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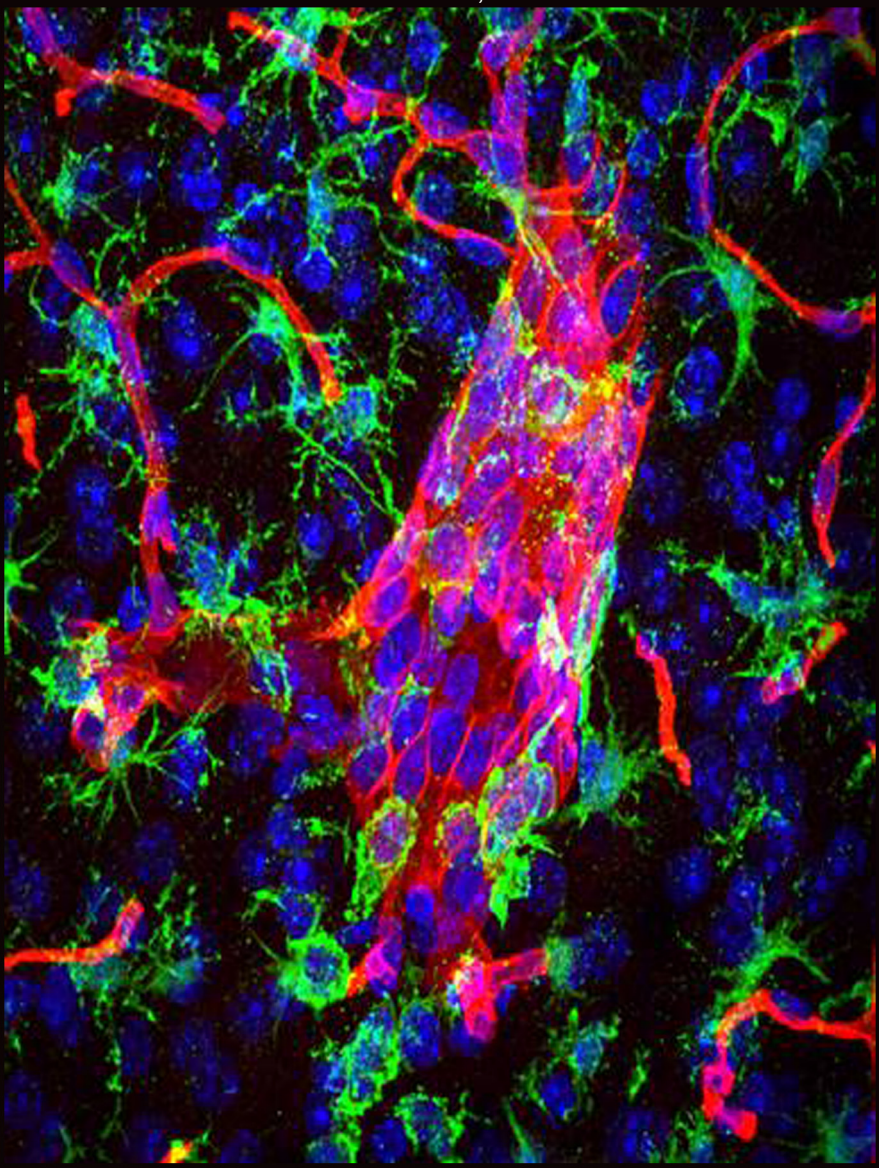

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THE IMPACT OF TRANSFERRIN RECEPTOR TARGETING ON IMMUNOLIPOSOMAL CARGO DELIVERY ACROSS THE BLOOD-BRAIN BARRIER

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Transferrin receptor expression is exclusive to the endothelial cells of the brain capillaries as opposed to endothelial cells in other organs of the body. This makes the transferrin receptor an interesting target for drug delivery to the brain. However, evidence on the intracellular trafficking mechanism of the transferrin receptor does not support the possibility of full transcytosis of the receptor. Still, the transferrin receptor could be an important tool to transport nanocarriers to the brain vasculature and subsequently depend on BCEC processing of the nanocarrier to mediate drug release.

We studied transferrin receptor-targeted liposomes containing oxaliplatin as a model drug cargo with the aim of quantifying the nanocarrier and cargo uptake in BCECs and the remainder of the CNS. A parallel approach using both in vitro and in vivo assessments was employed to study this aspect. For in vitro studies, a primary culture model of the rat blood-brain barrier was used to study the uptake of the immunoliposomes. For in vivo studies, 18 day old rats were used (due to their high expression of transferrin receptor on their brain capillaries) to study the passage of oxaliplatin into the brain parenchyma.

The uptake of OX26-conjugated immunoliposomes by BCECs were significantly higher both in vitro and in vivo when compared to isotypic IgG-conjugated liposomes. Quantitative analyses after capillary depletion revealed cargo transport from BCECs to the remaining CNS, but no differences could be detected between OX26-conjugated and isotype IgG control immunoliposomes in vivo, whereas isotype IgG control immunoliposomes were superior in vitro. In conclusion, OX26-targeted immunoliposomes are suitable for uptake by BCECs, which may be exploited for controlled release of a drug compound within the BCEC.