European School of Molecular Medicine

2025 summer call PhD selections

AVAILABLE POSITIONS

Principal Investigator	Giuseppe Testa
Affiliation	Human Technopole
Title of the proposed project:	Dissecting the intergenerational and neurodevelopmental impact of environmental perturbations through organoid modelling
Short description of the project	Whether and how the impact of environmental exposures can be inherited, with parental environments shaping phenotypes across generations independent of DNA sequence, is a fundamental question in biology with far-reaching implications for human health. Despite evidence of such epigenetic inheritance in animals, the mechanisms and relevance to humans remain elusive due to lack of (i) multi-generational human data, and (ii) access to germ cells and tissues from exposed individuals. Considering the paradigmatic case of the heritable impact of the exposure to endocrine disruptors (EDC), a widespread and hazardous class of chemicals that interfere with hormonal signaling causing a wide range of adverse health effects, including adverse neurodevelopmental outcomes, we are overcoming these challenges by leveraging (i) a unique multigenerational human cohort, SELMA (Bornehag et al., 2021; Caporale et al., 2022), where we are measuring the exposure to EDC and relating it to quantified neurodevelopmental outcomes (ii) an innovative hiPSC-derived in vitro system we recently developed (Stucchi et al., 2025) to model epigenetic dynamics across generations, thus making epigenetic inheritance tractable in humans. In the context of a multi-disciplinary and international consortium, the student will expose this in vitro model (namely hiPSC differentiated into gametes precursors, converted back into a pluripotent state and then further differentiated in neural organoids) to mixtures of EDCs at epidemiologically relevant concentrations derived from the SELMA cohort and profile transcriptome and selected epigenetic layers in each developmental stage of the above in vitro system to assess, by performing multi-omics computational analysis, what transcriptomic and epigenetic changes are induced in the germline by the EDCs and which are inherited and maintained in the next generation and with what neurodevelopmental consequences. The identified targets will be validated and the underlying mechanisms dissected by precision epigenome editing (Policarpi et al., 2024). Carrying out this project, the student will develop expertise in the areas of stem cell biology, human germ cells and neurobiology, epigenome editing, experimental toxicology and computational biology.
Main research area for the project	Neurobiology
Second research area for the project	Computational Biology
3 key words for project	Epigenetic inheritance; Organoid modelling; Neurodevelopment
Main topic/s of the lab	High definition disease modeling

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Short description of the lab activity	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	Stucchi, S. et al. High resolution multi-scale profiling of embryonic germ cell-like cells derivation reveals pluripotent state transitions in humans. **biorXiv** (2025) Caporale, N. et al. Multiplexing cortical brain organoids for the longitudinal dissection of developmental traits at single-cell resolution. **Nature Methods** 1–13 (2024). He, Z. et al. An integrated transcriptomic cell atlas of human neural organoids. **Nature** 635, 690–698 (2024). 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). Cheroni, C., Caporale, N. & Testa, G. Autism spectrum disorder at the crossroad between genes and environment: contributions, convergences, and interactions in ASD developmental pathophysiology. **Molecular Autism** 11, 69 (2020).
Group composition	8 PhD student, 7 postdocs, 3 technicians, 1 staff scientist
Institutional page link	https://humantechnopole.it/en/research-groups/testa-group/
Lab website link	https://github.com/GiuseppeTestaLab
Social media links	https://x.com/gtesta72