Scientific achievement

Non-canonical nucleic acid structures induced by specific binding of metal ions

Interactions between nucleic acid molecules and metal ions are typically weak, with dissociation constants in the millimolar range, and to a large degree nonspecific. Despite this fact, such interactions are a crucial factor in shaping nucleic acid structural preferences and, in case of systems exhibiting catalytic properties (ribozymes and DNAzymes), also their activity. There exists, however, a subset of DNA and RNA molecules capable of forming metal binding sites of improved affinity and specificity that are based on the formation of specific structural motifs, such as G-quadruplexes or metal ion aptamer domains.

My main research goal is to improve our understanding of the proficiency of DNA and RNA for strong and site-specific binding of metal ions, as well as of the potential of such interactions to shape the structures and activities of these biomolecules. Using NMR spectroscopy methods I determined the spatial structures of three distinct nucleic acid molecules and characterized the metal-binding sites that they form. The studied systems include:

1) *A four-stranded RNA G-quadruplex r(UGGUGGU)$_4$ stabilized by potassium K^+ ions.* Within this system I identified a new structural motif available for G-quadruplex molecules, that I dubbed a “reversed U-tetrad”, and explained how its presence leads to an unexpectedly strong thermal stabilization of tetramolecular G-quadruplex folds.

2) *A lanthanide-binding DNA aptamer*. In this system I structurally characterized a DNA-metal interaction site that is specific for lanthanide ions and exhibits an affinity value rarely encountered in similar interactions ($K_d \approx 0.3$ μM). Moreover, I demonstrated that for this system a direct interaction between DNA and paramagnetic lanthanide ions allows for the observation of the full range of paramagnetic NMR effects, that constitute an invaluable source of long-range structural information. This discovery opens up an avenue toward a broader use of paramagnetic NMR restraints in strucutral studies of DNA and RNA molecules.

3) *The catalytically proficient structure of the 8-17 DNAzyme, induced by zinc Zn^{2+} binding*. Within this research branch, apart from the determination of the DNAzyme structure induced by Zn^{2+} ions, I formulated a new model explaining how interactions with divalent metal ions shape the structural preferences of this system. The proposed model allows to reinterpret the results of over 20 years of 8-17 DNAzyme studies and provides the first structural basis to understand the mode of action of this system in the presence of Mg^{2+} ions, most relevant in the context if its usage in cells.

The results obtained within the presented scientific achievement allowed to decipher the conformational preferences of a series of DNA and RNA molecules of nano- and biotechnological importance. Apart from contributing to our general understanding of the properties of nucleic acid folds induced by metal ion binding, they also led to, among others, broadening the experimental toolbox available to NMR spectroscopy of nucleic acids and opening a perspective towards rational design of improved DNAzyme systems.