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From the lungs to the brain: The fantastic voyage of nanoparticles targeting beta-amyloid (A β)

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The brain is always confronted with the dilemma of the protection from noxious substances from the blood and the delivery of vital metabolites. Endothelial cells, forming together with other cells the blood-brain barrier (BBB), are known as the “Gatekeepers” of this trafficking. On the one hand, the protection from toxic molecules is achieved by the obstruction of the paracellular pathway with tight junctions that fuse brain capillary endothelia into a continuous tubular cell layer. On the other hand, vital molecules are transported from the blood by means of active trans-cellular mechanisms. Recent applications in nanomedicine focuses 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 (A β) 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 A β (–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 Assistant Professor of Physiology; 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, winner of The Best Project award in the field of Industrial Technologies) and FP6 (BONSAI project). 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 at the Dept. of Medicine and Surgery of the University of Milano-Bicocca.

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