P62 Genetically engineered brain drug delivery vector through the blood-brain barrier

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The blood-brain barrier (BBB) expresses high concentrations of transferrin receptor, and it was revealed that anti-transferrin receptor mouse monoclonal antibody (OX26) undergoes transcytosis through the BBB. This property allows the OX26 to serve as a brain drug delivery vector. In an attempt to produce broadly useful targeting agents, genetic engineering and expression techniques have been used to produce antibody-avidin (AV) fusion protein (OX26 IgG3C_H3-AV). In the present study we estimated the BBB permeability and stability of genetically engineered vector.

Transcytosis through the BBB of [^{3}H]biotin bound to genetically engineered vector was measured with an internal carotid artery perfusion/capillary depletion technique and pharmacokinetics was measured by intravenous injection technique. The brain uptake of [^{3}H]biotin bound to OX26 IgG3C_H3-AV expressed as %ID/g was 0.25 ± 0.09. The area under the plasma concentration curve (AUC) of OX26 IgG3C_H3-AV at 60 min was 134 ± 29 %ID×min/㎖ and total plasma clearance (CL_{ss}) was 1.54 ± 0.29 ㎖/min/kg.

Therefore genetically engineered vector can be used as an efficient brain drug delivery vector and it is stable in plasma according to HPLC analysis. But genetically engineered vector is required to be tested immunogenicity, and humanization method must be considered to get rid of possible toxicity and immunogenicity.