P-selectin Inhibitors for Controlling Inflammation

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Therapeutic Opportunity in Inflammation

Inflammation Associated Diseases
• Bacterial/viral infection
• Traumatic/Ischemic Injury
• Cancer
• Autoimmune
• Genetic (Sickle Cell)

Current Therapies that Fight Inflammation
• NSAIDS
• Cortiosteroids
• Immune System Inhibiting Antibodies

Remaining Unmet Need
Molecules that can be administered over weeks/months without shutting down the immune system or other adverse affects
P-selectin Mediates “Cellular” Response to Injury
**Peptide Mimetic of PSGL-1**

- Small functional peptide
- More chemically stable
- Appropriate glycosylation
- Binds as well as natural ligand
In vivo Inhibition of P-selectin

GSnP-6 reduced leukocyte sticking to blood vessel wall
# Current P-Selectin Inhibitors

<table>
<thead>
<tr>
<th>Molecule</th>
<th>$IC_{50}$</th>
<th>Indication</th>
<th>Molecule Type</th>
<th>Binding Pocket</th>
</tr>
</thead>
<tbody>
<tr>
<td>GsnP-6</td>
<td>22 nM</td>
<td><strong>Multiple Inflammatory Diseases</strong></td>
<td>Peptide</td>
<td>SO3, Sugar</td>
</tr>
<tr>
<td>GMI 1070</td>
<td>423 μM</td>
<td>Sickle Cell Disease, Cancer Metastasis</td>
<td>Glycomimetic</td>
<td>Sugar</td>
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<tr>
<td>Bimosiamose</td>
<td>70 μM</td>
<td>COPD, Psoriasis</td>
<td>Glycomimetic</td>
<td>Sugar</td>
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<tr>
<td>PSI-421</td>
<td>250 μM</td>
<td>Deep Vein Thrombosis</td>
<td>Small Molecule</td>
<td>Sugar</td>
</tr>
<tr>
<td>SelG1*</td>
<td></td>
<td>Sickle Cell Disease</td>
<td>Antibody</td>
<td>?</td>
</tr>
</tbody>
</table>
Summary

• Validated biological target
• Blocks early “cellular” stage of inflammatory process
• nM potency
• IP (pending provisional application) on composition, method of use and methods of synthesis