In vivo models for the assessment of metabolic effects of EDs

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WP3 leader

WP3 major aims

- To establish methods and protocols for in vivo detection of metabolism disruption
- To address disruption of metabolism in vulnerable individuals
- To understand mechanisms of metabolic disruption and to develop AOPs

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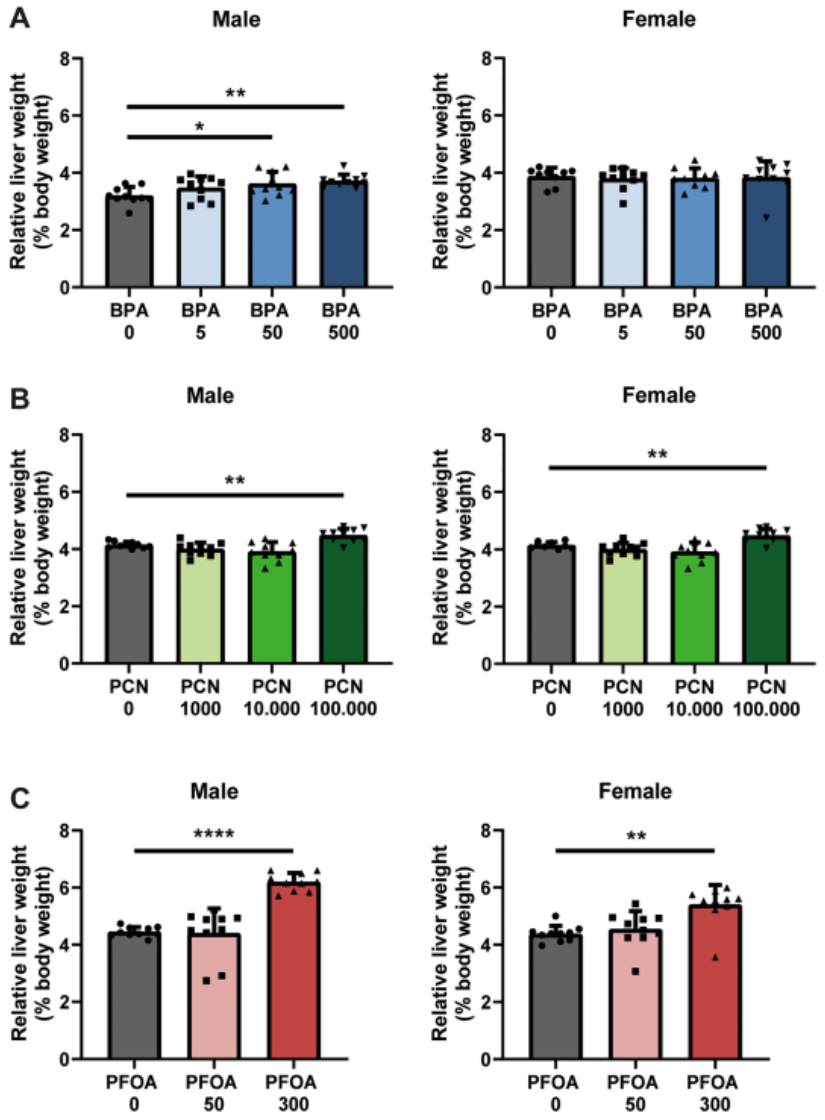
ORGAN TOXICITY AND MECHANISMS

Metabolic effects of nuclear receptor activation in vivo after 28-day oral exposure to three endocrine-disrupting chemicals

Brecht Attema[1] · Outi Kummu[2] · Sini Pitkänen[3] · Jonna Weisell[4] · Taina Vuorio[3] · Erika Pennanen[3] · Maria Vorimo[2] · Jaana Rysä[5] · Sander Kersten[1] · Anna-Liisa Levonen[3] · Jukka Hakkola[2]



The repeated dose 28-day oral toxicity protocol may not be a very sensitive approach for studying the metabolic effects of EDCs. Future models should focus on the incorporation of predisposing factors in the experimental setup.

MOLECULAR METABOLISM 66 (2022)
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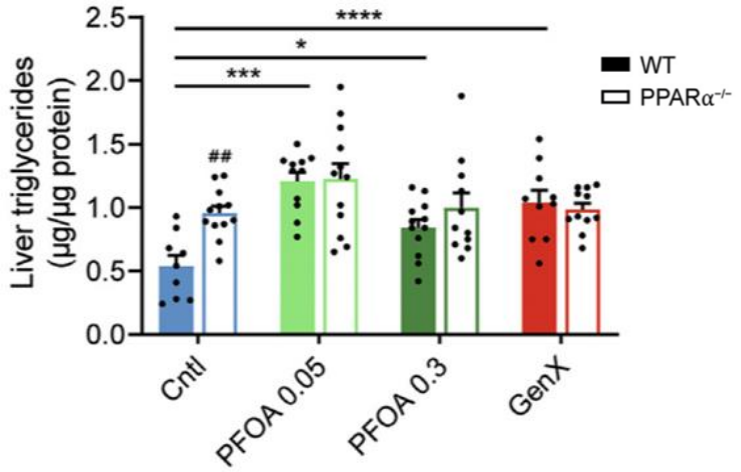
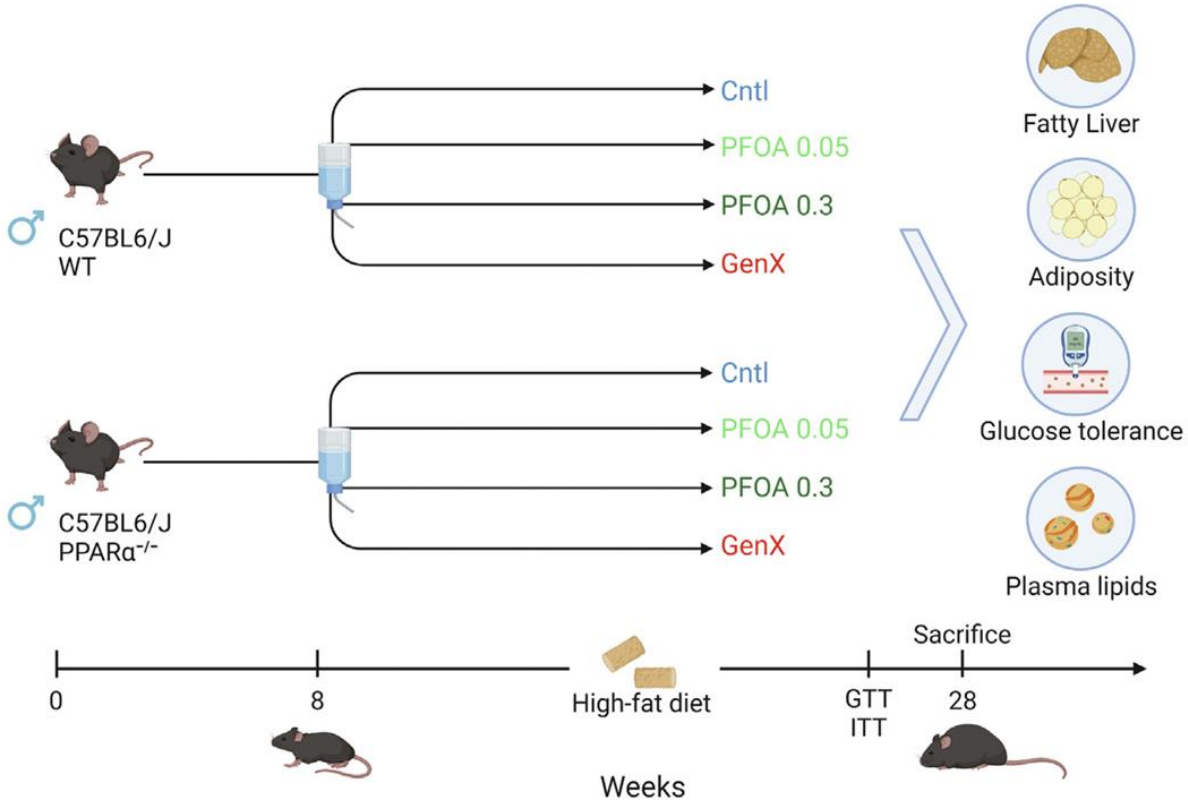
Original Article

MOLECULAR METABOLISM

Exposure to low-dose perfluorooctanoic acid promotes hepatic steatosis and disrupts the hepatic transcriptome in mice

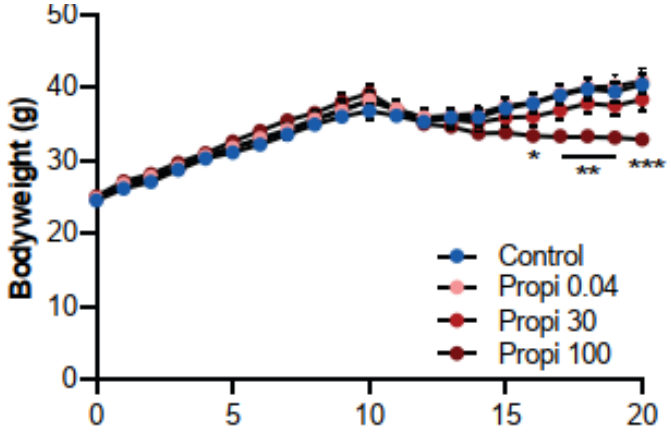
Brecht Attema [1], Aafke W.F. Janssen [2], Deborah Rijkers [2], Evert M. van Schothorst [3], Guido J.E.J. Hooiveld [1], Sander Kersten [1,*]

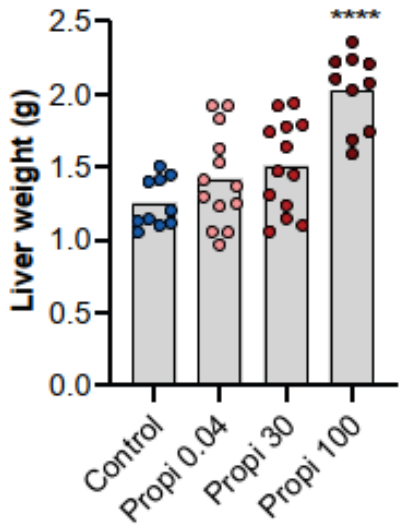


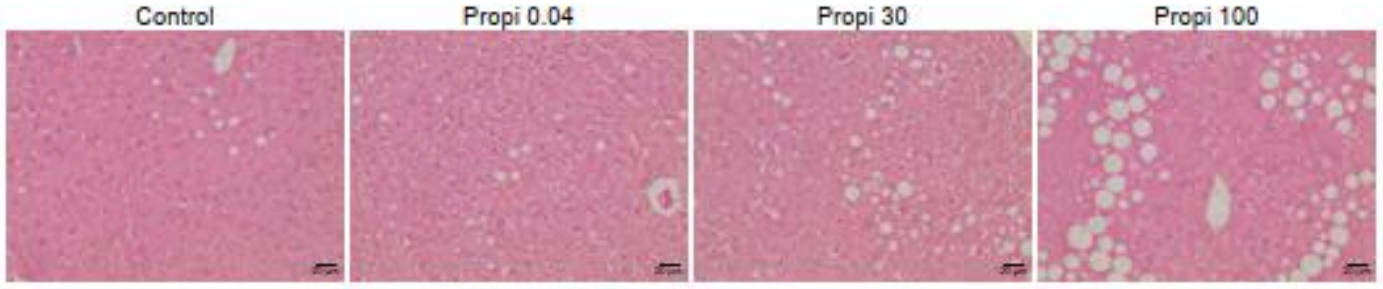


➡ High fat-diet sensitizes mice to the effects of EDCs

20-week propiconazole exposure with high-fat diet

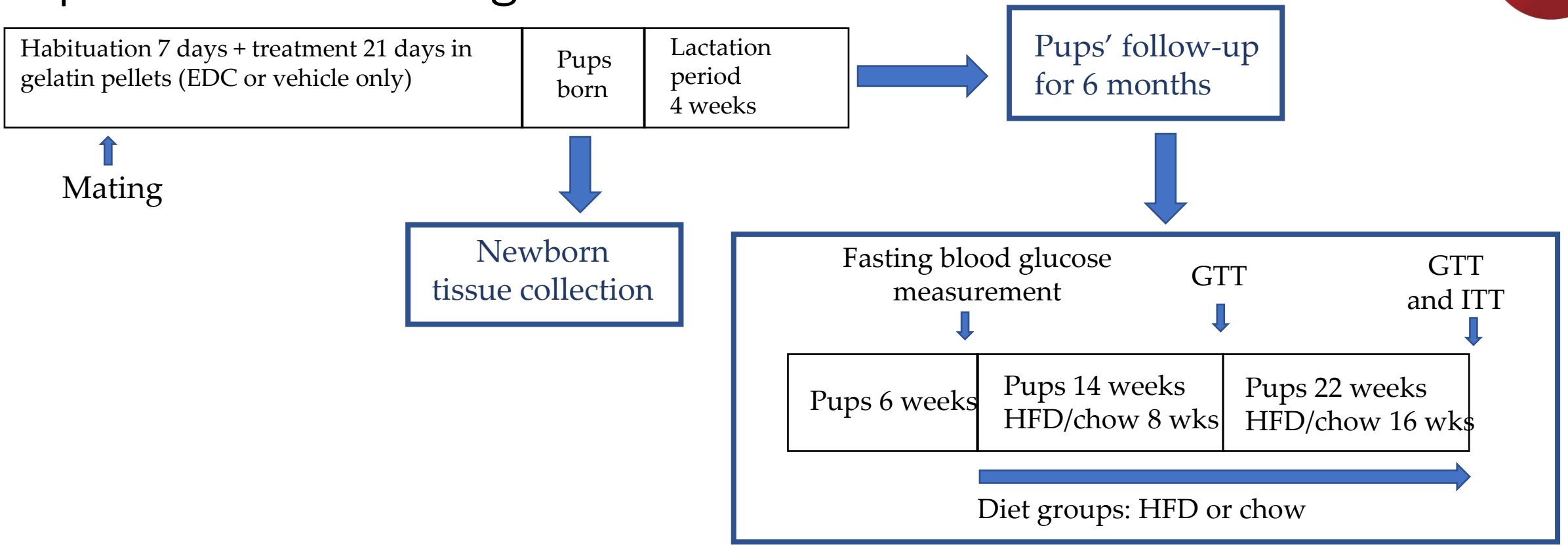






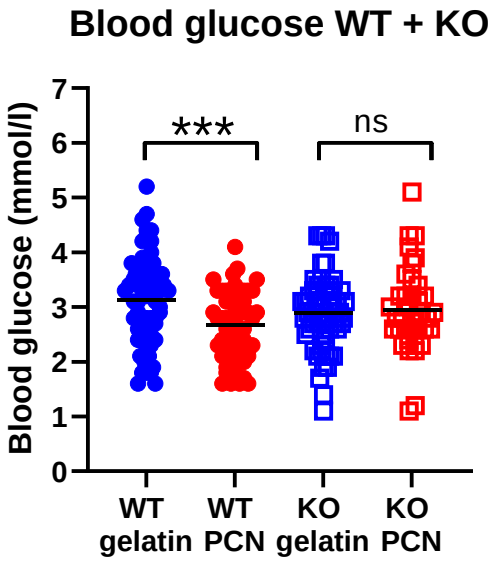
In utero exposure

Experimental setting

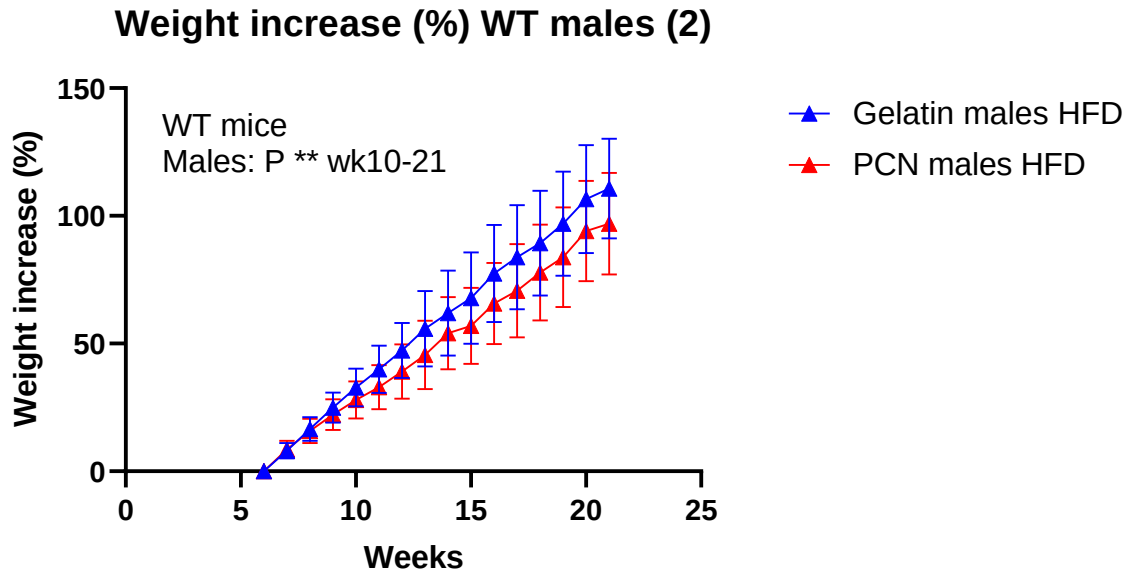


Testing of the method with a PXR ligand pregnenolone 16 α-carbonitrile (PCN)

Newborns



Follow-up



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RESEARCH PAPER

Activation of pregnane X receptor induces atherogenic lipids and PCSK9 by a SREBP2-mediated mechanism

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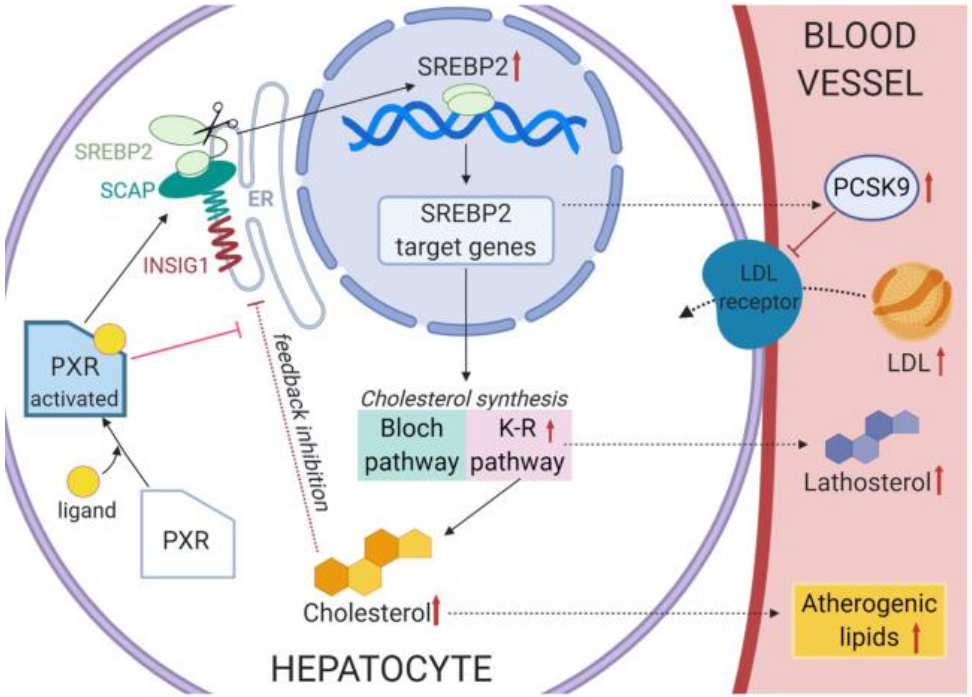

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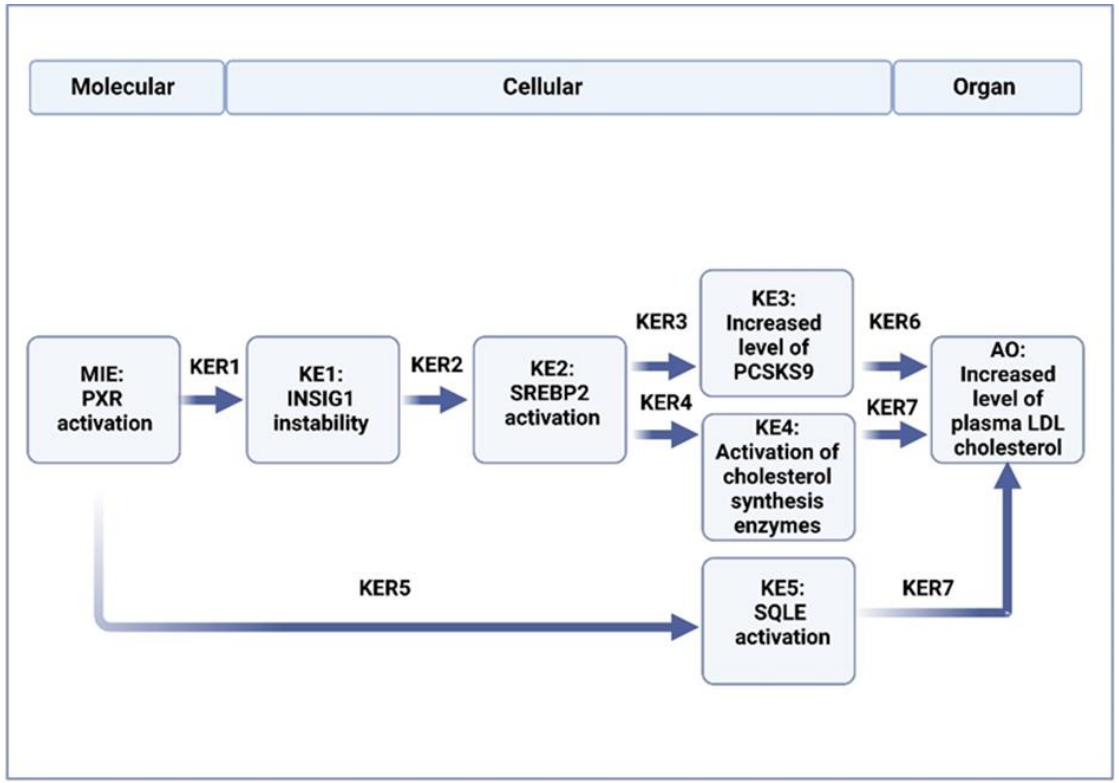
REVIEW ARTICLE

Adverse outcome pathway for pregnane X receptor-induced hypercholesterolemia

Anna Itkonen[1] · Jukka Hakkola[2] · Jaana Rysä[1]



Conclusions

- Two useful protocols for detection of metabolic disruption
  - HFD + ED compound exposure protocol
  - In utero exposure protocol
- New mechanistic data and understanding on metabolic toxicity pathways

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Thank you!

www.uef.fi/edcmet

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EURION