Alternative methods and animal models for research in perinatal development

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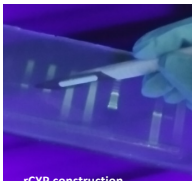
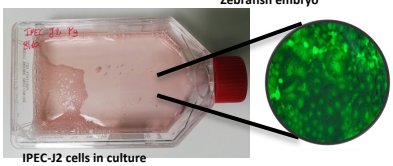
Alternatives to animal use in experiments

We aim to contribute to the **3Rs** by developing different *in vitro* models, including the construction of zebrafish and minipig **recombinant CYP enzymes** (rCYPs), the use of **cell culture** to model **pig and chicken** intestinal oxidative stress, development, and angiogenesis, and the use of **zebrafish embryos** as an alternative model for teratogenicity testing by pharmaceutical companies. The methods developed will partially replace animals used for scientific purposes. **The developed alternatives relate to own research stemming from animal studies (see other boxes).**



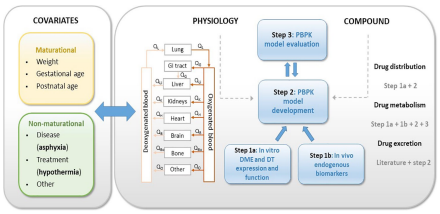

Zebrafish embryo


IPEC-J2 cells in culture

Research questions:

- Are rCYPs the future for less lab animal use during (early) drug development?
- How can we optimize and standardize the Zebrafish Embryo Developmental Toxicity Assay?
- Is the angiogenetic potential of pig umbilical cord endothelial cells different in the case of IUGR?

The neonatal pig as a translational model




Minipig © Ellegaard


Minipig under anaesthesia with catheters

We investigate the pharmacokinetics of drugs (**paediatric drug development**) used in **neonatal intensive care** units in a neonatal (**minipig**) model under special conditions, such as asphyxia and hypothermia, as this can provide critical information for neonatologists. Also, since immature and less developed neonatal pigs show similar disorders as premature and low birth weight babies, our group is interested in examining the translational value of the **neonatal low birth weight domestic** piglet in this regard. We study the molecular mechanisms underlying their higher vulnerability for disorders during the child- and adulthood (DOHAD principle).

Research questions:

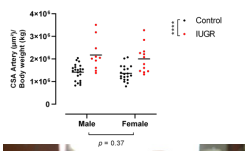
- Does cooling therapeutic hypothermia (TH) influence drug metabolism in asphyxiated neonates? A study in the neonatal Gottingen Minipig is a translational model.
- Are preterm piglets a valuable model for Phase I and Phase II drug metabolism in preterm newborns?
- Do intra-uterine growth-restricted piglets phenotypically mimic IUGR infants?

The neonatal pig in pig production

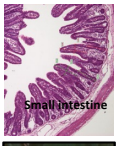
Intra-uterine growth restriction (IUGR) has a negative impact on neonatal survival, growth, and animal welfare. The male IUGR piglet suffers higher morbidity and mortality. We aim to detail the phenotype of the IUGR piglet (performance, morphology, behaviour), link this description to changes in intestinal development, vascularization, and placenta development, and look for biomarkers in the umbilical cord. In addition, we assess the effects of different strategies **(artificial rearing, nutritional supplements, etc.)** on the pig's resilience and development.

Research question:

- Sex-related differences in intra-uterine growth restricted piglets: what is the role of the umbilical cord?




Umbilical cord


Small intestine


IUGR piglet with normal littermate


Artificial rearing in brooder


Drenching

Techniques:

- PCR, qPCR, cloning, rCYP expression, enzyme activity, LC-MS, cell culture (o.a. ROS production and wound healing), etc.
- *In vivo* and *ex vivo* functionality assays, fluorogenic and luminogenic assays, permeability measurements, etc.
- Field studies, immunohistochemistry, image analysis, stereology, western blot, ELISA, etc.

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