

GESINAS - ImmunoTools Award 2023



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Unmasking sex-linked patterns in neonatal immune-brain axis

The orchestration of brain immune homeostasis relies on a delicate interplay between the central nervous system and the peripheral immune system, facilitated by various blood-brain interfaces. These interfaces, including the meninges, blood-brain barrier (BBB), and choroid plexus, collectively form a complex network that regulates the passage of immune cells and molecules into and out of the brain. The meninges, as a protective membrane enveloping the brain and spinal cord, serve as both a physical barrier and an active participant in immune surveillance. The BBB, a specialized endothelial barrier, meticulously regulates the passage of immune cells and molecules, ensuring a controlled immune environment within the central nervous system. Simultaneously, the choroid plexus, nestled within the brain's ventricular system, acts as a pivotal gateway, influencing the cerebrospinal fluid's immune composition and facilitating communication between the peripheral immune system and the brain. Likewise, it has become clear that sex exerts a profound biological influence on development, extending its impact far beyond reproductive functions. Indeed, males are at higher risk for developmental disorders including autism and early onset schizophrenia, diseases associated with neonatal infections and neuroinflammation. The central hypothesis of this project is that inherent sex differences in neonatal immune-vascular cell trafficking increases male vulnerability to neurodevelopmental disorders in response to immune activation. The rationale and long-term goal for this work is to elucidate sex differences in the immune-vascular profile during brain development, to better understand the aetiology of neurodevelopmental disease. It is crucial to further characterize sex differences in immune-vascular axis across the postnatal periods in order to add valuable insight into the how innate immune cells influence sex specific brain development. This will be addressed by three aims. 1) Quantify the immune cell composition of the meninges, brain, and choroid plexus neuropil (CD11b⁺Gr-1⁺), infiltrated blood-derived macrophages (CD11b⁺CD45^{high} - different from microglia CD11b⁺CD45^{low}), mast cells (CD117), and dendritic cells (CD45, MHC-II), antigen presenting cells (CD80, TCR α/β), markers of lymphocytes and monocytes (CD48), leucocytes (CD4⁺, CD8⁺) during the neonatal period. Will be also accessed the levels of cytokines (TNF- α and IL-6) by ELISA and important growth factors (GM-CSF). 2) Evaluate BBB maturation and integrity in neonatal mice, comparing between males and females. This will be assessed by investigating sex-specific variations in BBB integrity, the arrangement of endothelial tight junctions,

markers related to immune cell adhesion and extravasation, and examining the correlation between BBB permeability and immune cell migration. 3) Determine the effect of neonatal infection, using lipopolysaccharide (LPS) as an infection model on BBB function and immune cell trafficking (same as in aim 1 and 2) impact in the developing brain, maintaining sex as a factor. LPS is a bacterial endotoxin which promotes secretion of proinflammatory cytokines and activates the immune response.

Collectively, this study will contribute to delineating the influence of sex on immune cells at the brain-barrier borders on developmental processes and elucidate how these factors may contribute to both advantageous and pathological responses during the course of development and neuroinflammation. The **ImmunoTools** reagents will prove invaluable for executing this research endeavours.

GESINAS-ImmunoTools-Award - In my journey, I go beyond the confines of the laboratory, driven by a fervour to communicate science and bridge the gap between intricate concepts and the wider public. My active engagement in outreach activities is centred on inspiring curiosity and fostering understanding. I have made substantial contributions to sessions promoting science among young students, participating in impactful events such as *Escola de Verão* ICNAS-CIBIT 2023, European Researchers' Night, and Brain Awareness Week. My commitment extends to diverse committees and organizations. Serving as a Board Member at the Office for Teaching, Education, and Research in Seattle Children's Research Institute, I've assumed roles like Social Media Chairperson and Liaison at the University of Washington's Postdoctoral Association. Moreover, my dedication as Communications Co-Chair at Women in Bio spans several years, where I have passionately encouraged young women to embark on exciting journeys in science.

GESINAS - ImmunoTools AWARD for Vanessa Coelho-Santos

includes 20 reagents

FITC - conjugated anti-mouse CD8, CD48, CD45, TCR α/β

PE - conjugated anti-mouse CD11b, CD19, CD80, CD117, goat anti-mouse

APC - conjugated anti-mouse CD4, Gr-1, NK-cells

non-conjugated anti-mouse GM-CSF, MHC-II, Erythroid cell, ICAM

Mouse ELISA-set: TNF-alpha

[DETAILS](#) more [AWARDS](#)