www.wep-ltd.co.uk

Selective Binding of Glycopolymers (GlycoPol^{TM}) to Human Tissue Microarrays: A Novel Approach to Tissue Targeting

R. Palmer*, P. Williams*, G.Tekle*, D. M. Haddleton*, and K. Page+

* Warwick Effect Polymers Ltd., + Asterand plc

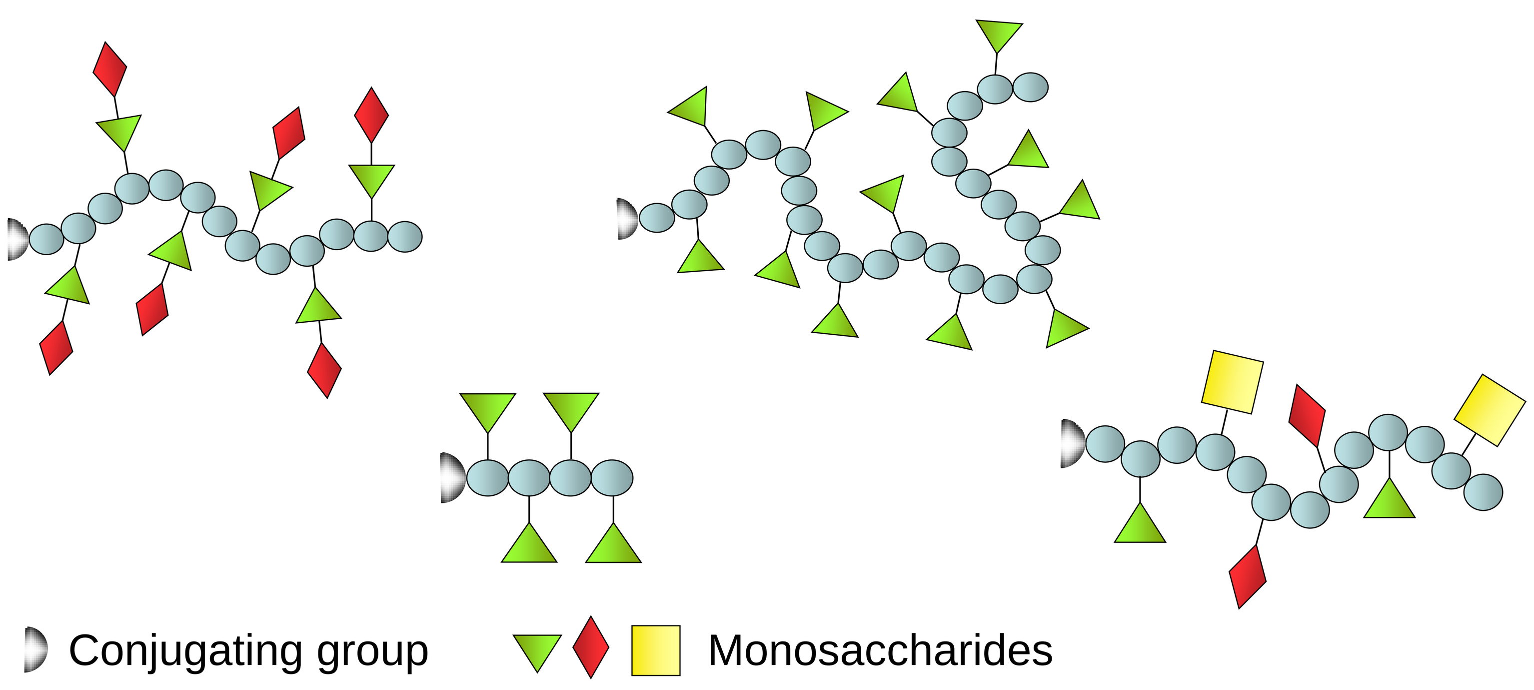
Introduction

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^{TM} polymers comprise a polymethacrylate scaffold with individual sugar molecules attached along the chain by 'click' chemistry[1-2]. In the present study, we have examined the binding of a range of GlycoPols™ to human tissue microarrays and cultured cells.

Methods

GlycoPol^{TM} polymer scaffold lengths (6 to 100 monomer units) were clicked with a range of sugars including: mannose, galactose, fucose, sialic acid, lactose or N-Acetyl galactosamine. Human tissue microarrays, comprising 33 different tissues, or cultured cells, were incubated with GlycoPols^{TM} alone, or after pre-incubation with un-labelled GlycoPols^{TM}. Tissue staining was visualised by fluorescence microscopy.

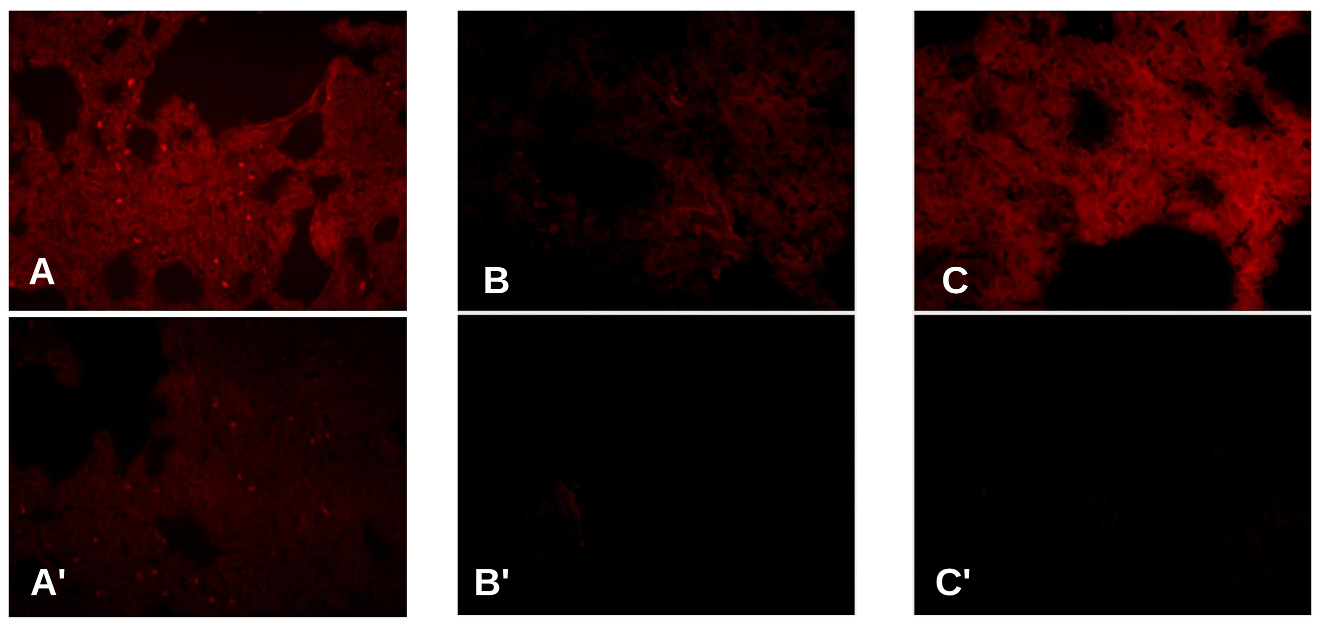
Figure 1. Schematic representation of the structure of GlycoPol^{TM}



Results

Specific binding of GlycoPols^{TM} to normal human tissues and to inflamed human lung and liver has been observed, indicating targeting of the GlycoPol^{TM} polymers to carbohydrate receptors on 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 GlycoPols^{TM} and with tissue or cell types, e.g. epithelial cells. GlycoPol^{TM} was also taken up into cells following specific binding to the cell surface.

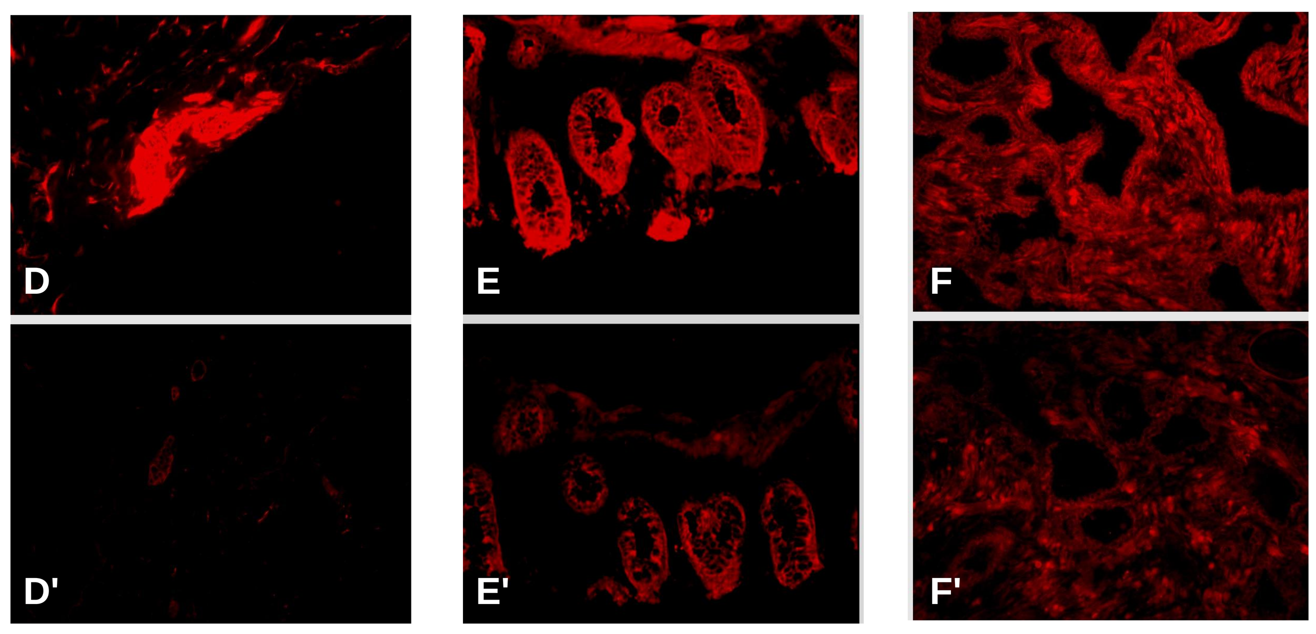
Figure 2. Binding of GlycoPols^{TM} to inflamed human lung



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

Figure 3. Binding of GlycoPols^{TM} to normal breast, colon and prostate tissues

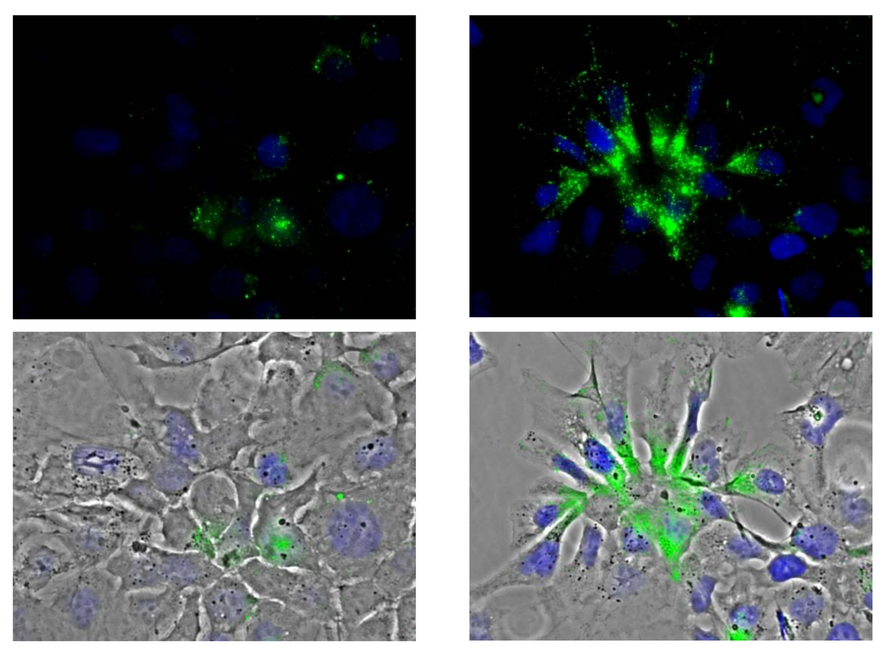
Breast Colon Prostate



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

Figure 4. Cell binding and uptake of GlycoPol^{TM}

4 h 24 h



Conclusions

Selected GlycoPols™ bind to specific receptors on human tissues and cells. By exploiting tissue-specific sugar binding properties, GlycoPol™ offers a novel approach to the selective targeting of therapeutic cargos e.g. proteins, peptides, siRNA, oligonucleotides and nanoparticles to cells and tissues. GlycoPols™ can be taken up into cells by receptor mediated uptake, offering the potential for intracellular delivery.

References

1.Ladmiral, et al *J. Am. Chem. Soc.* 2006, 128 (14), 4823-4830
2.Geng, et al *J. Am. Chem. Soc.* 2007,129 (49), 15156-15163

Warwick Effect Polymers Ltd T +44 (0)24 7669 2476 F +44 (0)24 7669 2456 E enquiries@wep-ltd.co.uk