DNA Constraints for Rational Control of Macromolecular Structure and Folding

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The DNA double helix is stable and rigid, making it an ideal nanoscale construction element. Duplex DNA has been used as a static framework to organize DNA, proteins, or nanoparticles, and dynamic DNA nanomachines have been built. However, assemblies in which DNA controls the structures of other macromolecules are rare. Here we use short (10-20 bp) DNA duplexes as structural constraints to control RNA structure.

Based on the X-ray crystal structure of the 160-nucleotide P4-P6 RNA domain of the *Tetrahymena* group I intron, pairs of sites for DNA constraint attachment were chosen rationally. When the DNA constraint is either incompatible or compatible with the folded RNA structure, RNA misfolding or folding is observed, respectively. The DNA constraint is modulated reversibly by adding complementary DNA strands. Alternatively, the DNA constraint is destroyed irreversibly by cleavage with a protein enzyme or by chemical scission of the DNA-RNA linkage. These findings will have substantial practical impact on DNA nanotechnology. The use of DNA constraints to control structure and folding should be applicable to other macromolecules like proteins and non-biological foldamers.