

Internship Proposal

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Proposal At: 2023-02-02

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Project Title:

PsychoGlia

Level:

Master

Project Summary:

Psychoactive substances are recognized as substances that dysregulate the monoaminergic systems with profound impact in behavior. However, increasing evidence supports a relevant role for glial cells in addiction. Our research group has established that exposure to psychoactive drugs, such as methamphetamine (Meth), induces microgliosis in mice through a crosstalk between microglia and astrocytes, that leads to impaired ability to evaluate risk. We have also demonstrated that binge alcohol administration to adult mice causes aberrant synaptic pruning and loss of prefrontal excitatory synapses, increasing anxiety-like behavior. Little is yet known on how chronic use will modulate glial reactivity, but in early abstinence microglia seems to be highly responsive, exacerbating the release of proinflammatory cytokines and increasing the likelihood of relapse. Here we will use different transgenic mice models to understand how glial reactivity progresses under chronic exposure.

Work to be developed by the student:

Available projects

- 1) Characterization of chronic effects - We are using an escalating dosing of Meth to define the timeline of the Meth-induced inflammatory signalling (characterisation of FACS-sorted microglia, impacts on neuronal morphology and function, proteomic evaluation, running a Mouse Cytokine Array, behavioural studies)
- 2) Characterization of immune populations (innate or adaptive) and cytokine release,
- 3) In vitro use of primary microglia and hippocampal, co-cultured in microfluidic platforms, to address contact dependent communication, release of soluble factors and other interesting pathways.
- 4) Take advantage of transgenic mouse models with controlled overexpression of IL-10

(pMT-10-IL-10) or the IL-10R/ (missing the IL-10 receptor1) to investigate the protective mechanisms elicited by IL-10 under exposure to Meth.

5)Unravelling how Meth modulates both neuronal and microglial cytoskeletons and how this impacts behavior



References:

Canedo, T., et al., Astrocyte-derived TNF and glutamate critically modulate microglia reactivity by methamphetamine. bioRxiv, 2021: p. 2021.02.22.432170.

2.Socodato, R., et al., Daily alcohol intake triggers aberrant synaptic pruning leading to synapse loss and anxiety-like behavior. Sci Signal, 2020. 13(650): p. eaba5754.