

Structure of a 10-23 Deoxyribozyme Captured in a Precatalytic State

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Deoxyribozymes (DNAzymes) are *in vitro* selected DNA sequences capable of catalyzing chemical reactions. The RNA cleaving 10-23 DNAzyme was one of the first DNAzymes to be evolved and possesses clinical and biotechnical applications as a knockdown agent. DNAzymes do not require the recruitment of other components to cleave RNA and can turnover, thus they have a distinct advantage over other knockdown methods (siRNA, CRISPR, morpholinos). Despite this, a lack of structural and mechanistic information has hindered the optimization and application of the 10-23 DNAzyme. Here, we report a 2.7 Å crystal structure of the RNA cleaving 10-23 DNAzyme captured in a precatalytic state. The DNAzyme adopts a dimer conformation coordinated between extensive interaction between the catalytic core sequence. In addition, the substrate adopts a sharp kink at the cleavage site that exposes the scissile phosphate to three coordinated magnesium ions. This structure provides preliminary insight into the catalytic activity of the 10-23 DNAzyme, and factors that limit the application of the DNAzyme *in vivo*.

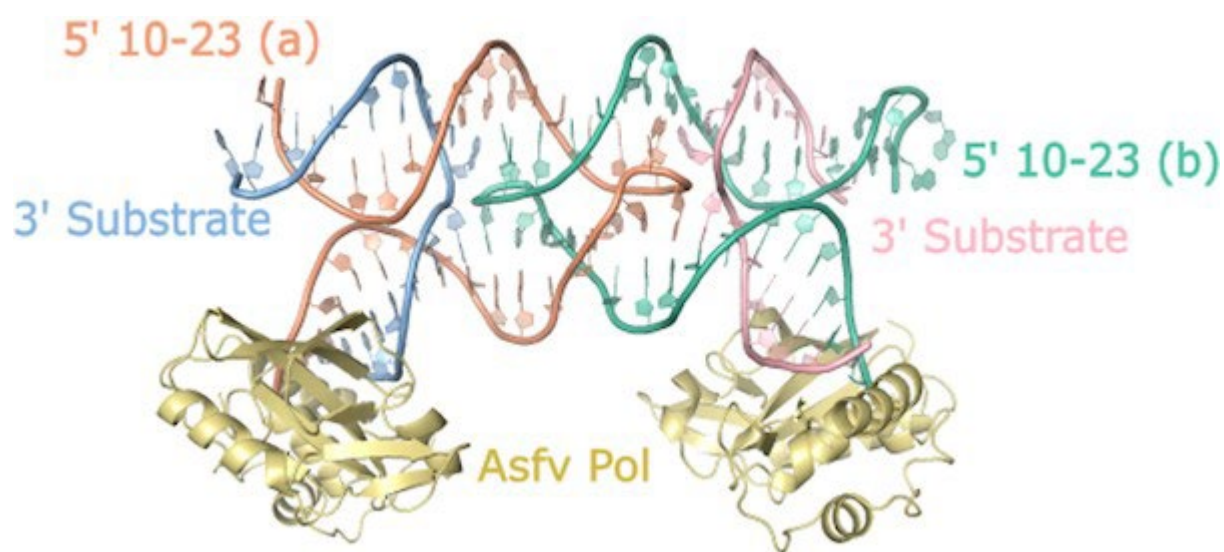


Figure 1