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The fantastic voyage of nanoparticles targeting Aβ

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Pharmacological treatment of brain diseases is still a difficult task. Many potential therapeutic compounds fail to reach their molecular targets in the brain parenchyma limiting the development of clinically relevant therapeutics. Indeed the concentration of therapeutic compounds into the brain parenchyma depends on various factors but it is clear that the capability to cross the blood brain barrier (BBB) is of paramount importance. The difficulties encountered in the treatment of brain disease with conventional pharmacological tools have created the need for alternative and innovative strategies. Nanotechnology-based approaches might improve the unfavorable pharmacokinetic of molecules unable to overcome the BBB. Recent applications in nanomedicine focus on nanoparticles (NP) as they are promising tools for site-specific delivery of drugs and diagnostic agents, through the possibility to functionalize their surface with target-specific ligands. Treatment options for Alzheimer's disease (AD) are limited because of the inability of drugs to cross the BBB. Previously, we showed that intraperitoneal administration of liposomes functionalized with phosphatidic acid and an ApoE-derived peptide (mApoE-PA-LIP) reduces brain beta-amyloid (Aβ) burden and ameliorates impaired memory in AD mice. Among the different administration routes, pulmonary delivery is a field of increasing interest not only for the local treatment of airway diseases but also for the systemic administration. We investigated lung administration as an alternative, non-invasive NP delivery route for reaching the brain. Our results show that mApoE-PA-LIP were able to cross the pulmonary epithelium *in vitro* and reach the brain following *in vivo* intratracheal instillations. Lung administration of mApoE-PA-LIP to AD mice significantly decreased total brain Aβ (–60%; $p<0.05$) compared to untreated mice. These results suggest that pulmonary administration could be exploited for brain delivery of NP designed for AD therapy.

Biography

Giulio Sancini is an Assistant Professor of Human Physiology and Specialist in Applied Pharmacology. He has focused his research activity mainly on Neurosciences, Nanomedicine, and Nanotoxicology. His research has been funded by European FP7 (NAD Project, Nanoparticles for diagnosis and therapy of Alzheimer's disease and FP6 (BONSAI project, Bio-imaging with Smart Functional Nanoparticles). He has published more than 45 papers in reputed journals and has been serving as an Editorial Board Member of repute. He is Head of the Physiology Unit in Department of Medicine and Surgery at University of Milano-Bicocca.

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