

**P014** Evaluation of 60 nm nanoparticles as delivery systems of proteins on an *in vitro* model of blood brain barrier  
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Blood–brain barrier (BBB) is composed of specific structures by brain capillary endothelial cells and its sheathing by astrocytic endfeet through basement membrane, which maintains homeostasis of central nerve system (CNS) by its specific properties. Approximately 100% of large molecule drugs do not cross BBB (Pardridge, 2003). In order to by-pass BBB, using the Trojan horse strategy, we studied the ability of 60 nm nanoparticles to interact and deliver proteins through BBB and to astrocytes.

Neutral and cationic 60 nm polysaccharidic nanoparticles were prepared from maltodextrins reticulated with epichorhydrin (De Miguel et al, 2000).

The studies were performed on an *in vitro* model of BBB (Dehouck et al, 1992) at 4°C and 37°C. The mechanisms of interactions of these nanoparticles (cytoadhesion, cytoadhesion-cytoinvasion-passage) with endothelial cells and protein delivery to astrocytes was evaluated.

Neutral nanoparticles were found to enter the cells via the caveolae pathway while cationic nanoparticles were found to use another pathway under investigation.

Loaded cationic nanoparticles with BSA were found to increase the delivery of BSA to astrocytes by 7 fold.

Neutral nanoparticles were found to use the caveolae pathway and had a high degree of transcytosis. Cationic nanoparticles were mainly trapped within the cells and had a low degree of transcytosis. In the brain cationic nanoparticles strongly increase protein delivery to astrocytes (7 fold increase).

These results taken together demonstrate the interest to use nanoparticle to deliver proteins to the brain through BBB and to astrocytes