



BLOOD / BRAIN INTERFACE EXPLORATORY PLATFORM

OUR AIM IS TO PROVIDE SERVICES TO EVALUATE THE CEREBRAL BIOAVAILABILITY OF DRUGS AND THE MIGRATION OF IMMUNE CELLS AND PATHOGENS IN THE BRAIN THROUGH BLOOD / BRAIN INTERFACES

While brain capillaries and microvessels form the blood / brain barrier, the choroid plexus is the main site of the blood / cerebrospinal fluid (CSF) barrier.

Both interfaces control the overall cerebral bioavailability of drugs by restricting the paracellular route (presence of tight junctions) and by modulating drug exchange between the blood and the brain via the transcellular pathway (involvement of efflux mechanisms and metabolic processes). These barriers also represent potential sites of entry into the central nervous system for pathogens and/or immune cells.

In vitro approaches (isolated brain capillaries, isolated choroid plexus and in vitro cellular models) are adequate tools to evaluate and investigate the role of the blood / brain interfaces in these mechanisms.

EXPERTISE AND BIOANALYTICAL SERVICES

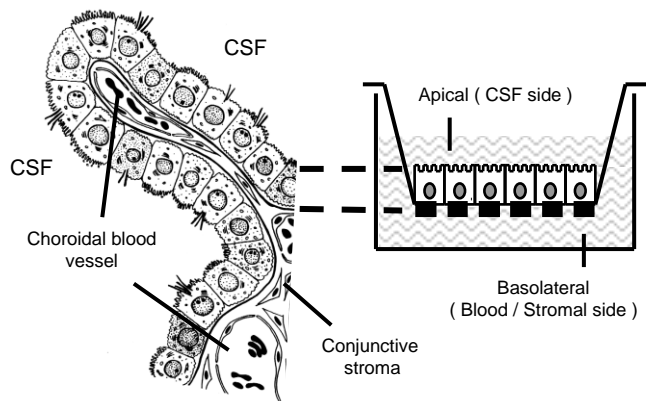
➤ Isolated capillaries and choroid plexuses

Freshly isolated intact tissues or homogenates are available for uptake and / or metabolic studies.

➤ In vitro cellular model

An in vitro cellular model of the blood / CSF interface that recapitulates the specific features of the in vivo choroidal epithelium was developed and extensively characterized. Being set up on a permeable filter, it delimits two compartments and is appropriate for both blood to CSF and CSF to blood transfer measurements.

In a reverse configuration, it also enables to investigate the transepithelial migration of immune cells or to evaluate the possible alteration of barrier properties following exposure to inflammatory molecules or activated/infected cells.



➤ Analytical expertise

HPLC - radiodetection - spectrophotometry – immunocytology - flux cytometry - RNA isolation - protein extraction.

APPLICATIONS

➤ In Neuropharmacology :

- Evaluating drug penetration through the choroid plexus and identifying the mechanisms possibly limiting this penetration (metabolism, multiple drug resistance phenotype)
- Evaluating drug elimination from the CNS through the choroid plexus and the blood / brain barrier, and identifying the transporters involved in the efflux processes
- Evaluating the efficacy of pharmacological compounds to modulate and control the migration of activated / infected immune cells across the choroid plexus
- Identifying pharmacological compounds to be used in association with CNS drugs in order to increase the cerebral bioavailability of the latter (by inhibiting efflux systems, or transiently opening the barrier).

➤ In Neuropathophysiology :

- Evaluating the penetration of inflammatory cells in the brain and characterizing the mechanisms involved in the migration (interest in multiple sclerosis and other CNS inflammatory diseases)
- Evaluating the penetration of infectious pathogens in the brain and investigating the mechanisms involved in the invasion (interest in bacterial and viral infectious diseases)
- Evaluating the effects of inflammatory mediators (cytokines, metalloproteases...) on the morphological and biochemical barrier properties of the blood / CSF interface (interest in CNS inflammatory and infectious diseases)

PARTNERSHIPS

We conduct both basic and applied research studies (pharmacology, toxicology, immunology, infectiology).

Research and development services are being provided to worldwide pharmaceutical industries (Neurogen/USA, Novartis/Suisse, Athena/USA, Servier/France, VectHorus/France), and academic research laboratories (INSERM, CNRS, IRSN, CEA, INSA, CLARA, Tokyo's University, King's College London, Providence's University).

We are working in collaboration with Brain-*i*, a private entity eligible for SME participation to EU Programmes for Research. Brain-*i* is a partner in the FP7 project "*Neurobid*".

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