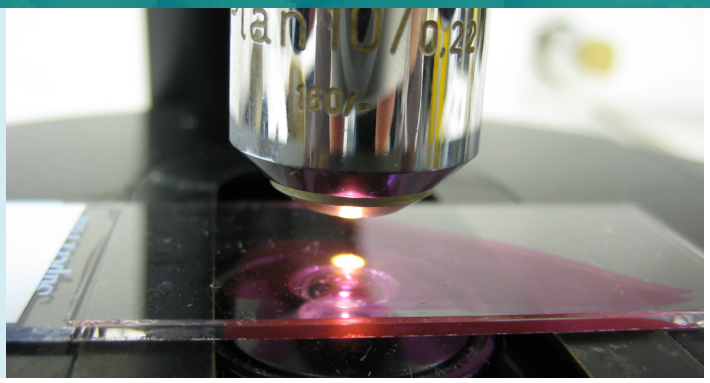
NETHERLANDS BRAIN BANK

Supporting preclinical research on post mortem human brain

NBB Research Services provides tailored solutions designed to answer research questions from biotechnology and pharmaceutical companies. Uniquely positioned between the world-renowned professional brain bank and excellent neuroscience research facilities, NBB will guide partners from research project definition, to optimal tissue selection and custom sample processing and analyses.



HISTOLOGICAL SERVICES

We offer a wide range of histological services

> Classical histological staining

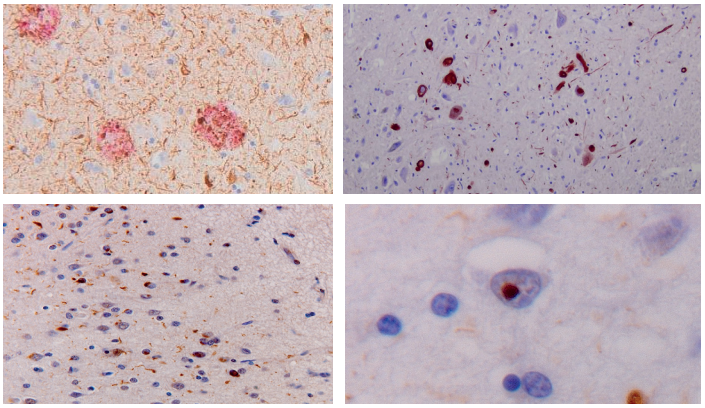
> Morphological evaluation of tissue blocks

> Immunohistochemistry on FFPE and frozen samples

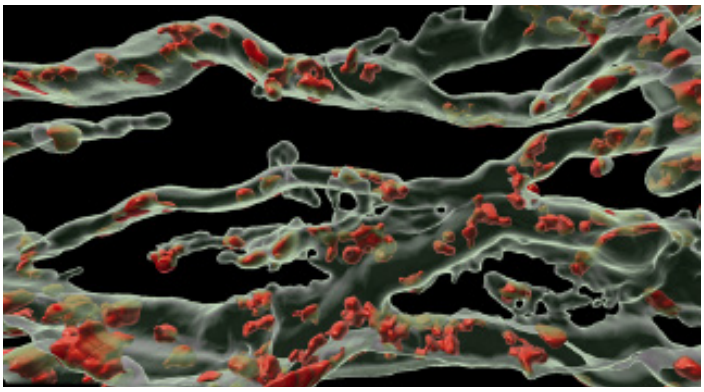
> Pre-screening of selected tissue blocks

> High-resolution fluorescent microscopy

> Tailored fixation and protocol optimization



Immunohistochemical analysis for neuropathological evaluation. *Top left: Extracellular deposits in plaques (pink) and Tangles and neuropil threads (brown) in Alzheimer's Disease. Top right: alpha-synuclein staining in Parkinson's Disease. Bottom left: TDP-43 staining in Frontotemporal lobe degeneration. Bottom right: P62 in Frontotemporal lobe degeneration.*



High- resolution Stimulated Emission Depletion (STED) microscopy in PFA fixed tissue sections. *Reconstructed 3-dimensional axons (SMI312 in green) and mitochondria (Tomm20 in red) of an MS donor. Figure adapted from Van den Bosch et al. Annals of Neurology, 2022.*

DONOR SELECTION SUPPORT

Quality research on post mortem brain tissue from a heterogeneous population of donors requires careful selection of donors and tissue samples to achieve optimal experimental results.

Contact the NBB if you require support in selection of donors and tissues based on the NBB **clinical, neuropathological and genetic data.**

www.brainbank.nl

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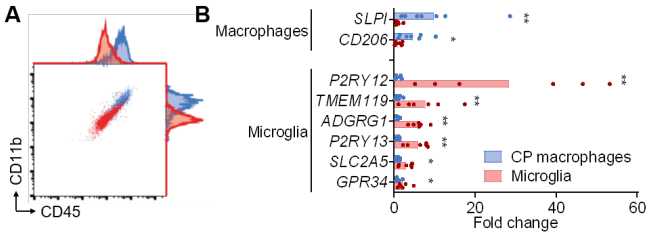
ISOLATION OF PRIMARY CELLS

Primary cells derived from human brain samples represent unique source material for molecular profiling in relation to a donor's clinical history and neuropathological characteristics. NBB Research Services relies on validated published methods to isolate microglia, B-cells and T-cells and prepare samples for subsequent RNA sequencing studies. Due to a short postmortem delay and rapid procedure the primary cells show preservation of gene expression and phenotype, reflecting the neuropathological status of the donor.

PRODUCTS

- Isolated primary microglia, T cells and B cells from fresh most-mortem cortical grey matter and subcortical white matter.
- Donors are selected based on clinical diagnosis.
- Cells can be provided frozen in DMSO, lysed, or in culture medium (fresh).

MICROGLIA ISOLATION



Isolated microglia from post-mortem human brain tissue are distinguishable from autologous macrophages. *Pure microglia are isolated using a rapid procedure based on Percoll density gradient centrifugation followed by CD11b+ magnetic beads-positive selection or fluorescence activated cell sorting. (A) FACS plot showing white matter microglia (red) and choroid plexus (CP) macrophages (blue) (B) Expression of microglia and macrophage signature genes in microglia and CP macrophages.*

REFERENCES

Mizee, M. R., Poel, M. van der & Huitinga, I. in Handbook of Clinical Neurology vol. 150 273–283 (Elsevier, 2018).

Van der Poel, M. et al. Nat. Commun. 10, 1139 (2019).

Fransen, N. L. et al. Brain 143, 1714–1730 (2020).

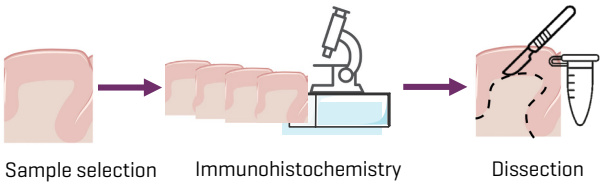
SINGLE CELL RNA SEQUENCING

Exploration of hnRNA from isolated populations of glial or neuronal cells allows to measure cell type specific gene expression in samples from nearly 5,000 donors.

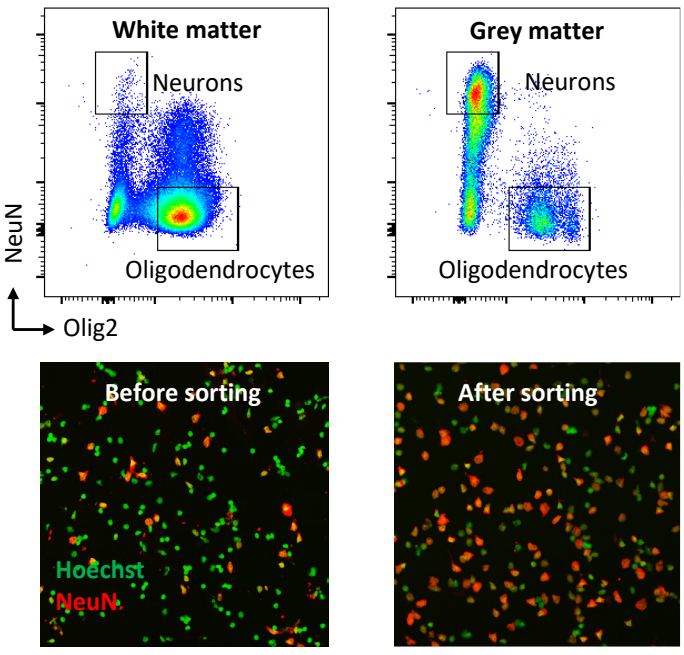
NUCLEUS ISOLATION SERVICE

- Isolated nuclei from frozen samples from neuropathologically characterized donors
- Sample selection, dissection and preparation for single nucSeq
- Cell type enriched nuclei for increased RNA sequencing depth

SAMPLE SELECTION AND DISSECTION



CELL TYPE ENRICHMENT



Sorted cell-type specific nuclei from cortical grey and white matter. *(Top) FACS sorting was applied to enrich cell-type specific nuclei from brain donors selected based on clinical, neuropathological, and genetic background. Distinct enrichments of neuronal (NeuN) and oligodendrocyte (Olig2) nuclei are shown. (Bottom) The grey matter sample before and after NeuN sorting.*