P047 Mass spectrometric screening for quadruplex DNA-selective ligands

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Telomeres contain DNA sequences that are thought to form four stranded DNA structures known as quadruplex DNA. Since telomeres are maintained in ~90% of cancer cells, and not in normal somatic cells, compounds which bind selectively to quadruplex DNA may be able to interfere with DNA replication in tumour cells. Electrospray ionization mass spectrometry (ESI-MS) can be used to investigate non-covalent complexes of ligands bound to DNA. Our laboratory has established conditions for the ESI-MS observation of both double stranded and quadruplex DNA structures and their respective ligand-bound complexes.
In this work ligands based on the alkaloid drug berberine, which has antimalarial and antitumor properties, have been investigated for their DNA binding. These included an ortho-, meta- and para-phenylmethylnitroindolyl-substituted berberine as well as a 2-naphthalene substituted analogue. Each of the ligands showed pronounced selectivity for quadruplex DNA over double stranded DNA. These compounds may represent useful leads towards new therapeutics as well as probes into the presence and functions of quadruplex DNA in cells.