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CHO glycosylation mutant cells as potential hosts for production of therapeutic biologics with enhanced efficacy

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Glycosylation can significantly affect the efficacy of recombinant therapeutics. Glycoprotein drugs require a high degree of sialylation of their N-glycans for a longer circulatory half-life. Mannose-terminated N-glycans can specifically target the proteins to macrophages and dendritic cells via mannose-binding receptors. Removal of core fucose from human IgG1 has been shown to significantly enhance its affinity to FcγRIIIa and thereby dramatically improves its antibody-dependent cellular cytotoxicity (ADCC). Cancer cells generally express glycoproteins with shortened O-glycans. Therefore, recombinant anti-cancer vaccines carrying these short tumor-associated O-glycans are more ideal for triggering specific anti-tumor immune responses. With cytotoxic lectins and the newly-developed genome editing technologies, such as ZFNs, TALENs and CRISPR-Cas9, we have generated more than 20 CHO glycosylation mutant cell lines. Some of these mutant lacks one specific glycosylation genes whereas others lack more than 10 glycosylation genes. With these CHO cell mutants, we have been able to produce highly sialylated EPO, recombinant human β-glucocerebrosidase with mannose-terminated N-glycans (like Cerezyme, but no need for *in vitro* glycan modification) and fucose-free antibodies. Furthermore, these mutant CHO cells can produce recombinant antibodies carrying different N-glycans with highly homogenous structures (90-97%). These are invaluable tools for antibody PK/PD studies on the impact of different N-glycans.

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