Supramolecular recognition of DNA and RNA junction structures for anti-viral and anti-cancer therapy

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We have developed metallo-supramolecular cylinders (helicates) that bind strongly to DNA and RNA Y-shaped junctions, forks and bulges, and prevent DNA transactions. They enter cells and rapidly localise in cell nuclei, where the fork-binding agents interfere with the processing of DNA leading to cell cycle arrest followed by apoptosis, without inducing genotoxicity or mutagenicity.[1] As a route to control the activity of these agents, we can encapsulate them in a curcubituril ring to create a rotaxane structure, with release from the rotaxane switching on the junction-binding activity.[2]

Recognition of a specific nucleic acid shape is a powerful alternative to traditional sequence-recognition. In RNA-viruses the ends of the genome are non-coding parts which fold into specific structures and regulate viral replication. The same structures are common to many different viruses and an exciting new anti-viral target. We have shown that some of our agents can bind junction and bulge structures (Fig 1) in the untranslated regions of both SARS-CoV-2 and HIV-1 and show potent anti-viral activities at concentration levels where they are not cytotoxic to mammalian cells.[3]

A new nano-scale form of usual DNA-recognition by nanoparticles (Fig 2) will also be discussed.[4]

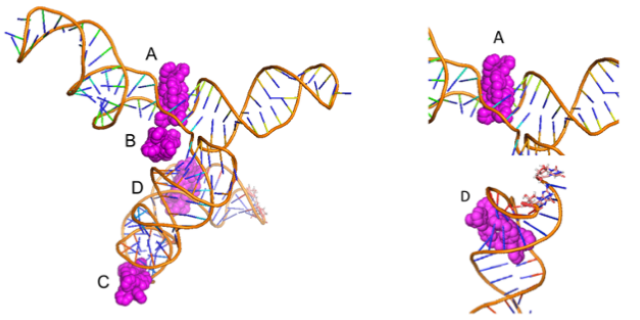

Fig.1 *Cylinders recognise SARS-CoV-2 RNA.*

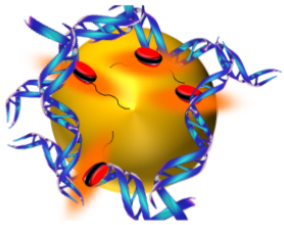

Fig. 2 *Coiling DNA around a gold nanoparticle*

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