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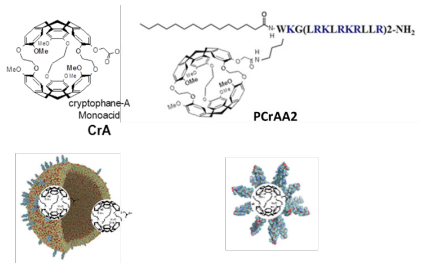
Peptide-modified micelles and liposomes: Carriers for xenon hyper-CEST MRI of blood brain barrier endothelial cells

Margitta Dathe, Matthias Schnurr, Heike Nikolenko, Karl Sydow and **Leif Schröder**
Leibniz-Forschungsinstitut für Molekulare Pharmakologie, Germany

Selective imaging of pathological areas and targeted drug delivery are crucial for efficient diagnostics and therapy. Drug delivery to the brain is a particular challenge. We generated highly cationic lipopeptides that form micelles and bind to liposomes. Cargos, covalently bound or incorporated into such carriers are selectively transported into blood brain barrier endothelial cells. Basis for the selective uptake of the different systems is the activation of clathrin-mediated endocytosis, a process which is not addressed in other vessel endothelial cells. Here we present the development of peptide-modified micellar and liposomal carriers for the selective transport of cryptophane-A (CrA) into human brain capillary endothelial cells. 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 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 and might be a promising MRI tool.



Scheme of peptide-tagged CrA-loaded liposomes and PCrAA2 micelles for Xenon Hyper-CEST MRI

Recent Publications

1. 1. Gehne S et al. (2013) Characterization of cell-penetrating lipopeptide micelles by spectroscopic methods. J Phys Chem B 117: 14215-14225.
2. 2. Keller S et al. (2005) Membrane-mimetic nanocarriers formed by a dipalmitoylated cell-penetrating peptide. Angew Chem Int Ed 44: 5252-5255.
3. 3. Leupold E et al. (2009) Apolipoprotein E Peptide-modified Colloidal Carriers: The Design Determines the Mechanism of Uptake in Vascular Endothelial Cells. BBA 1788(2) 442-449.
4. 4. Sydow K et al. (2016) Lipopeptide-based micellar and liposomal carriers: Influence of surface charge and particle size on cellular uptake into blood brain barrier cells. Euro J Pharm Biopharm 109: 130-139.
5. 5. Schnurr M et al. (2015) Brain Endothelial Cell Targeting via a Peptide-functionalized Liposomal Carrier for Xenon Hyper-CEST MRI. Adv Healthcare Mat, 4: 40-45.

Biography

Margitta Dathe studied Physics at the Humboldt University of Berlin and completed her PhD in 1978 from the Academy of Sciences of the GDR. Since 1999, she has been working as Head of the Peptide-Lipid Interaction Research Group of the Leibniz Research Institute of Molecular Pharmacology. Her research interest is focused on targeting, cellular uptake promoting peptides and lipid-based carrier systems as well as on antimicrobial peptides. She has published more than 100 papers in reputed journals.

dathe@fmp-berlin.de