

**Institute :** Institute of Zoology and Biomedical Research.

**Topic:** PFAS exposure and premature ovarian insufficiency: molecular mechanism

**Name of supervisor:** dr hab. Anna Ptak, prof. UJ

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**Background information:**

Per- and polyfluoroalkyl substances (PFAS) have been produced in large quantities for several decades, and as time passes, some of them have been identified in wildlife from remote regions of the world. Some studies showed higher levels of PFAS in human blood and human ovarian follicular fluid (FF), indicating their ability to reach the ovary. It is important to note that together with the increasing levels of PFAS in human blood, a gradual increase in the appearance of premature ovarian insufficiency (POI) is observed. The diagnosis of POI is a serious event for women. It is a condition with medical, psychological, and reproductive implications. The etiology of POI is still poorly defined because, in more than 70% of cases, the cause is not determined. Despite the determination of PFAS in FF, current data are limited to conclude whether there is an association between PFAS concentrations and idiopathic POI.

**The main question to be addressed in the project** is as follows.

We postulate that PFAS, present in follicular fluid, acts as mitochondrial disrupting chemicals, disrupts normal ovarian function directly and indirectly, and leads to signs of POI.

**Information on the methods/description of work:**

To test the hypothesis, we propose the following three objectives, which will be carried out in *ex vivo*, *in vitro*, and *in vivo* approaches. The *ex vivo* study aims to assess whether associations exist between PFAS concentrations in human ovarian FF and POI infertility etiology, as well as the energy phenotype of human granulosa cells. The next, *in vitro* study aims to describe the effects of PFAS on mitochondrial function such as OXPHOS, ROS homeostasis, apoptosis, and steroidogenesis with a description of the molecular mechanism. Finally, the *in vivo* study aims to identify whether specific inhibition of the PFAS affected pathway is beneficial in the mouse model.

**Additional information (e.g Special requirements from the student):**

Candidates' competence: Original publication in the field of endocrinology. Practical experience in work with cell cultures, skills in laboratory techniques, especially in operating scientific advanced equipment used in gene expression analysis (real-time PCR instruments), protein expression analysis (western blotting equipment, luminescent image analyser), and enzyme activity assays (microplate reader).

**Place/name of potential foreign collaborator:**

Department of Instrumental Analysis and Environmental Chemistry, Institute of Organic Chemistry (IQOGCSIC). Juan de la Cierva 3, 28006, Madrid, Spain

**References:**

- [1] Chon SJ, et al. 2021. Premature Ovarian Insufficiency: Past, Present, and Future. *Front Cell Dev Biol.* 10;9:672890.
- [2] Ding N, et al. 2020. Perfluoroalkyl and polyfluoroalkyl substances (PFAS) and their effects on the ovary. *Hum Reprod Update.* 1;26(5):724-752.
- [3] Kang Q, et al. 2020. Nontargeted identification of per- and polyfluoroalkyl substances in human follicular fluid and their blood-follicle transfer. *Environ Int.* 139:105686.