Photophysical insight on the interaction between an RNA G-quadruplex and fluorescent platinum(II) complexes

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G-quadruplexes (G4s) are believed to play crucial roles in regulating gene expression.[1] In contrast to DNA G4s, which have been extensively investigated, there are much less studies on RNA G4s. In particular, studies on the interaction of RNA G4s with metal complexes are still missing to date. As various clinically relevant genes are known to harbor G4s forming sequences,[1] small molecules, especially metal complexes which can target to RNA G4s are potential regulators for gene expression.

Here we applied photophysical methods to understand the interaction between an RNA G4 and two fluorescent platinum(II) complexes. The investigated RNA sequence is a triple-mutant that forms one specific conformational state of the wildtype G4 forming BCL-2 (B-cell lymphoma 2) RNA, present in the mRNA of the BCL-2 onco-gene.[2] Fluorescence lifetime measurements show the binding affinities of both metal complexes to the G4 to be in the nM range. Further, we find 1:1 and 1:2 binding equilibria of this G4 RNA to the metal complex depending on the concentration ratio. Interestingly, the binding to the G4 RNA can also induce a conformational change of both complexes, which is indicated by a change of the fundamental fluorescence anisotropy. These findings, which enlight the particular interaction of the RNA G4 with the platinum(II) complexes, are beneficial for the design of metal complexes as particular RNA G4 binders.

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[1] Shankar Balasubramanian, Laurence H. Hurley, Stephen Neidle, *Nat. Rev. Drug Discov.* **2011**, 10, 261-275.
[2] KW Yip, JC Reed, *Oncogene*. **2008**, 27, 6398–6406.