MID-TERM REVIEW

TOWARDS BETTER IDENTIFICATION OF ENDOCRINE DISRUPTING CHEMICALS THAT HARM FEMALE REPRODUCTIVE HEALTH

MARCH 2023

WHAT IS THE FREIA PROJECT?

The FREIA project is an EU-funded project dedicated to advancing test methods to identify endocrine disrupting chemicals (EDCs) that are toxic to female reproduction.

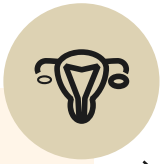
THE FREIA PROJECT HAS THREE MAJOR GOALS:

To gain new understandings and insights into adverse effects of endocrine disruption on women's health.

To develop new test methods and improve existing ones to detect EDCs toxic to female reproduction and support protective regulation.

To promote sustainable options for a healthy society and improve women's health.

HOW DO WE ACHIEVE THIS:



PERFOM EXPERIMENTAL STUDIES

- Human ovary, follicles, follicular fluid, and adrenal
- Computer models and studies in a culture dish
- Rat studies

FIND BIOMARKERS OF EFFECT

- Human-relevant biological measures of harmful effects
- Descriptions of biological events, during specific life-stages, leading to female reproductive toxicity

DEVELOP TEST STRATEGIES

- Novel or improved computer models, and test methods with cells in a culture dish or animal models
- Test strategy to identify EDCs toxic to female reproduction

HIGHLIGHTS FROM THE FIRST 3 YEARS OF THE FREIA PROJECT:

The main findings of the **experimental studies** include:

- Classical toxicity endpoints in female rats are insensitive to the human endocrine disruptors diethylstilbestrol and ketoconazole.
- The developing brain appears to be more sensitive for EDC effects with respect to puberty than the developing ovary.
- Targeting steroid hormone formation appears to have worse effects on the ovary and oocytes than targeting the estrogen receptor (ER).

The main findings of the **analysis of human data** include:

- EDCs reduce the number of germ cells in human fetal ovaries after exposure in culture dishes.
- Several potential biomarkers for ovarian disruption were identified and are under further investigation.
- Fluids surrounding oocytes are filled with EDCs, including phthalates, parabens and PFAS. These exposures are linked to lower ovarian responses in women undergoing fertility treatment.

Highlights of our work to **develop test strategies** include the development of:

- 16 mechanistic descriptions on how EDCs can lead to female reproductive toxicity.
- Improved computer models to predict interaction with PPARg and aromatase.
- Test methods that investigate ovarian cell toxicity, estrogen receptor-beta (in)activation, and oocyte maturation and quality.
- A multi-lab evaluation to expand the standard H295R steroidogenesis assay from three to 19 steroids.
- An evaluation of the mammary gland as a sensitive endpoint in female rats in order to measure EDC actions.

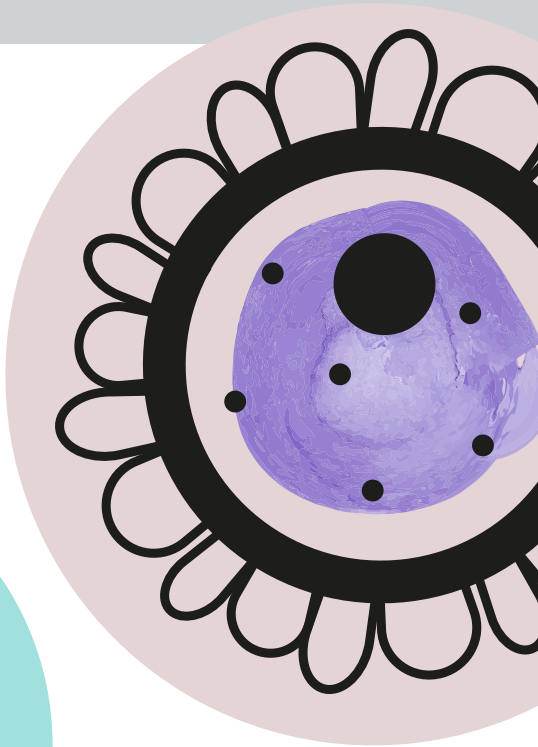
ENTERING THE FINAL PHASE OF THE FREIA PROJECT:

In 2023, the FREIA project plans to...

1 Integrate our knowledge and methods into human-relevant test strategies to identify EDCs toxic to female reproduction

2 Publish strategies to promote women's health

3 Organise the final FREIA event to present our results



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FREIA is part of the EURION cluster
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