ArmaGen engineers brain-penetrating amyloid antibody for Alzheimer's disease

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Alzheimer's disease (AD) is caused by the deposition of amyloid plaque in brain, and the leading plaque disaggregation therapeutic is the anti-amyloid antibody (AAA). Plaque disaggregation is caused by physical contact between the AAA and the plaque. However, the plaque in brain is behind the blood-brain barrier (BBB), and the AAA does not penetrate the brain in the absence of BBB disruption. Another problem with the current class of AAA biologics is that these drugs have prolonged blood mean residence times (MRT) of 30 days, and cause large and sustained elevations in blood concentrations of amyloid peptides, which are toxic molecules. ArmaGen has engineered AGT-160, which is a brain penetrating AAA for AD (Biotechnology & Bioengineering, 2010). The brain-penetrating AAA is also rapidly removed from blood with a MRT of <3 hours. The efficacy of a brain penetrating AAA was tested in a transgenic AD mouse model. A single chain Fv (ScFv) form of the AAA was engineered and fused to a genetically engineered monoclonal antibody (MAb) against the mouse transferrin receptor (TfR). The TfRMAb-ScFv fusion protein was administered twice-weekly to AD mice for 12 weeks by IV injection at a dose of 1 mg/kg. Treatment caused a 40% decrease in the brain concentration of Abeta amyloid peptide, but caused no elevation in Abeta amyloid peptide in blood, and caused no cerebral micro-hemorrhage (Molecular Pharmaceutics, 2011). AAAs that are re-engineered to cross the BBB can disaggregate plaque without causing toxic side effects associated with high blood amyloid peptide levels.