Piano Nazionale di Ripresa e Resilienza (PNRR), Missione 4 "Istruzione e ricerca" – Componente 2 "Dalla ricerca all'impresa", Investimento 1.3 "Partenariati estesi"
Iniziativa finanziata dall'Unione europea –- NextGenerationEU.
A multiscale integrated approach to the study of the nervous system in health and disease (MNESYS)
Codice progetto MUR: **PE00000006** – CUP UNINA: **E63C22002170007**

Project title: Neuronal control of intestinal barrier function

Tutor: Prof Gabriella Aviello

Intestinal homeostasis relies on the synergistic action of multi-layered defense mechanisms, involving mucus production, epithelium integrity, immune tolerance, and redox balance[1]. Over the past few decades, research has established that substantial communication exists between the enteric nervous system (ENS), situated in the intestinal wall, and several components of the mucosa. This neuro-immune interaction is emerging as crucial for the whole body's health[2]; indeed, a wide range of intestinal and extraintestinal diseases are associated with ENS dysfunction, including monogenic neuropathies, early-onset neurodevelopmental disorders, and neurodegenerative diseases. Recent single-cell RNA sequencing of human and mouse colons has revealed distinct genetically-identified classes of enteric neurons[3]. However, our understanding of the role of ENS in regulating gut barrier function is incomplete due to longstanding challenges related to the rare, fragile, and isolated nature of these neurons. We have previously demonstrated that an altered redox state in the gut influences mucus production[4]. Preliminary data leading up to this proposal suggest that, in a model of neurodevelopmental disorder, the gut barrier is dysfunctional, and reduced mucus production seems to be associated with an altered redox state. Using a multi-model approach, we propose a multidisciplinary project involving neuroscience, immunology, and pharmacology to study the neuronal control of gut mucosal defense mechanisms and the role of the redox balance in preserving the crosstalk between the ENS and the mucosa. This project will benefit from longstanding collaborations with internationally recognized research groups in Ireland and the UK, thanks to which the Ph.D. student will benefit from additional research support and training opportunities. The research enabled by this project has the potential to reveal an important conundrum in the neuronal control of gut barrier function. Thus, disclosing the mechanisms regulating neuro-immune interaction might identify novel therapeutic approaches to preserve or re-establish gut homeostasis.

References

1. Aviello G, Knaus UG. NADPH oxidases and ROS signaling in the gastrointestinal tract. Mucosal Immunol. 2018 Jul;11(4):1011-1023. doi: 10.1038/s41385-018-0021-8.
2. Wang H et al. Enteric neuroimmune interactions coordinate intestinal responses in health and disease. Mucosal Immunol. 2022 Jan;15(1):27-39. doi: 10.1038/s41385-021-00443-1.
3. Morarach K et al. Diversification of molecularly defined myenteric neuron classes revealed by single-cell RNA sequencing. Nat Neurosci. 2021 Jan;24(1):34-46. doi: 10.1038/s41593-020-00736-x.
4. Aviello G et al. Colitis susceptibility in mice with reactive oxygen species deficiency is mediated by mucus barrier and immune defense defects. Mucosal Immunol. 2019 Nov;12(6):1316-1326. doi: 10.1038/s41385-019-0205-x.