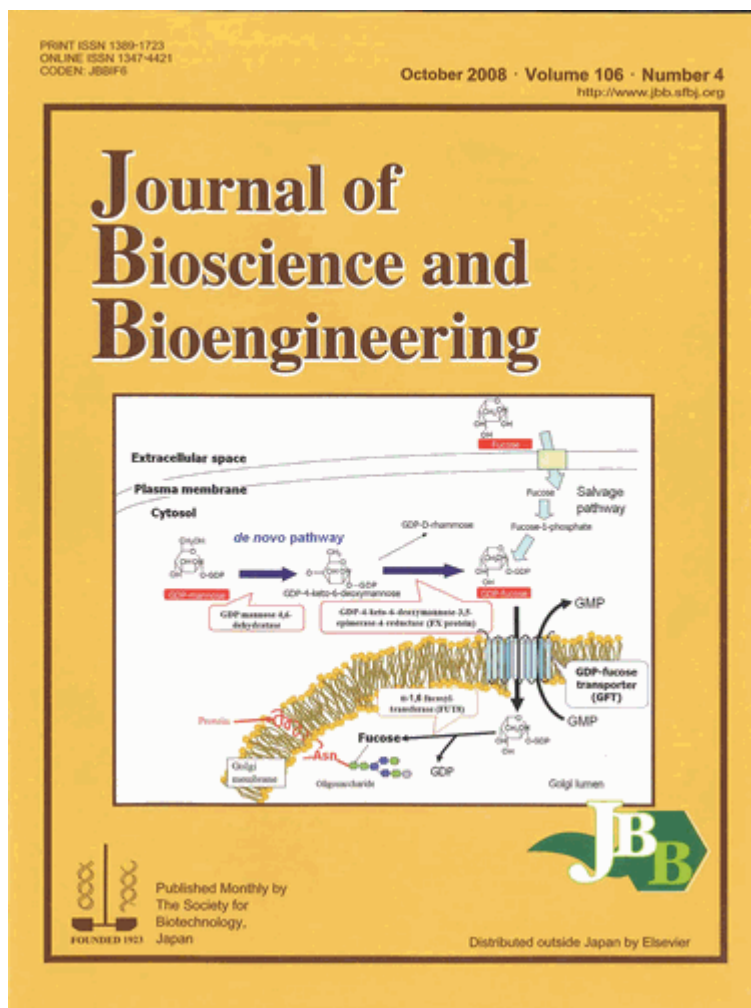


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Glycosylation is the most extensive of all post-translational modifications and plays an important role in secretion, antigenicity, *in vivo* function, and the clearance of glycoproteins in blood. Glycosylation control is an important issue for the industrial production of therapeutic proteins. Human antithrombin III (AT-III) is a plasma glycoprotein and is used as a biopharmaceutical for preventing and regulating blood coagulation. The  $\alpha$ -1,6 fucosylation of AT-III, which has four N-asparagine glycosylation sites, significantly reduces antithrombin–heparin affinity. Hence, defucosylation is one of the most important issues for quality control of commercial AT-III production using mammalian cell culture.

Figure illustrates the biosynthesis of GDP-fucose and protein fucosylation in a mammalian cell. Cytosol GDP-mannose is converted to GDP-4-keto-6-deoxymannose by GDP-mannose dehydratase (GMD). This intermediate is converted to GDP-fucose by GDP-4-keto-6-deoxymannose-3,5-epimerase-4-reductase (GMER). GDP-fucose is transported through Golgi membrane by GDP-fucose transporter (GFT). In the Golgi apparatus, fucose is transferred from GDP-fucose to N-linked-type complex glycoprotein by  $\alpha$ -1,6 fucosyltransferase (FUT8).

Related article: Omasa, T., Tanaka, R., Doi, T., Ando, M., Kitamoto, Y., Honda, K., Kishimoto, M., and Ohtake, H., "Decrease in antithrombin III fucosylation by expressing GDP-fucose transporter siRNA in Chinese hamster ovary cells", *J. Biosci. Bioeng.*, vol. 106, 168-173 (2008).

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