P1.46

Functionalization with curcumin-derivative and TAT peptide enhances the interaction with human brain capillary endothelial cells of nanoliposomes binding amyloid-beta peptide

SANCINI G[1], GREGORI M[1], CAMBIANICA I[1],SALVATI E[1], ZONA C[2], MASSERINI M[1]

[1]Dept of Experimental Medicine, Univ. of Milano-Bicocca, Monza, Italy

[2]Dept of Biotechnology and Biosciences, Univ. of Milano-Bicocca, Milano, Italy

In the field of nanomedicine, nanoparticles (NP) are one of the most studied tools for drug delivery and transport of contrast agents across the blood-brain-barrier.

Alzheimer's Disease (AD) is a neurodegenerative disorder that affects millions of individuals worldwide. Accumulation of amyloid-β peptide (Aβ) in the brain, and its aggregation into oligomers, fibrils and plaques, plays a central role in the onset and development of AD. The E.C. FP7 project "NAD" (Nanoparticles for therapy and diagnosis of Alzheimer's disease) is involved in the design of NP that recognize and remove brain Aβ. Starting from this point, we are performing double-functionalized nanoliposomes (NL) with a ligand for Aβ, the curcuminderivative and the TAT cell-penetrating peptide. Click chemistry method was used to decorate the NP with the curcumin derivative, while TAT peptide was covalently attached to the NP surface via a thiol-maleimide reaction. NL exposing the curcumin derivative and the TAT peptide have extremely high affinity for Aβ fibrils with Kd value of 3-15 nM. Curcumin-NL did not show any relevant membrane nor cellular accumulation within human brain capillary endothelial cells (hCMEC/D3) while the functionalization with TAT-peptide mediated an efficient NL cell uptake. Moreover, we studied their ability to cross hCMEC/D3 monolayer in-vitro. Again, their endothelial permeability was enhanced only with TAT peptide.