There is a need to develop novel anticancer drugs which bypass multidrug resistance pathways (namely DNA damage) and exhibit high selectivity against tumours over healthy tissue. In particular the prognosis for those suffering from colon cancer, especially at later stages, is poor. The development of novel pharmaceuticals that successfully tackle these key issues is paramount.

Host defence peptide α-helices (a) help us to resist various diseases including cancers and infection, but suffer from poor pharmacokinetics as drug targets; therefore there is a drive to develop synthetic systems which mimic the function of these innate molecules. Among other mimetics strategies, metallohelices (e.g. helicates) – being of a similar size, shape and charge to α-helices – have risen to the fore. Unfortunately these metal complexes are unsophisticated in comparison to the natural systems, rarely contain functional groups and invariably have high symmetry.

Our research lab developed new water compatible systems known as flexicates (b), which form in an optically pure manner, are easily functionalised and have shown great potential as extremely potent and selective anticancer and antimicrobial agents. They are found to cause significant changes to the cell cycle and induce early apoptosis in colon cancer.

More recently we have established a novel asymmetric architecture, which employs directional ligands to form triplex metallohelices (c). These soluble, stable, and functionalisable compounds show exceptional activity as anticancer agents. They are found to act on the cell cycle and induce apoptosis without damaging DNA: they appear to act in a similar manner to the peptidic α-helices that they were designed to emulate. They have also been found to be extremely selective against colon cancer cells over healthy cells. These compounds take a significant step towards using metallohelix architectures as highly adaptable peptidomimetic systems in the fight against cancer.