LANTHANIDE BINDING APTAMER AS A TOOL FOR PARAMAGNETIC NMR SPECTROSCOPY OF NUCLEIC ACIDS

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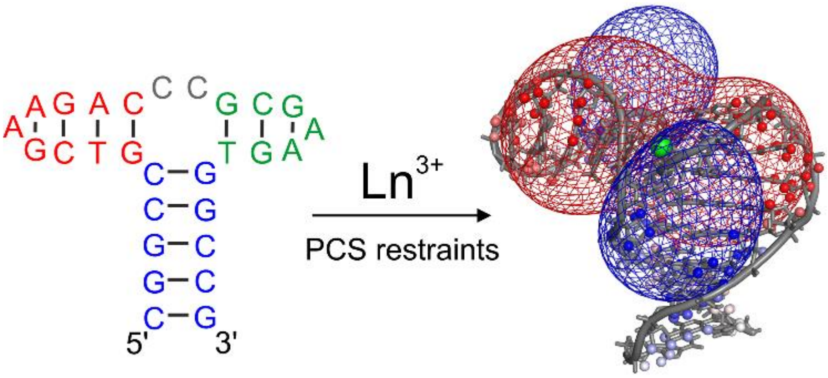
NMR spectroscopy is among the primary techniques used for high resolution structural studies of nucleic acid systems. Classical approaches to biomolecular NMR structure determination rely of the measurement of inter-proton distances up to 5-6 Å, through the means of the Nuclear Overhauser Effect (NOE). The local nature of these distance restraints can lead to a poor reproduction of some global structural features of the studied molecule (e. g. the degree of helical bending). Long-range NMR structural restraints derived from the presence of a paramagnetic ion in the studied system can radically change this situation and have already found much success in NMR studies of proteins, beyond just structure determination[1]. However, the potential of paramagnetic NMR methods remains largely unrealized for nucleic acids due to lack of general methods to rigidly and site-specifically introduce paramagnetic ions into these systems.

Here we present the high-resolution NMR structure of a lanthanide-binding DNA aptamer and demonstrate that lanthanide ions bound to this system induce large magnitude paramagnetic effects (pseudocontact shifts; PCS), readily interpretable in terms of structural parameters. We propose that the lanthanide binding motif uncovered for this system can be exploited to introduce lanthanide binding sites into a broad range of different DNA and RNA molecules to facilitate their structural and functional NMR studies. The presented structure is also of interest by itself, as it constitutes the first high-resolution structure of a metal-binding aptamer deposited in the PDB, furthering our understanding of high-affinity metal binding by DNA.



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