

**Title:** Destabilization of neuronal morphology in chronic inflammation: molecular mechanisms and identification of potential therapeutic agents (NCN/OPUS)

**Supervisor:** Professor Jacek Jaworski

**Institute:** International Institute of Molecular and Cell Biology in Warsaw

**Laboratory:** Laboratory of Molecular and Cellular Neurobiology

**www:** <https://url-shortener.me/1LOC>

**Project description:**

Dendritic arbors play a crucial role in the integration of synaptic information, and their structure typically remains stable throughout most of life. However, under pathological conditions such as chronic inflammation, stress, or aging, this stability may be disrupted, contributing to cognitive decline. Dendritic simplification is one of the most consistently documented markers of brain aging and dementia progression.

Despite the importance of these changes, the molecular mechanisms that drive the destabilization of mature dendrites remain poorly understood. In our cellular models, we have shown that the pro-inflammatory cytokine IL-1 $\beta$  induces broad transcriptional changes and dendritic destabilization, yet the protein mediators of these processes remain unidentified. Moreover, it is unclear whether inflammation-regulated factors contribute to cognitive deficits observed in infection, depression, neurodegeneration, or aging. Identifying these mechanisms may pave the way for new therapeutic approaches aimed at supporting neuronal function.

**Aim:**

The goal of the project is to identify inflammation-regulated genes and proteins that contribute to dendritic arbor destabilization and cognitive impairment associated with chronic inflammation and aging.

The PhD project will focus on understanding how inflammatory signaling affects gene regulation in mature neurons and which molecular mechanisms lead to dendritic destabilization. To address these questions, the project will combine molecular and cellular approaches with transcriptomic analyses. In particular, the student will investigate inflammation-induced changes in gene expression using single-cell RNA sequencing and study their impact on dendritic structure.

The work will involve experiments in rodent models, neuronal cell culture, and human neurons generated from fibroblasts through cellular reprogramming. The student will gain experience in modern neurobiology methods including neuronal imaging, transcriptomic data analysis, and cellular models of neuroinflammation.

**Requirements:**

- Master's or Master's Eng degree in biology, biotechnology or related fields
- Strong interest in cell biology and/or neurobiology
- Proficiency in written and spoken English
- Excellent interpersonal skills, initiative, good work organization, and strong collaboration abilities
- Strong analytical and critical-thinking skills, including the ability to independently evaluate data
- Willingness to work with animal models (rodents)
- Prior experience in the following techniques will be an advantage (but is not a prerequisite):
  - Cell culture (primary and/or established cell lines)
  - Work with rodents
  - Ability to code in R and/or Python and experience in data science

- Sequencing data analysis and/or multiomic data analysis

**Number of positions available: 1**

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