The role of the histone modification H3K27me3 in developing and adult neurons

Summary

Neurons are born early in development and are not replaced during the organism's lifetime. Therefore, once neurons have matured and become functional, they must remain so for a long time—in humans, up to a hundred years or more. Epigenetic regulation plays a crucial role in establishing and maintaining neuronal function by regulating correct gene expression patterns. The overall goal of this PhD project is to understand how histone modifications regulate gene expression and chromatin architecture throughout neuronal development and adulthood. This research will help us understand the fundamental principles of epigenetic regulation in brain development and function.

Research field:	Chemistry and biotechnology
Supervisor:	Kärt Mätlik
Availability:	This position is available.
Offered by:	School of Science Department of Chemistry and Biotechnology
Application deadline:	Applications are accepted between June 01, 2025 00:00 and June 30, 2025 23:59 (Europe/Zurich)

Description

The research

Neuronal development is controlled by epigenetic mechanisms, including modifications of histones and DNA, which regulate gene expression patterns during lineage decisions, differentiation, and maturation. Epigenetic modifications, such as histone methylation, influence chromatin accessibility and interactions with transcription factors. Histone proteins can be methylated at different amino acids, leading to different outcomes on chromatin compaction and gene expression. For example, histone 3 lysine 27 trimethylation (H3K27me3) induces gene expression silencing, whereas H3K4me3 is associated with active gene expression. Histone methylation patterns are tightly regulated during neuronal maturation, ensuring that appropriate genes are expressed at each stage of development.

Using cerebellar granule cells as a model of neuronal development, we have previously found that the genomic localisation of H3K27me3 changes during neuronal maturation. The changes in H3K27me3 during neuronal maturation are associated with two distinct genomic and epigenetic features: a local remodelling of H3K4me3/H3K27me3 bivalent domains at gene promoters, and a global increase in H3K27me3 at broad intergenic regions. The goal of this research is to define the mechanisms of H3K27me3 regulation in neurons and investigate how developmental changes in H3K27me3 regulate gene expression and chromatin structure.

Specifically, the thesis should address the following questions:

1) Which mechanisms regulate the global increase of H3K27me3 during neuronal maturation?

2) What is the function of H3K27me3 developmental accumulation in the adult brain?

3) What is the importance of histone bivalency in mature neurons?

Responsibilities and (foreseen) tasks

- Design and plan experiments
- Collect data using a range of next-generation genomics, molecular biology, biochemistry, microscopy, and cell culture techniques
- Analyse genomic and transcriptomic datasets using bioinformatics tools
- Present data at seminars and conferences
- Write manuscripts on the results of the project

Applicants should fulfil the following requirements:

- a Master's degree in life sciences

- a clear interest in the topic of the position
- experience in molecular and cell biology techniques
- experience in or willingness to learn bioinformatics
- excellent command of English
- capacity to work both as an independent researcher and as part of an international team

The following experience is beneficial:

- Cell culture methods
- Gene expression analysis
- Microscopy
- Programming in R/RStudio

To apply, please submit a research plan on the topic, including the overall research and data collection strategy.

We offer:

- A 4-year PhD position focusing on fundamental mechanisms of gene regulation in the brain
- Opportunities for supervising bachelor's and master's degree students
- Opportunities for conference visits and networking with leading universities in biomedical sciences

About the laboratory

The Laboratory of Neuroepigenetics is located within the Department of Chemistry and Biotechnology and is a member of the Health and Food Technologies Focus Centre at Tallinn University of Technology (TalTech). For further information, please contact Dr. Kärt Mätlik at kart.matlik@taltech.ee or visit the Mätlik lab website at https://matliklab.org.

To get more information or to apply online, visit https://taltech.glowbase.com/positions/937 or scan the the code on the left with your smartphone.