A high-throughput approach to develop self-assembling, glycosolated materials for biomedical applications

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Carbohydrate based drugs are underrepresented in the field of therapeutics despite the discovery of numerous carbohydrate binding proteins.\textsuperscript{1} Examples are found in the treatment of diabetes (eg miglitol), thrombosis (eg fondaparinux) and influenza (zanamivir and oseltamivir). The major obstacle for drug-development in this area is the high polarity of sugars which restricts their ability to cross the enterocyte layer in the small intestine, dramatically reducing bioavailability. Moreover, when administered intravenously carbohydrates suffer from fast renal excretion. It is anticipated that by formulating carbohydrates as self-assembling nanoparticles, we can increase the lifetime of such molecules \textit{in vivo} and therefore open up a whole new area of drug discovery.

Utilising the copper catalysed azide-alkyne cycloaddition (CuAAC) ‘click’ reaction between azide-tethered sugars and alkyne substituted hydrophobic chains, our target is to produce a library of glycosolated self-assembling materials. High-throughput (HT) techniques are being employed to synthesise a collection with systematic variations in headgroups, chain lengths and chain unsaturation. Upon addition of water, amphiphilic compounds self-assemble into various phases, influenced by a variety of factors including temperature, polar surface area, and chain splay. In order to determine the optimum conditions, we will carry out HT formulation studies at the Australian synchrotron, and have developed a high-throughput phase characterisation technique so that complete libraries can be characterised in rapid time.\textsuperscript{2} This data will enable us to telescope our studies to create amphiphilic carbohydrate based drugs for a specific therapeutic or transportative role. Work on the synthesis of our library will be presented.

Carbohydrate azide head group + Hydrophobic alkyne tail $\xrightarrow{1) \text{Cu}(s)} \xrightarrow{2) \text{H}_2\text{O}}$ Self-assembled material