Peptides binding to LDL-receptor as carriers for crossing the blood brain barrier

KEYWORDS

LDL receptor
Peptides
Phage display
Blood-brain barrier
Receptor-mediated transcytosis

PATENT

Title : *Peptides binding to LDL receptor as carriers for crossing the blood-brain barrier*
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LICENSING

Research collaboration
Licence agreement

INVENTORS

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PROBLEM

The blood-brain barrier (BBB) is a structure at the interface between the brain and the blood that strictly controls the brain homeostasis in association with the blood-cerebrospinal fluid barrier and the ependymal barrier. BBB is composed of a monolayer of endothelial cells joined by tight junctions, limiting the paracellular crossing, and surrounded by astrocytes and pericytes. Due to the presence of the BBB, most drugs are not able to passively access the brain if they do not meet certain characteristics, such as the lipophilicity and a size smaller than 400 Daltons.

Blood-brain barrier crossing and brain penetration are really challenging for the delivery of therapeutic agents and imaging probes. The development of new crossing strategies is needed and a wide range of strategies (invasive or not) have been proposed so far.

The receptor-mediated transcytosis is an attractive mechanism allowing the non-invasive penetration of the BBB and offers the advantage to be specific. It involves the binding of a vector (i.e. endogenous ligand, antibody or peptide), coupled with the molecule of interest, to a receptor that initiates the endocytosis of this receptor and leads to the transcytosis of the complex across the endothelial cells. The most studied receptors used for this purpose are the transferrin receptor (TfR), the insulin receptor (IR) and the Low-Density Lipoprotein receptor (LDLR) and its related proteins (LRP1 and LRP2).

SOLUTION

Among available targets for receptor-mediated transcytosis, LDLR shows favorable characteristics mainly because of the lysosome-bypassed pathway of LDL delivery to the brain, allowing an intact discharge of the carried ligand to the brain targets.

The invention discloses a dodecapeptide targeted to the extracellular domain of LDLR In vitro, our peptide is endocytosed by endothelial cells by the caveolae-dependent pathway, preventing its degradation and suggesting its transcytosis. The in vivo studies performed by Magnetic Resonance Imaging and Fluorescent Lifetime Imaging suggest the brain penetration of the peptide.

This peptide could be used to transport molecules of pharmaceutical or diagnostic interest across the BBB.

INNOVATION

- Non-invasive BBB crossing strategy

TECHNOLOGY STATUS

TRL 2-3

MARKETS

- **Healthcare & pharmaceutical**

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