Modifications of IgG Antibody

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Alzheimer's Disease (AD), is the most common type of dementia, a progressive neurodegenerative disease that involves parts of the brain that controls memory and thought. The prevalence of Alzheimer's Disease is expected to triple by 2050. A number of drugs used in clinical trials to alter the course Alzheimer's Disease are immunoglobulin G (IgG) antibodies that target forms of the beta-amyloid peptide, which comprise amyloid plaques found in the brains of patients with Alzheimer's Disease. IgG drugs may be able to prevent the onset of Alzheimer's Disease but are limited in their ability to penetrate the blood-brain barrier. Previous work shows that a mouse antibody 4G8 presenting a Fab glycan exhibited increased retention in the brain after delivery. Furthermore, this retention was shown to correlate with the presence of the carbohydrate sialic acid on the Fab glycan. However, this Fab glycan proved to contain a mixture of acetylated and glycolated sialic acid, as well as alpha-galactose, which is not likely to be well-tolerated by humans. This study investigated the feasibility of altering the glycan carbohydrates on 4G8 to get a homogeneous Fab glycoform, consisting exclusively of acetylated sialic acid. This study was performed by the enzymatic modification of the 4G8 Fab glycan, followed by removal, isolation, and profiling of Fab glycan by HPLC. The results of this study were unfortunately inconclusive. While the controls showed the analysis method to be working, as there were no visible peaks of the modified Fab glycan on the HPLC. This is likely due to poor recovery from synthesis and purification steps and a streamlined method is currently being investigated.