Studies of Endocrine disrupter pollutants in zebrafish embryos: Contribution of genetically modified models (transgenic, Knock out) to predict toxicological impacts.

Description
Endocrine disruptors are molecules that can affect the expression of hormone-regulated genes. Early exposures during developmental stages are likely to lead to long term effects. We previously highlighted environmental pollutant-linked transcriptional dysregulation of genes involved in the hormonal biosynthesis in the central nervous system during the embryonic development of zebrafish (Brion et al., 2012; Vosges et al., 2012; Vosges et al., 2010; Cano-Nicolau et al., 2016). The question of the long term consequences of these pollutants on central estrogenic signaling remains to be explored. This thesis aims at understanding how the developmental regulation of estrogen receptors and cerebral aromatase expression affect the long term organization of the central nervous system, using zebra fish models. Such an approach is made possible thanks to the recent development of knockout lines for the ERs receptors and Cyp19a1b available in our laboratory. The prediction of developmental effects also implies integrative approaches combining spatio-temporal analysis of the expression of target genes and physiological process modulated by the presence of neuro-steroids. The candidate will also work toward the integration of these biological and toxicological data into mathematical models (quantitative Adverse Outcome Pathway, qAOP) to predict the (eco) -toxicological impacts of endocrine disruptors on human and environmental health (collaboration with F. Bois, Modeling Unit in France, toxicology and ecotoxicology, as part of the EU-ToxRisk project). The thesis will be co-supervised by Francois Brion (Ineris) and Thierry Charlier (University of Rennes 1, IRSET).

Location
INERIS (National Institute of Industrial Environment and Risks (http://www.ineris.fr ) is a Public Institution of Industrial and Commercial (EPIC) placed under the supervision of the Ministry of Ecological and Solidarity Transition in FRANCE. Its mission is to carry out or commission studies and research to evaluate and prevent accidental or chronic risks to humans and to the environment, and more particularly those risk related to industrial installations, chemical substances and underground operations. The head office of INERIS is located in the Verneuil-en-Halatte, on a park of more than 40 hectares in a privileged green setting, 40 minutes from Paris and 10 minutes from Senlis / Chantilly (A1) - 30 minutes from Paris Nord + shuttle bus.

This project will be developed in collaboration with IRSET. Irset is a joint research unit of the Inserm institute, Rennes 1 University and the EHESP - School of Public Health, in partnership with the Universities of Angers and the French Antilles, the CNRS, and the Teaching Hospitals of Rennes, Angers and Pointe-à-Pitre. Its mission is to study the biological processes and the environmental factors (whether chemical, biological, physical, social and cultural, occupational, geographical or economic) that affect human health, and to help public health authorities make informed decisions on the basis of scientific data.

Scientific and technical skills required by the candidate
The potential candidate should have a master or equivalent in biology. Previous experience in laboratory setting is mandatory (Practical knowledge in cell biology, biochemistry and/or physiology).

Application: Application, including transcripts, CV and motivation letter should be sent to Francois Brion (Francois.BRION@ineris.fr) and Thierry Charlier (thierry.charlier@univ-rennes1.fr) or can be uploaded on the Ineris web site: https://www.abg.asso.fr/fr/candidatOffres/show/id_offre/77264