



RESEARCH TOPIC MECM5

Investigating the gender-based molecular mechanisms underlying synaptic refinement in neurodevelopmental and neurodegenerative disorders.

Curriculum MECM standard

Research Area

Neuroscience

Laboratory name

Pharmacology and brain pathology

Research Supervisor

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Abstract

During postnatal development, the removal of excess synapses by microglia - the brain's resident immune cells - is a key process for proper neurodevelopment of the adolescent brain. Impaired synapse clearance has been associated with the development of neurodevelopmental disorders such as autism spectrum disorder (ASD) and attention deficit/hyperactivity disorder (ADHD). Interestingly, pathological reactivation of this same process is thought to occur in neurodegeneration. Of note, these disorders exhibit gender differences in both prevalence rates and symptomatology. While the causes of such gender diversity remain to be fully elucidated, several experimental lines of evidence suggest that gender differences in microglia may impact the development and outcome of these disorders. This project aims to characterize the gender differences underlying synaptic remodeling in adolescent mice and understand whether these mechanisms are dysregulated in preclinical models of ASD and Alzheimer's Disease. To this end, we will analyze gender differences in synapses and microglia in the brain of mouse models at different ages using morphological, molecular and functional techniques.

Main technical approaches

Preferred:

- Previous experience with primary neuronal cultures, immunocytochemistry techniques and confocal microscopy.
- Willingness to work with animals

Scientific references

1. De Bellis MD, Keshavan MS, Beers SR, Hall J, Frustaci K, Masalehdan A, Noll J, Boring AM. Sex differences in brain maturation during childhood and adolescence. *Cereb Cortex*. 2001 Jun;11(6):552-7. doi: 10.1093/cercor/11.6.552. PMID: 11375916.

2. Breach MR, Lenz KM. Sex Differences in Neurodevelopmental Disorders: A Key Role for the Immune System. *Curr Top Behav Neurosci*. 2023;62:165-206. doi: 10.1007/7854_2022_308. PMID: 35435643; PMCID: PMC10286778.
3. Prengel TM, Brunne B, Habiballa M, Rune GM. Sexually differentiated microglia and CA1 hippocampal synaptic connectivity. *J Neuroendocrinol*. 2023 May;35(5):e13276. doi: 10.1111/jne.13276. Epub 2023 May 11. PMID: 37170708.
4. Uhl M, Schmeisser MJ, Schumann S. The Sexual Dimorphic Synapse: From Spine Density to Molecular Composition. *Front Mol Neurosci*. 2022 Feb 18;15:818390. doi: 10.3389/fnmol.2022.818390. PMID: 35250477; PMCID: PMC8894598.
5. Lynch MA. Exploring Sex-Related Differences in Microglia May Be a Game-Changer in Precision Medicine. *Front Aging Neurosci*. 2022 Mar 31;14:868448. doi: 10.3389/fnagi.2022.868448. PMID: 35431903; PMCID: PMC9009390.

Type of contract

Position not supported by any scholarship or equivalent contract.