

# Molecular mechanisms of activity-regulated expression of the neurotrophin BDNF

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## Summary

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*Brain-derived neurotrophic factor (BDNF) is regulated by activity in brain neurons and is associated with several human psychiatric and cognitive disorders. The aim of the project is to characterize novel mechanisms involved in neuronal activity-regulated BDNF gene expression by using molecular and cell biology approaches and animal experiments.*

Research field:	Chemistry and Biotechnology
Supervisor:	Tõnis Timmusk
Availability:	This position is available.
Offered by:	School of Science Department of Chemistry and Biotechnology
Application deadline:	Applications are accepted between May 03, 2021 00:00 and May 31, 2021 23:59 (Europe/Zurich)

## Description

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Functioning of the nervous system is activity-dependent. Dendrites and axons of neurons allow neurons to be appropriately interconnected to other neurons, and the formation of functional neural circuits. Modifiability of such neuronal connectivity by formation of new synapses, and alteration of the strength and stability of existing synapses – is regarded as the main cellular basis of many neuronal functions, including behaviour. Neuronal activity-regulated transcription plays a crucial role in synaptic development and function, and its deregulation gives rise to disorders of human cognition.

Brain-derived neurotrophic factor (BDNF) is one of the best-studied genes regulated by activity in the brain neurons and its polymorphisms are associated with several human psychiatric and cognitive disorders. Also, mutations of genes that control activity-dependent transcription result in several disorders of human cognition. For example, Rubinstein-Taybi syndrome, a disorder characterized by severe mental retardation, is caused by mutation of the transcription factor CREB cofactor CBP. Both CREB and CBP are involved in activity-dependent transcription of BDNF. Rett syndrome, which is characterized by mental retardation and defects in socialization, is caused by mutation of MeCP2, an activity-regulated repressor of BDNF transcription.

Discovery and characterization of activity-regulated transcription factors is of great importance in neuroscience field. The aim of this project is to characterize novel transcriptional and posttranscriptional mechanisms involved in neuronal activity-regulated BDNF gene expression by using molecular and cell biology approaches and animal experiments used before by our group (Pruunsild et al., J. Neuroscience 2011; Koppel et al., Neuropharmacology 2013, J. Neurochem. 2015, Glia 2018; Tuvikene et al., J. Neuroscience 2016, eLife 2021; Esvald et al., J. Neuroscience 2020).

### **Applicants should fulfil the following requirements:**

- strong expertise in cell and molecular biology techniques
- additional expertise in animal work, primary neuron, glia and live cell imaging will also be assets to the project



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