DNA Catalysts with Tyrosine Kinase Activity

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Deoxyribozymes that catalyze many different chemical reactions have been identified, including many DNA catalysts that use triphosphate electrophiles. Nevertheless, deoxyribozymes that catalyze the phosphorylation of a peptide side chain have not been reported. Here we used in vitro selection to identify deoxyribozymes that transfer the γ-phosphoryl group from either a 5'-triphosphorylated RNA oligonucleotide donor or guanosine 5'-triphosphate (GTP) donor to the tyrosine hydroxyl acceptor of a DNA-anchored hexapeptide. Tyrosine kinase deoxyribozymes were identified from each of N_{30}, N_{40}, and N_{50} random-sequence pools and require both Zn^{2+} and Mn^{2+} for their activity. The new deoxyribozymes have little selectivity with regard to the amino acid identities near the tyrosine. These findings demonstrate that DNA has the fundamental catalytic ability to phosphorylate the tyrosine side chain of a peptide substrate. Future efforts will pursue peptide sequence selectivity, reactivity of free peptide and protein substrates, and improved reactivity of small-molecule phosphoryl donors such as GTP.