**Inserm U1103, CNRS UMR6293–Université Clermont Auvergne : Laboratoire Génétique Reproduction & Développement (C. Vaury)**

**PhD Supervisor:** David Volle (DR2 Inserm, HDR)

david.volle@uca.fr

**Identification of the molecular mechanisms leading to the transgenerational effects of exposure to bile acids.**

So far little is known about the mechanisms responsible for the transmission over several generations of pathologies induced by endo- or xeno-biotics. Our data in mice show transmission of metabolic disorders over two generations in the descendants of fathers exposed to bile acids. In that context, the objective of this project is to understand the cellular mechanisms leading to the transmission of alterations over several generations by focusing on germ cell homeostasis. We will work with a powerful genetic model, the nematode C. elegans. We will study the impacts of bile acid treatments, using the nematode bile acid-like moleculcules, named dafachronic acids, on population size, nematode growth, lifespan, fertility and the impact on descendants. We will validate the involvement of the various players selected by a gene candidate approach, focusing particularly on those involved in the control of metabolism or epigenetic processes. The impacts of these candidates will be defined through a genetic screen (siRNA) that will be supported by approaches in histology, biochemistry and molecular biology. For some candidates, we will validate their initial impact on germ cell lines of C. Elegans and mice. This project will identify the role of bile acids in the paternal and maternal transmission of pathologies, in order to understand the programming of the transmission of pathologies that can affect the health or quality of life of future generations

**Baptissart et al.** (2018). [Multigenerational impacts of bile exposure are mediated by TGR5 signaling pathways.](https://www-ncbi-nlm-nih-gov.gate2.inist.fr/pubmed/30443025) ***Sci Rep***. PMID: 30443025

**Baptissart et al.** (2014). Bile acids alter male fertility through TGR5 signaling pathways. ***Hepatology***. PMID: 24798773.