Glycan Modulation To Prevent Fucosylation

Technology and Cell Systems for Enhanced Antibody-Dependent Cellular Cytotoxicity (ADCC) Activity for Cancer and Anti-Infectious Disease Antibodies
Antibody-Dependent Cellular Cytotoxicity (ADCC)

Cancer:
ADCC Dominates Anti-Tumor Cell-Killing Effect of Cancer Antibodies
ADCC: Also Important for Removal of Infected Cells

Infectious Diseases:
ADCC to Kill Infected Cells

Viral Antigen or Antigen Exposed During Infection

Infected Cell

NK Cell

FcyRIIIa

GlymaxX®
The Fc Glycan Determines ADCC Activity

Figure: GlymaxX® enzyme deflects fucose biosynthesis pathway which results in a 10-100-fold decrease in mAb concentration
A New Concept for Metabolic Intervention: Pathway Deflection

Fucose synthetic pathways:
The internal pathway matters.

GlymaxX®
A New Concept for Metabolic Intervention: Pathway Deflection

Knock-out of enzymes involved are patent protected
A New Concept for Metabolic Intervention: Pathway Deflection

Extracellular space
Plasma membrane
Cytosol

Lysosome

α-fucosidase
Fucose
Fucose kinase
Fucose-1-phosphate
GDP-fucose
GDP-fucose pyrophosphorylase
GDP-fucose
FX
3,5-epimerase
FX
GDP-4-keto-6-deoxygalactose
GDP-4-keto-6-deoxymannose
GDP-mannose
GMD
NADP+
NADPH
Deflecting Enzyme removes intermediate substrate

Golgi lumen

ProBiogen®

GlymaxX®
GlymaxX® Depletes Fucose as Efficient as Knock-out Strategies

Introducing the GlymaxX® Enzyme into an Existing Trastuzumab Clone Removes Fucose from G0/G1 and G2 Structures, Without Changing Their Relative Abundance
Case Study: GlymaxX®-Modified Trastuzumab

Afucosylated Fc Glycan Shows Increased FcγRIIIa Binding

Receptor Binding Assays:

<table>
<thead>
<tr>
<th>Samples</th>
<th>Factor vs WT</th>
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<tbody>
<tr>
<td>WT</td>
<td>---</td>
</tr>
<tr>
<td>Clone 1</td>
<td>16-fold</td>
</tr>
<tr>
<td>Clone 2</td>
<td>18-fold</td>
</tr>
<tr>
<td>Clone 3</td>
<td>20-fold</td>
</tr>
</tbody>
</table>

Assay Performed in the Absence of Plasma IgG!
(Which will compete with rec. antibody for receptor binding.
In vivo the different ADCC activities (fucosylated vs afucosylated)
will be even greater)

Outcome:
About 20-fold increased ADCC Activity in vitro
(in this assay setting)
GlymaxX® Glycan Modulation...

- ...is a stable and permanent cell modification
- ...boosts ADCC-Mediated Cell Killing Activity in cancer & infectious diseases
- ...induces cell-killing at lower antibody concentrations (much lower doses!)
- ...can be applied to new & existing cell lines, and entire expression platforms
- ...can be accessed via ProBioGen‘s existing GlymaxX® CHO cell lines
- ...can be applied in less than 10 weeks to existing cells or platforms
- ...and does not negatively affect cell productivity & product quality
- ...is simple, stable and robust
- ...works by preventing fucose biosynthesis and minimized fucose content
- ...is well-known to increase FcγRIIIa binding to boost ADCC cell-killing
- ...is royalty-free
- ...is licensed to many biotechs and big pharmas world-wide
Contact ProBioGen

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