PROGETTO 1/ PROJECT 1

Supervisore/*Supervisor:*	Dr. Gianvito Martino
Titolo/*Title:*	Unveiling the Consequences of Neural Precursor Cell Dysfunction in Aging.
Corso */PhD Course*	Scienze Cognitive e Comportamentali
Curriculum:	
Link alla pagina personale OSR/UNISR/ *Link to OSR/UniSR personal page:*	

Descrizione del progetto/Project description (Tra i 2.000 e 3.000 caratteri spazi inclusi/ *Number of characters, including spaces*: 2.000 - 3.000):

Recent findings have revealed that adult neural precursor cells in the subventricular zone have the ability to regulate not only neurogenesis in the olfactory bulbs but also maintain striatal homeostasis in pathological conditions. Using a transgenic mouse model, we observed significant morphological and functional changes in striatal neurons upon selective ablation of these precursor cells, suggesting their crucial role in the proper functioning of decision-making tasks involving fast-spiking interneurons. Interestingly in the process of aging, it is known that a gradual reduction in neurogenesis and in NPC number, leading to a globally reduced functioning of the neural stem cell niche, occurs.

This project investigates the dysfunction of neural precursor cells (NPCs) in the aging brain, aiming to understand the mechanisms of age-related cognitive decline and explore strategies for rejuvenation and improved brain health.

Aims of this project include the characterization of alterations in the aging striatum adjacent to the neurogenic niche, assessing morphological, neurophysiological changes, and their impact on behavior and brain functioning. Further we will investigate molecular changes in the aging striatum and its relationship to the neurogenic niche using scRNA-seq data analysis, focusing on NPC-secreted signaling molecules and signaling alterations. Finally, we will explore rejuvenation techniques such as neural stem cell transplantation and gene therapy interventions to address NPC dysfunction and restore the neurogenic niche, identifying molecular changes associated with rejuvenation.

This project enhances understanding of NPC dysfunction in the aging brain, reveals molecular mechanisms of age-related changes, and explores rejuvenation strategies. Findings could lead to interventions improving cognitive skills, reversing aged brain dysfunction, and potentially benefiting other neurodegenerative disorders.

This project aims to advance our understanding of NPC dysfunction in the aging brain, elucidate the underlying molecular mechanisms of age-related changes, and explore rejuvenation strategies. The findings from this research have the potential to have significant clinical implications. By characterizing age-related changes and investigating

the molecular mechanisms involved, this project seeks to shed light on the dysfunctional processes occurring in NPCs within the aging brain. Understanding these mechanisms can provide valuable insights into the development of targeted interventions.

In summary, the objectives of this project, which include characterizing age-related changes, investigating molecular mechanisms, and exploring rejuvenation strategies, highlight its translational orientation. The research findings have the potential to advance our understanding of NPC dysfunction in the aging brain, identify molecular targets for intervention, and pave the way for future clinical applications that can enhance cognitive function and alleviate age-related brain disorders.

Competenze che deve acquisire lo studente/Skills to be acquired by the student (Max 600 caratteri spazi inclusi/ *Number of characters, including spaces*: max 600):

Handling transgenic mouse lines, administering in vivo injections using a stereotactic technique, conducting confocal microscopy, immunohistochemistry, and immunofluorescence staining, performing flow cytometry, rt-PCR, RNA-seq, and bioinformatics analysis, carrying out PCR, administering compounds and drugs in vivo. Maintaining a thorough understanding of the latest literature in the field, constructing hypotheses, developing experimental plans to investigate these hypotheses, writing regular scientific reports, analyzing and discussing results, and critically evaluating published papers (e.g., Journal Club).

Bibliografia/References (max. 15)

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-Butti E, Bacigaluppi M, Rossi S., Cambiaghi M, Bari M., Cebrian Silla A, Brambilla E, Musella A, De Ceglia R, Teneud L, De Chiara V, D'Adamo P, Garcia-Verdugo JM, Comi G, Muzio L, Quattrini A, Leocani L, Maccarrone M, Centonze D and Martino G. (2012) Subventricular zone neural progenitors protect striatal neurons from glutamatergic excitotoxicity. Brain

-Butti E, Cusimano M, Bacigaluppi M, Martino G. (2014) Neurogenic and non-neurogenic functions of endogenous neural stem cells. Front Neurosci

-Friedman A, Homma D, Bloem B, Gibb LG, Amemori KI, Hu D, Delcasso S, Truong TF, Yang J, Hood AS, Mikofalvy KA, Beck DW, Nguyen N, Nelson ED, Toro Arana SE, Vorder Bruegge RH, Goosens KA, Graybiel AM.(2017) Chronic Stress Alters Striosome-Circuit Dynamics, Leading to Aberrant Decision-Making. Cell

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