Antibody production in plants: advances and challenges in glycoengineering

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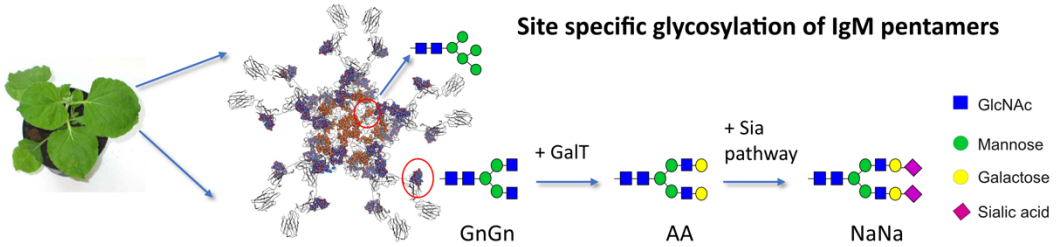
Monoclonal antibodies (mAbs) are amongst the most important biopharmaceutical products and demands are increasing. One reason for the need of large product quantities (several tons /year) is the generation of products with suboptimal efficacies. A possibility to approach this shortcoming is the expression of mAbs with optimized glycosylation profiles.

In line, recent serological profiling suggests that combatting infections requires a bouquet of Ab isotypes and subclasses, with glycosylation playing a central role1,2. Notably, while IgGs carry only one glycosite (GS), the glycosylation status of other Abs, like IgM and IgA is more complex, carrying up to 7 GSs and site specific glycosylation. This makes its controlled production difficult.

The ability of plants to produce mAbs with targeted glycosylation has been demonstrated in multiple studies3. A modular cloning and expression toolbox, which consists of single and multi gene expression vectors and glycoengineered production hosts, was developped3. The versatile approach enables (i) rapid Ab iso- and subtype switch and (ii) the generation of mAbs with engineered glycosylation profiles4,5.

The starting point is a glycoengineered tobacco related Nicotiana benthamiana line that generates GlcNAc-terminated N-glycan structures (GnGn), a conserved N-linked glycoform in higher eukaryotes. This structure is then subsequently modified by the coexpression of respective glycosylation enzymes, e.g. β1,4 galactosyltransferase (GalT) for the generation of galactosylated (AA), and the sialylation pathway (Sia) for sialylated (NaNa) structures. Advances and challenges in the expression of various mAbs, including multimeric IgA and IgM glyco-variants, are discussed.



IgM glycosylation

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