Laboratory title : CNRS UMR 5297 - Daniel Choquet

Supervisor
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Thesis title :
Nanoscale AMPA receptor organization during autistic syndrome

Keywords : AMPA receptors, synaptic transmission, Super resolution microscopy, autism, scaffolding proteins

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Abstract
Autism spectrum disorder is clearly identified as a synaptic disease. The vast majority of the mutations implicated in this syndrome impact proteins which molecularly organize the synapse, as the trans-synaptic couple of proteins neurexin-neuroligin, or the various scaffolding protein of the post-synaptic density, PSD95 or all members of the Shank family.

We are working to the development of super-resolution techniques coupled to electrophysiology to understand how dynamic organization of AMPA receptors at the nanoscale impacts the synaptic transmission. During last years, we demonstrated for example that AMPA receptors are clustered in domains of 80 nm size, acting like a quantum of post-synaptic response. Other studies showed that exchange between trapped inside domain receptor and freely diffusive ones tunes the fidelity of synaptic transmission. The aim of the presenting project consists to transfer our imaging and electrophysiology expertise to decipher the molecular modification of the synapse responsible of autism disorder. This project will necessitate to the development of d-STORM technique in brain slices to go to a more integrated level. The study will be focused on the effect of various PSD95 mutations on the dynamic organization of AMPA receptors and their effect on synaptic transmission.

Qualification required
The student should have some notion in microscopy and some knowledge in molecular biology