

The Role of antibodies in Alzheimer's disease

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Alzheimer's is an aging disease, considered to be the most common form of dementia. It affected about two to three percent of the population back in 2000 and will eventually increase to about six percent by 2050. For every one person who has it, it takes about three people to impact. The goal is to delay its appearance and extend cognitive health so it matches physical health. With Alzheimer's beta-amyloid accumulates outside of the cell and not inside which is one of the first hallmarks of Alzheimer's. One FDA approved drug Aducanumab, an antibody infused into the body, makes heterotetramers (four polypeptide chains) specifically sticky to beta-amyloid. The problem is getting this drug into the brain which we eventually discovered has some steps to be done. Antibody 4G8 has sugars in structure or glycans. Antibody 6E10 has no sugar present. It is found that there is no difference between the two going into the brain, but 4G8 increased the drug flow three times. Sialylated Fab glycans improve antibody drug delivery to the brain. This type of antibody contains a galactose at 1,3 position (alpha-gal) which is not produced in humans. The goal is to get rid of the alpha-gal and the glycolytic form of sialic acid and make pure sialylated Fab glycan on antibody 4G8 (G2FS2). In order to achieve this we used 26ST, SNA column column to purify, added alphaGal and performed a protein A spin. HPLC analysis will reveal glycan products. Expecting a single peak for G2FS2. If G2FS2 is produced, we will test this against G2F to determine blood-brain barrier permeability with collaborators at the VA.