Postdoctoral Position « Environment-Metabolism-Spermatogenesis-Pathophysiology-&-Inheritance» Institute Genetic, Reproduction & Development, Inserm U1103, CNRS UMR 6293, Université Clermont Auvergne. 28 place Henri Dunant, 63001 Clermont-Ferrand Cedex, France https://www.gred-clermont.fr/directory/team/en/team-13-environment-spermatogenesispathophysiology-and-inheritance/

Duration: 2 to 3 years Starting date: To define due to international confinement. Contact: david.volle@inserm.fr or david.volle@uca.fr

The Volle lab investigates the mechanisms that lead to testicular pathophysiologies such as fertility disorders or testicular germ cell cancers in the context of altered metabolism and/or of exposures to environmental molecules. In order to perform such work, we use pharmacological approaches combined with specific genetic models such as C. elegans, transgenic mice and culture cell of tumor cell lines.

<u>The background of the project.</u> The incidence of testicular germ cell tumors (TGCT) has increased in the last decades. TGCTs are the most common solid cancers in young adults. Moreover, 10 to 20% of patients have forms that are resistant to treatment.

It is thus essential to improve the treatments in order to provide better care to people with cancers that are resistant to current treatments. This is even more important as it has been clearly established that patients who received chemotherapy or radiotherapy are at higher risk of developing a secondary malignant tumor. To answer the key question of treatment efficiency, there is a need to better understand the etiology of TGCT, which remains poorly known.

In order to explore the questions of TGCT biology *and their sensitivity to chemo-drugs*, we have started a new field of research in our team focusing on nuclear receptors, which has been associated with the development of cancers.

Description of the project. To achieve this project, we will use genetically modified mice that are predisposed to TGCT and testicular organotypic culture system. In addition, we will develop single cell approach to decipher the molecular mechanisms involved in tumor development, aggressiveness or chemo-resistance. This analysis will be key to study switches of homeostasis and metabolism between normal to tumor cells. Through these models combined with high-throughput approaches (such as RNAseq), candidate will analyze the biology of germ cell tumors (initiation, progression and invasion) as well as their sensitivity to therapy in order to decipher the roles of targeted signaling pathways. In addition, candidate will use *C. elegans* as a powerful genetic model to validate candidates defined in mouse models. This transposition will be useful to develop new model to study germ cell tumor in regards with the 3R ethical rules.

Expected results. The validation of these models will allow us to first extend their use in the context of TGCT biology in order to provide mechanistic connections between selected signaling pathways and TGCT etiology. Secondly, this work should provide new insights for providing novel prognostic markers and potential therapeutic targets.

<u>Candidates.</u> Qualified candidates should be self-driven and highly motivated individuals with an established track record of success, including first author publications.

Experience in cancer biology, developmental biology, reproductive biology, cell and molecular biology, or related field(s) is desirable. The candidate must have experience on genetically modified mouse models and/or *C. elegans* biology, cell culture, single cell and molecular biology techniques (RNAseq, etc.), bioinformatics skills.

For prompt consideration, please email the following items to Dr. David VOLLE: <u>david.volle@inserm.fr</u> *A one-page cover letter describing areas of research interests and career goals

*Curriculum vitae with bibliography

*Contact information for 3 references