Introduction

BBB is a critical barrier in the brain that regulates the entry of molecules into the brain parenchyma. The selective permeation of molecules across the BBB is crucial for both the delivery of therapeutic agents and the normal function of the brain. The BBB is formed by tight junctions between endothelial cells, which limit the diffusion of molecules into the brain. These tight junctions are regulated by various factors, including cytokines and growth factors.

Transport of Molecules Across the BBB

The transport of molecules across the BBB occurs through passive diffusion, active transport, and paracellular diffusion. Passive diffusion occurs through the paracellular pathway, which is mediated by tight junctions. Active transport occurs through specific transporters, such as the P-gp pump, which is highly expressed in the BBB.

Experimental Models

1. Brain tumor distribution after IV injection of fluorescent conjugates
   - Experiments were conducted in vivo in nude mice to evaluate the distribution of fluorescent conjugates across the BBB.
   - Fluorescent conjugates were injected intravenously, and brain tissue was collected at various time points post-injection.
   - Tumor distribution was analyzed using fluorescence microscopy.

2. Brain permeation of drugs
   - Drugs were administered intravenously to mice, and brain tissue was collected at various time points post-injection.
   - Drug concentrations were measured using high-performance liquid chromatography (HPLC).

3. Brain tumor distribution after IV injection of fluorescent conjugates
   - Flow cytometry was used to analyze the expression of specific markers on tumor cells.
   - Tumors were harvested at various time points post-injection, and tumor cell samples were analyzed using flow cytometry.

Conclusions

- ANG1005 is a new peptide, ANG1005, a conjugate of Paclitaxel and Angiopep new vector peptide, able to cross the Blood-Brain Barrier for the treatment of brain cancers.

- Animals were perfused in the carotid artery with physiological saline to remove excess physiological saline from the brain and to ensure that the BBB was not disrupted.

- Mice were treated with ANG1005, and brain tissue was extracted 15 minutes after injection.

- Brain tissue was analyzed using HPLC to measure the concentration of ANG1005 in the brain.

- The concentration of ANG1005 was higher in the brain than in other tissues, indicating that ANG1005 can cross the BBB.

- ANG1005 allows delivery of 100 times the concentration of paclitaxel required for activity, demonstrating the potential of ANG1005 as a new therapeutic agent for brain cancer.

- ANG1005 shows higher distribution in brain tumors compared to other regions of the brain, indicating its potential for targeted therapy.

- ANG1005 delivers therapeutic concentrations of paclitaxel to the brain, indicating its potential for targeted therapy.

- ANG1005 inhibits intracranial tumor growth as measured by MRI in rats.

- ANG1005 is a promising new therapeutic agent for the treatment of brain cancers.