Glycosylation of recombinant anti-cancer therapeutics in different expression systems with their emerging technologies

Abstract

Glycosylation, a post translational modification, has a great role in recombinant anticancer therapeutic proteins, as most of the approved recombinant therapeutics are glycoproteins. The constant amino acid sequence of therapeutics determines the enzymatic activity while the glycan associated influence their pharmacokinetics, solubility, distribution, serum half-life, effector function and binding to receptors. Glycoproteins expressed in different expression systems get their own oligosaccharides, which increases the diversity of proteins. Glycan structure also varies from batch to batch in a single expression system, depending on culturing conditions and medium. Heterogeneity of glycan creates hurdles in downstream processing, ultimately leading to variable anticancer therapeutic efficacy. Therefore, glycoproteins require appropriate expression system to catch structurally and functionally identical glycan, like human. In different types of glycosylation, N-glycosylation has acquired great attention because much is known about it. In many expression systems, its pathway remains conserved in endoplasmic reticulum but divergence has been observed when it enters the Golgi complex. Hence, in the recent decades, numerous approaches have been adopted for the engineering of Golgi's N-glycosylation pathway to attain human like glycan. Some of the researchers have tried to engineer the Nglycosylation pathway of expression systems by introduction and knock down of various genes. Others have worked on the site-directed mutagenesis of glycosylation potential sites and in vitro glycosylation remodeling via chemo-enzymes. In this review, we have emphasized on glycosylation pattern in various expression systems with their emerging technologies for glycosylation engineering of anticancer therapeutic drugs.

Key words: N-glycosylation; Glycoproteins; Glycoengineering; GlycoSwitch; GlycoFi; GlycoDelete; Yeast expression system; Mammalian expression system.