**Background**

Protein-carbohydrate interactions mediate a multitude of critical biological recognition processes. The proteins responsible for deciphering this information are termed lectins.

- Polymers with pendent carbohydrate moieties (glycopolymers) interact with lectins and have demonstrated binding affinities several orders of magnitude greater than a single carbohydrate.
- Interference at this early stage is known as anti-adhesion therapy and does not kill the pathogen. Importantly, it prevents binding and hence internalisation which markedly reduces the chance of becoming resistant.

**Comparison of Surface Binding with Inhibitory Activity**

**Glycopolymer–Lectin Interactions**

The nature of the interactions between glycopolymers and lectins, and the structural features necessary to obtain high-affinity materials are not fully understood. In this study, we probed multivalent interactions in the α-mannose-Concanavalin-A (ConA) pairing:

- Post-polymerisation Modification: α-β-mannose was ‘clicked-on’ to a poly-(propargyl methacrylate) backbone.
- Polymer Chain Lengths: 2 (P1), 6 (P2) and 11 nm (P3).
  - Binding and inhibition was assessed using Quartz-crystal microbalance with dissipation monitoring (QCM-d) and Fluorescence-linked sorbent assay (FLSA).
  - Higher binding affinity = increased mass of glycoside binding to the lectin surface. This property is used to screen new inhibitors.

**Inhibition of Bacterial Toxins**

**Bacterial Toxin Binding**

The cholera toxin (CTx) secreted by *Vibrio cholerae* binds glycosides expressed on the cell surface. Materials with high-affinity and selectivity for these lectins could find applications as anti-adhesive agents.

- PNA binding site
- CTx binding site

**Tandem Post-Polymerisation Modification**

‘Clickable’ units are not compatible with controlled radical polymerisation. Instead, tandem-post polymerisation modification techniques were used.

- Poly(pentafluorophenyl methacrylate) for easy modification.
- β-α-galactose was ‘clicked-on’ to pendent alkyne moieties.
- Results in biocompatible methacrylamide based (co)polymers.

**Role of Linker Length and Carbohydrate Density**

- Polymers synthesised with ~6 Å (short) and 16 Å (long) linkers.
- Linker length has no effect on PNA inhibition (A).
- Longer linker has 2 – 3 fold lower MIC compared to shorter linker in inhibiting CTx (B).
- 100X more active than free galactose.

**Binding Modes**

- QCM-d also probes the viscoelasticity of films formed on a surface.
- Large changes in dissipation (ΔD) indicate a flexible film, whilst small ΔD values suggest a rigid, non-flexible coating: The longer chain polymer (P3) spans the binding site of ConA whereas the shorter polymers (P1/P2) can only bind one site.

- A combination of techniques is required to assess the efficacy of an inhibitor.

**Summary**

- Tandem post-polymerisation modification allows synthesis of polymers from same chain length distribution.
- Longer linker has better binding site accessibility.
- Carbohydrate density has an effect.
- Inhibitors have to be developed for the binding site.