ArmaGen develops biologics brain amyloid imaging agent for Alzheimer's disease

May 29, 2012

The most potent agent for imaging the amyloid plaque in brain of Alzheimer's disease (AD) is the Abeta(1-40) amyloid peptide. However, the Abeta peptide cannot be developed as a peptide radiopharmaceutical for the *in vivo*imaging of the amyloid burden in brain, because the peptide does not cross the blood-brain barrier (BBB). The Abeta(1-40) peptide was re-engineered for BBB penetration with a unique 2-vial pharmaceutical approach. ArmaGen's brain imaging technology combines the molecular Trojan horse technology and avidin-biotin technology with peptide radiopharmaceutical technology. The Abeta(1-40) peptide was synthesized with a single biotin moiety on the amino terminus and an internal tyrosine residue was radiolabeled with 125-iodine. The [N-biotinyl, 125I]-Abeta(1-40) was formulated in one vial. A second vial contained AGT-3 (see Products), which is a genetically engineered IgG-avidin fusion protein, where the IgG domain is an engineered monoclonal antibody (MAb) against the human insulin receptor (HIR). The HIRMAb acts as a molecular Trojan horse to ferry the attached Abeta peptide radiopharmaceutical across the BBB. The avidin domain of the AGT-3 fusion protein binds with very high affinity to the mono-biotinylated peptide radiopharmaceutical. The stable conjugate of AGT-3 and [N-biotinyl, 125I]-Abeta(1-40), which is designated AGT-3100 (see Products), is formed immediately upon mixing of the 2 vials prior to intravenous administration. AGT-3100 binds selectively to the amyloid plaques in tissue sections of AD brain, as described in the 2012Bioconjugate Chemistry. AGT-3100 can also be modified by conjugation with a chelator groups for radiolabeling with heavy metals suitable for either PET or SPECT external imaging of the brain in humans.