Poly- and perfluoroalkyl substances (PFAS) are a family of fluorinated aliphatic compounds manufactured for diverse applications. For these reasons, PFAS have been detected in carpets, furniture, papers, building materials, food contact materials, impregnation agents, cleansers, polishes, paints, and ski waxes, among many other items commonly found in offices, households, and cars. Releases of PFAS to the environment can occur near chemical manufacturing locations, at industrial sites where PFAS are used, and at various stages of use and disposal of the product. It has resulted in their accumulation in the environment and drinking water contamination. The carbon-fluorine bond in these compounds is extremely strong, and thus many PFAS are not appreciably degraded under environmental conditions. Due to their environmental persistence and bioaccumulation, some congeners of PFAS are called “forever chemicals”.

Human exposure to PFAS occurs through the ingestion of contaminated drinking water and seafood, and inhalation of indoor air. Therefore, the vast majority of the population is exposed to PFAS daily, but the level of exposure to each PFAS differs. For this reason, PFAS are present in blood samples and even in human ovarian follicular fluid, indicating their ability to reach the ovary. Exposure to PFAS is a public health concern because epidemiological data suggest a potential association between exposure to PFAS and infertility. In addition, several PFAS have been identified in patients with premature ovarian insufficiency (POI); however, we cannot draw a direct link between PFAS exposure and POI.

POI is characterized by the loss of ovarian function before the age of 40 and is one of the leading causes of female infertility. The diagnosis of POI is a serious event for women. It is a condition with medical, psychological, and reproductive implications. In about 70% of POI cases, the cause remains unknown. Although the possible environmental impact of POI is often a topic of discussion, the evidence for this relationship has not yet been evaluated. However, it is well recognized that women’s ovarian follicular fluids contain high levels of some PFAS; therefore, the mixture of specific PFAS can represent a link between environmental impact and idiopathic POI. Our pilot study indicated that mitochondria are a target organelle for the action of PFAS in the human ovary.

Thus, the emerging concept in this project is that PFAS act as “mitochondrial disrupting chemicals” and by these actions are the cause of POI. We believe that PFAS present in follicular fluid directly disrupts mitochondrial function, induces oxidative stress and apoptosis in granulosa cells, or acts indirectly inhibiting steroid hormone biosynthesis and by both mechanisms leads to signs of POI. These studies will close a critical knowledge gap on the link between exposure to a mixture of PFAS and POI. Our technically innovative approaches will be the bridge methodologies in cellular bioenergetics with PFAS contamination and POI etiology. The results will advance the field of ovarian biology by characterizing the biological mechanism by which PFAS regulate ovarian metabolism and thus induce toxic effects that can lead to POI. Our long-term goal is to indicate novel therapeutic approaches that target crucial steps in PFAS-induced POI.