Internship opportunity in Molecular Neuroscience: Characterizing Cerebral Amyloid Angiopathy Subtypes in Human Brain Tissue using Immunohistochemistry and Immunofluorescence

Project description:

Cerebral amyloid angiopathy (CAA) involves the progressive deposition of amyloid β (Aβ) within the cerebral vasculature. It is a cause of cognitive decline and intracerebral hemorrhages in the elderly. Diagnosis of probable CAA relies on the neuroimaging-based 'Boston criteria 2.0' which includes non-haemorrhagic MRI markers. However, these criteria tend to underestimate the true occurrence of CAA since the MRI markers are not CAA-specific and reflect late-stage manifestations. On neuro-pathological examination, CAA can be classified into subtypes I (capillary CAA or capCAA) and II (large vessel arterial CAA or artCAA), distinguished by the involvement of capillaries next to that of larger vessels (arteri(ol)es). This projects aims to characterize the presence of capCAA or artCAA in a well-described cohort of cases (human brain tissue from AD and CAA patients and control individuals), as well as to determine whether candidate subtype-specific biomarkers are specifically expressed in either capillary or arterial CAA cases. With this knowledge, we will be able to expand our studies into investigating the potential of candidate biomarkers for each CAA subtype.

Your role:

You will be able to perform a (semi-)quantitative analysis of a cohort of amyloid β (Aβ)-stained sections from patients with Alzheimer's Disease (AD) and/or Cerebral Amyloid Angiopathy (CAA), as well as controls subjects. To confirm the immunohistochemistry results, you will optimize a double immunofluorescent staining protocol using anti-Aβ and anti-Actin antibodies to distinguish cap/artCAA. In addition, previous research has shown candidate biomarkers for cap/artCAA. Therefore, you will conduct pilot experiments to optimize staining protocols of these candidate subtype-specific biomarkers using immunohistochemistry and immunofluorescence.

Techniques:

- Immunohistochemistry + Light microscopy
- Immunofluorescence + Fluorescent microscopy

Project timeline (6+ months, depending on number of candidate markers to be studied):

(1) (Semi-)Quantitative assessment of Aβ-stained sections (n=106) following a protocol for determining cap/artCAA.
(2) Confirmation of the immunohistochemistry results with double-immunofluorescence staining for Aβ and Actin
    a. Optimization of protocol conditions
    b. Sub-cohort staining
    c. Qualitative staining assessment
(3) Pilot experiments with preselected candidate biomarker studies with immunohistochemistry
    a. Optimization of protocol conditions
    b. Small cohort staining and assessment
    c. Confirmation with triple-immunofluorescence staining
        i. Triple-staining protocol optimization
        ii. Small cohort staining and assessment
(4) Preparing report
(5) Presentation of results

Project timeline and candidate

The project's expected timeframe is September 2024 - March 2025. The candidate may be a Bachelor or Master student, preferably with knowledge of the employed techniques and a high level of motivation to conduct research in the field of neurovascular diseases. The student is expected to gain expertise in the aforementioned techniques during the first one to two months of the internship, after which they will be able to work independently. Upon receipt of internship application, a short meeting (online or onsite) will be scheduled to meet the daily supervisor and exchange expectations.

Research Group: Neurochemistry of Neurodegeneration

Head: Prof. dr. ir. Marcel Verbeek

Daily Supervisor: Carla Hernández Utrilla MSc