Proposal of Master Research Project (MRP) for the Academic Year 2026-27

Group Name: Plasticity and Remodeling of Neural Circuits
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Title of the MRP: GluN3A-dependent spine plasticity in the frontal cortex of the stressed adult brain

Summary of the MRP:

Dendritic spines are the primary locus for excitatory synapse formation in the mammalian brain and a central hub for effecting synaptic plasticity. Although some spines are stable for extended periods, a significant proportion is enormously dynamic and experience large structural changes that reshape circuit connectivity in response to environmental challenges. These structural rearrangements thus providing a fundamental mechanism for brain plasticity and associated behavioral adaptations.

The project builds on previous research from our laboratory demonstrating that GluN3A, a non-conventional NMDA receptor subunit typical of juvenile brains, is retained in specific adult brain regions involved in higher-order cognitive and emotional processing. Our recent findings demonstrated that GluN3A-NMDARs in prefrontal cortex excitatory pyramidal neurons mediate maladaptive plasticity responses to stress and provided a target to promote resilience. The molecular mechanisms involve modulation of synaptic mTORC1 complexes and *di novo* protein synthesis.

We will investigate whether targeting GluN3A and associated signaling in prefrontal cortex works at the level of structural spine plasticity in naive and stressed mice, as seems to be the case for ketamine and serotonergic psychedelics; and map the subpopulations of pyramidal neurons targeted by stress using viral delivery of genetically-encoded spine fillers and 2-photon *in vivo* longitudinal approaches.

The specific aims will be:

1. Determine how GluN3A deletion in projection-defined pyramidal neuron subpopulations impacts dendritic spine dynamics and morphology in basal and chronically stressed mice.
2. Determine how GluN3A deletion in projection-defined pyramidal neuron subpopulations impacts calcium dynamics and network connectivity.

The student will participate in surgical animal procedures, *in vivo* multiphoton microscopy, image processing and quantification, and statistical analysis.

Methods and technology involved in the MRP:

- Viral intracerebral injections of retrograde tracers and calcium indicators in genetically modified mice
- *In vivo* multiphoton imaging of dendritic spines and calcium dynamics through cranial window across different time-points
- Brain processing and confocal analysis of dendritic spine morphology
- MATLAB-based image processing and quantification

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