DNA-Catalyzed Amide Hydrolysis

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DNA catalysts (deoxyribozymes) for a variety of reactions have been identified by in vitro selection. However, for certain reactions this identification has not been achieved. One important example is DNA-catalyzed amide hydrolysis, for which a previous selection experiment instead led to DNA-catalyzed DNA phosphodiester hydrolysis. Subsequent efforts in which the selection strategy deliberately avoided phosphodiester hydrolysis led to DNA-catalyzed ester and aromatic amide hydrolysis, but aliphatic amide hydrolysis has been elusive. In the present study, we show that including modified nucleotides that bear protein-like functional groups (any one of primary amino, carboxyl, or primary hydroxyl) enables identification of amide-hydrolyzing deoxyribozymes. In one case, the same deoxyribozyme sequence without the modifications still retains substantial catalytic activity. Overall, these findings establish the utility of introducing protein-like functional groups into deoxyribozymes for identifying new catalytic function. The results also suggest the longer-term feasibility of deoxyribozymes as artificial proteases.