



UNIVERSITÀ DEGLI STUDI DI MILANO

D-MEM



PhD-UNIMI

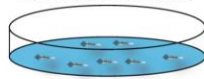
Doctorate program
Milan
EXPERIMENTAL
MEDICINE

In vivo zebrafish model to dissect novel pathological pathways and potential therapies for congenital highly disruptive diseases

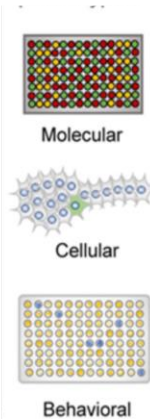
Whole Exome Sequencing



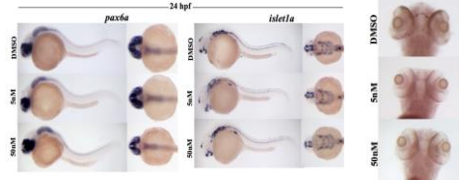
Zebrafish disease models



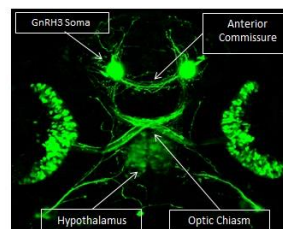
Analysis of phenotypes



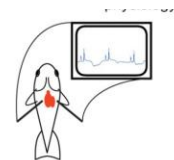
Whole-Mount In Situ Hybridization



High resolution imaging



Physiological assays



So far, zebrafish has been used primarily as a model system to study vertebrate development, and most zebrafish endocrine research has been concerned with the development of the different endocrine axes, which are already settled within the first days of development. Research of these early events can take full advantage of major strengths of the zebrafish system: the small size and transparency of the embryos and larvae and their accessibility for forward genetics, chemical compound screening, in vivo imaging, and rapid antisense-mediated gene knockdown. Besides human genetics has revealed that impaired endocrine function in many human patients originates from developmental defects. Thus, studying endocrine development can be unquestionably crucial for a better understanding of endocrine deficits during later human life. Recent studies revealed that crucial principles and players of endocrine axes previously identified in mammals are well established and conserved in zebrafish. Thus, the present PhD project aims to use zebrafish as a model organism to dissect novel pathological pathways and potential players for congenital endocrine diseases.

Specific Aims of the project:

- 1) Zebrafish as tool for screening new candidate genes in congenital HD diseases by forward genetics
- 2) Zebrafish as a model organism for investigating EDCs effect in thyroid and gonads

Bibliography:

- Löhr H et al., **Zebrafish in endocrine systems: recent advances and implications for human disease**. doi: 10.1146/annurev-physiol-012110-142320. PMID: 21314433.
- Marelli F, Persani L. **How zebrafish research has helped in understanding thyroid diseases**. doi: 10.12688/f1000research.12142.1. PMID: 29263787; PMCID: PMC5730863.
- Rurale G et al., **Short-Term Exposure Effects of the Environmental Endocrine Disruptor Benzo(a)Pyrene on Thyroid Axis Function in Zebrafish**. doi: 10.3390/ijms23105833. PMID: 35628645; PMCID: PMC9148134

Candidate specific requirements:

Experience in endocrine regulatory mechanisms of reproduction and/or thyroid development, whole exome sequencing technique and analysis, molecular biology techniques for gene expression studies, zebrafish model

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