3 PhD-students in Cellular Neuroscience (life cell imaging, cell biology, neurophysiology)

Specification

Location	De Boelelaan 1105, Amsterdam
Function types	PhD positions
Scientific fields	Natural Sciences
Hours	40.0 hours per week
Salary	€ 2191 - € 2801
Education	University Graduate
Job number	CNCR86
About employer	Vrije Universiteit Amsterdam (VU)
Short link	www.academictransfer.com/39546

Apply for this job before April 13, 2017

Job description

The projects are part of a EU-funded project on cellular trafficking (H2020 COSYN) and a national grant on neuromodulators. The PhD-projects will be integrated in these larger project groups.

Communication between neurons in the brain depends on the secretion of chemical messengers from synaptic and dense core vesicles and the trafficking of these vesicles to and within the synapse. Several genes involved in these processes are now firmly implicated in brain disorders like schizophrenia, autism, epilepsy and mental retardation. The aim of the projects is to unravel the mechanisms of vesicle trafficking and secretion in neurons and to analyze how these processes are affected by disease.

Tasks
All projects use cultured rodent and human neurons and modern genome editing to delete/modify candidate genes or introduce/correct disease-relevant variation. As main analysis tools, you will primarily use patch clamp electrophysiology and fluorescence imaging (project 1) or life cell imaging and cellular trafficking assays (project 2-3). All projects will test their main findings in more integrated models (brain slices and in vivo). You will be part of international research networks and will be able to exploit a variety of other analysis methods available within the networks. All projects are in Amsterdam and you will work primarily in Amsterdam with regular visits to the participating labs. The PhD-students will be trained on site and in specialized courses on campus.
During the PhD you will write several scientific publications that will be combined in a PhD thesis.

Requirements

We are looking for candidates that hold, or will soon hold, a master degree in (Medical) Biology, Biophysics or Physics, preferably with hands-on experience in (neuronal) cell culture and microscopy, and a strong motivation to pursue a career in science. Experience with cellular imaging and/or patch clamp physiology are an advantage.

Conditions of employment

You can find information about our excellent fringe benefits of employment at http://www.workingatvu.nl like:
• remuneration of 8,3% end-of-year bonus and 8% holiday allowance;
• solid pension scheme (ABP);
• generous contribution (65%) commuting allowance based on public transport;
• a wide range of sports facilities which staff may use at a modest charge.

The salary will be in accordance with university regulations for academic personnel, and amounts € 2,191 gross per month in the first year up to € 2,801 in the fourth year (salary scale 85/PHD) based on a full-time employment.

Employer

Vrije Universiteit Amsterdam

Vrije Universiteit Amsterdam (VU) is a leading, innovative and growing university that is at the heart of society and actively contributes to new developments in teaching and research. Our university has ten faculties, and provides work for over 4,500 staff and scientific education for more than 23,000 students.

Department

The Faculty of Earth and Life Sciences (FALW) offers a range of Bachelor and Master programmes. Research at the faculty focuses on the fields of the life sciences, health sciences, environmental sciences and earth sciences. World-class teaching and cutting-edge research activities go hand in hand. FALW works together with other faculties like economics, medicine, exact sciences, psychology and social sciences. The faculty's research facilities can be categorized as excellent. The faculty's international focus fosters cross-border collaboration, leading to substantially improved quality and greater impact of our research results.
The Center for Neurogenomics and Cognitive Research in Amsterdam (see http://www.cncr.nl) participates in the Neuroscience Graduate School Amsterdam Rotterdam (http://www.onwar.nl) and is seeking applications for 3 PhD students in cellular neuroscience (life cell imaging, cell biology, neurophysiology).

Additional information

Project 1 (COSYN1): Effect of genetic variation in human brain disorders on synaptic transmission

Several exon variants and single gene CNVs are now firmly associated with schizophrenia, autism and mental retardation. We have previously identified synaptic gene networks where many such risk factors accumulate. Using two reduced and highly standardized model systems, we aim to systematically analyze the synaptic effects of different exonic variants and single gene CMVs in a large European collaboration named COSYN. In this project, we will focus on presynaptic function. As model system we will exploit human iPS-cell derived neurons from patients and controls, sampled by others in the COSYN team and analyze synaptic transmission using patch clamp physiology. We will exploit modern gene-editing methodology to generate models for schizophrenia, autism and mental retardation, introducing mutations and gene deletions to study the synaptic function of disease-associated genes. Life cell imaging experiments will be used for independent analysis of synaptic functions. Together these studies yield roughly 50 functional parameters which together assist in predicting the synaptic consequences of genetic variation associated with schizophrenia.

Project 2 (COSYN2): Effect of genetic variation in human brain disorders on DCV trafficking & fusion

In addition to synaptic transmission, we have obtained evidence that the secretion of neuromodulatory signals such as neuropeptides and trophic factors, is dysregulated in schizophrenia, autism and mental retardation. Within COSYN, we have found associations with several new genes that point in this direction. In this project, we will investigate the mechanisms of trafficking and secretion of secretory vesicles that contain these neuromodulators (dense cored vesicles, DCVs) in human, iPSC-derived neurons. Primary mouse hippocampal neurons and intact rodent tissue (brain slices, in vivo) will be used as controls and for initial tests. We will identify the common and unique aspects of DCV trafficking and fusion, relative to synaptic vesicles, and the links to human disorders, especially for the genes that we found associated with disorders. This project uses life cell imaging (2-photon imaging and confocal microscopy) and genetically encoded reporters to detect DCV trafficking and fusion. We have previously established detection of DCV secretion in living neurons at the single vesicle level and characterized several molecular factors that regulate secretion of neuropeptides in chromaffin cells. In this project we will exploit these tools/methods to test whether these principles operate in neurons and how these principles might be altered in human disease.

Project 3 (DCV1): Molecular mechanisms of trafficking and fusion of secretory vesicles in neurons

Many of the modulatory signals that change our brain state (arousal, sleep, euphoria) are secreted from dense cored vesicles (DCVs) in neurons. Dysregulation of DCV trafficking and release is at the basis of many disorders, like neuropsychiatric disorders. The aim of this project is to unravel the mechanisms of DCV trafficking and secretion in neurons at the single vesicle level from the initial biogenesis at the Golgi to the final fusion at synapses. This project uses life cell imaging (2-photon imaging and confocal microscopy) in intact rodent tissue (brain slices, in vivo) and human iPSC-derived neurons, and genetically encoded reporters to detect DCV trafficking and fusion. This project will work together with project 2 where similar methods are being used. We have previously established detection of DCV secretion in living neurons at the single vesicle level2 and characterized several molecular factors that regulate secretion of neuropeptides in

chromaffin cells3. In this project we will exploit these tools/methods to test whether these principles operate in neurons and how the secreted cargo affects network activity and behavior. Using two recently acquired/rebuilt microscopes, we are now able to witness the behavior of individual vesicles prior to secretion in normal and mutant neurons in intact tissue.

Application

Please send CV and cover letter (together as 1 PDF) to Els Borghols at els.borghols@vu.nl with 'CNCR86' and the project number(s) in the subject line.
Deadline: 13 April 2017. Start date: no later than July 1st 2017.

More info at http://cncr.nl/jobs/vacancies, via http://www.cncr.nl or from prof. M. Verhage (project leader, m.verhage@vu.nl).