EuroNanoMed3

INTREPIDUS

**Nanoporous-Membranes for Intrathecal (Pseudo)Delivery of Drugs**

## RESULTS OVERVIEW - 2022

In the middle stage of the EURONANOMED project the preclinical animal model was developed and validated by genotyping. Subsequently, cerebrospinal fluid from heterozygous animals (mutant genotype) was used for *ex vivo* testing of the experimental filtering devices.

The preclinical model for evaluating the effectiveness of nanoporous membranes was performed on APP/PS1 transgenic mice, provided by the partner University of Oveido, consisting of 2 pairs of APP/PS1 transgenic mice, each pair consisting of a trio: 2 females and a male. After the quarantine period, the animals were mated to obtain the offspring needed for the experiments. Mating was performed between a wild-type (wt) male and a mutant transgene (mt) purebred female. Biological samples (tips of tails) were taken from the offspring and their genotyping was carried out to identify the presence of the mutation (in the heterozygous state) and to separate the animals carrying the mutation from the wild-type ones.

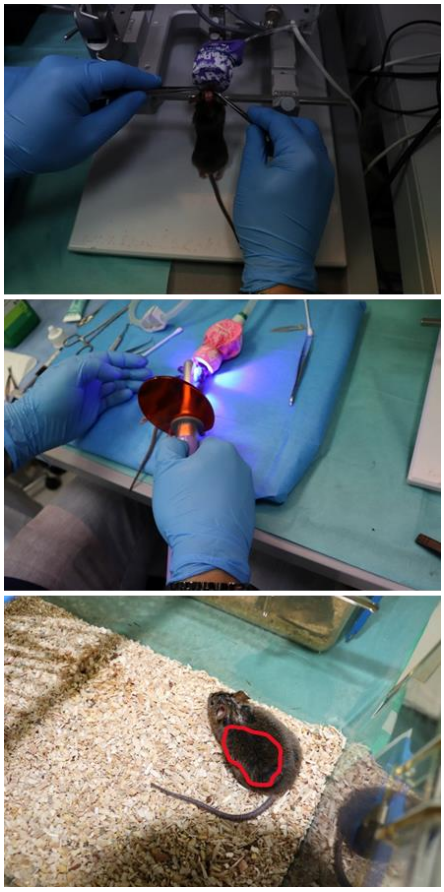

*Figure 1 Different steps in the stereotaxic surgery for the filtering devices implantation.*

The use of CSF from transgenic animals was necessary to verify that the presence of β-amyloid (which readily adheres to various structures) in the CSF would not lead to clogging of the device. The tests carried out did not lead to the recording of device malfunctions due to this aspect.

The surgical interventions for the implantation of the device consisted in the creation of subcutaneous pockets, on the dorsal side of the animal, in which the reservoir of the device was placed, the Alzet cannula was placed in the cisterna magna and the catheter was adjusted in length to unite the cannula with the - the reservoir placed subcutaneously.

The selective molecular permeability, molecular entrapment, and biofouling was assessed.