

## **PROBING TRANSITION METAL BINDING SITES ON DNA USING ELECTROSPRAY MASS SPECTROMETRY**

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Nucleic acids provide a multitude of opportunities for metal ion binding as a consequence of the diversity of functional groups and heteroatoms present in their structures. For example, magnesium and potassium ions interact electrostatically with the phosphodiester backbone and also stabilise specific secondary and tertiary structures such as those present in ribozymes and telomeres. In contrast, transition metals generally form covalent bonds with the nitrogen atoms present in nucleic acid bases. The latter interactions are central to the mechanism of action of clinical anticancer drugs such as cisplatin and carboplatin, and may also be important for other transition metals with anticancer or antimetastatic activities. We are currently evaluating the application of electrospray ionisation mass spectrometry (ESI-MS), in conjunction with enzymatic digestion of metal-oligonucleotide reaction products for routine determination of metal binding sites on nucleic acids.

This paper will present the results of our recent work into the binding of cis- and trans-platinum(II) complexes, as well as palladium(II), ruthenium(II) and ruthenium(III) complexes, with both single-stranded and double-stranded DNA. Crude reaction mixtures were monitored by ESI-MS and reaction products were purified by HPLC. ESI-MS spectra were also obtained after purified reaction products had been subjected to partial or total nuclease digestions. These latter experiments provide information about the number, identity and sequence position of the bases involved in coordination to the metal. Finally, these results have been compared to the data obtained from ESI-MS/MS spectra of metal-oligonucleotide adducts. Overall, the two approaches are complementary and together enable complete characterisation of the metal binding sites on DNA.

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