

P004 The snRNP 15.5K protein folds its cognate K-turn RNA: a combined theoretical and biochemical study
Vlad Cojocaru¹, Stephanie Nottrott^{2,3}, Reinhard Klement¹, and Thomas M. Jovin¹

¹ *Department of Molecular Biology, Max Planck Institute for Biophysical Chemistry, Am Fassberg 11, 37077 Göttingen, Germany*

² *Department of Molecular Biology, Max Planck Institute for Biophysical Chemistry, Am Fassberg 11, 37077 Göttingen, Germany*

³ *Program in Molecular Medicine, University of Massachusetts Medical School, Worcester, MA 01605, USA*

The human 15.5K protein binds to the 5' stem-loop of U4 snRNA, promotes the assembly of the spliceosomal U4/U6 snRNP, and is required for the recruitment of the 61K protein and the 20/60/90 protein complex to the U4 snRNA. In the crystallographic structure of the 15.5K-U4 snRNA complex, the conformation of the RNA corresponds to the family of kink turn (K-turn) structural motifs. We simulated the complex and the free RNA, showing how the protein binding and the intrinsic flexibility contribute to the RNA folding process. We found that the RNA is significantly more flexible in the absence of the 15.5K protein. Conformational transitions such as the inter-conversion between alternative purine stacking schemes, the loss of G-A or G-C base pairs, and the opening of the K-turn occur only in the free RNA and reveal the flexible regions critical to the RNA folding. We performed chemical RNA modification experiments and observed that the free RNA lacks secondary structure elements, a result in excellent agreement with the simulations. Based on these observations we propose a protein-induced RNA folding mechanism in which the RNA intrinsic flexibility functions as a catalyst.