

par **Pierre Paoletti**
Ecole Normale Supérieure de Paris
Institut de Biologie

NMDA receptors: allosteric machine in neurotransmission

The function of the human brain, and its remarkable capacity for experience-dependent change, hinges on the organization and dynamics of chemical synapses, primary sites of neuronal communication. Our lab has a long-standing interest in studying the molecular principles underpinning the structure and function of chemical synapses. Our research focuses on NMDA receptors (NMDARs), a family of glutamate-gated ion channel receptors that are essential mediators of excitatory neurotransmission and synaptic plasticity. These receptors have also been implicated in various neurological and psychiatric disorders thus receiving strong interest as potential therapeutic targets. Recent years have witnessed major progress in our understanding of the structure, mechanisms and regulation of NMDARs, with highlights including the decoding of the first full-length atomic structures. Studies from our team have also contributed to the emerging view that NMDARs are particularly complex molecular machines, endowed with unique allosteric capacity and exquisitely sensitive to their native microenvironment. I will present current knowledge on the anatomical and functional diversity of NMDARs, their molecular architecture and structural mechanisms, and the recent identification of key regions that allosterically control their subunit-specific gating and pharmacological profile. I will also present results obtained with genetically-modified mice showing how endogenous brain modulators, such as zinc ions, interact with specific NMDAR populations to regulate excitatory synapses and behavior. I will conclude by showing our latest developments in molecular engineering and optogenetics with the design of optically-controlled NMDAR subunits for precise manipulation and interrogation of receptor structure and function.

Hôte : Jacques Neyton (IBS/Groupe Transporteurs Membranaires)