Post-doctoral position

University Hospital of Clermont-Ferrand

University of Clermont Auvergne

IMoST UMR 1240 INSERM/UCA

Clermont-Ferrand, FRANCE

Starting date: 1rst of September 2023

Duration: 1 year and a half

Post-doctoral topic:

"Women's Fertility Preservation: optimization of the *in* vitro activation and growth of human primordial follicles"

Research team:

This position is proposed by the **ART department of the University Hospital of Clermont-Ferrand led by Pr Florence Brugnon** who is also the head of **the Fertility and Cancer task group of the Robust team of IMoST laboratory UMR 1240 INSERM/UCA** (https://imost.uca.fr). Our research task group has developed innovative projects to reach a better understanding and improvement of fertility preservation. Briefly, we have been optimising ovarian tissue cryopreservation [1], [2] and testing innovative methods to analyse ovarian tissue quality post freezing/thawing [3], amongst them an original ovarian cortical tissue culture model [1], [4]. We have also developed methods to detect residual disease in ovarian fragments [4], [5] to ensure a safe fertility restoration achieved by ovarian grafting [6]. More recently, our group started to investigate the effect of cancer and its treatments on the human reproductive functions.

Through this fundamental and applied research, innovative methods have been developed and proposed to patients to ensure their fertility preservation and restoration.

Post-doctoral project:

Recent advances in cancer treatments have significantly improved the survival of cancer patients. Nevertheless, these treatments are potentially gonadotoxic and often reduce ovarian reserve (Gerstl *et al.*, 2018); therefore, fertility preservation options should be offered to patients. The routinely used protocol for fertility preservation in women consists in freezing mature oocytes (halted at the metaphase stage of the second meiotic division) after hormonal stimulation (Rienzi *et al.*, 2010). However, ovarian stimulation may be contraindicated (therapeutic emergencies …) or impossible (prepubertal girls). In such circumstances, ovarian tissue cryopreservation for later transplantation is the only currently available option to preserve fertility (Donnez *et al.*, 2004). Importantly, ovarian tissues will not be grafted if residual disease is detected in the cryopreserved ovarian fragments (Rosendahl *et al.*, 2010). To date, there is no approach to restore patient fertility in such circumstances.

One area of research is the development of *in vitro* systems to culture isolated follicles from ovarian fragments to produce mature oocytes (Telfer, 2019). This strategy successfully produced offspring in mouse in the late 90's (Eppig and O'Brien, 1996). In humans, all studies performed revealed that a multi-step *in vitro* culture is required to obtain mature oocytes from ovarian cortex (Xiao *et al.*, 2015; McLaughlin *et al.*, 2018). The first step of this procedure is the activation of the ovarian reserve (primordial and primary follicles) within *in vitro* cultured ovarian fragments (McLaughlin *et al.*, 2018). The second step is the growth and subsequent maturation of antral follicles from preantral follicles. In the context of *in vitro* human folliculogenesis, all the currently developed

systems failed to yield good quality mature oocytes from primordial follicles. Therefore, an optimization of the *in vitro* growth of human ovarian follicles is essential for a future implementation of this fertility preservation approach in clinical practice for patients. In this project, the post-doctoral researcher will optimize the first step, namely the activation of the ovarian reserve (primordial and primary follicles) within *in vitro* cultured ovarian fragments, using innovative techniques.

Once the protocol for the *in vitro* activation and growth of primordial follicles is optimized, the post-doctoral researcher will evaluate the effects of cancer treatments, such as PARP inhibitors, on the activation and growth of primordial follicles within ovarian fragments. Indeed, the effects of novel classes of anti-cancer therapies, such as PARP inhibitors, on the ovarian function remain unexplored. Altogether, this project aims to contribute to the development of novel approaches to preserve fertility of cancer patients by innovative technologies.

Implemented technics:

- Organotypic culture of human ovarian tissue
- Immunohistochemistry
- Histochemistry
- RNA seq

Post-doctoral fellow required qualifications:

Individuals holding a PhD in cell biology, reproductive biology or with related research experience are eligible. Experience in ovarian tissue culture and/or transcriptomics and proteomics is preferred but not indispensable.

Candidates must email the following items to Pr Florence Brugnon (fbrugnon@chu-clermontferrand.fr) and Dr Gaëlle Marteil (gaelle.marteil@uca.fr)

- A one-page cover letter describing areas of research interests and career goals
- Curriculum vitae with a list of publications
- Contact information for two references

Location:

Clermont- Ferrand is located at the heart of Auvergne, surrounded with dormant volcanoes. Clermont-Ferrand is a young and dynamic city, with approximately 40 000 students. Clermont-Ferrand offers a pleasant living environment to its citizens with numerous activities such as hiking, visiting historic buildings, attending festivals and Rugby games…

Clermont-Ferrand is located in the center of France and is 2,5 hours away from Lyon and 3 hours from Paris by train. Aulnat airport also connects Clermont-Ferrand to Paris, Corsica and Portugal.

Publications of the team:

[1] S. Sanfilippo et al., “Quality and functionality of human ovarian tissue after cryopreservation using an original slow freezing procedure,” J. Assist. Reprod. Genet., vol. 30, no. 1, pp. 25–34, Jan. 2013, doi: 10.1007/s10815-012-9917-5.

[2] S. Sanfilippo et al., “Vitrification of human ovarian tissue: a practical and relevant alternative to slow freezing,” Reprod. Biol. Endocrinol., vol. 13, p. 67, Jun. 2015, doi: 10.1186/s12958-015-0065-5.

[3] S. Sanfilippo et al., “Viability assessment of fresh and frozen/thawed isolated human follicles: reliability of two methods (Trypan blue and Calcein AM/ethidium homodimer-1),” J. Assist. Reprod. Genet., vol. 28, no. 12, pp. 1151–1156, Dec. 2011, doi: 10.1007/s10815-011-9649-y.

[4] L. Chaput et al., “Sensitive and Specific Detection of Ewing Sarcoma Minimal Residual Disease in Ovarian and Testicular Tissues in an In Vitro Model,” Cancers (Basel), vol. 11, no. 11, Nov. 2019, doi: 10.3390/cancers11111807.

[5] V. Grèze et al., “Highly sensitive assessment of neuroblastoma minimal residual disease in ovarian tissue using RT-qPCR-A strategy for improving the safety of fertility restoration,” Pediatr Blood Cancer, vol. 64, no. 5, 2017, doi: 10.1002/pbc.26287.

[6] J.-B. Pretalli, S. Frontczak Franck, L. Pazart, C. Roux, C. Amiot, and DATOR Group, “Development of Ovarian Tissue Autograft to Restore Ovarian Function: Protocol for a French Multicenter Cohort Study,” JMIR Res Protoc, vol. 8, no. 9, p. e12944, 30 2019, doi: 10.2196/12944.