Molecular and Neural Correlates of Memory and Cognition

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Session 1  Molecular substrates of memory and cognition

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Presynaptic homeostatic plasticity contributes to the activity-driven remodelling of cortical networks

Neuronal homeostatic plasticity is a mechanism, by which neurons regulate their excitability and synaptic strength to keep network activity in physiological range independently of frequency of incoming stimulation. Monocular deprivation-induced ocular dominance plasticity (MD-ODP) in the visual cortex represents an established in vivo paradigm, where inactivity-driven homeostatic reconfiguration of cortical networks plays a key role. Main cellular mechanisms underlying synaptic homeostatic plasticity are the activity-induced regulation of availability of postsynaptic glutamate receptors and the modulation of presynaptic release efficiency. While postsynaptic mechanisms contributing to homeostatic plasticity are well established, little is known about the presynaptic molecular players.

Bassoon is presynaptic scaffolding protein involved in the spatial and functional organisation of synaptic vesicle recycling. I will report on a new role of bassoon in the regulation of homeostatic synaptic plasticity. We observed aberrant MD-ODP in a constitutive knock-out model of bassoon. To dissect the role of bassoon in this process we tested functional correlates of inactivity-induced homeostatic scaling in cultured neurons from bassoon knock out animals using electrophysiology and imaging of synaptic vesicle recycling using sypHy. Bassoon deletion resulted in a defect in inactivity-induced homeostatic adaptation of neurotransmitter release at excitatory synapses leaving homeostatic remodelling of postsynaptic receptor apparatus unaffected. In vivo experiments in a conditional mouse model revealed that selective removal of bassoon from cortical excitatory synapses prevented normal MD-ODP. Taking together, our results put homeostatic plasticity of neurotransmitter release machinery as an important mechanism contributing to activity-dependent functional shaping of cortical cirucuity and the presynaptic scaffold bassoon as an indispensable molecular player in this process.