

Glycan Derivatization to Improve IgG Permeability Through the Blood Brain Barrier to Effectively Treat Alzheimer's

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Alzheimer's is a neurodegenerative disease that has affected more than 6 million families. Although there have been many attempts to find a cure for the disease, none have been successful in either the prevention or curing of Alzheimer's. The biggest obstacle that makes Alzheimer's so hard to treat is the inability to transport medicine through the blood-brain barrier (BBB). Prior research indicates that human antibodies, IgG, are not able to cross this blood-brain barrier successfully. 4G8, however, has been reported to have a reduced efflux, meaning decreased 'traffic out of the brain' with a non-impacted influx, referring to the 'traffic' into the brain, with the treatment of neuraminidase. 4G8 is an IgG antibody that has a sialylated Fab Glycan that specifically binds to and recognizes amyloid plaques in the brain; these plaques are the driving factor in causing Alzheimer's. In order to increase the permeability of IgG through the BBB, we will use glycosylation, the addition of a sugar molecule, to make these antibodies homogenous to 4G8 by removing IgG's sialic acid group and replacing it with that of 4G8's. We are hoping that making the Fab Glycan of IgG homogeneous to 4G8 should allow for a more effective means of treating Alzheimer's. Although we were able to glycosylate the antibodies successfully, we were not yet able to determine if this would be an effective method to promote the crossing of the blood-brain barrier.