



Peptide-Modified Micelles and Liposomes: Carriers for Xenon Hyper-CEST MRI Of Blood Brain Barrier Endothelial Cells

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Diagnostics and treatment of the brain is a particular challenge. We developed a micelle forming and lipid binding lipopeptide (P2A2) which selectively recognizes human brain capillary endothelial cell (HBMEC), the major components of the blood brain barrier (BBB).

Here we present the development of lipopeptide-modified micellar and liposomal carriers for the selective transport of cryptophane-A (CrA) into HBMECs. Chemical exchange saturation transfer with hyperpolarized Xenon nuclei (Hyper-CEST) allows highly sensitive detection of supramolecular cages such as CrA in non-invasive Magnetic Resonance Imaging (MRI). Incorporation into liposomes distinctly reduced the toxicity of the hydrophobic CrA and a one nanomolar concentration generated sufficient contrast to distinguish between brain capillary and aortic endothelial cells. Covalent attachment of CrA to the peptide did not influence the micelle characteristics and provided additional advantages as it results in high local cage concentration and allows more reliable quantification of the signal molecule. The peptide-modified carriers combine a high selectivity for human brain capillary endothelial cells with the great sensitivity of Xe Hyper-CEST MRI. In addition, liposomes or labelled micelles for Hyper-CEST applications were significantly less invasive. 80 amole biosensor/cell correspond to a loading of 3.4 % of the cell volume with micelles whereas covalently bound spin reports such as e.g. PFCE (perfluoro crown ether) nanodroplets occupy with 2 pmole/cell about 65 % cell volume.

We consider CrA-A2 micelles and liposomes highly promising as future potential MRI reporters for the monitoring of highly vascularised brain regions such as tumors.

Biography

Dr. Dathe has completed her PhD in Physics by the Academy of Sciences of the GDR and started her scientific carrier at the Institute of Drug Research and the Biocenter of the Basel University, Switzerland. Since 1992 she has been working as research group leader at the Leibniz Institute of Molecular Pharmacology, Berlin with the focus on cell penetrating and antimicrobial peptides and their application. She has published more than 120 papers in reputed journal as well as a number of book contributions.