

## バイセクティング GlcNAc 含有複合型糖鎖を持つ均一な抗体医薬品の作製

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Preparation of homogeneous antibody drugs having complex-type glycan containing bisecting GlcNAc (<sup>1</sup>*Department of Science and Technology, Seikei University*, <sup>2</sup>*KH Neochem Co., Ltd*) ○ Hasumi Muto<sup>1</sup>, Yuto Nakamachi<sup>2</sup>, Taiki Kuribara<sup>1</sup>, Kiichiro Totani<sup>1</sup>

Antibody drugs are expected to be highly effective and to reduce side effects as therapeutic agents for cancer and other diseases. Glycans are attached to the surface of antibodies, and their glycan structures regulate antibody-dependent cellular cytotoxicity (ADCC) activity, which is important for the efficacy of therapeutic antibodies. However, the glycans structures of currently used therapeutic antibodies are heterogeneous, resulting in reduced efficacy of therapeutic antibodies and differences in therapeutic efficacy between lots. In this study, we replaced the heterogeneous glycans on the antibody to Gal<sub>2</sub>GlcNAc<sub>3</sub>Man<sub>3</sub>GlcNAc<sub>2</sub> (G2B) type glycan, which are considered to have the highest ADCC activity, and produced an antibody drug with uniform G2B type glycans. The G2B-type glycans were extracted from chicken egg yolk. The heterogeneous sugar chains on the antibody drug were cleaved by enzyme and then transferred G2B-type glycans by glycosyltransferase. A comparison of the ADCC activity of the antibody drug with the homogeneous G2B-type glycans and the original antibody drug on the market will also be reported.

**Keywords :** Antibody drugs; Bisecting GlcNAc; ADCC

抗体医薬品はがんなどの治療薬として高い効果と副作用の軽減が期待されている。抗体表面上には糖鎖が付加されており、その糖鎖構造は抗体医薬品の効果に重要な抗体依存性細胞傷害 (ADCC) 活性を制御している。しかしながら、現在治療に使用されている抗体医薬品の糖鎖構造は不均一であり、これが抗体医薬品の効果低下やロット間の治療効果の差をもたらしている。そこで本研究では抗体上の糖鎖を ADCC 活性が最大とされる Gal<sub>2</sub>GlcNAc<sub>3</sub>Man<sub>3</sub>GlcNAc<sub>2</sub>(G2B) 型糖鎖に均一化し、均一 G2B 型糖鎖を有する抗体医薬品を作製した (Figure 1)。G2B 型糖鎖は鶏卵から抽出し、抗体医薬品上の不均一糖鎖を酵素によって切断した後に G2B 型糖鎖を糖転移酵素によって転移した。均一 G2B 型糖鎖を有する抗体医薬品と、元の市販されている抗体医薬品の ADCC 活性の比較も合わせて報告する予定である。

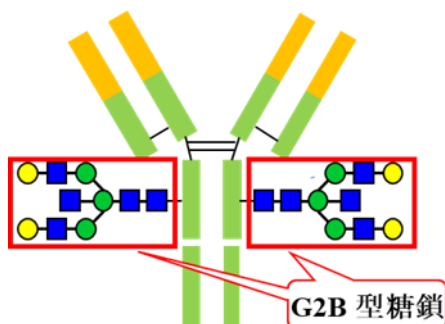


Figure 1 G2B 型糖鎖に均一化した抗体医薬品