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Study of the interaction between polysaccharide nanocapsules and biological barriers for the targeted administration of drugs

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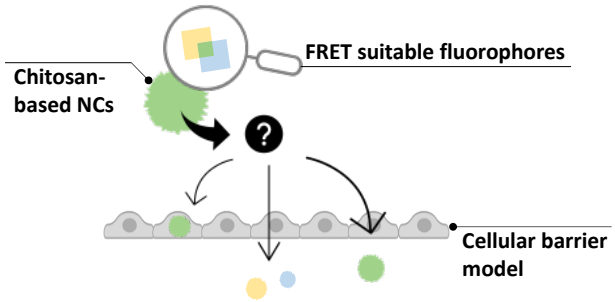
Nowadays, in clinical trials, efficient drug delivery remains a major challenge due to the hindrance offered by the complexity of biological barriers. The anatomy and physiology of each barrier is different and the ways to overcome them need to be taken into account when designing a new drug delivery system. For instance, the blood brain barrier and the corneal barrier are two examples of highly restrictive membranes.[1] The intranasal administration is an option to overpass the blood brain barrier in a non-invasive way to treat neurodegenerative illnesses. Likewise, transcorneal administration would improve drug delivery to the posterior segment of the eye, which is impaired by the corneal barrier.

In this context nanotechnology aims at designing nanocarriers that can improve the transport of the desired molecules through biological barriers.[2] The improved delivery and drug residence time would also enhance the efficacy of the treatment. But to do so, nanocarriers are required to cross the biological barriers without losing their integrity and without leaking the active molecule. Therefore, it is important to define the fate of the carrier after the administration: characterize the interaction between the nanocarrier and the biological environment, decipher if the release kinetics depend on the degradation of the whole carrier or the drug diffusion through it.

The main goal of this work is to track the integrity and the fate of a nanocarrier through two examples of barriers, the nasal and the corneal one. To do so, two sets of nanocapsules (NCs), composed by an oily core and a chitosan shell, are used to encapsulate two fluorophores. Both fluorophores are suitable for the appearance of Förster Resonance Energy Transfer (FRET) effect if the NC is intact, but this effect will be lost when the NC is broken. Therefore, FRET will be used to monitor the NCs integrity during *in vitro* tests. To take into account the interaction with biological barriers after administration, simplified *in vitro* models of nasal and corneal monolayers have been settled using Transwell® inserts. Calu-3 cells were chosen as a suitable *in vitro* barrier model of the respiratory area, since they preserve the characteristics of differentiated, functional human epithelia. On the other hand, SIRC cells were chosen as corneal epithelial barrier model.

The NCs will be tested in both models to study the interaction mechanism between these biological barriers and chitosan-based NCs, evaluating the NCs fate and integrity (Scheme 1)



Scheme 1 Interaction of NCs with cellular barrier model

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2. Casadomé-Perales Á, M. L., et al., Inhibition of p38 MAPK in the brain through nasal administration of p38 inhibitor loaded in chitosan nanocapsules. *Nanomedicine (Lond.)* **2018,** *14* (18), 13.