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Control of synaptic connectivity, diversity and function by cell-surface interactions

SEMINAR & VISITING SPEAKER SERIES

WORLD WIDE NEURO PLATFORM

DATE

Monday, June 20, 2022
12:00 PM CST

WORLD WIDE NEURO LINK

This talk willl be hosted on zoom:

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SPEAKER

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BIO

Joris de Wit obtained his PhD degree at the VU University (Amsterdam, The Netherlands) in 2004. He performed his postdoctoral training with Matthijs Verhage (VU University, The Netherlands; 2004-2006) and Anirvan Ghosh (University of California San Diego, USA; 2006-2012). In 2013, he started the Laboratory of Synapse Biology at the VIB-KU Leuven Center for Brain & Disease Research (Leuven, Belgium) as VIB Group Leader and Associate Professor at KU Leuven. In 2018, he became Deputy Science Director of the VIB-KU Leuven Center for Brain & Disease Research, and in 2019 he was promoted to Professor in the Department of Neurosciences. Work in his laboratory aims to understand the molecular and cellular mechanisms that determine where and when synapses form; how these connections change with experience, and how they are affected in disease. Joris de Wit is recipient of an ERC Starting Grant and FWO Odysseus grant.

RESEARCH

Neural circuits are composed of distinct neuronal cell types connected in highly specific patterns. Unraveling how neurons form appropriate synaptic connections during development is a key challenge in neuroscience and is essential to understand brain function and disease. Neural circuit formation critically relies on cell-cell recognition and communication mediated by cell-surface ligands and receptors. The complexity of the cell-surface interactions that regulate precise synaptic connectivity and specify synaptic properties is only beginning to emerge. In this talk, I will discuss our recent work dissecting the cell-surface interaction networks that control connectivity, structure and function of specific synapses in hippocampal circuits. In addition, I will discuss how alterations in ligand-receptor communication may be relevant for brain disorders, in particular Alzheimer's disease.

OBJECTIVES

My research aims to understand the molecular mechanisms that control the development and maintenance of neural connectivity. My work focuses on the role of cell-surface interactions in these processes. I have made innovative use of proteomic approaches to uncover the network of ligand-receptor interactions that regulate connectivity, revealing a prominent role for leucine-rich repeat-containing receptors in synapse development (De Wit Neuron 2009, 2013; O'Sullivan, De Wit Neuron 2012; DeNardo Neuron 2012; Savas, De Wit Nat Protoc 2014). Work from my laboratory elucidated the intracellular sorting mechanisms that control the distribution and composition of cell-surface receptors at synapses (Savas Neuron 2015; Ribeiro PLOS Biol 2019). To understand how cell-surface interactions specify synapse development in neural circuits, my lab demonstrated that cell-surface receptors act in an input-specific and combinatorial fashion to shape the structural and functional properties of specific synaptic inputs of pyramidal neurons (Condomitti Neuron 2018; Schroeder Neuron 2018). To move beyond the study of single candidate genes and gain a comprehensive view of synaptic cell-surface receptor networks, we developed an approach to analyze the cell-surface proteome and interactome of a specific hippocampal synapse type (Apóstolo Nat Commun 2020). Relevant to neurological disease, my lab uncovered a role for the amyloid precursor protein as a modulator of the GABABR1a receptor in synaptic transmission (Rice Science 2019; Rice Mol Neurodegen 2020), and identified dysregulation of a neuromodulatory peptide involved in sleep as an underlying cause of aberrant neural activity in the early stages of Alzheimer's disease (Calafate bioRxiv 2021).

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