30. Impact of oligosaccharide modification on therapeutic antibody

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IgG1 has two *N*-linked oligosaccharide chains bound to the Fc region. The oligosaccharides are the complex biantennary type, composed of a trimannosyl core structure with the presence or absence of core fucose, bisecting *N*-acetylglucosamine (GlcNAc) and terminal galactose, giving rise to structural heterogeneity. Antibody-dependent cellular cytotoxicity (ADCC), a lytic attack on antibody-targeted cells, has been found to be one of the critical effector functions responsible for the clinical efficacy of therapeutic antibody such as anti-CD20 IgG1 (Rituxan^{TM}) and anti-Her2/neu IgG1 (Herceptin^{TM}). ADCC is triggered upon binding of lymphocyte receptors (FcγRs) to the antibody Fc region, depending on the amount of fucose attached to the innermost GlcNAc of *N*-linked oligosaccharide via α1,6-linkage, and is dramatically enhanced by the fucose reduction. Importantly, fucose-negative therapeutic antibodies are not expected to be immunogenic as their carbohydrate structures are a normal component of natural human serum IgG. Thus, the application of fucose-negative antibodies should be a powerful and elegant approach as a next generation of therapeutic antibody with improved efficacy.