

## Psychiatry and Neuroscience Seminar Series 2024

**Pr. Frédéric MEUNIER**

(Host T Galli)

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# Greasing the wheel of memory via a novel phospholipase A1 pathway



**Tuesday, January 23<sup>rd</sup>, 2024, noon**

Room D Levy, 102-108 rue de la santé - 75014 Paris

**Pr Frédéric A MEUNIER**

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The goal of our research is to determine how brain cells communicate and survive in health and disease. We are focused on the molecular events that govern vesicular trafficking within presynaptic nerve terminals and neurosecretory cells. Our discoveries have led to a deep understanding of how secretory vesicles interact with the cortical actin network prior to fusing with the plasma membrane to release the neurotransmitter. One of the last frontiers in neurobiology is to understand how our brain can learn and store memories - some of them enduring for a lifetime. Saturated FFAs, particularly myristic and palmitic acids, strongly increase during neuronal stimulation and memory acquisition, suggesting the involvement of phospholipase A1 (PLA1) activity in synaptic plasticity. I will present some of our work demonstrating that the DDHD2 isoform of PLA1 generates these saturated FFAs across the brain, thereby controlling memory performance in reward-based learning and spatial memory models prior to the development of neuromuscular deficits. We found that DDHD2 interacts with the key synaptic protein STXBP1/Munc18-1. Both DDHD2 knockout and haplo-insufficient STXBP1<sup>+/-</sup> mice display intellectual disability and motor dysfunction. We also show that STXBP1 controls the targeting of DDHD2 to the plasma membrane and the generation of saturated FFAs in the brain. Our findings suggest key roles for DDHD2 and STXBP1 in the lipid metabolism underlying synaptic plasticity, learning and memory.

**Keywords:**

Botulinum Toxins

Neurobiology

Synapses

Single Molecule Imaging

Neuroscience

Neuroprotection

Neurotransmitter

Molecular Biology

Cell Biology

Microscopy

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