

## Key Facts about GlycoExpress®

GlycoExpress® (GEX®) are human cells for the production of authentic human glycosylated proteins with no immunogenic non-human carbohydrate residues.

It provides an established expression platform for different biopharmaceuticals:

- **Antibodies of different isotypes (e.g., IgG, IgM, IgA)**
- **Defucosylated antibodies**
- **Bispecific antibodies/ fragments (e.g., NK-cell/ T-cell recruiters)**
- **Difficult-to-express and complex glycosylated proteins (e.g., FSH, rhSP-D and others)**
- **Blood factors (e.g., FVII)**
- **Protein hormones (e.g., FSH, HCG)**
- **Fusion proteins with extended serum half-life**
- **Enzymes (e.g., for enzyme replacement therapy)**



## GlycoExpress® - The toolbox for the production of human glycosylated biopharmaceuticals

GlycoExpress® (GEX®) technology is a well-established human expression platform for the screening and production of biotherapeutics. It consists of a toolbox of glycoengineered cell lines optimized for producing biotherapeutics with desired glycan structures to improve their clinical performance.

Glycosylation of a glycoprotein depends on the host cell line and strongly affects a biotherapeutic's properties such as bioactivity, solubility, stability, serum half-life and immunogenicity. Thus, modification and control of glycosylation are important aspects in developing such products.

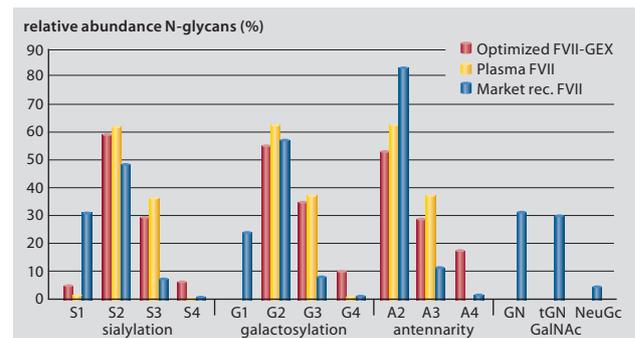
Because different products need different glycosylation characteristics for their optimal activity, we have generated a set of GEX® cell lines with the following attributes:

- **mAB-Express®** for optimized glycosylation of antibodies, including low core-fucosylation, high galactosylation, bisGlcNAc, and sialylation
- **SialoMax®** used for products where high sialylation and high core fucosylation is required
- **SialoFlex®** allows gradual adjustment of the sialylation degree for screening of the optimal content of sialic acid on a product
- **FucoFlex®** allows the adjustment of the fucosylation degree for screening of the optimal content of fucose for the respective product

Further glycoengineered cell lines are continuously developed. Examples include a cell line for the production of glycoproteins with high amounts of mannose-6-phosphate (e.g., in the field of enzyme replacement therapy) and SialoMax® glycoengineered to eliminate

N-glycan-linked GalNAc for products with further reduced serum clearance.

By using this toolbox of cell lines, we can mimic glycosylation of the respective human endogenous protein, for example for coagulation factor VII:



**Glycosylation of coagulation factor VII from different sources. FVII-GEX® exhibits almost identical glycosylation features as seen with plasma FVII. Marketed FVII derived from BHK significantly differs from GEX®-optimized and plasma derived FVII and furthermore carries immunogenic NeuGc: S: sialylated, G: galactosylated, A: antennarity, 1-4: mono-tetra, GN: GalNAc, t: terminal.**

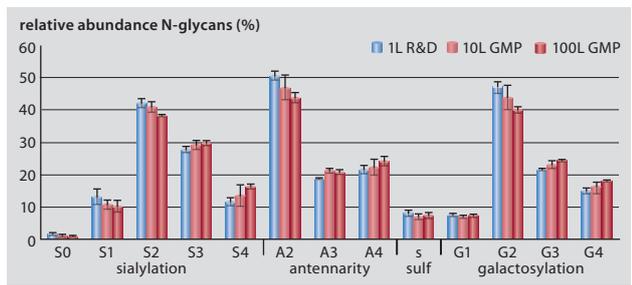
Because GlycoExpress® cells are of human origin, immunogenic glycans such as nonhuman sialic acid (NeuGc), the Galili epitope or core  $\alpha$ 1,3 fucose are absent. Those unwanted structures are known to cause immunogenic reactions and can increase serum clearance of the glycoprotein. Furthermore, human specific glycosylation features (e.g., bisGlcNAc,  $\alpha$ 2,6 linked sialic acid) are present whereby  $\alpha$ 2-6 linkage is not found in hamster derived cell lines such as CHO or BHK.

**GlycoProcess**

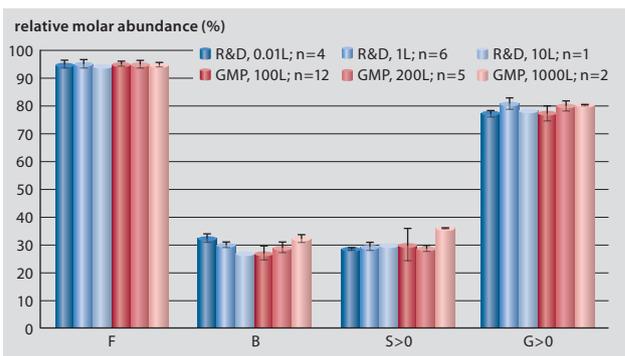
**Production Yield:** The preferred production technology for GlycoExpress® platform is based on perfusion processes leading to high productivity and stable product quality across all scales and batches. The following table shows current yields for different molecule classes. In two customer projects, we compared the productivity of difficult-to-express proteins in CHO and GEX® cells and found up to a 10-fold increased productivity and dramatically improved product quality when produced in GEX® cells.

| Yields for different product classes                           |               |
|--|---------------|
| Product Class  | Productivity* |
| IgG (high and low core-fucose)                                 | 15-30 g/L     |
| IgA  | 10-15 g/L     |
| IgM  | ~3 g/L        |
| Factor VII   | ~2 g/L        |
| *Yield per 30-40 day perfusion run per liter bioreactor volume |               |

**Product Quality:** As shown in the following two figures for a glycoprotein and an IgG antibody produced in several production scales, glycan parameters are nearly identical, even when produced in glass, stainless steel, or single-use bioreactors.



Glycan profile across scales for a glycoprotein hormone



Glycan profile across scales for an IgG1 antibody (F: Fucosylated, B: Bisected, S: Sialylated, G: Galactosylated structures)

The reasons for this are the favorable biotechnological features of GEX® cells, including

- Exceptionally high stability of production clones in terms of productivity, even without selection pressure
- High shear force resistance of the cells, which originate from robust blood cells
- High cell densities
- Low cell doubling time.

**Regulatory and Safety**

The GlycoExpress® production platform and derived products were approved for clinical trials by regulatory agencies in the major countries as depicted in red in the following figure.



**We are open and ready to discuss your project and to help you find the suitable GEX® cell line for your demands.**

For more information please contact us

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