

Establishing *ex vivo* brain-pituitary and gonadal models for PFAS toxicity assessment



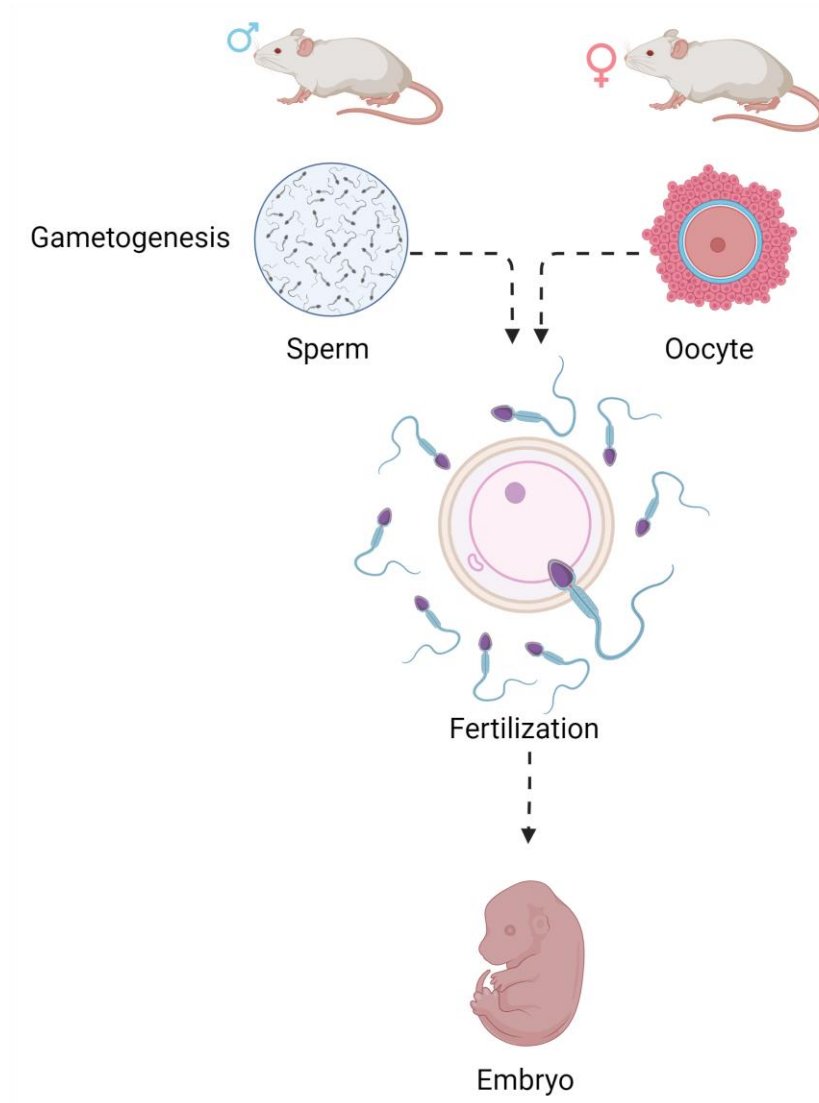
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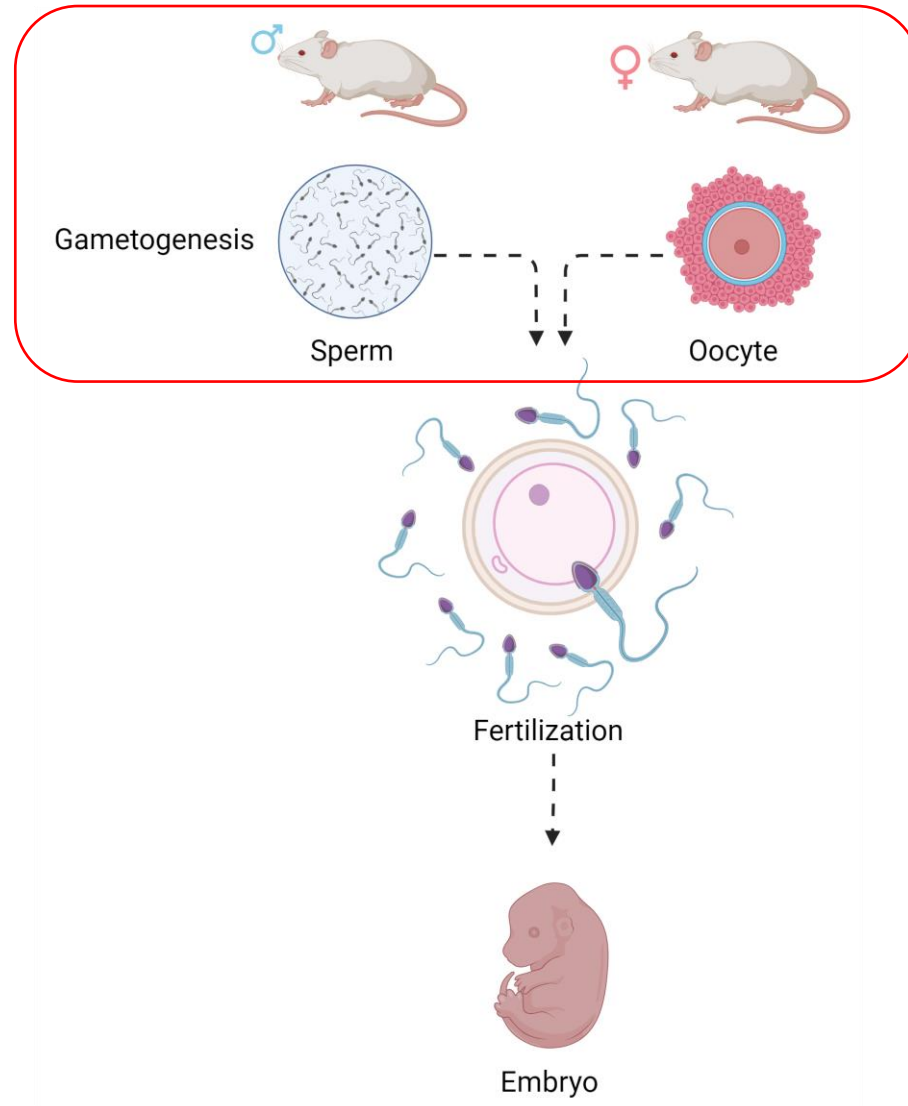
NSFT Winter Meeting 2025



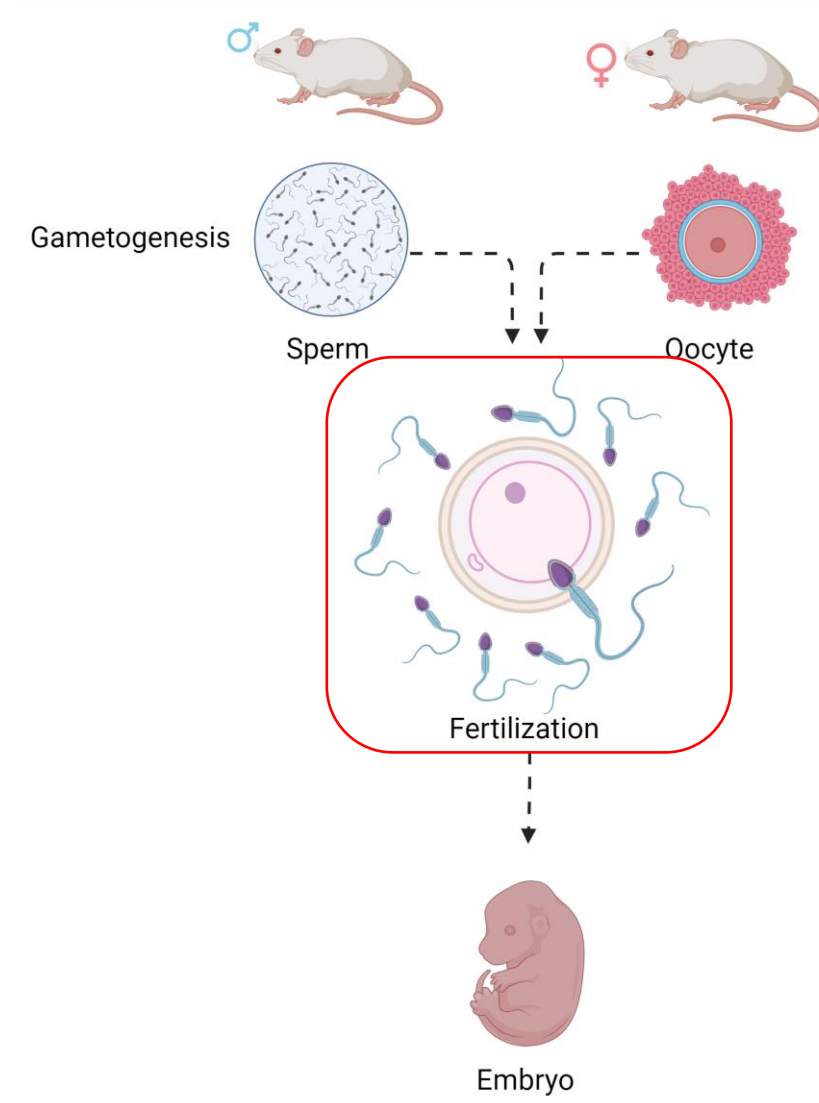
Reproduction in living organisms



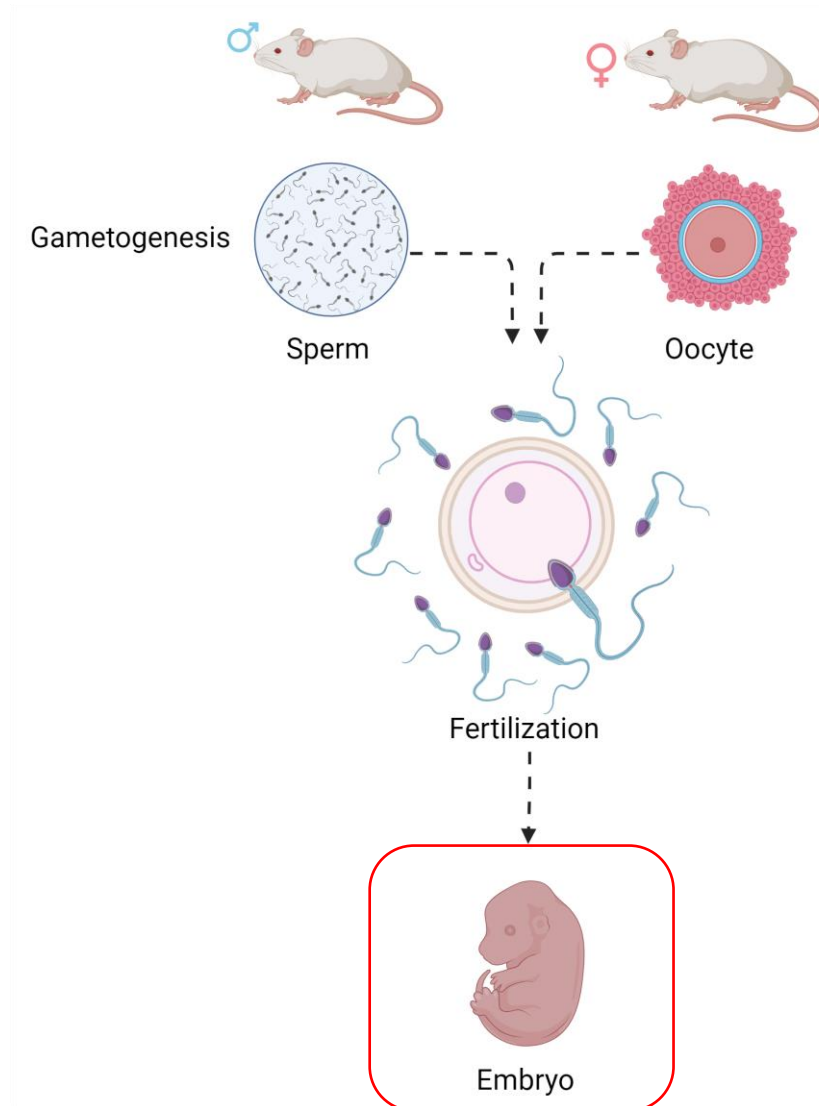
Reproduction in living organisms



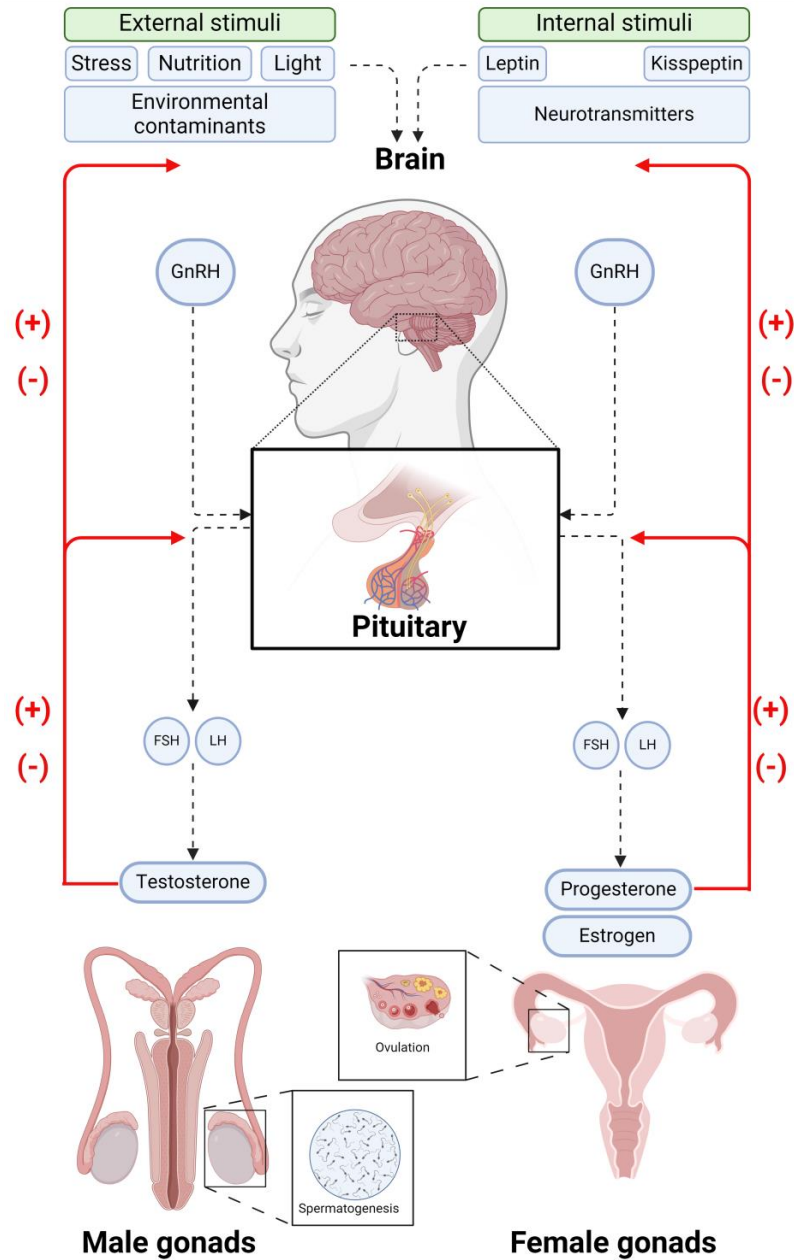
Reproduction in living organisms



Reproduction in living organisms



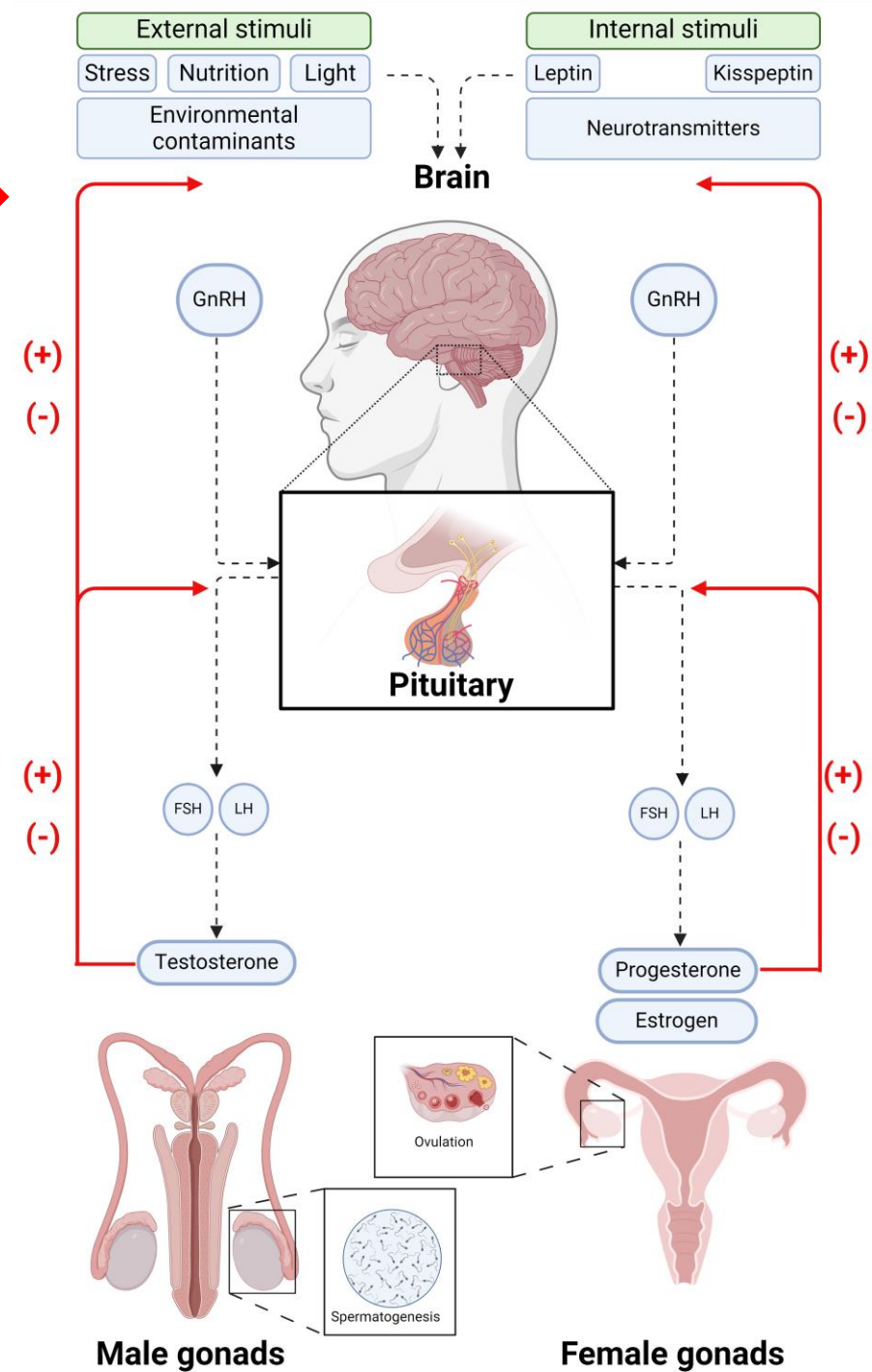
Brain-pituitary-gonadal (BPG) axis



Brain-pituitary-gonadal (BPG) axis

➤ Brain:

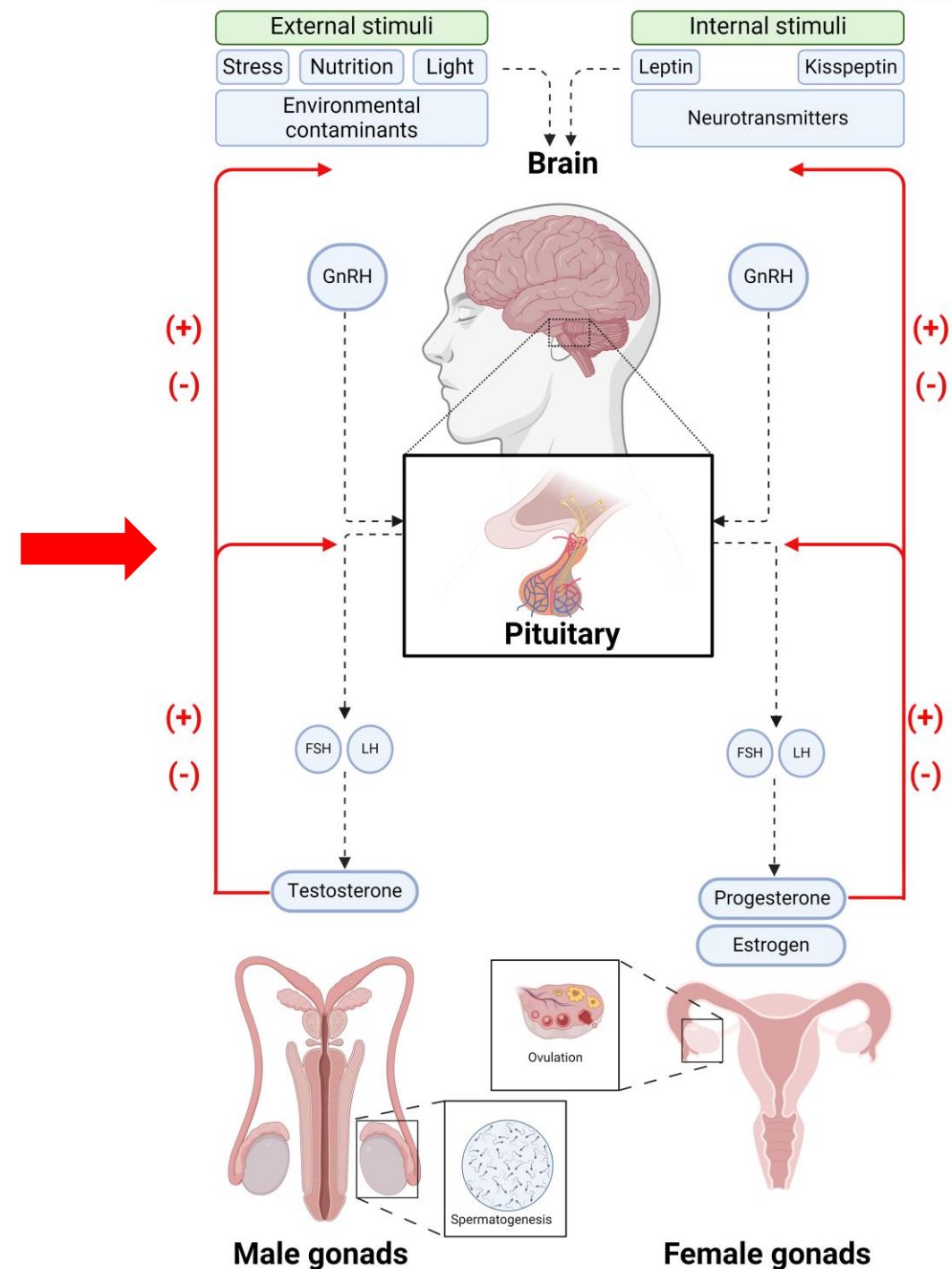
- Releases gonadotropin-releasing hormone (GnRH) in response to external and internal stimuli.



Brain-pituitary-gonadal (BPG) axis

➤ Pituitary gland:

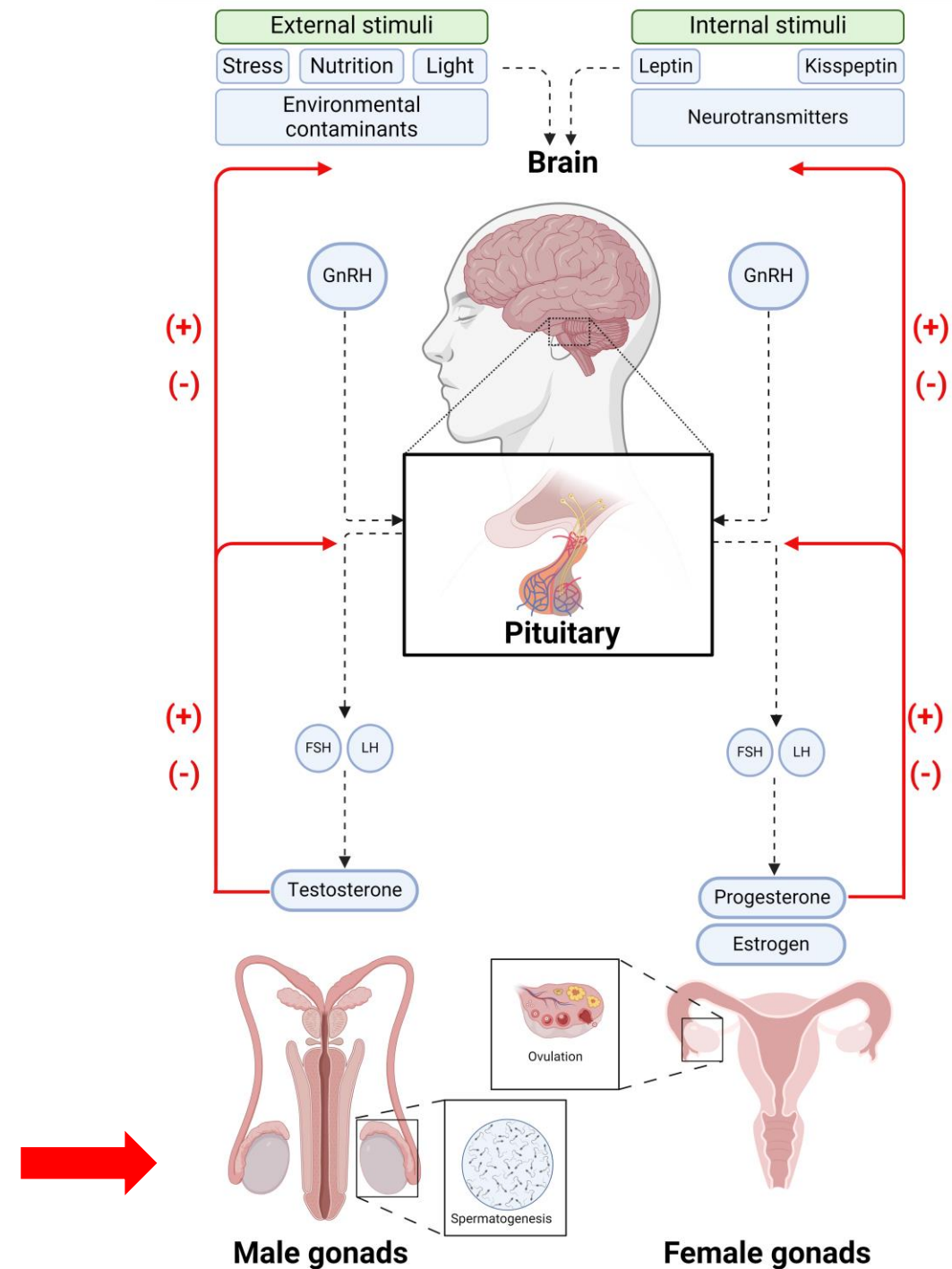
- Responds to GnRH by releasing Luteinizing hormone (LH) and Follicle-stimulating hormone (FSH)
- These hormones travel through the bloodstream to the gonads



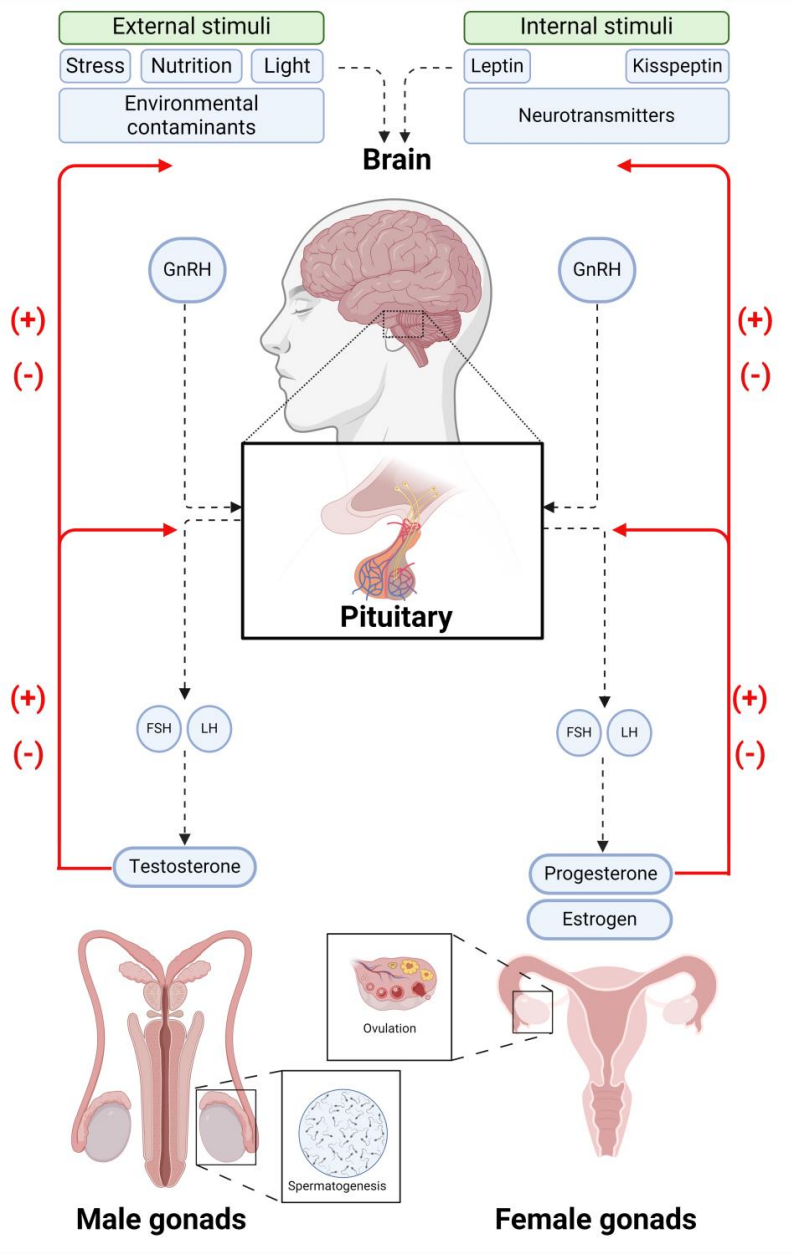
Brain-pituitary-gonadal (BPG) axis

➤ Gonads

- Respond by producing sex hormones (testosterone, estrogen, and progesterone).
- These hormones are responsible for sexual development and gametogenesis.



Brain-pituitary-gonadal (BPG) axis



Endocrine-disrupting chemicals (EDCs)

EDCs are substances that **interfere** with the endocrine system.



Cosmetics



Water-repellent Clothing



Cleaning Products

Polyfluoroalkyl substances (PFAS), are an important group of EDCs that:

- Bioaccumulate in organisms
- Resist degradation



Fish



Water



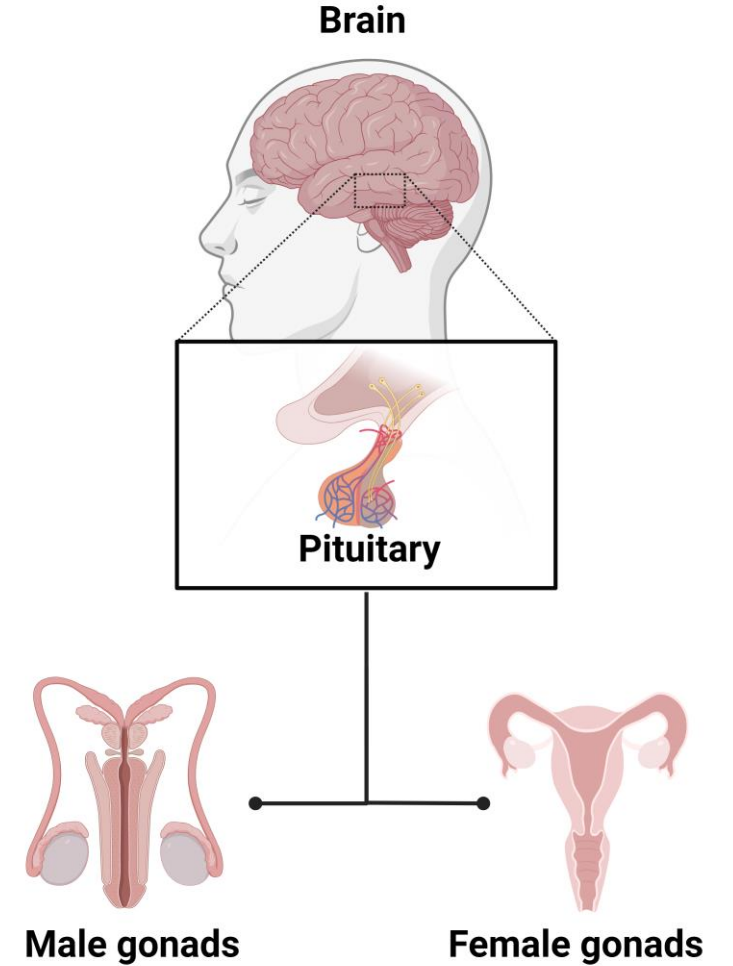
Food processing/packaging

How do EDCs cause endocrine disruption?

Interference with hormone **synthesis**

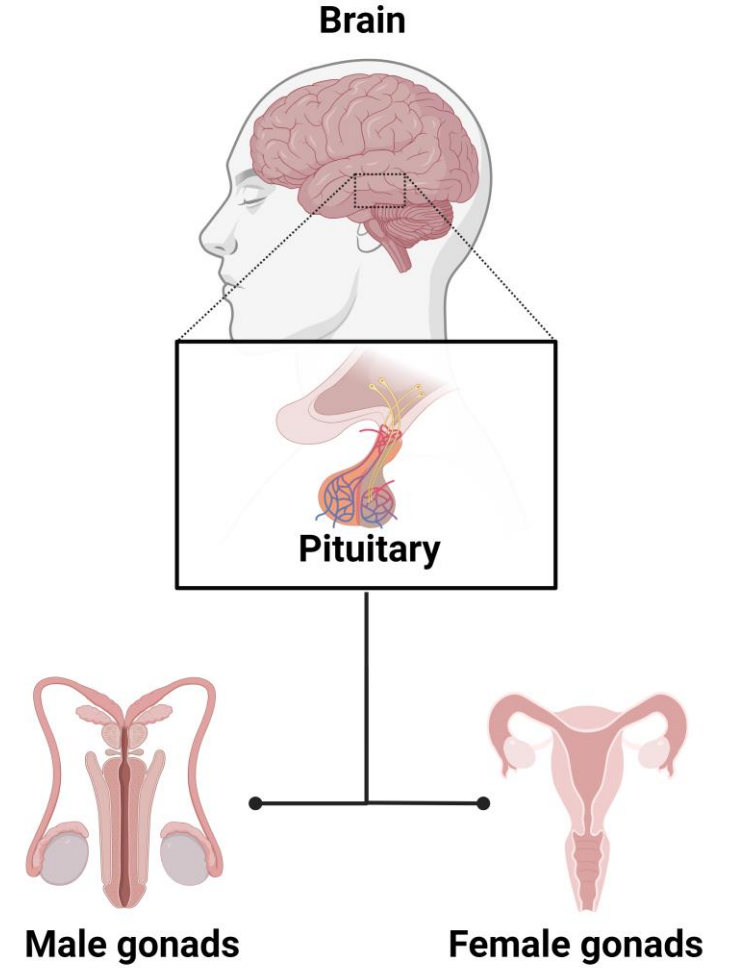
Interference with hormone **transport**

Interference with hormone **storage**



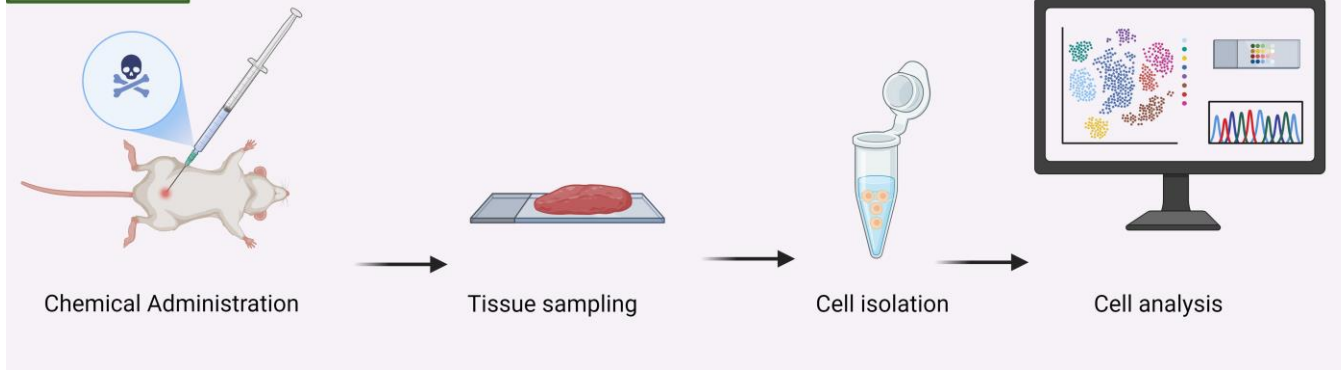
How do EDCs cause endocrine disruption?

Interference with hormone **synthesis**

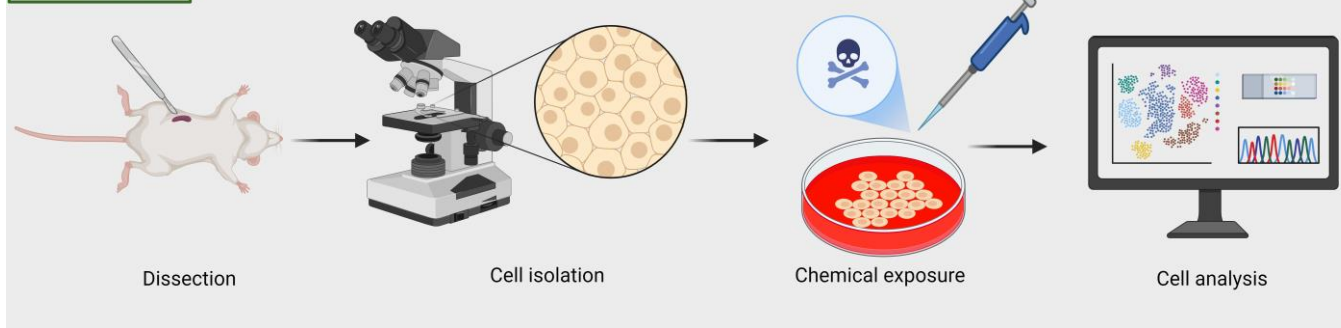


Experimental models for toxicology studies

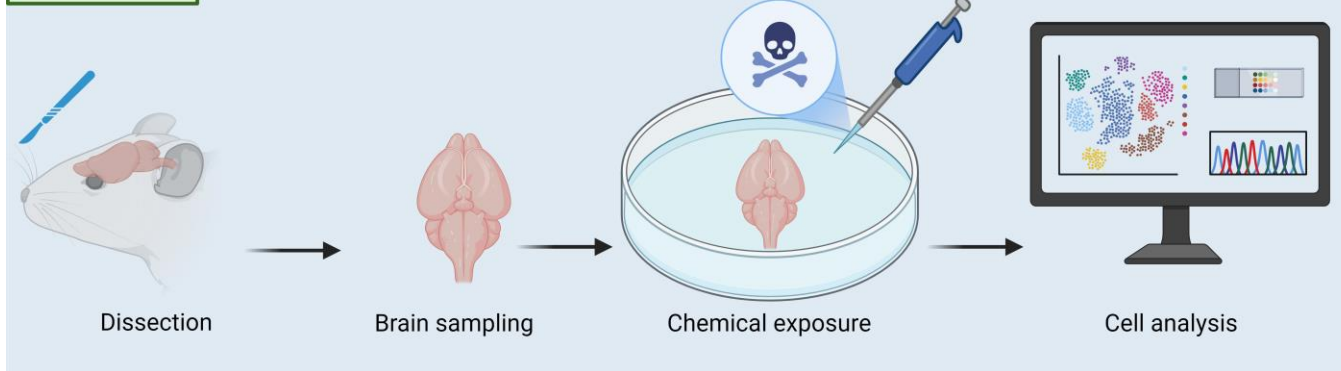
In vivo studies



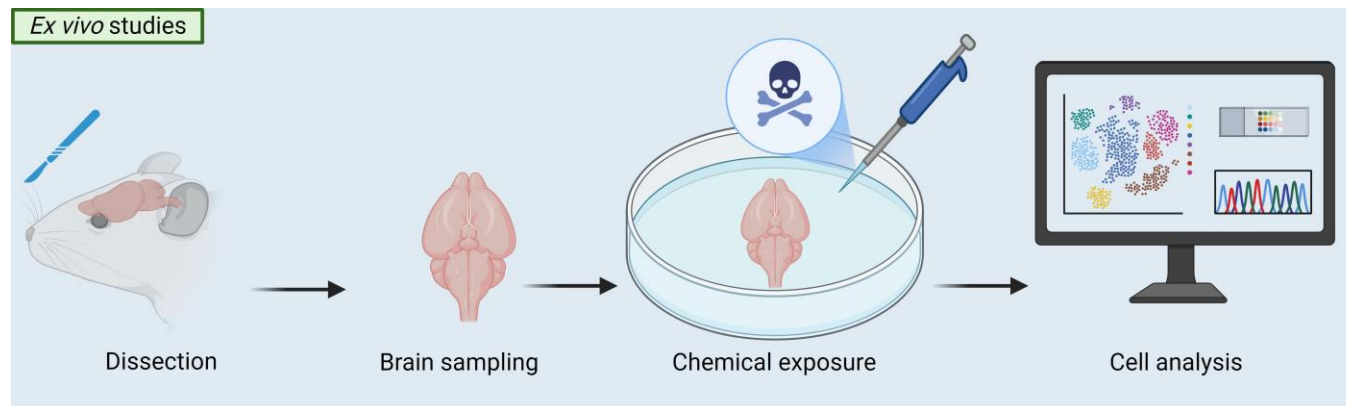
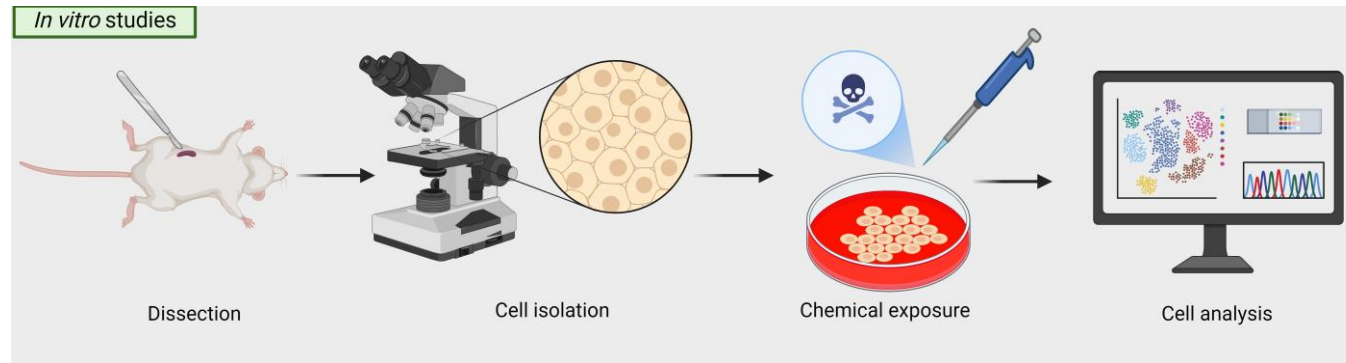
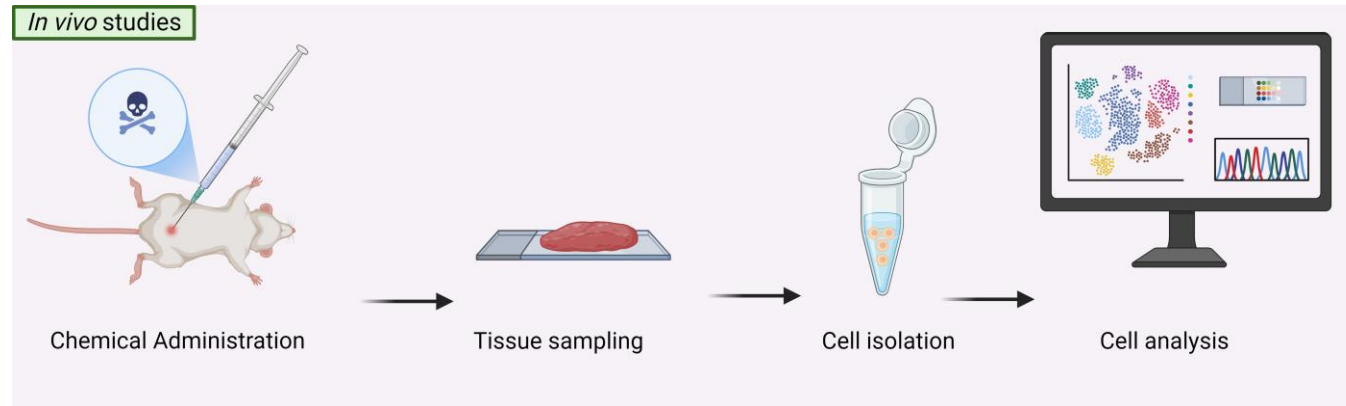
In vitro studies



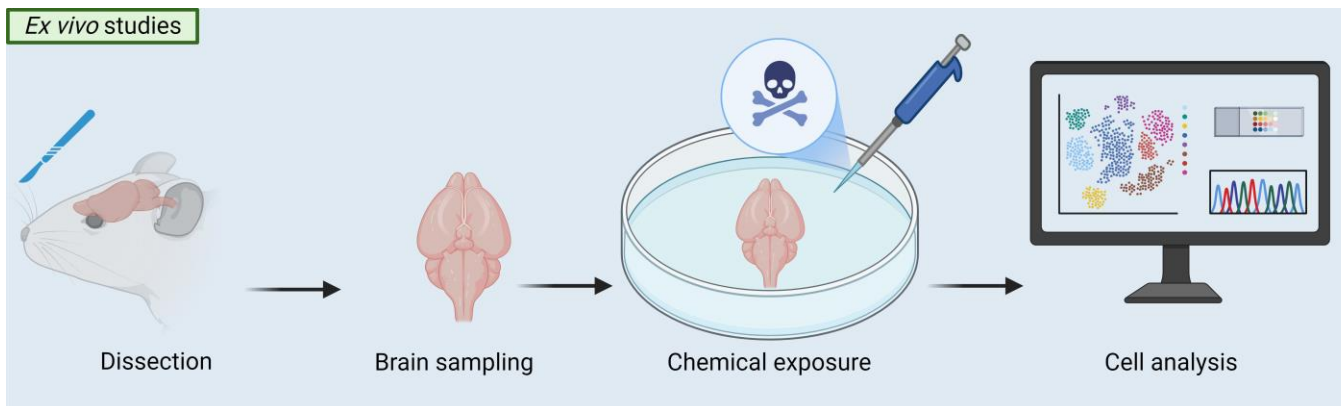
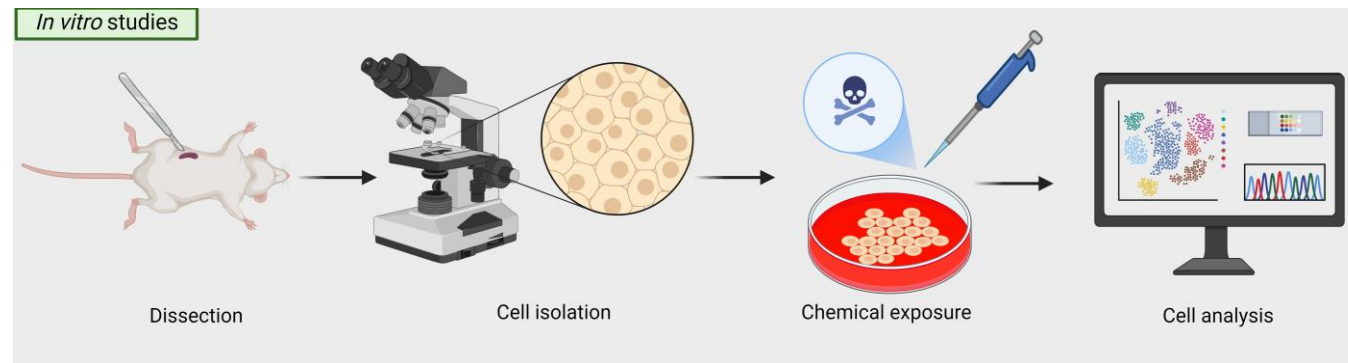
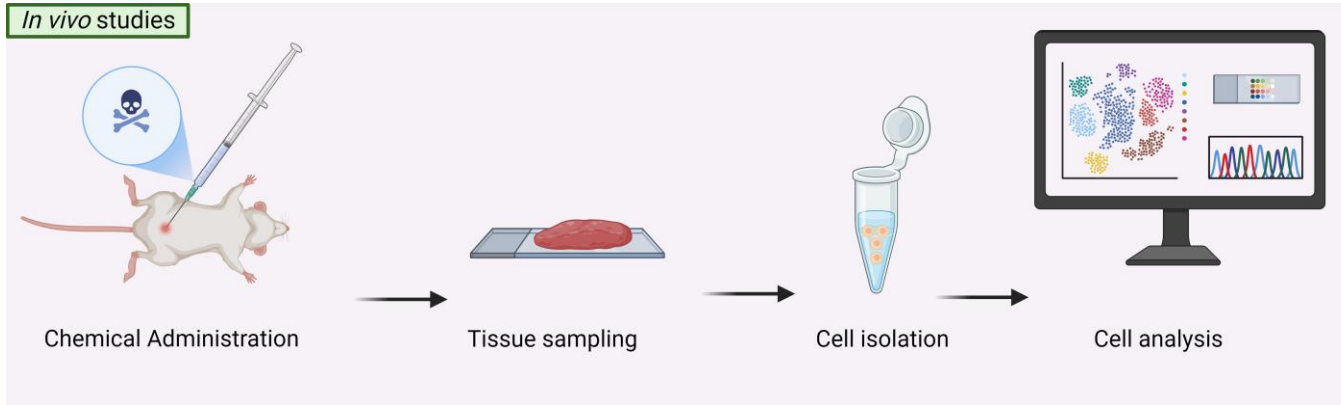
Ex vivo studies



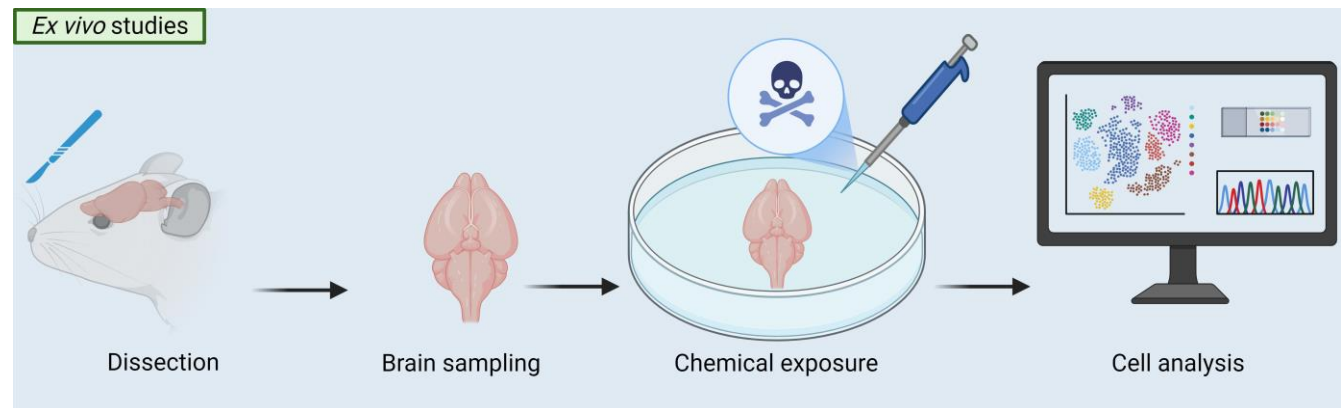
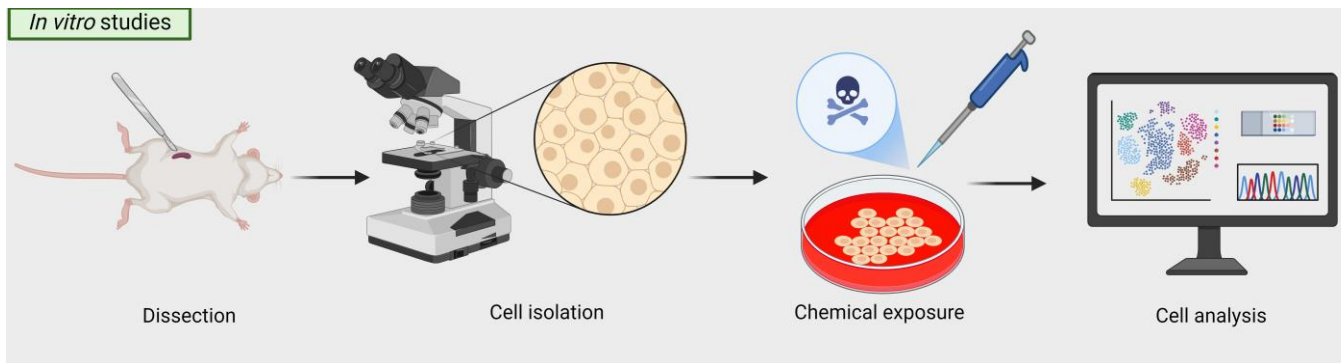
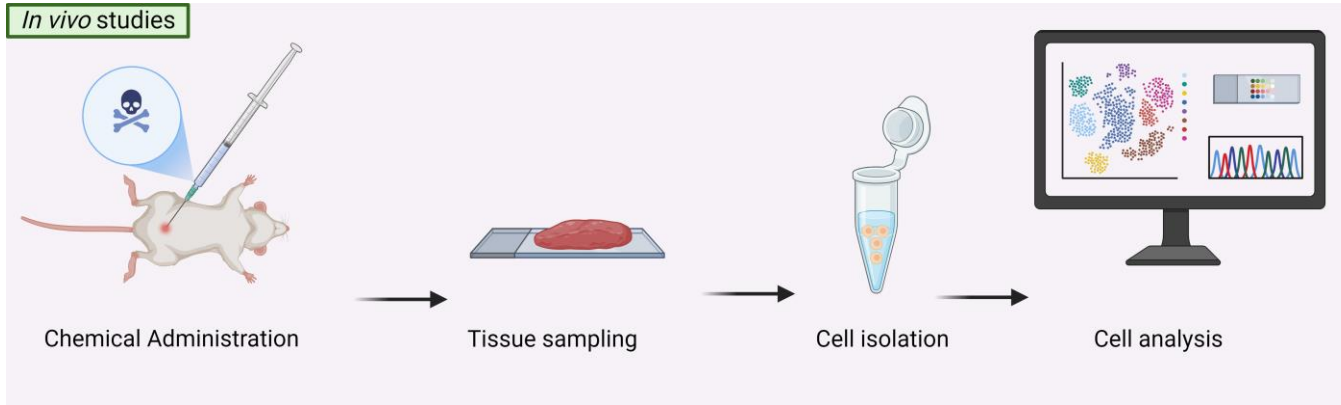
Experimental models for toxicology studies



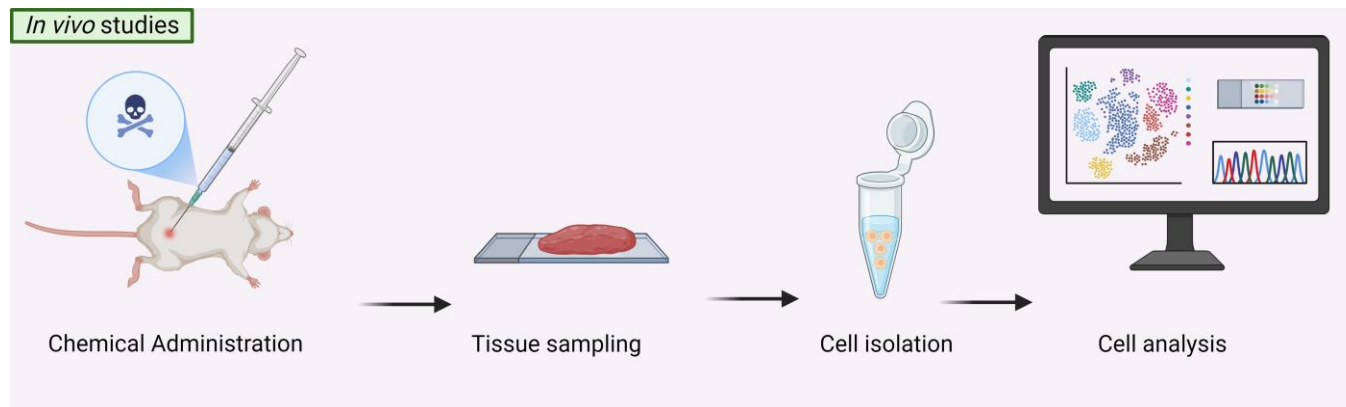
Experimental models for toxicology studies



Experimental models for toxicology studies



Experimental models for toxicology studies



CHIASMA - Accessible Innovative Methods for the Safety & Sustainability Assessment of Chemicals & Materials

Simona Kavaliauskienė¹, Bina Vetal², Romain Fontaine³, Armin Baygen⁴, Christian Herkner⁵, Erik Ropstad⁶, Mette H.B. Müller⁷
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Objectives

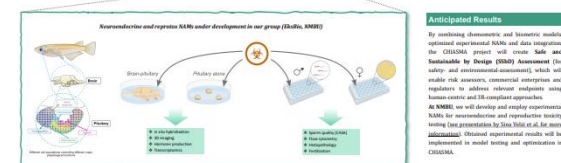
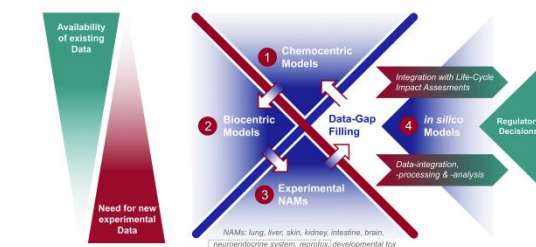
The shift to ethical and sustainable toxicology is one of the goals set by EU Commission for the next generation based and risk assessment of chemicals and materials. However, the shift is hindered by the reliance on animal testing, lack of validated alternatives, standardized methods, multi-stakeholder coordination, and accessible data. To address this, a large collaborative project namely CHIASMA - Accessible Innovative Methods for the Safety & Sustainability Assessment of Chemicals & Materials - has been funded by the European Union's Horizon Europe Research and Innovation program and will run during 2024-2027. The project involves more than 20 partners from across the globe and aims at developing and implementing a comprehensive set of *Non-Animal Methods* (NAMs) for a more ethical, reliable, and robust evaluation of human and environmental safety within regulatory context.

Methods

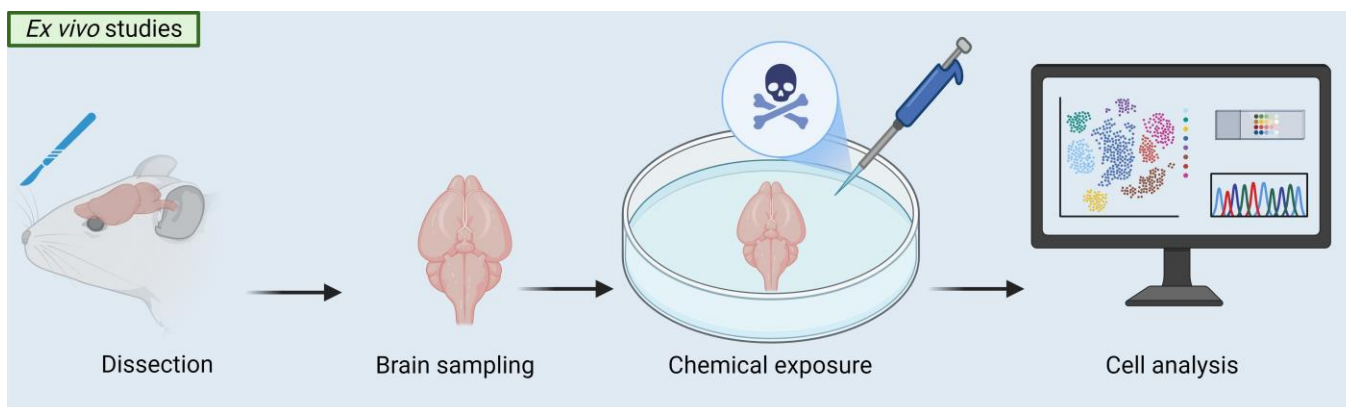
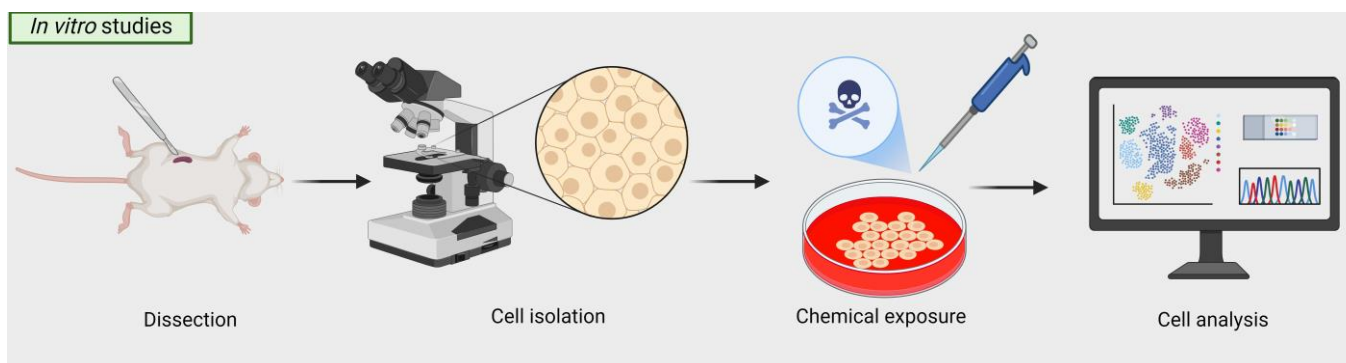
NAMs will be based on both *in vitro* and experimental methods, including *in vitro* methods, human or animal cells and tissues, and *in vivo* experimental methods. The *in vitro* and experimental NAMs will be "top-down" validated against three groups of chemicals and materials: (i) *Pharmaceutical Substances* (PPSs), (ii) *Novel pesticides*, and (iii) *2D materials* for energy applications, which were chosen based on their high health impact, environmental persistence, and large industrial use in the Norwegian University of Life Sciences (NMBU). We will use an *in vivo* *Brain Primary Cerebral slice* system based on model fish (*Danio rerio* and *Medaka*) to develop NAMs within CHIASMA Research and Innovation and Sustainability by Data (R&I) by Data (R&I) by Data (R&I).

CHIASMA - Accessible Innovative Methods for the Safety & Sustainability Assessment of Chemicals & Materials (Grant Agreement 101019123, Horizon Europe, 2024-2027) is a project funded by the European Union's Horizon Europe Research and Innovation program.

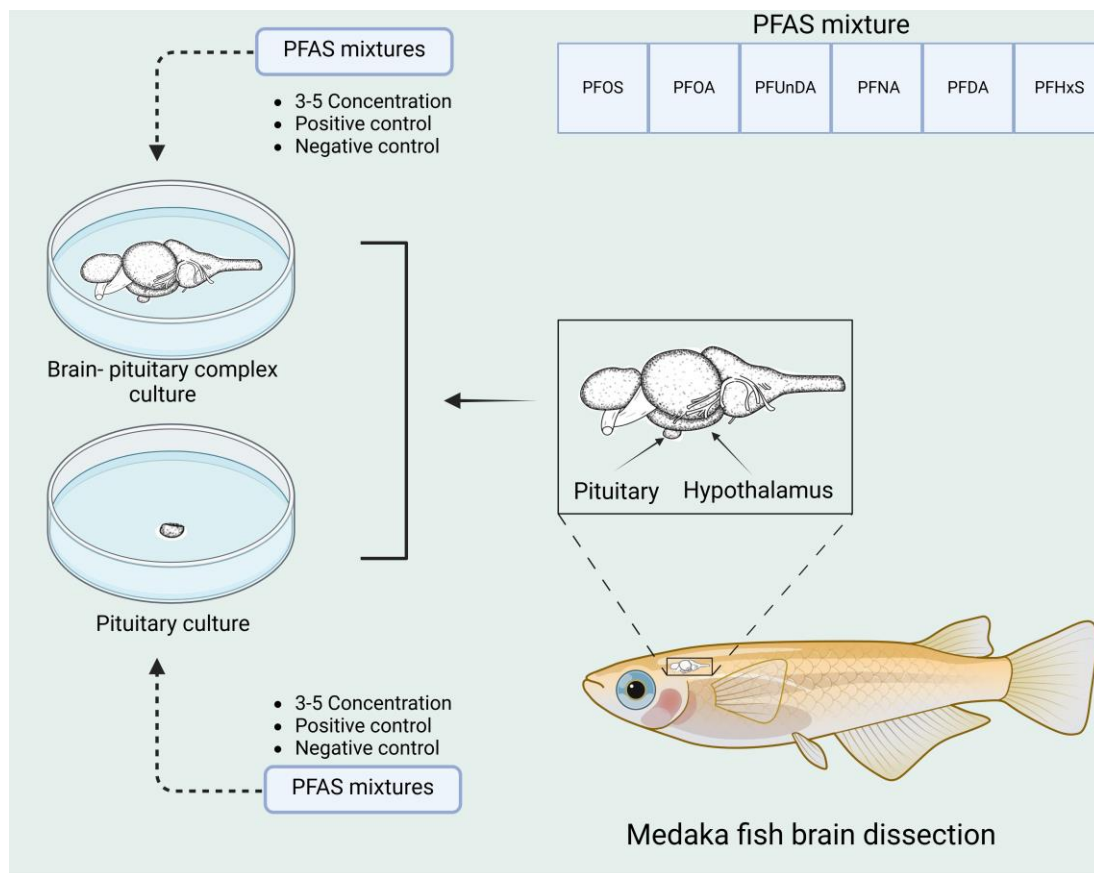
Illustration of the CHIASMA R&I approach to testing and assessment of materials using an iterative approach based on the integration of (1) chemocentric, (2) biocentric and (3) new experimental models into a convergent framework for data integration and processing.



Poster ID PT9 by Simona Kavaliauskienė et al.



Ex vivo brain-pituitary model



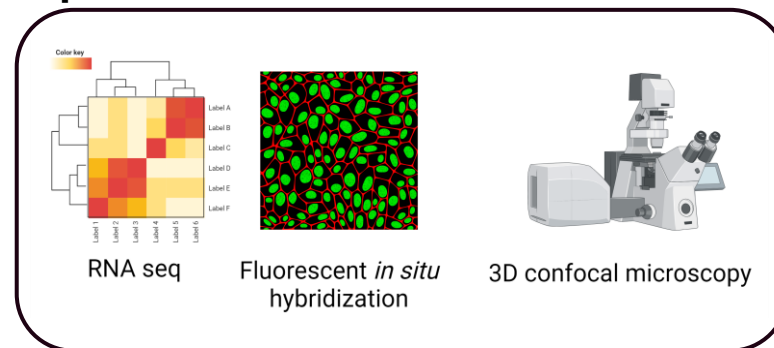
Brain/pituitary cell viability:



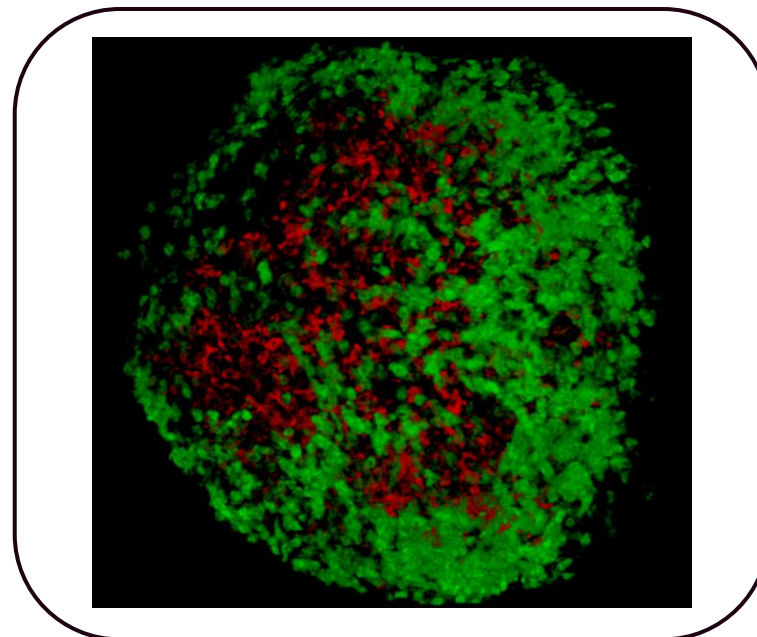
This method has a current viability of up to **2-5 days** is particularly important for testing chemicals that may impact the BPG axis.

Methods to be applied

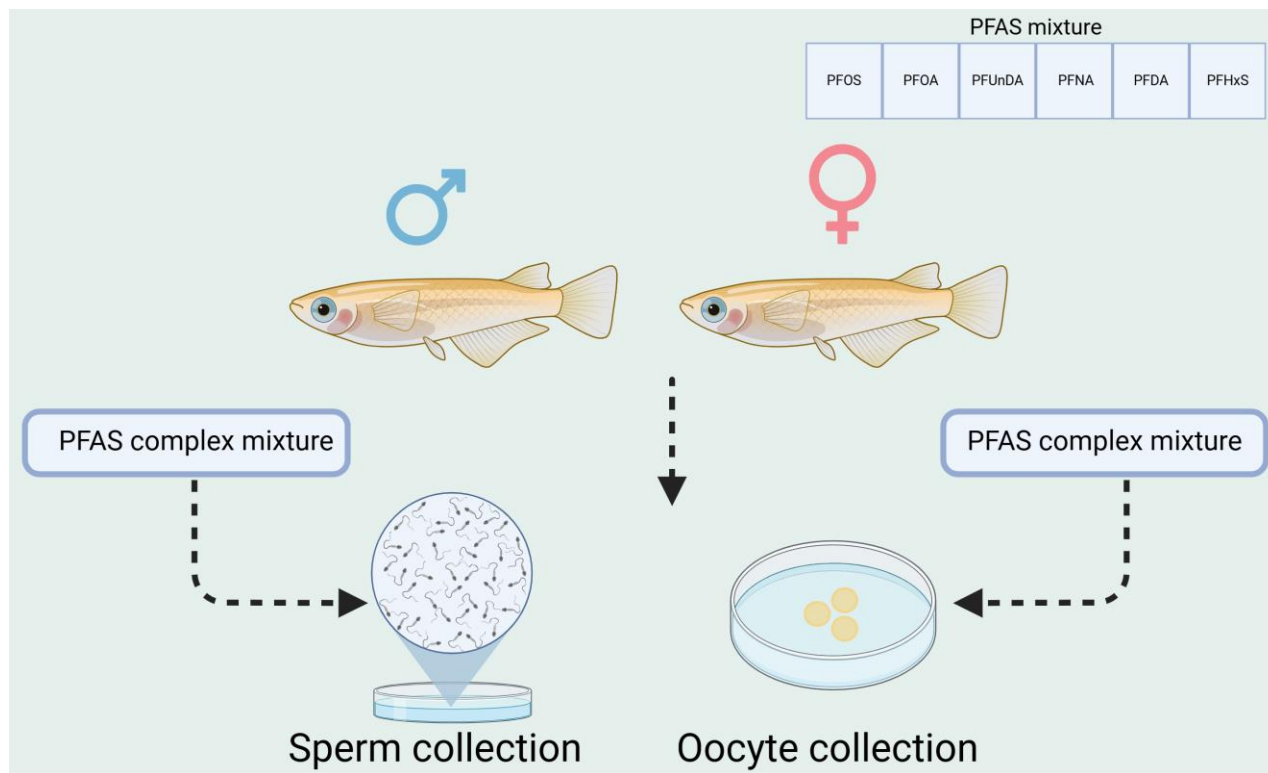
Gene expression effects:



Changes in cell numbers in transgenic line:

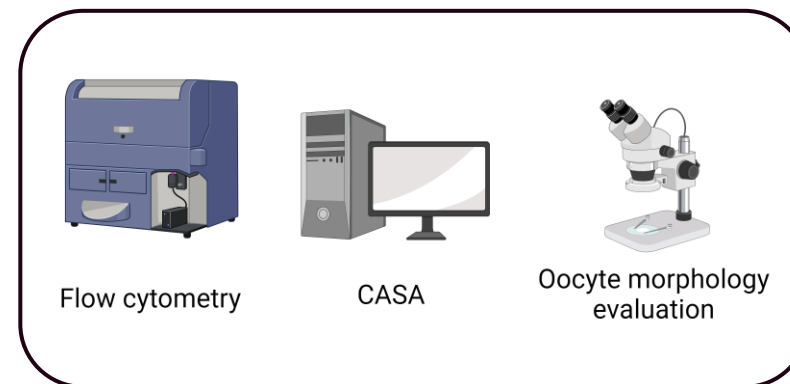


In vitro gamete toxicity models



Methods to be applied

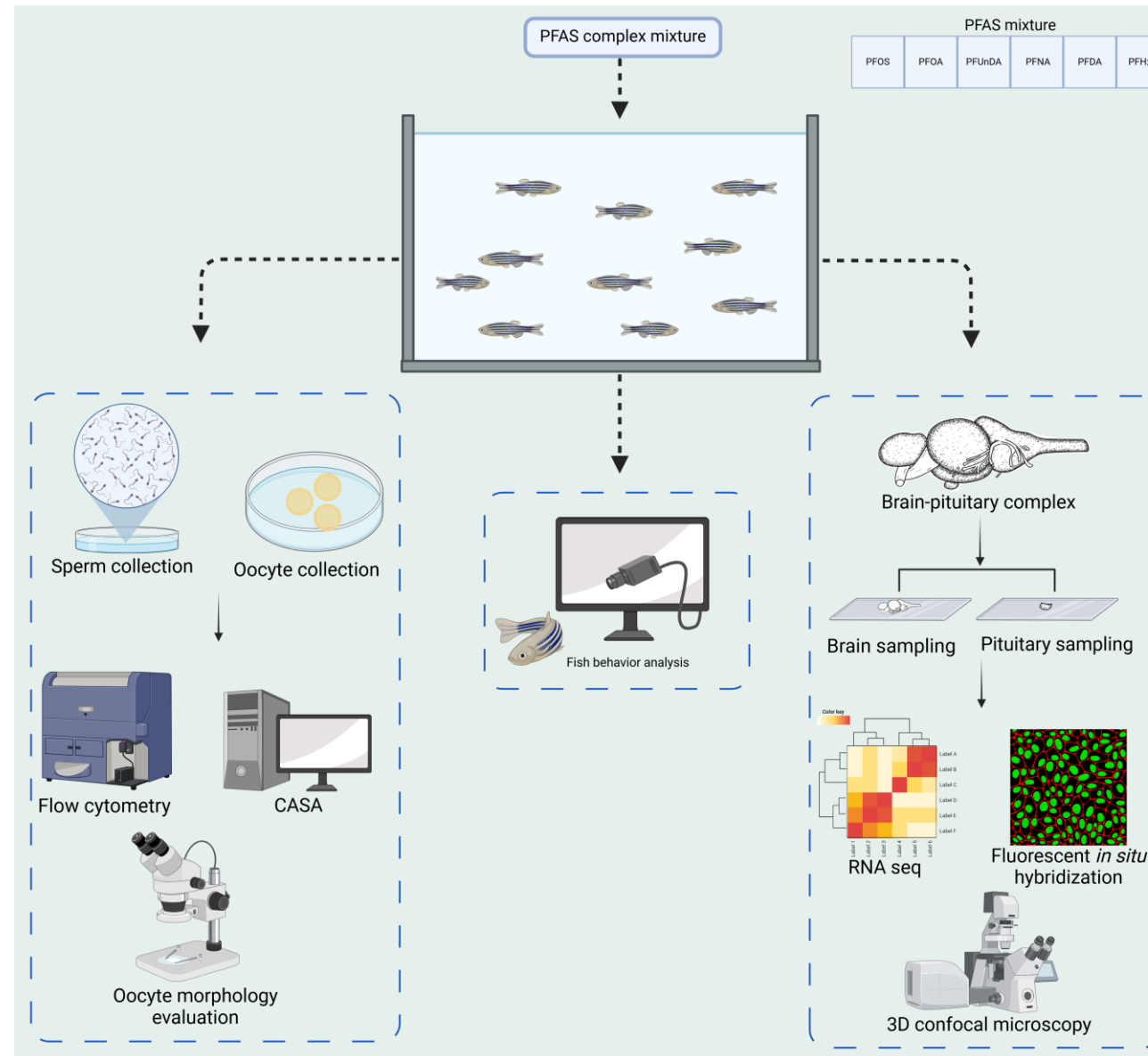
Sperm/oocyte quality evaluation:



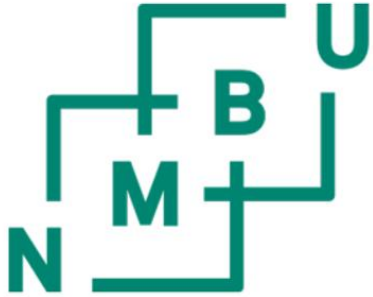
Validate the brain-pituitary and gamete model



Validate the brain-pituitary and gamete model



Acknowledgment



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Mette H.B. Müller**



**Researcher
Romain Fontaine**



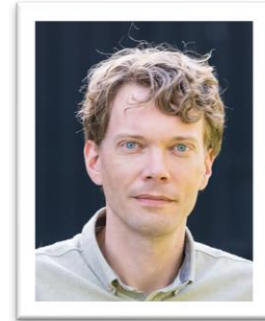
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