ProBioGen
Intelligent Biopharmaceutical Solutions

GlymaxX®
Fucose Targeted Glyco-Engineering

ADCC Enhancement by Fucose Glyco-Engineering

GlymaxX®: Fucose-targeted Glyco-Engineering to boost antibody-mediated cell-killing potency.

Therapeutic Antibodies with low fucose content show a much higher Antibody-Dependent Cellular Cytotoxicity (ADCC), i.e. a higher killing activity against tumorigenic or infected.
Several therapeutic antibody drugs on the market rely on ADCC as a mechanism of action. ADCC Enhancement has the potential to increase the therapeutic effect and/or to strongly reduce antibody dosage requirements, eventually resulting in fewer side-effects and treatment costs.

The GlymaxX® technology is based on the introduction of a gene into the cell, encoding an enzyme which deflects the cellular fucose biosynthesis pathway. This leads to literally afucosylated antibodies, both on the core part (no core fucose) or to the variable part (no antennary fucose) of an N-glycan. (It also inhibits the fucosylation of O-glycans and protein-O-fucosylation.) On top, GlymaxX® also allows adjusting specific intermediate fucosylation levels via fucose addition to the culture medium.
The GlymaxX® technology is universally applicable, robust, simple and potent, and it can be rapidly applied to any existing or newly created antibody producer cell lines, as well as entire expression platforms. GlymaxX® CHO host cell lines or vectors are available under a research license or commercial license. GlymaxX® has been globally out-licensed non-exclusively to Pharma and Biotech companies.

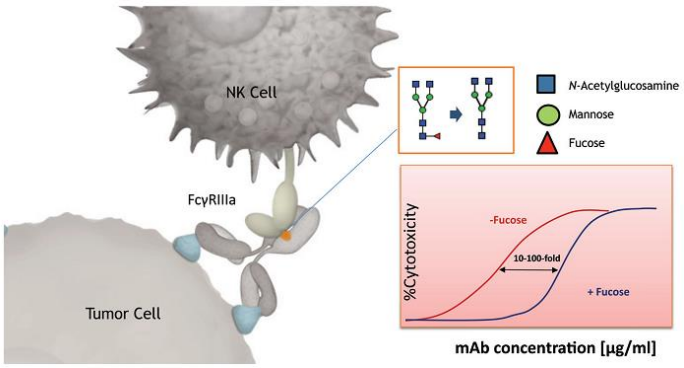

Figure 1: Antibodies produced from GlymaxX®-engineered cells contain a reduced amount of core-fucose, show an increased ability to bind to FcγRIIIa and recruit NK-cells, and mediate an increased ADCC response.

Advantages of GlymaxX®:

- Yields antibodies with increased ADCC activity due to minimized fucose content
- Applicable to **new** and **existing** clones
- Speed: Modification in less than 10 weeks
- Permanent and stable modification
- No negative effects on upstream or downstream process, productivity, cell growth, etc.
- No culture additives required
- Proven batch-to-batch consistency
- Scalability up to 2000 L under GMP confirmed
- Applicable in cells of various species origin
- Full effect with very low enzyme levels
- Currently undergoing clinical trials
- **Free of Revenue-Based Royalties!**

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GlymaxX® - A New Concept for Metabolic Intervention

This technology is based on the heterologous, cytosolic expression of a bacterial enzyme that redirects the *de novo* fucose synthesis pathway towards a sugar-nucleotide that cannot be metabolized by eukaryotic cells. Even low levels of the deflecting enzyme expression are sufficient to block the *de novo* pathway. This independence directly contributes to a stable level of afucosylation over an extensive number of cumulative population doublings. The deflecting enzyme expression of the GlymaxX® technology does not inhibit cell growth and productivity but mediates the secretion of antibodies with minimized fucose content. The overall antibody structure is not altered by the absence or presence of fucose residues. The absence of fucose has no impact on its pharmacokinetics, stability, and immunogenicity.

As a unique feature, the GlymaxX® technology can also be applied to existing antibody producer cell lines or even entire cell expression platforms in a very short timeframe without altering their productivity.

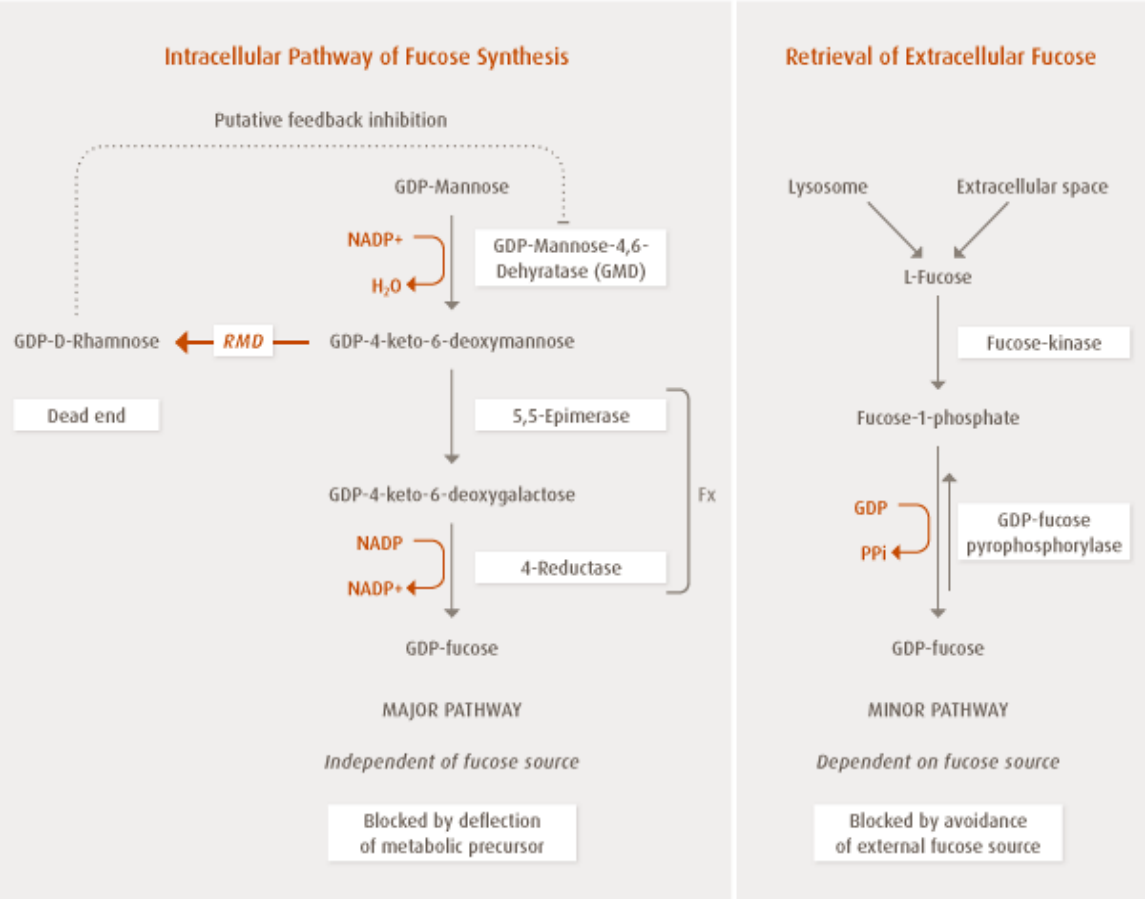

Figure 2: Working principle of the GlymaxX® technology. In the absence of fucose, cells are unable to synthesize GDP-fucose via the salvage pathway. The de novo pathway, the dominant source of activated GDP-L-Fucose, is efficiently blocked by enzymatic conversion of the intermediate GDP-4-keto-6-deoxymannose into GDP-D-Rhamnose, a dead end product that typically does not occur in vertebrate cells.