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INTREPIDUS

Nanoporous-Membranes for Intrathecal (Pseudo)Delivery of Drugs

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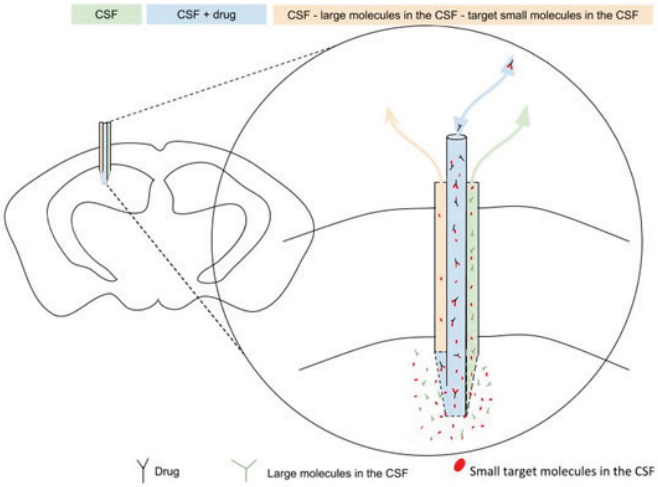

Representation of the device implanted in the lateral ventricle of a mouse. The mechanism of action relies on the selective permeability of the nanoporous membranes and on the different size and electrochemical characteristics of target molecules in the CSF compared to drugs.

Drug delivery to the Central Nervous System (CNS) is limited by complex biological barriers generally termed the blood–brain barriers (BBB). The nanotechnology-enabled innovation to be developed in INTREPIDUS is a drug delivery system that will lay the foundations for a new route of administering drugs to the CNS. This new concept is called pseudodelivery and is based on a patented implantable device able to put in touch target molecules present in the Cerebrospinal Fluid (CSF) with drugs infused inside of the device. This is achieved by means of a smart architecture of selectively-permeable nanoporous membranes that allow the influx of small molecules (targets) at the time of preventing the efflux of therapeutics of larger molecular size (nanosieve). Acting directly on the CSF is expected to be highly effective while no immune responses are expected from biological drugs as they do not enter in contact with cells (immunoisolation). Thus, the ultimate aim is to change the paradigm of route of administration of drugs for a wide number of neurological conditions: from peripherally delivered to intrathecally pseudodelivered.

Specifically in this project, we will develop and test an intrathecally implantable device to be used in combination with two types of drugs: enzymes and antibodies. The project is composed of interconnected work packages aimed at refining the design of the device, manufacturing all components, and assembling the prototype. Proof-of-concept will be made at multiple levels: in vitro, ex vivo (human and mice CSF) and in vivo.

Strategies to optimize biocompatibility and biofouling of nanoporous membranes are implemented throughout the project since membranes need to be fully biocompatible and remain operational for the long term.