

MS7-O4 From sequence to nanostructure: a critical base pair in RNA k-turns that confers folding and structural characteristics, and correlates with biological function

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Kink turns (k-turns) are ubiquitous sequences that generate tight kinks within RNA helices that mediate tertiary interactions in the folding of large assemblies such as the ribosome, and often serve as targets for specific binding proteins. Because of this, k-turns play a key role in the assembly of ribosomes, the spliceosome and box C/D and H/ACA snoRNPs, as well as seven distinct riboswitch species.

Both tertiary contacts and protein binding can stabilize the kinked conformation, and some, but not all, sequences may fold in the presence of sufficient metal ion concentrations. These differential folding properties must be very important in the assembly and function of their RNA species. Another important structural characteristic is that most k-turns fall into one of two classes, depending on whether the acceptor of the H-bond donated by the -1n O2' is N3 or N1 of the conserved A2b (termed the N3 or N1 conformation). This changes the trajectory of the NC (Non-canonical) helix, thus potentially affecting tertiary contacts. Such conformational influences are likely to be very important in the biogenesis of large RNA protein assemblies.

By systematic analysis of Kt-7 variants we have identified the single base pair that follows the conserved A•G pairs (the 3b•3n basepair) as the critical determinant of ion-dependent folding, and we have enunciated rules for ion-induced folding together with a molecular explanation.

Here we determined more than 25 structures and found that 3b•3n basepair is the critical determinant of a k-turn's structure conformation (N3 or N1), and the results also agree with phylogenetic analysis. We also confirmed this observation by X-ray scattering interferometry (XSI), to probe the solution structural conformation of the k-turn.

The deduced sequence rules for k-turn folding and structure conformation have strong predictive value, and can be applied to many natural RNA sequences. To show those sequence rules are well understood and applicable to modeling and design, we successfully designed a nanostructure comprising six k-turns in a circular arrangement, the structure of which has been determined by X-ray crystallography at 3.0 Å resolution.

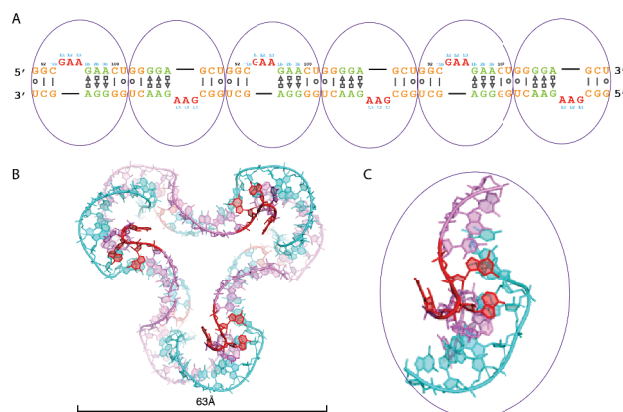


Figure 1. Design and structure of the RNA triangle. (A) Design of the RNA triangle with 6 Kt-7 sequences. (B) Structure of the RNA triangle. One strand colored blue, another strand colored violet, all the loop regions colored red. (C) One Kt-7 structure.

Keywords: RNA structure, kink-turn, X-ray crystallography, nanostructure