Glycosylated Nanomaterials: Neutralisation and Detection of Bacteria and Toxins

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Protein-Carbohydrate Interactions

Cell signalling

Fertilisation

Inflammation

Cellular adhesion of
• Viruses
• Bacteria
• Bacterial toxins

Miura, *JPOLA*, 2007, 45, 5031

Gamblin, *Chem. Rev.*, 2009, 109, 131
Why Materials?

Kiessling, Angew. Chem., 2006, 45, 22348
Alexander et al, JACS, 2007, 129, 11014
Applications: Anti-adhesion Therapy

Interactions can be inhibited at \( \text{nM} \) of glycopolymers

\[
\text{(LacNAc)}_3\text{-glycopolymer}
\]

Survival (%)

Days postinfection

\( \text{Neu5Ac} \alpha 2-6^* \)
\( (n=6) \)
\( \text{Non-sialyl} \)
\( (n=5) \)

Influenza inhibition in mice

Sharon, N. Biochimica et Biophysica Acta, 2006, 527–537
Hidari et al. Glycobiology 2008, 18, 779
Glycopolymers by Post-Polymerisation Modification


- Easy to make 50 gram scale
- 1 column/distillation
- Compatible with RAFT/ATRP
- Quantitative functionalisation with non-hindered amines
- Density control
- Sequentially modified polymer libraries

Theato, P.; *J. Pol. Sci. A.*, **2008**, *46*, 6677
Selective Binding of Cholera-Toxin

Enzymatic domain \(\rightarrow\) Induces toxic effect

Carbohydrate binding domain \(\rightarrow\) Binds to epithelial cells to promote cell uptake

Anti-adhesion therapy does not target bacteria, so less evolutionary stress

Galectins – at least 13

Sigma-Aldrich – 8 Galactose-’specific’ lectins

How do we engineer a high-affinity binder for cholera toxin, without total synthesis of complex carbohydrates?
Glycan Accessibility as a Tool for Lectin Specificity

Cholera Toxin

Peanut Agglutinin

16 Å

6.3 Å

Kiick et al.; Macromol. 2007, 40, 7103 and Biomac., 2006, 7483
**Glycopolymer Library**

<table>
<thead>
<tr>
<th>Polymer</th>
<th>DP[^a]</th>
<th>Linker[^b]</th>
<th>Density[^c]</th>
<th>M&lt;sub&gt;w&lt;/sub&gt;/M&lt;sub&gt;n&lt;/sub&gt;[^d]</th>
</tr>
</thead>
<tbody>
<tr>
<td>GP1</td>
<td>18</td>
<td>Short</td>
<td>100</td>
<td>1.29</td>
</tr>
<tr>
<td>GP2</td>
<td>33</td>
<td>Short</td>
<td>100</td>
<td>1.27</td>
</tr>
<tr>
<td>GP3</td>
<td>70</td>
<td>Short</td>
<td>100</td>
<td>1.26</td>
</tr>
<tr>
<td>GP4</td>
<td>18</td>
<td>Long</td>
<td>100</td>
<td>1.32</td>
</tr>
<tr>
<td>GP5</td>
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<td>1.32</td>
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<tr>
<td>GP6</td>
<td>70</td>
<td>Long</td>
<td>100</td>
<td>1.28</td>
</tr>
<tr>
<td>GP7</td>
<td>33</td>
<td>Long</td>
<td>50</td>
<td>1.23</td>
</tr>
<tr>
<td>GP8</td>
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<td>1.21</td>
</tr>
<tr>
<td>GP9</td>
<td>33</td>
<td>Long</td>
<td>10</td>
<td>1.20</td>
</tr>
</tbody>
</table>

[^a]: Degree of Polymerization
[^b]: Type of Linker
[^c]: Polymer Density
[^d]: Molecular Weight Ratio

**Chemical Structures:**

- Glycopolymer 1 (GP1): n = 25, 50, or 100
- Glycopolymer 2 (GP2): n = 25, 50, or 100
- Glycopolymer 3 (GP3): n = 25, 50, or 100
- Glycopolymer 4 (GP4): x = 10, 25, 50, 100
- Glycopolymer 5 (GP5): x = 10, 25, 50, 100
- Glycopolymer 6 (GP6): x = 10, 25, 50, 100
- Glycopolymer 7 (GP7): x = 10, 25, 50, 100
- Glycopolymer 8 (GP8): x = 10, 25, 50, 100
- Glycopolymer 9 (GP9): x = 10, 25, 50, 100

**Graphs:**

- Molecular Weight Distribution (M<sub>w</sub>)
- Transmission Spectroscopy
- Wavenumber (cm<sup>-1</sup>)


Applications: Detection

- Direct
- Label-free
- Easy
- Sensitive
- Quantifiable in real-time
Potential Sensor for Ricin

![Chemical structure and experimental setup](image)

![Graphs and data](image)
Colour Change ◯ ☒
Fast ☒
Specific ☒
Saline Stability

Colour Change ✔
Fast ✔
Specific ✔
Saline Stability ✔

Richards, S-J., Fullam, E., Besra, G. S. Gibson, M. I., In Preparation
Summary

- Tandem Post-Polymerisation Modification
- Multivalent inhibitors that have good affinity AND specificity
- Glycogoldnanoparticles
- Optimised polymer coating for lectin detection
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Gibson Group Members

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