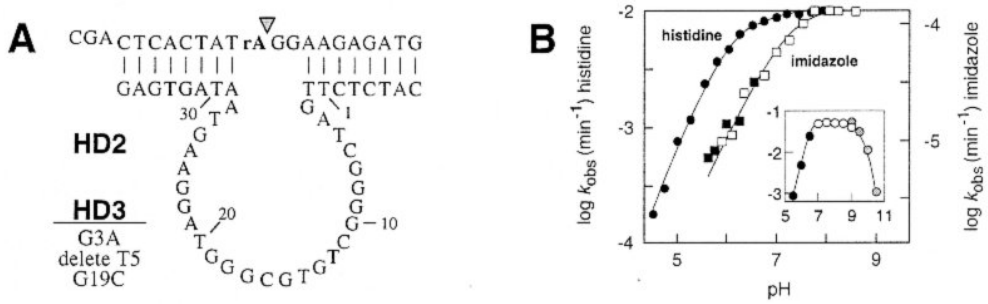
Breaker Laboratory

Molecule of the Year

1998

Histidine-dependent Deoxyribozymes

Fig. 1. Features of a histidine-dependent deoxyribozyme.[1] (**A**) Sequences and secondary structures of HD2 and HD3 - RNA-cleaving DNAs that requires L-histidine as a cofactor. Arrowhead indicates cleavage site. (**B**) The pH dependency of the rate constants for HD3 suggest a general-base function for the amino acid.



In recognition of the first demonstration of cooperation between amino acids and nucleic acids to achieve enzymatic function, the status of Breaker Laboratory "Molecule of the Year" has been conferred upon the "HD3" deoxyribozyme, which cleaves RNA using L-histidine as a cofactor.

Nucleic acids carry a limited repertoire of chemical groups that are used to form higher-ordered structures and that are used to form active sites. Thus, it has been suggested that nucleic acids could augment their limited chemical composition by using peptides and other compounds as cofactors to generate greater catalytic potential. The isolation of a new class of histidine-dependent (HD) deoxyribozymes that cleave RNA provides the first experimental evidence that nucleic acids can co-opt the catalytic power of proteins by employing amino acids as cofactors. This finding reveals a broader catalytic potential for nucleic acids, and suggests that ribozymes in the putative "RNA World" might have used similar strategies to foster the emergence of more complex metabolic processes.

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[1] Roth, A. and Breaker, R. R. (1998) An amino acid as a cofactor for a catalytic polynucleotide. *Proc. Natl. Acad. Sci. USA* **95**, 6027-6031.