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Genetic glycoengineering for improvement of biopharmaceuticals

Glycotope's GEX™ platform comprises a comprehensive portfolio of proprietary glycoengineered human suspension cell lines. Gene editing technologies like the zink finger nuclease (ZFN), transcription activator-like effector nuclease (TALEN) or Crispr/Cas technology as well as classical overexpression techniques are very efficient tools to further gear up the glycosylation machinery for specific needs of human biopharmaceuticals. Optimization of glycosylation can target the amount of e.g. fucose, galactose and sialic acid (NANA). As an example, the glycan influenced binding to liver based receptors like the asialoglycoprotein receptor is the key step to eliminate the molecule from the blood stream. As case study, we show on the example of human factor VII expressed in a portfolio of different genetically modified GEX cell lines, the specific improvement of the glycosylation profile especially with regards to the reduction of liver receptor binding properties. Besides the generation of glycan with highest sialylation degree, the GalNAc moiety which exhibits high affinity towards the asialoglycoprotein receptor was removed by knockout of the respective transferases simultaneously on multiple alleles. Interestingly, the knockout of the *GalNT* genes led to unexpected changes in other N-glycan features like antennarity of the N-glycans, sialylation degree as well as the amount of bisecting GlcNAc present. By these technologies, a FVII molecule was generated which resembles human plasma derived FVII to high extend.

Biography

Steffen Goletz founded Glycotope in 2001 and has more than 16 years of experience in the life sciences industry. Prior to this, he worked for several renowned research institutions, including the Max Delbrueck Centre for Molecular Medicine (Berlin), the MRC Centre for Protein Engineering (Cambridge, UK) and the German Cancer Research Centre in Heidelberg. As CSO, he is responsible for the development of Glycotope's platform technologies and product pipeline of glyco-optimized biotherapeutics. He studied biology, biochemistry and molecular biology at the universities in Heidelberg, Kaiserslautern, Manchester (UK) and Berlin and holds a PhD in Biochemistry from Freie Universiät, Berlin.

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