European School of Molecular Medicine

YOUR DETAILS

* Name & Surname

Giuseppe Testa

* Affiliation HT

PHD PROJECT DETAILS

* Title of the proposed project

Dissecting gene-environmental interactions in human brain development through advanced organoid modelling

* Short description of the project (up to 300 words)

The development of the human brain is characterized by highly complex, specific and coordinated series of biological events that give rise to a variety of cell populations, organized in intricate and interconnected brain structures. To investigate these processes, this project will employ human pluripotent stem cell lines reprogramming to generate models of neural development. Furthermore, (epi)genome engineering techniques will be utilized to manipulate and study the impact of genetic and environmental factors on brain development. Cortical brain organoids modelling will serve as a modelling approach for overcoming the inaccessibility of the spatial and temporal dynamics of human neurodevelopment, recapitulating its most salient features. Integrating these experimental models with single-cell omics we will investigate the molecular mechanisms of human neurodiversity and how genetic and environmental factors interact in the context of sensitive windows of neurodevelopment. This project will leverage comprehensive atlases of the human brain and brain organoids at the single cell level, relying on both publicly available and in-house produced single cell multi omics data (transcriptomics, spatial transcriptomics, epigenomics, and metabolomics), using advanced computational approaches for data integration and analysis. We aim to bridge cellular dynamics to neurobehavioral phenotypes through analysis of developmental trajectories. We will study brain organoids multi-omic data from cohorts of neurodiverse individuals moving beyond traditional diagnostic categories

* Indicate the main research area for the project described above - Neurobiology

If needed indicate a second research area for the project described above -
Computational biology

* Provide up to 3 key words for project:

Neurodiversity; Organoid modelling; Developmental trajectories

YOUR LABORATORY ACTIVITIES DETAILS

* Main topic/s of the lab

High definition disease modelling

* Short description of the lab activity (up to 500 words)

We focus on the dynamics of brain disorders, with a strong emphasis on human experimental models and straddling multiple scales of analysis from single cell resolution to organismal function, working in close integration with national and international deeply phenotyped cohorts that provide unique edges for the study of gene/environment interactions in mental health vulnerability and resilience. Our research environment includes transformative facilities encompassing reprogramming, editing and brain organoids automation, state of the art genomics and microscopy infrastructures along with a HT-wide architecture of high performance computing (HPC) attuned to the needs of contemporary computational biology.

* Recent bibliography (max 5 references)

Caporale, N. et al. Multiplexing cortical brain organoids for the longitudinal dissection of developmental traits at single-cell resolution. **Nature Methods** 1–13 (2024).

Bosone, C. et al. A polarized FGF8 source specifies frontotemporal signatures in spatially oriented cell populations of cortical assembloids. **Nature Methods** 1–13 (2024).

He, Z. et al. An integrated transcriptomic cell atlas of human neural organoids. **Nature** 635, 690–698 (2024).

López-Tobón, A. et al. GTF2I dosage regulates neuronal differentiation and social behavior in 7q11.23 neurodevelopmental disorders. **Science Advances** 9, eadh2726 (2023).

Caporale, N. et al. From cohorts to molecules: Adverse impacts of endocrine disrupting mixtures. **Science** 375, eabe8244 (2022).

Cheroni, C. et al. Benchmarking brain organoid recapitulation of fetal corticogenesis. **Transl. Psychiatry** 12, 520 (2022).

* Group composition: total members, and roles distribution (PhD, postdoc, technician, etc.)

7 PhD student, 7 postdocs, 3 technicians, 1 staff scientist

Institutional page link

https://humantechnopole.it/en/research-groups/testa-group/

Lab website link, if any

https://github.com/GiuseppeTestaLab

Social media links, if any

https://x.com/gtesta72

If you prepare a video to promote your lab/project, please include the link below