

# Transport of cationic liposomes in a human Blood Brain Barrier model: role of the stereochemistry of lipid components on liposome physico-chemical and biological feature

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**Beatrice Simonis**<sup>1\*</sup>, Francesca Ceccacci<sup>2</sup>, Cecilia Bombelli<sup>2</sup>, Giovanna Mancini<sup>3</sup>, Nunzia Maisto<sup>1</sup>, Rudaba Zaman Raya Syeda<sup>1</sup>, Luciano Galantini<sup>1</sup>, Enrica Donati<sup>3</sup>, Giulio Auciello<sup>4</sup>, Antonella Cellucci<sup>4</sup>, Ivan Fini<sup>4</sup>, Domenico Vignone<sup>4</sup>, Odalys Gonzalez Paz<sup>4</sup>, Annalise Di Marco<sup>4</sup>

<sup>1</sup> Chemistry Department, Sapienza University, Rome, Italy

<sup>2</sup> CNR-ISB-SOU of Rome c/o Chemistry Department, Sapienza University, Rome Italy

<sup>3</sup> CNR-ISB, Rome 1 Resarch Area, 00015 Montelibretti (RM)

<sup>4</sup>IRBM SpA, Pomezia, Rome 00071

\*e-mail: [beatrice.simonis@uniroma1.it](mailto:beatrice.simonis@uniroma1.it)

Neurological diseases are one of the greatest medical emergencies and although new neuropharmaceuticals have the potential for treating specific central nervous system (CNS) diseases, the treatment is often complicated by the drug inability to cross the blood brain barrier (BBB). The main problem in the treatment of CNS diseases is the delivery of the drug rather than their efficacy, so a primary objective is the development of novel nanocarriers able to cross the BBB. Nanosystems such as liposomes are ideal drug delivery systems because their features can be easily and properly tuned, they usually show low toxicity as well as biocompatibility and biodegradability. We designed and investigated cationic liposomes functionalized to promote the crossing of BBB. The formulations were composed of natural phospholipids and cholesterol in mixture with synthetic diastereomeric cationic *gemini* amphiphiles (SS, RR or MESO) and/or a *mannosylated* amphiphiles (MAN-PEG3-PE) that should favor the interaction and the uptake by BBB (Figure 1). All formulations were analyzed with the aim of investigating how the different stereochemistry of these *gemini* and the co-presence of both a cationic surface and a glucosyl residues can affect liposome physicochemical and biological features. For all formulations the mean diameter, the polydispersity index (PDI), the Transition temperature ( $T_m$ ) and stability over time were investigated by dynamic laser light scattering measurements (DLS). The most promising formulations were evaluated in uptake experiments on a monolayer of brain microvascular endothelial cells and their permeability was investigated on an *in vitro* BBB model.