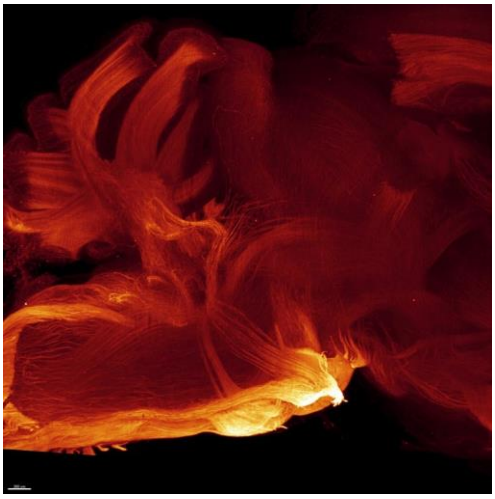
CiMUS International PhD Programme

1. Project title:

Role of estrogen in shaping brain neuromodulator circuits.

2. Research Project:

Estrogens are central regulators of physiological homeostasis and nervous system function. Periods of transition in estrogen production (such as puberty or menopause) are associated with an increased incidence of metabolic and psychiatric disorders. Thus, changes in adiposity, glucose homeostasis or mood disorders are commonly associated to those life stages. A growing body of evidence suggests that part of these effects are mediated by the direct actions of estradiol through modulatory neuronal populations in the brain. Previous studies showed that estrogen induces cellular, morphological and synaptic plasticity, via increased proliferation of neural progenitor cells, increase of dendritic spine density and synaptogenesis; however, it is largely unknown how estradiol affects to the long-range connectivity of neurons, potentially shaping the brain-wide architecture of neuromodulator circuits. This gap in our knowledge is largely due to the difficulties to study changes in adult brain connectivity at high resolution. This has recently changed with the development of 3D histology technologies which allow the detection, visualization and quantitatively analysis in a highthroughput and unbiased manner.



Light-sheet capture of long-range projecting axons in the brain of an adult mouse.

Building in our combined expertise in circuit plasticity mapping and estradiol brain actions, we will interrogate how estradiol shapes the connectivity of neuromodulator centers in the brain, focusing in the two main life stages where its action switches on and off: puberty and menopause. To this, we will use a series of genetically targeted technologies in different rodent models of those two life stages, combined with iDISCO-lightsheet microscopy whole-brain imaging, and advanced bioinformatic tools to automatically map axonal tracings at whole-brain scale. This will be combined with a series of pharmacological, metabolic, behavioral experimental paradigms to understand its pathophysiological implications on the metabolic and psychiatric disorders associated to puberty and menopause. Understanding the cellular effects of estrogen over different modulatory populations in the brain will open new avenues to understanding the etiology of endocrine-transition associated pathology.

Cofinanciado por la Unión Europea
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3. Job position description:

We are seeking a candidate enthusiastic about neural circuits and endocrinology. The candidate will join two laboratories led by specialists in neuroendocrinology and brain circuit plasticity, offering close and dynamic supervision, hands-on training, access to specialization courses, and access to a wide network of international collaborators. The successful candidate will receive training in state-of-the-art methods for 3D histology, animal experimentation, and molecular biology, among others.

Key Responsibilities: The candidate will implement methods for animal surgery, animal behavior, metabolic phenotyping, molecular biology, 3D histology (iDISCO, TRIC-DISCO), microscopy and image analysis.

Requirements for candidates: A BSc in Biology, Biochemestry, Pharmacy or similar, and a MSc in Neurosciences, Biomedical sciences or similar, are requested. The candidate is expected to be highly interested in Neurosciences. Previous experience in Python programming is a plus but is not requested.

4. Supervisor and Co-Supervisor

Name: Alba Vieites-Prado
Email: alba.vieites.prado@usc.es
Research group: Brain plasticity
Link to group website: https://cimus.usc.gal/gl/grupos/brain-plasticity

Selected publications on the topic:

- Houser G, **Vieites-Prado A**, …[+3], Renier N (AC). Organization and development of bilateral somatosensory feedback projections in mice. **iScience**. May 21;28(6):112725. DOI: 10.1016/j.isci.2025.112725. [Original Article]
- Gabanyi I (AC), Lepousez G, Wheeler R, **Vieites-Prado A**, …[+11], Eberl G (AC), Lledo PM (AC). 2022. Bacterial sensing via neuronal Nod2 regulates appetite and body temperature. **Science**, Vol 376(6590):eabj3986. DOI: 10.1126/science.abj3986. [Original Article]
- Kirst C*(AC), Skriabine S*, **Vieites-Prado A***, Topilko T, Bertin P, …[+5], Renier N (AC). 2020. Mapping the fine-scale organization and plasticity of the brain vasculature. **Cell**. Vol 180(4):780-795. DOI: 10.1016/j.cell.2020.01.028. *Co-First author [Original Article]
- **Vieites-Prado A,** Renier N (AC). 2021. TISSUE CLEARING AND 3D IMAGING IN DEVELOPMENTAL
- BIOLOGY. **Development**, Vol 148 (18): dev199369. DOI: 10.1242/dev.199369. [Review]

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Funding supporting the research proposed:

- ED431F 2025/37 - *Programa de Consolidación e Estruturación de Unidades de Investigación Competitivas, Proxectos de excelencia*. Entity: GAIN-Xunta de Galicia. Call: 2025. Budget: 65.000€. Role: PRINCIPAL INVESTIGATOR.
- PID2022-143059NA-100. *Activity-dependent structural rewiring of adult brain circuits* (ActiReWire). Entity: Spanish Research Agency, Ministerio de Ciencia e Innovación, Gobierno de España. Call: 2022. Timing: 2023-2026. Budget: 162.500€. Role: PRINCIPAL INVESTIGATOR.

Name: Ismael González-García
Email: ismael.gonzalez@usc.es
Research group: NeuRoMet group
Link to group website: https://cimus.usc.gal/es/grupo/neuroendocrine-regulation-metabolism

Selected publications on the topic:

- **González-García I** (CA), Xu Y (CA) (2025) Hypothalamic actions of estrogens in the regulation of energy and glucose homeostasis. **Rev Endocr Metab Disord**. DOI: 10.1007/s11154-025- 09994-1
- **González-García I**, García-Clavé E, Cebrian-Serrano A, (…) García-Cáceres C (2023) Estradiol regulates leptin sensitivity to control feeding via hypothalamic Cited1. **Cell Metabolism**. 35, 438-455. DOI: 10.1016/j.cmet.2023.02.004
- **González-García I*** (CA), Freire-Agulleiro O*, Nakaya N, (…) López M (CA) (2022) Olfactomedin
- 2 deficiency protects against diet-induced obesity. **Metabolism**. 129: 1-5. DOI: 10.1016/j.metabol.2021.155122 *Co-First author
- **González-García I**, Contreras C, Estévez-Salguero A, (…) López M (2018) Estradiol regulates energy balance by ameliorating hypothalamic ceramide-induced ER stress. **Cell Reports**. 25: 413-423. DOI: 10.1016/j.celrep.2018.09.038
- **González-García I**, Martínez de Morentin PB, Estévez-Salguero A, (…) López M (2018) mTOR signaling in the arcuate nucleus of the hypothalamus mediates the anorectic action of estradiol. **J. Endocrinol**. 238: 177-186. DOI: 10.1530/JOE-18-0190

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Funding supporting the research proposed:

- European Research Council, ERC-2025-STG. Reference: 101219072. Timing: 2026-2031.
- 1,498,325 €. Principal investigator
- Xunta de Galicia, Axudas do Programa de Consolidación e Estruturación de Unidades de Investigación Competitivas Ano 2024, Proxectos de Excelencia. Reference: ED431F 2024/14. Timing: 2024-2027. 90,000 €, Principal investigator
- Agencia Estatal de Investigación, Proyectos de Generación de Conocimiento 2022. Reference: PID2022-141115NA-I00. Timing: 2023-2026. 232,500 € + FPI Fellowship, Principal investigator