Supramolecular chemistry as a multi-modality platform for radiotracers design

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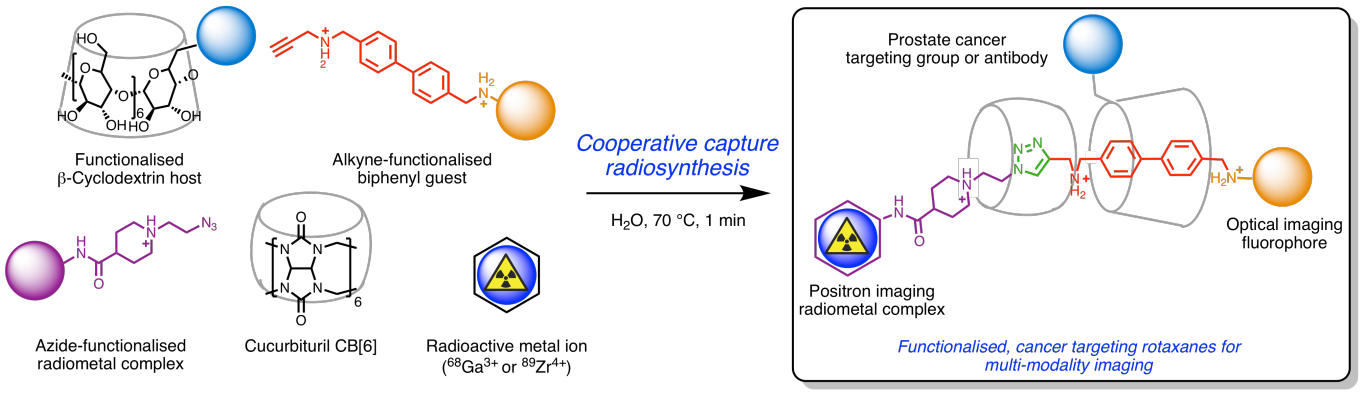
The design opportunities offered by supramolecular chemistry hold promise in the development of drug delivery systems targeting cancer. Our goal is to implement supramolecular structures into the medical domain building multi-modality imaging agents for positron emission tomography (PET). To this end, we report the synthesis and characterisation of functionalised supramolecular, cancer targeting radiotracers.

The mechanically interlocked molecules (rotaxanes) synthesis was designed in a one-pot strategy around a four-component cooperative capture approach involving the cucurbituril (CB[6]) catalysed alkyne-azide 'click' chemistry with β-CD as a catalyst. An efficient preorganisation between the azide and alkyne derivatives, CB[6] and β-CD via hydrogen bonds, facilitated a rapid synthesis of the rotaxanes. β-CD was monofunctionalised to expand the versatility of our construct. To demonstrate its flexibility, we synthesised various radioactive rotaxanes functionalised with radioactive ^{68}Ga and ^{89}Zr metal ion complexes, fluorescein and cancer-specific ligand or monoclonal antibodies. Reactions to make multi-functional rotaxanes were complete in less than one minute at 70 °C in water. All constructs were characterised by multinuclear NMR, high-resolution electrospray ionisation mass spectrometry and high-performance liquid chromatography. Radiolabelling reactions gave ^{68}Ga-rotaxanes and ^{89}Zr-rotaxanes in high radiochemical yield and purity. Following binding assays and positron emission tomography (PET) imaging were achieved to demonstrate the viability of our constructs as the first use of supramolecular chemistry to access cancer specific radiotracers.



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