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Delivery of nanoformulated antiretroviral drugs across the blood brain barrier

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In HIV management, eradication of virus by sanctuary sites remains a main challenge. In fact, although current antiretroviral (ARV) therapies suppress plasma HIV below detectable levels in a consistent proportion of subjects, total virus eradication is still beyond our possibilities. An important barrier to achieve such goal is related to the suboptimal concentrations of ARVs within the HIV sanctuaries. The central nervous system (CNS) is a key example of sanctuary where viral replication occurs despite of a complete viral suppression in the peripheral blood. In recent years, nanotechnology has provided great promise in the eradication of HIV from CNS. However, this is the first time in which a complex and heavy peptide like enfuvirtide (Enf), which normally does not penetrate in the CNS, is found to cross the blood brain barrier (BBB) of mice, by conjugation with a nanoconstruct. We demonstrated that iron oxide nanoparticles coated with an amphiphilic polimer (MYTS), labeled with FITC, increased AF660-Enf translocation across BBB *in vitro*, using a validated BBB model composed of rat BMVECs and astrocytes, and in mice i.v. injected with the nanoformulated Enf. We describe a delivery mechanism involving the uptake of MYTS-Enf in the endothelial cells, the nanocomplex dissociation and the release of the peptide, which is efficiently excreted into the outside environment (Figure 1). The dissociation seems to involve the degradation of the PMA shells bearing the peptide into the more mature endosomal compartments, as an effect of the increased acidity and enzymatic activity of their inner environment, to be then completed within lysosomes.

Biography

Luisa Finandra is a Post-doc fellow in Centro di Microscopia Elettronica per lo sviluppo delle Nanotecnologie applicate alla medicina at University of Milano, Italy. She is expert in transport physiology with a specific competence in permeability processes through intact epithelia and cellular membranes, my present field of research is the study of fluorescent tracers biodistribution in animal models. A particular interest in cancer diagnosis is currently pursued by *in vivo* detection of targeted nanoparticles by CCD camera or confocal microscopy analysis.

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