Title:	Editorial: Nucleic Acid Polymerases: The Two-Metal-Ion Mechanism and Beyond.
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Abstract:	Nucleic acid polymerases are essential for all forms of life, performing diverse functions from genome replication and repair to the transcription of a wide variety of RNAs. Although these enzymes differ widely in substrate specificity, efficiency, accuracy, and evolutionary origin, they all catalyze the same nucleotidyltransferase reaction. This eBook on “Nucleic Acid Polymerases: The Two-Metal-Ion Mechanism and Beyond” highlights both the similarities and differences among these enzymes. The two-metal-ion catalytic mechanism for polymerases was proposed in 1993 by Thomas A. Steitz (Steitz, 1993), based on structural studies of the 3′-5′ exonuclease active site of the Klenow fragment of E. coli DNA polymerase I (Beese and Steitz, 1991; Beese et al., 1993) and mutagenesis of the polymerase active site (Polesky et al., 1992). Structural support for this mechanism came over the next several years, when crystal structures were determined with primer-template DNA and dNTP poised for catalysis at the polymerase active sites of several different DNA polymerases and HIV-1 reverse transcriptase (Pelletier et al., 1994; Doublié et al., 1998; Huang et al., 1998; Li et al., 1998). These and subsequent structures show that polymerases have two absolutely conserved aspartate residues that coordinate two divalent cations in the polymerase active site (Figure 1A), demonstrating that the two-metal-ion catalytic mechanism is also applicable to DNA synthesis (Brautigam and Steitz, 1998).
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