extension efficiency correlates well with the observed distance ( $d$ ) between the primer 3'-OH and  $\alpha$ -phosphate of the incoming nucleotide. This distance ranges from 3.4 Å (correctly paired primer terminus) to > 9 Å. Mismatches with distances between 4 – 6 Å were extended, albeit poorly. When the observed distance increases further ( $d > 6$  Å), extension was nearly completely impeded.

Beard, W.A., Shock, D.D., and Wilson, S.H. (2004) Influence of DNA structure on DNA Polymerase  $\beta$  active site function: Extension of mutagenic DNA intermediates. *J. Biol. Chem.*, 279, 31921-31929.