【Seminar】How synaptic plasticity regulates Intracellular Transport of AMPAR

Date-Time
Wednesday, April 8, 2026 - 10:00 to 11:00

Location Seminar room C210, Ctr Bldg

Description

Title: How synaptic plasticity regulates Intracellular Transport of AMPAR

Speaker: Dr. Françoise Coussen
Research Director at the CNRS

Interdisciplinary Institute for Neuroscience (IINS)
University of Bordeaux and CNRS

https://www.bordeaux-neurocampus.fr/en/?s=Coussen

https://www.iins.u-bordeaux.fr/

Short Bio:

Françoise Coussen is a biochemist, molecular biologist, and cell biologist whose career has focused on signal transduction and synaptic receptor biology.

She obtained her PhD at Université de Paris at the Institut Pasteur, where she achieved the first purification of mammalian adenylate cyclase (1985). She then pursued postdoctoral training in the laboratory of Alfred G. Gilman in Dallas, where she successfully cloned adenylate cyclase type 1 (1986-1988).

Upon returning to France, she joined the CNRS in Paris. In the laboratory of Jean Massoulié at the École Normale Supérieure, she worked on the purification, cloning, and biophysical characterization of acetylcholinesterase (1988-1994).

After a sabbatical in Durham (1994-1996), she contributed to the establishment of a new neurobiology laboratory in Bordeaux alongside Christophe Mulle and Daniel Choquet. In Christophe Mulle's laboratory, she performed the first proteomic analysis of proteins associated with kainate receptors (1996-2008). She later joined Daniel Choquet's laboratory to characterize the intracellular trafficking of AMPA receptors (2008-2024).

She served as Director of Research at the CNRS and retired one year ago. In recognition of her scientific contributions, she was awarded a CNRS medal for her career achievements.

Summary:

AMPA receptors (AMPAR) are the principal ionotropic glutamate receptors regulating fast excitatory transmission in mammalian brain. AMPAR are highly dynamic complexes undergoing constant turnover through endo- and exocytosis from the cell surface. Changes in the number of synaptic AMPA subtypes of glutamate receptors underlie many forms of synaptic plasticity. These variations are controlled by a complex interplay between their intracellular transport (IT), export to the plasma membrane, stabilization at synaptic sites, and recycling. The differential molecular mechanisms involved in these various trafficking pathways and their regulation remains partly unknown in particular for the IT of AMPAR.

Regulated vesicular IT, which allows cells to quickly distribute a large variety of cargos to specific cellular compartments, can greatly impact their function. Indeed, receptor IT is a key mechanism fundamental for the maintenance of the surface proteome, playing essential roles in establishing important neuronal properties, such as cellular excitability and synaptic efficacy. Moreover, initial synaptic recruitment of pre-existing extra-synaptic surface AMPAR, subsequent postsynaptic exocytosis to replenish the extra-synaptic surface pool of AMPAR, and AMPAR secretory transport are implicated in the synaptic incorporation of AMPAR at the plasma membrane during LTP.

In cultured neurons we have shown that under basal conditions, newly synthesized-AMPAR travel bidirectionally at a velocity around 1.5 um/s, to distribute receptors all along the dendrite, and it is highly modulated by neuronal activity. This is also the case in organotypic hippocampal slice. This transport in highly regulated during LTP in terms of speed of IT, exocytosis of the receptors and direction of the transport inside the dendrites.

The cytosolic C-terminus domain of AMPAR GluA1 is specifically associated with cytoplasmic proteins that could be implicated in the regulation of their IT such as 4.1N. We have shown how interaction between GluA1 and 4.1N regulates IT and exocytosis at the plasma membrane in basal condition and after LTP induction. We use sh-RNA against 4.1N and specific mutations and deletions of GluA1 C-terminus domain to characterize how this interaction is involved in coupling AMPAR to the transport machinery. 4.1N-GluA1 interaction plays an essential role during exocytosis of the receptor in basal transmission. Importantly, disrupting GluA1 interaction with 4.1N prevents the LTP induced increase in the number of GluA1 containing vesicles observed in control and GluA1 externalization. During basal transmission, the binding of 4.1N to GluA1 allows the fusion/fission membrane exocytosis whereas during LTP the interaction of 4.1N with GluA1 allows both IT and exocytosis of the receptor in hippocampal cultured neurons.

Short Abstract:

Abundance of AMPA receptors (AMPAR) at synapse is essential for the establishment and maintenance of synaptic function. Their synaptic localization is dependent on a highly dynamic exocytosis,

endocytosis and plasma membrane mobility events. Moreover, intracellular transport (IT) of newly synthetized AMPAR is important to maintain the pool of receptors at the plasma membrane.

Using our biochemical tool combined with photonic live imaging, we controlled and followed the intracellular transport of tagged GluA1 containing receptors in cultured rat hippocampal neurons and in organotypic hippocampal slices. Analyzes are performed for GluA1 WT and mutants of GluA1 C-terminus domain in basal condition and during LTP. Localization of AMPAR is regulated by their intracellular trafficking thru interaction of their C-terminus domains with different intracellular partners. These interactions play a major rule in the exocytosis and localization of the receptor at the plasma membrane both in basal condition of during cLTP.