PECSDDeli :Processable intelligent colloids for mucosal drug delivery

Programme P2N + édition 2010

Thierry Delair, IMP@Lyon1, Université de Lyon 69622 Villeurbanne CedeX

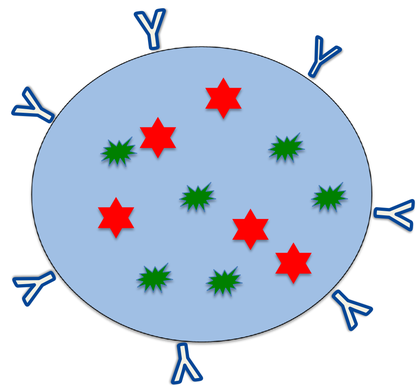
AGENCE NATIONALE DE LA RECHERCHE ANR

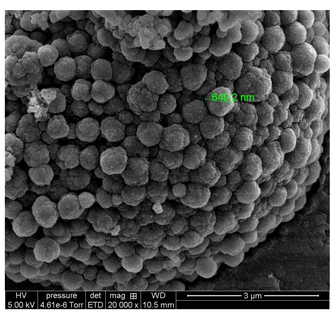
Contexte et résultats marquants

Objectives:

- To develop **a multi functional nano drug delivery system** simple to administer and to manufacture, **based on safe, biodegradable and biocompatible materials**.

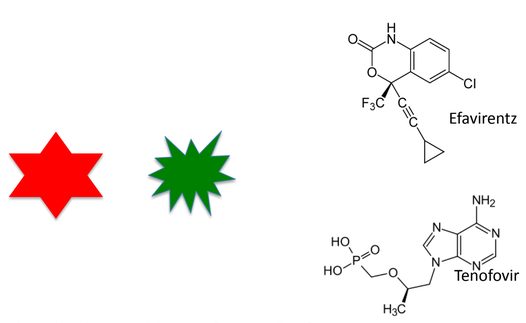
- To target the **natural reservoirs of the HIV virus** with antiretroviral drug loaded particles decorated with IgAs.





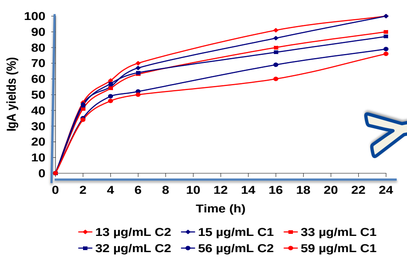
Submicronic PECs particles
(DLS: < 650 nm IP 0,17)
Conc. C-DS 0,01%

Polymer matrix with poly(lactic acid) from Anabior. Residual solvents maintained within the requirement of pharmacopeia.
Colloidal polyelectrolyte complexes of chitosan and dextran sulfate (PECs) were stable in physiological media, as a result of the fine tuning of chitosan degree of acetylation and molar mass.
The particle concentration during manufacturing was increased by a factor 15-30 by the new approach investigated within this project..



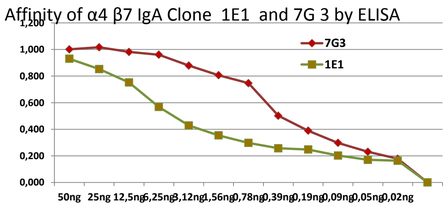
PLA particles were loaded with fluorescent markers. The fluorescence ranged from green to infra-red. Efavirenz (antiretroviral drug) was encapsulated with a 90% yield for a mass ratio of 5 to 45 mg per g of PLA with no alteration of particle size. PECs particles were loaded with Tenofovir at weight ratio of 10% with a quantitative adsorption yield.

Adsorption kinetics of α4 β7 IgA Clone 1E1 (C1) and 7G 3 (C 2) in PBS at C-DS 0.3 TF

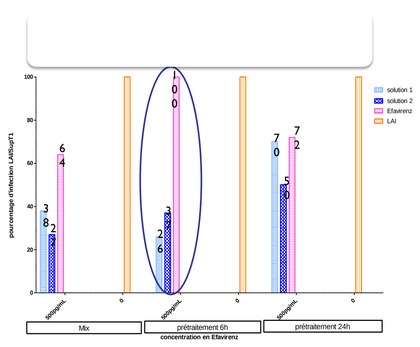


Various types of IgAs were adsorbed on PLA or PECs particles. Conditions were developed to maintain the colloidal character of the particle dispersions. The presence of the ARD at high concentration in the polymer matrix may decrease the adsorption yields.

Affinity of α4 β7 IgA Clone 1E1 and 7G 3 by ELISA



IgA antibodies were produced at B cell Design by immunization of HAMIGA mice with α4β7 antigen loaded onto PLA particles. Out of 20 clones, 2 were selected and allowed to produce respectively 20 mg and 8 mg of IgA. The specificities and affinities of these IgAs were demonstrated by ELISA and flow cytometry.



Efavirentz loaded PLA particles were tested *in vitro* for the protection against infection by the LAI viral strain of human peripheral blood mononuclear cells (PBMCs). Encapsulated Efavirentz featured a better protection than the soluble form of the antiretroviral drug.

Les NPs PLA / Efavirenz sont pré-incubés pendant 6h ou 24 avant l'infection par la souche LAI
La pré-incubation des NPs (sol. 1 / sol. 2) permet de protéger les cellules cibles de l'infection.

Production scientifique (publications, brevets)

Marie Costalat : "Elaboration de colloïdes par complexation polyélectrolytique contrôlée de polysaccharides", JEPO 40 Anduze, 2 Octobre 2012, Communication orale.
Marie Costalat : "Colloïdes par association contrôlée de polysaccharides", Colloque GFP Grenoble,19-22 Novembre 2012, Communication orale.
Marie Costalat : "Elaboration de particules submicroniques par association contrôlée de polysaccharides", 16ème Journée du Groupe Lyonnais des Glyco-Sciences (GLGS) Villeurbanne, 15 Novembre 2012, Communication orale.
Ramona Polexe : " Chitosan-dextrane sulfate polyelectrolyte complexe nanoparticles as delivery systems for antibodies" poster présenté à XXVIth GTRV, 5 décembre , 2011, Université Catholique de Louvain, Brussels

CONTACT :

xxx@Thierry.Delair@univ-lyon1.fr

ANaBior · Université Jean Monnet Saint-Etienne · IMP · CNRS · b cell design · CEA