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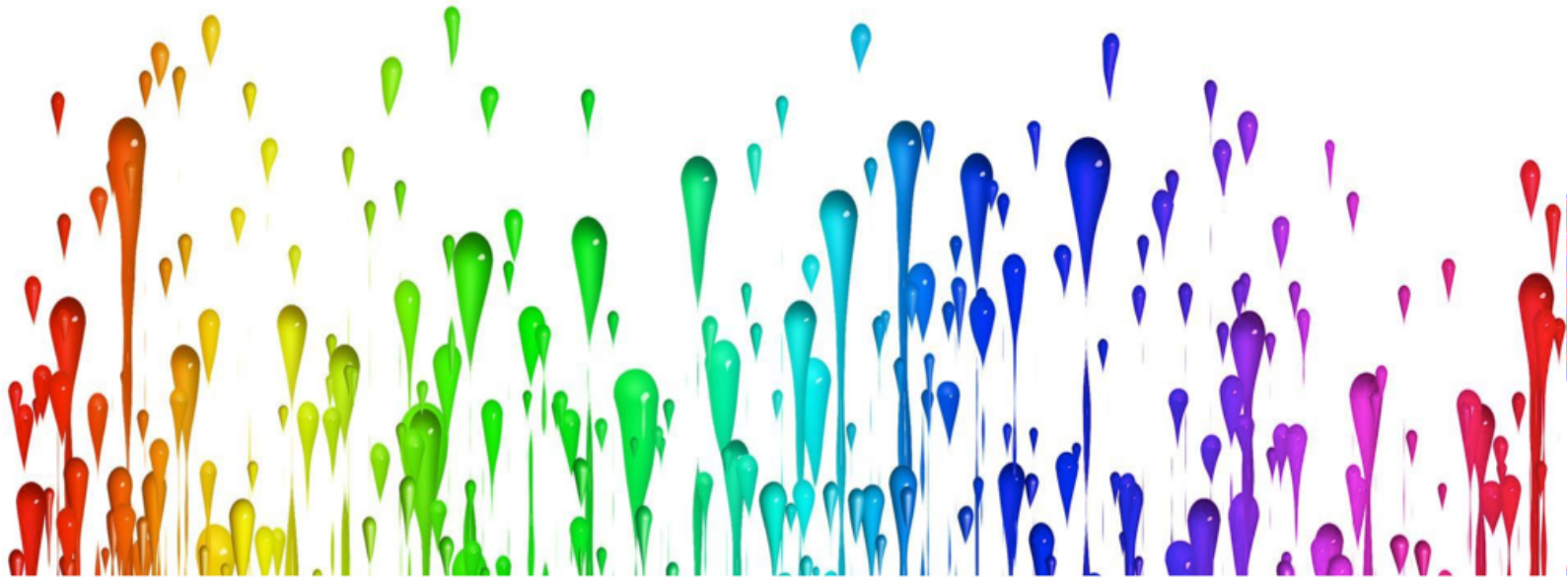
ATTI DEL CONVEGNO



Synthesis and characterization of peptide functionalized nanoparticles for the selective transport across the blood-brain barrier.

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The treatment of cerebral diseases such as brain tumors and neurodegenerative disorders is severely hindered due to the presence of the blood-brain barrier (BBB). The role of this barrier is to preserve brain homeostasis and to prevent toxic substances and invading organisms from reaching the brain. Therefore, an important feature of this barrier is the low and selective permeability to molecules, which excludes therapeutics from entering the brain parenchyma [1]. The development of new strategies for enhancing drug delivery to the brain represents a major challenge in treating cerebral diseases. Here we report on the synthesis and structural characterization of a biocompatible nanoparticle (NP) made up of poly(lactic-co-glycolic acid) (PLGA)-polyethylene glycol (PEG) co-polymer (namely PELGA) functionalized with the membranotropic peptide gH625 (gH) and the iron-mimicking peptide CRTIGPSVC (CRT) for transport across the blood-brain barrier (BBB). gH possesses a high translocation potency of the cell membrane. Conversely, CRT selectively recognizes the brain endothelium, which interacts with transferrin (Tf) and its receptor (TfR) through a non-canonical ligand-directed mechanism. We hypothesize that the delivery across the BBB of PELGA NPs should be efficiently enhanced by the NP functionalization with both gH and CRT. Synthesis of peptides and their conjugation to the PLGA as well as NP physical-chemical characterization are performed. Moreover, NP uptake, co-localization, adhesion under dynamic conditions, and permeation across in vitro BBB model are evaluated as a function of gH/CRT functionalization ratio. Results establish that the cooperative effect of CRT and gH may change the intra-cellular distribution of NPs and strengthen NP delivery across the BBB at the functionalization ratio 33% gH–66% CRT.

1. Farokhzad, O.; Langer, R. Nanomedicine: Developing smarter therapeutic and diagnostic modalities. *Adv. Drug Deliv. Rev.* **2006**, 58, 1456–1459.