



**Master 2 Reproduction et Développement**  
**Stage de recherche 2026-2027**

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**Prénom et NOM du/de la responsable d'équipe : David VOLLE**

**Intitulé de l'équipe d'accueil :**

**Environnement, Métabolisme, spermatogénèse, pathophysiologie et hérédité**

**Site internet de l'unité : [INSTITUT GENETIQUE, REPRODUCTION & DEVELOPPEMENT - iGReD](#)**

**Prénom et NOM du/de la directeur-riche du Laboratoire ou de l'Unité : Krzysztof JAGLA**

**Adresse du Laboratoire ou de l'Unité :**

28 place Henri Dunant  
63001, Clermont-Ferrand, FRANCE

**Résumé du thème de recherche de l'équipe d'accueil (une dizaine de lignes maximum) :**

These last decades, links between liver diseases and male fertility disorders have been highlighted. Interestingly, some reports have drawn attention to the regulation of liver and testis functions via a bi-directional dialog. However, this dialog between liver and testis has not been fully studied so far. Over the last years, liver agents, such as bile acids have been demonstrated as key regulators of testicular homeostasis and male fertility. Our project aims to understand how changes of local environment of the spermatogonial stem cell niche, due to xenobiotics and/or modulations of BA, could define their fate, and irreversibly alter their homeostasis leading to pathologies such as infertility and testicular germ cell tumors (TGT).

**Titre du projet de stage :**

Identification of the crosstalk between metabolic and epigenetic processes in stem cell homeostasis and their involvement in fertility disorders and/or testicular cancer as well as in chemo-resistance.

**Projet de stage : (une vingtaine de lignes maximum).** Understanding the mechanisms that drive stem cell fate decision is of major importance with clinical in the etiology of diseases such as infertility or cancer as well as in regenerative medicine and tissue rehabilitation after cancer therapy. Growing evidence show that metabolic pathways influence epigenetic changes associated with lineage commitment, specification, and self-renewal. In the other way round, epigenetic is also important in metabolic decision. However, the interplay between metabolism and epigenetics in deciding the fate of spermatogonial stem cells (SSC) remains largely unexplored. The study of SSC that self-renew while giving rise to



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differentiated germ cells appears as a useful strategy to decipher the mechanisms involved in stem cell homeostasis associated with cell fate specification and outcome of potential diseases. Our goal is to decipher the metabolic-epigenetic interplays through the study of "candidate genes" identified using RNAseq approaches. We will take advantage of genetically engineered mouse models in combination with cell culture experiments either treated by pharmacological agents or modified by genome editing (Crispr/CAS9). Our objectives are: 1/ to analyze the role of yet unidentified genes in the etiology of fertility disorders or germ cell cancers; 2/ to study the interaction between metabolic-epigenetic pathways in germ cell homeostasis and chemoresistance; and 3/ to transpose these data on human. The data obtained will shed light on the gene networks that drive stem cell fate and help to better understand the interaction between cellular metabolism and epigenetics for regulating stem cell homeostasis, cell state and differentiation capacity. This work should allow defining biomarkers of stem cell alterations leading to germ cell cancer, fertility disorders and/or transgenerational inheritance of disease to offspring. This project might also offer opportunities to develop new therapeutics in regenerative medicine following anti-cancer treatment.

**Techniques mises en œuvre par le stagiaire :**

***Rodent models, cell culture, viral transduction, transfection, SSC transplantation, histology/Imagery, molecular biology.***

**Publications du Responsable de stage au cours des 5 dernières années :**

**2025**

- RC Cattley, AJ De Roos, D Mandrioli, N Pearce, A Pronk, A Soshilov, SO Abarikwu, I Baldi, DB Barr, LEB Freeman, S Bortoli, A Connolly, MA Dalvie, MJ Ferreira, MB Genter, L Le Hégarat, S Lorenzetti, JR McLaughlin, P Møller, CC Montagner, HCS Silveira, T Toyoda, **DH Volle**, L Benbrahim-Tallaa, A de Conti, C Facchin, AT Kunzmann, F Madia, E Pasqua, ML Aix, X Deng, RA Dongoran, MT Olanipekun, E Suonio, S Viegas, H Mattock, R Wedekind, MK Schubauer-Berigan. Carcinogenicity of atrazine, alachlor, and vinclozolin. *Lancet Oncol.* 2025 Nov 21:S1470-2045(25)00702-8. doi: 10.1016/S1470-2045(25)00702-8. Online ahead of print. PMID: 41285132 No abstract available.
- L Sauzéat<sup>C</sup>, M Moreira, H Holota, C Beaudoin, **DH Volle**. Unveiling the hidden impact of long-term metal-rich volcanic pollution on male reproductive functions using isotope metallomics. *Environment International.* 2025 Apr:198:109388. doi: 10.1016/j.envint.2025.109388. Epub 2025 Mar 19.
- E Martinot, H Holota, A de Haze, C Beaudoin<sup>C</sup> and **DH Volle**\*. The Pregnane-X Receptor regulates steroid synthesis in mouse Leydig cells. *Frontiers in Endocrinology.* 2025 May 6;15:1430781. doi: 10.3389/fendo.2024.1430781. eCollection 2024.



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- M [Garcia](#), H Holota, A De Haze, JP Saru, P Sanchez, E Battistelli, L Thirouard, M Monrose, G Benoit, **DH Volle\***, C Beaudoin \*. Alternative splicing is an FXR $\alpha$  loss-of-function mechanism and impacts energy metabolism in hepatocarcinoma cells. 2024, **The Journal of biological chemistry** - pp 108022 (**co-last, co-corresponding**)

**2024**

- Monrose M, Holota H, Martinez G, Damon-Soubeyrand C, Thirouard L, Martinot E, Battistelli E, de Haze A, Bravard S, Tamisier C, Caira F, Coutton C, Barbotin AL, Boursier A, Lakhil L, Beaudoin C and **Volle DH\***. Constitutive Androstane Receptor Regulates Germ Cell Homeostasis, Sperm Quality, and Male Fertility via Akt-Foxo1 Pathway. 2024, **Advanced science (Weinheim, Baden-Wurtemberg, Germany)** - pp e2402082
- H Holota, A De Haze, E Martinot, M Monrose, JP Saru, F Caira, C Beaudoin\* and **DH Volle\***. Identification of the Role of TGR5 in the Regulation of Leydig Cell Homeostasis. 2022, **International journal of molecular sciences**, Dec 6;23(23):15398. doi: 10.3390/ijms232315398.
- L Sauzéat\*, J Eychenne, L Gurioli, M Boyet, DE Jessop, R Moretti, M Monrose, H Holota, C [Beaudoin](#) & **DH Volle**. Metallome deregulation and health-related impacts due to long-term exposure to recent volcanic ash deposits: New chemical and isotopic insights. 2022, **The Science of the total environment**, vol. 829-pp 154383, 022 Jul 10:829:154383. doi: 10.1016/j.scitotenv.2022.154383.

**2022**

- H. Holota, A. De Haze, E. Martinot, M. Monrose, JP Saru, F. Caira, C. Beaudoin, **DH Volle\***. Identification of the Role of TGR5 in the Regulation of Leydig Cell Homeostasis. **International journal of molecular sciences**. 2022 Dec 6;23(23):15398. doi: 10.3390/ijms232315398.
- L. Thirouard, H. Holota, M. Monrose, M. Garcia, A. de Haze, C. Damon-Soubeyrand, Y. Renaud, JP. Saru, A. Perino, K. Schoonjans, C. Beaudoin, **DH Volle\***. Identification of a Crosstalk among TGR5, GLIS2, and TP53 Signaling Pathways in the Control of Undifferentiated Germ Cell Homeostasis and Chemoresistance. **Adv Sci (Weinh)**. 2022 Apr 18:e2200626. doi: 10.1002/advs.202200626. Online ahead of print. PMID: 35435331 (IF 16.806).
- L. [Sauzeat](#), J. [Eychenne](#), L. Gurioli, M. Boyet, D. Jessop, R. Moretti, M. [Monrose](#), H. [Holota](#), C. [Beaudoin](#) and **DH Volle**, “Metallome deregulation and health-related impacts due to long-term exposure to recent volcanic ash deposits: New chemical and isotopic insights.”, **The Science of the total environment**, pp. 154383, 2022.

**2021**

- Y. Muranishi, L. Parry, M. Vachette-Dit-Martin, F. [Saez](#), C. Coudy-Gandilhon, P. Sauvanet, **DH Volle**, J. Tournayre, S. Bottari, F. Carpentiero, G. Martinez, J. Muronova, J. Escoffier, A. Bruhat, A. Maurin, J. Averous, C. Arnoult, P. Fafournoux and C. Jousse, “When idiopathic male infertility is rooted in maternal malnutrition during the perinatal period in mice.”, **Biol Reprod**, 2021.



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- L. Thirouard, H. Holota, M. Monrose, M. Garcia, A. De Haze, J. Saru, F. Caira, C. Beaudoin and **DH Volle\*** “Analysis of the Reversible Impact of the Chemodrug Busulfan on Mouse Testes.”, *Cells*, vol. 10 (9) , 2021.
- E. Martinot, L. Thirouard, H. Holota, M. Monrose, M. Garcia, C. Beaudoin and **DH Volle\*** “Intestinal microbiota defines the GUT-TESTIS axis.”, *Gut*, 2021. Letter to Editor.
- **DH Volle\***, “Molecular and Cellular Endocrinology: Special issue hypothalomo - Pituitary axis: Roles in integrative physiology and pathophysiology.”, *Molecular and cellular endocrinology*, vol. 525 , pp. 111198, 2021. Editorial from special issue as guest editor.

**Autres informations:**

**Etudiants actuellement en thèse ou en M2 dans l'équipe d'accueil.** Pour chaque étudiant indiquez le nom du responsable de thèse, l'année du début de la thèse et l'Ecole Doctorale de rattachement

Etudiant	Encadrant	Financements	Dates	
Ekaterina KUZNETSOVA	David VOLLE	MENRT, UCA	oct-23	SVSAE ED 65
Elhadji Mountaga DIALLO	Claude BEAUDOIN/ Lucie SAUZEAT	MENRT, UCA	mars-24	ED École Doctorale SF Clermont-Ferrand

**Etudiants ayant préparé ou soutenu leur thèse ou leur M2 dans l'équipe d'accueil au cours des six dernières années.** Pour chaque étudiant indiquez le nom du responsable de l'étudiant, l'année du début de la thèse et de fin de la thèse, l'Ecole Doctorale de rattachement et le devenir de l'étudiant.

Etudiant	Encadrant	Financements	Dates	
Manon GARCIA	Claude BEAUDOIN	Research Medical Foundation (FRM) fellowship and 4 <sup>th</sup> year on emergence from Pr Beaudoin	10/2017-09/2021	SVSAE ED 65
Laura THIROUARD	David VOLLE	MENRT, UCA and 4 <sup>th</sup> Year from FRM	10/2017-09/2021	SVSAE ED 65
Mélusine MONROSE	David VOLLE	MENRT, UCA and 4 <sup>th</sup> Year from ARC Foundation	10/2018-09/2023	SVSAE ED 65



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**Cette proposition de stage s'adresse-t-elle spécifiquement à un étudiant scientifique, médecin ou vétérinaire ou bien est-il ouvert à tous les profils ?**

**Ouvert à tous les profils**

**Ce sujet peut-il donner lieu à une thèse ?**

**Oui nous souhaitons présenter le/la candidate au concours de l'école doctorale de Clermont-Fd pour l'obtention d'un financement.**

**Nous étudierons également les autres possibilités de financement (demande bourse Ligue, FRM).**