

Selective Binding of GlycoPol™ polymers (GlycoPol™) to Human Tissue Microarrays: A Novel Approach to Tissue Targeting

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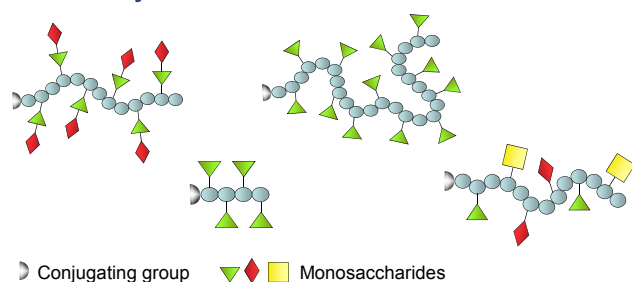
Introduction

Carbohydrates are information rich molecules involved in a number of biological processes including: cell-cell and receptor interactions and in targeting of biological mediators. Frequently these carbohydrate/polysaccharide effects are mediated by chemically complex structures that are beyond the scope of conventional chemistry. Pseudo-polysaccharides comprising sugars attached to polymers offer the potential to mimic some of these complex, multi-valent interactions to target therapeutics to specific cells and tissues. GlycoPol™ polymers comprise a polymethacrylate scaffold with individual sugar molecules attached along the chain by 'click' chemistry¹⁻².

Methods

GlycoPol™ polymers comprising four scaffold lengths (6, 20, 40 and 100 monomer units) were clicked with a range of sugars including: mannose, galactose, fucose, sialic acid, lactose and N-Acetyl galactosamine, and conjugated to biotin as a reporter. Human tissue microarrays, comprising 33 normal tissues, together with inflamed lung and liver tissues, were incubated with GlycoPols™ alone, or after pre-incubation with an equal concentration of un-biotinylated GlycoPols™. Tissue staining was visualised by normal streptavidin/hexaflor methods.

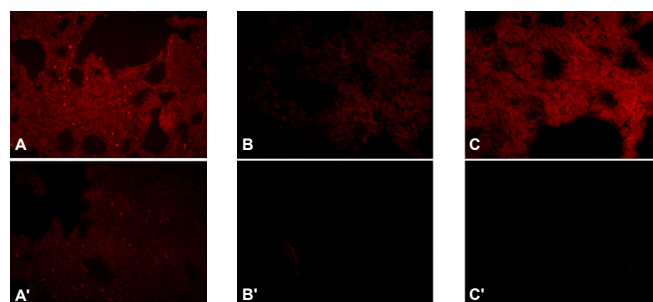
Figure 1. Schematic representation of the structure of GlycoPol™



Results

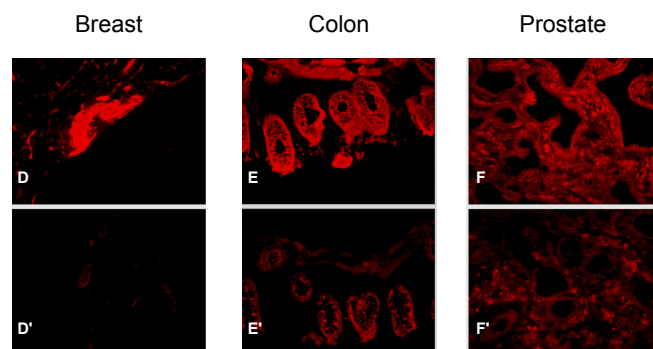
Specific binding of GlycoPol™ polymers to normal human tissues and to inflamed human lung and liver has been observed, indicating targeting of the GlycoPol™ polymers to carbohydrate receptors on specific cells and tissues. Targeting was observed on a number of tissues including: breast, lung, prostate, colon and liver. Binding specificity was associated with both sugar composition of the GlycoPol™ polymers and with tissue or specific cell types, e.g. epithelial cells.

Figure 2. Binding of GlycoPol™ polymers to inflamed human lung



GlycoPol™ A, Blocked A'; GlycoPol™ B, Blocked B'; GlycoPol™ C, Blocked C'

Figure 3. Binding of GlycoPol™ polymers to normal breast, colon and prostate tissues



GlycoPol™ D, Blocked D'; GlycoPol™ E, Blocked E'; GlycoPol™ F, Blocked F'

Conclusions

By exploiting tissue-specific sugar binding properties, GlycoPol™ offers a novel approach to the selective targeting of therapeutic cargos, including proteins, peptides, siRNA, oligonucleotides and nanoparticles to specific cells and tissues.

References

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2. Geng, J.; Mantovani, G.; Tao, L.; Nicolas, J.; Chen, G.; Wallis, R.; Mitchell, D.A.; Johnson, B.R.G.; Evans, S.D.; Haddleton, D.M. *J. Am. Chem. Soc.* 2007, 129 (49), 15156-15163.