

**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 overarching goals of the project are:

- (i) to identify key inflammation-regulated genes and proteins responsible for dendritic arbor destabilization and cognitive impairment, and
- (ii) to discover and preliminarily evaluate small-molecule compounds capable of protecting neurons from inflammation- and age-induced structural deterioration.

The prospective PhD student will be able to choose one of two research paths: Mechanistic path — focused on understanding how inflammation and aging affect gene regulation and which molecular processes lead to dendritic destabilization and associated cognitive deficits. Therapeutic path — focused on identifying small-molecule compounds that stabilize dendrites under inflammatory conditions and evaluating their potential as candidates to support cognitive function during aging.

**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
- 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:** 2

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