THE IMPERFECTIONS MAKE IT BETTER: AN INCREASED AFFINITY OF PNA-RNA TRIPLEXES WITH BULGES

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Controlling RNA structural dynamics is key in RNA biology and therapeutic targeting. Peptide nucleic acids (PNAs) enable stable, sequence-specific triplex formation with structured RNA, even under physiological conditions. They can recognize bulged purine residues and induce conformational changes that support continuous triplex formation. Using NMR spectroscopy, we found that PNA-induced remodeling is independent of the initial dsRNA conformation and is instead driven by a delicate balance between the type and number of bulge conformations within the triplex, with bulge composition further enhancing PNA affinity by up to tenfold — highlighting a tunable strategy for achieving high-affinity and sequence-specific RNA targeting.

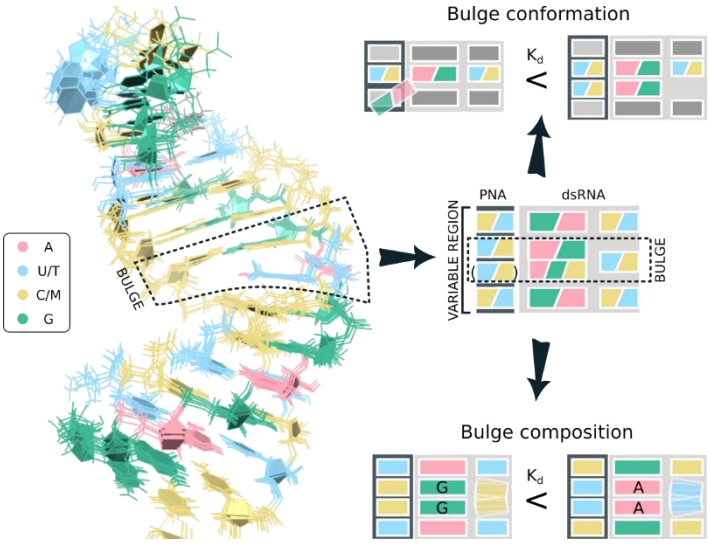

Figure 1. Mutations in the variable region of PNA-dsRNA triplexes affect the conformation and composition of the bulge, resulting in a markedly increased binding affinity.

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