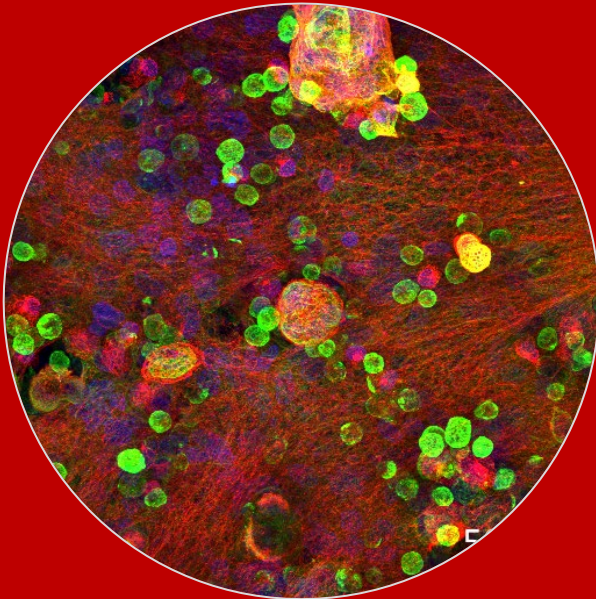


Micro- and Nanoplastics: Deciphering translocation and effects at the maternal-fetal interface



Dr. Tina Buerki-Thurnherr

Swiss Symposium on Endocrine Disrupting Chemicals, 28.10.24

Micro-/Nanoplastics (MNPs) in pregnancy



Hints for developmental toxicity of MNPs (animal studies):

Polystyrene NPs can reduce placental & fetal weight

Polystyrene NPs can cause defective neural tube morphogenesis

Polystyrene MNP co-exposure injures fetal thalamus

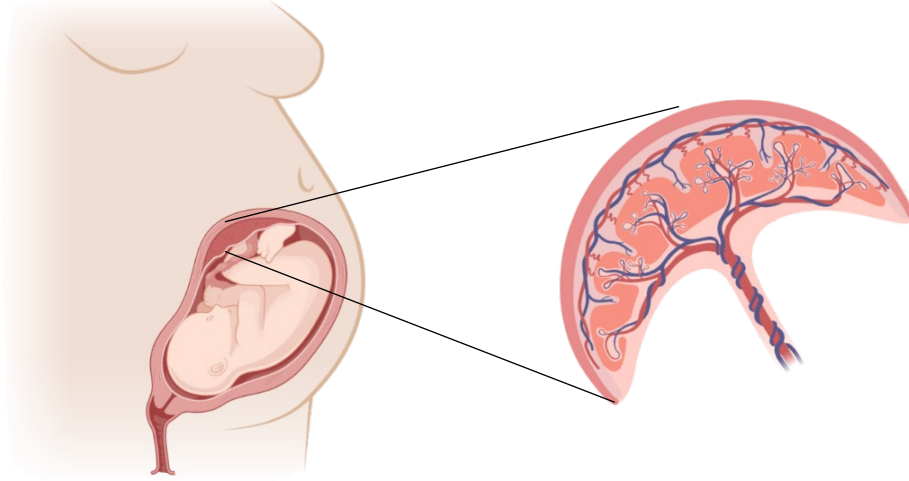
2020: Fournier et al., PFT

2021: Nie et al., Nanotoxicology

2022: Yang et al., Environm. Int.

- ➔ Can MNPs cross the placental barrier? Is this dependent on the particle properties?
- ➔ What are the health impacts of MNPs in human pregnancy?

Placenta – indispensable for successful pregnancy



- **Barrier function:** protection against infectious agents
- **Maternal-fetal exchange:** nutrients, waste products, gases
- **Immunological maternal tolerance:** prevents rejection of the fetus
- **Hormonal secretion:** important for fetal growth & development

➔ Placenta is central to proper embryo-fetal development and is **very sensitive to disturbances from toxic substances**

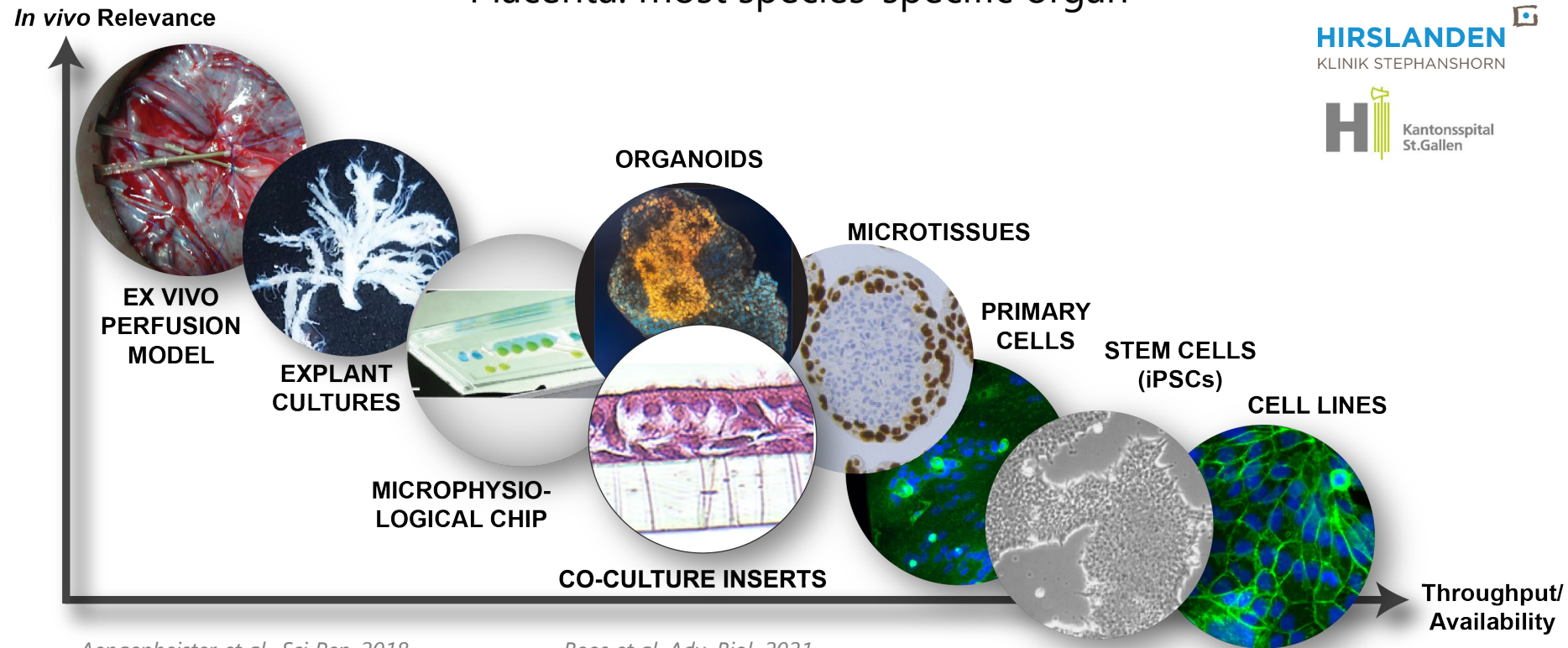
Advanced human-based models



-> Placenta: most species-specific organ

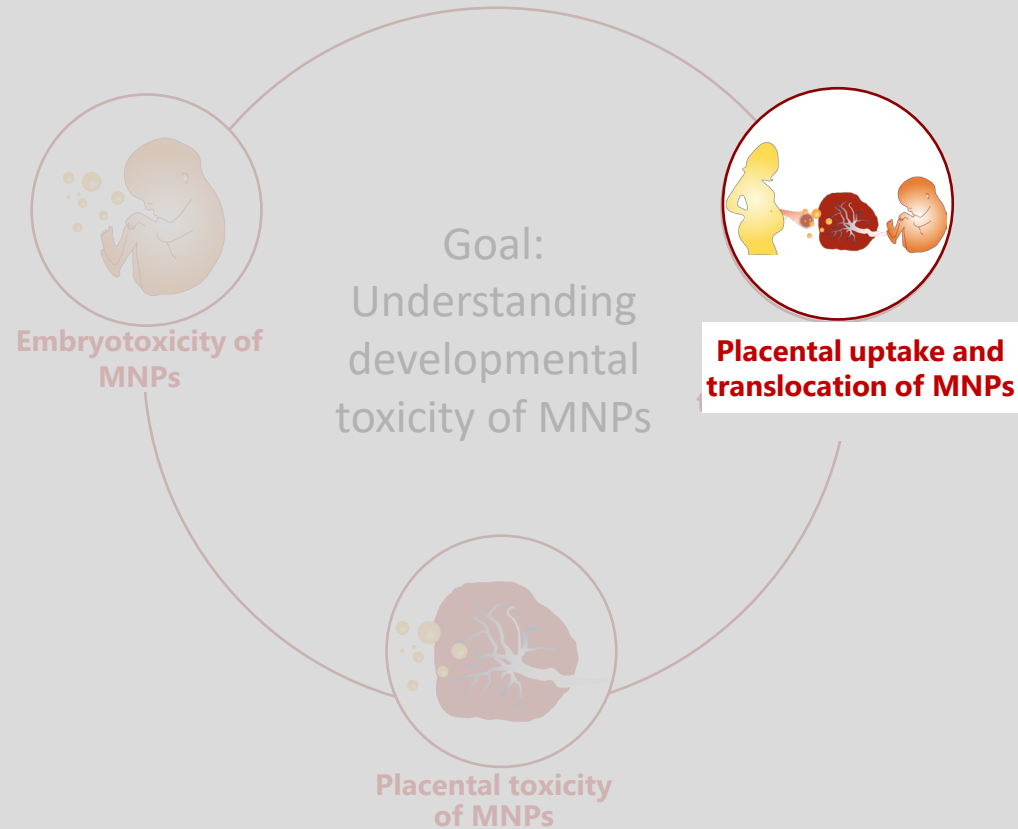
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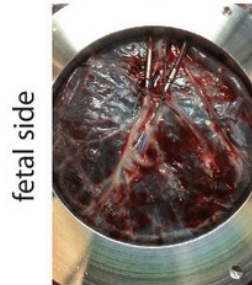
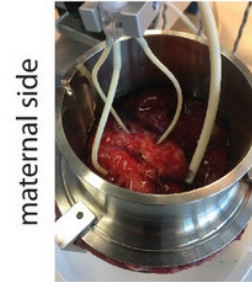
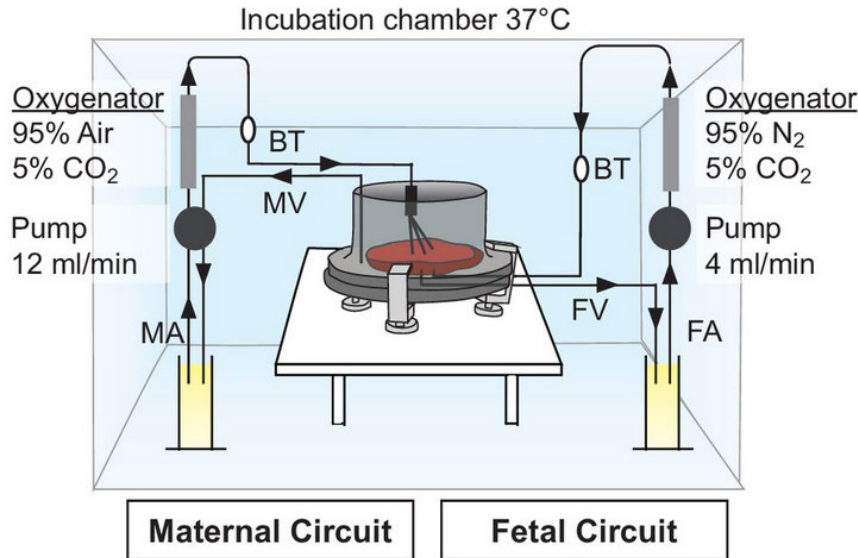
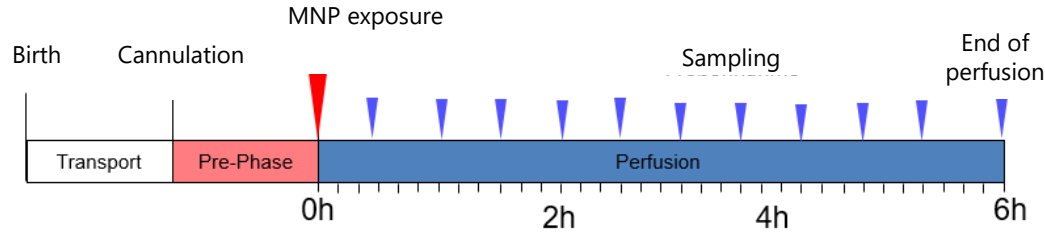


Aengenheister et al., *Sci Rep.*, 2018
Muoth, *Nanoscale*, 2016
Grafmüller et al., *J. Vis. Exp.*, 2013

Boos et al., *Adv. Biol.*, 2021
Dugershaw-Kurzer et al., *Adv. Sci.*, 2024



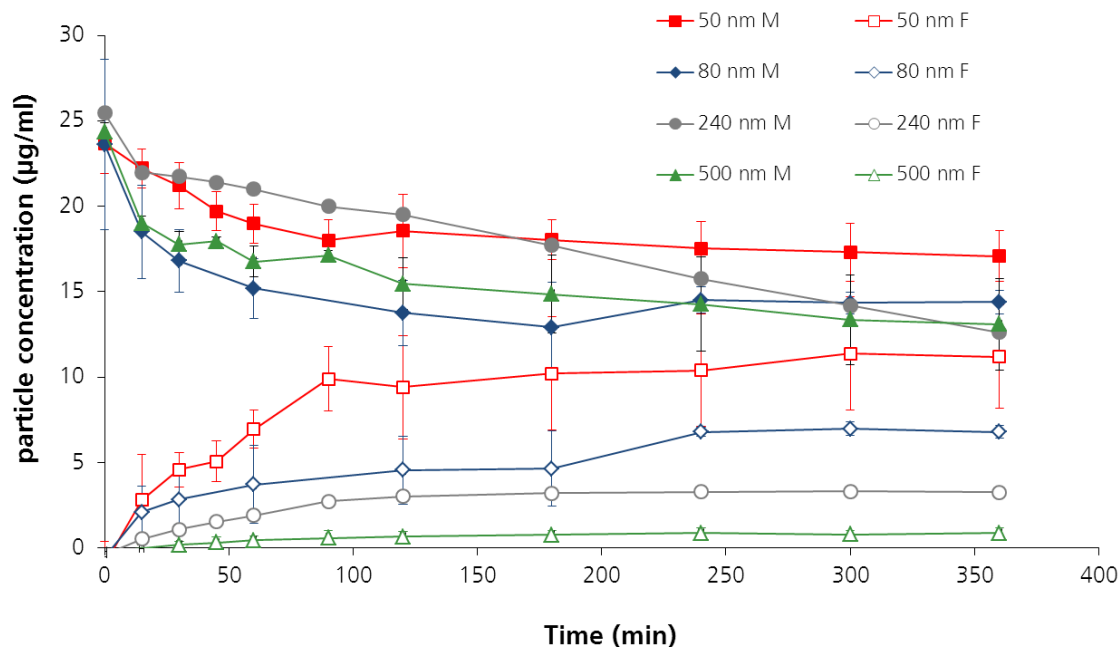
Placenta perfusion model to study MNP transfer



Placental translocation of micro/nanoplastics (MNPs)



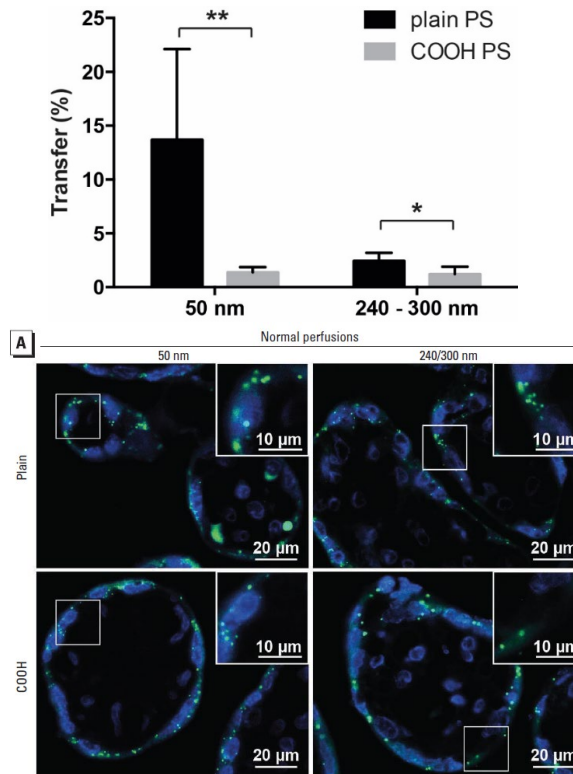
50-500 nm polystyrene (PS) MNPs



➔ Size matters! Higher translocation for smaller PS particles

Wick et al, EHP, 2010
Grafmüller et al, EHP, 2015

Plain vs carboxylate polystyrene NPs



➔ Surface modifications matters!

Confirmation from ambient MNP exposure

Microplastics detected in human placenta -> «Plasticenta»

2021: Ragusa et al., Environ. Int.

"It is like having a cyborg baby, no longer composed only of human cells, but a mixture of biological and inorganic entities." — Dr. Antonio Ragusa

Microplastics detected in meconium
(suggesting fetal transfer)

2022: Liu et al., Env. Sci and Technol.

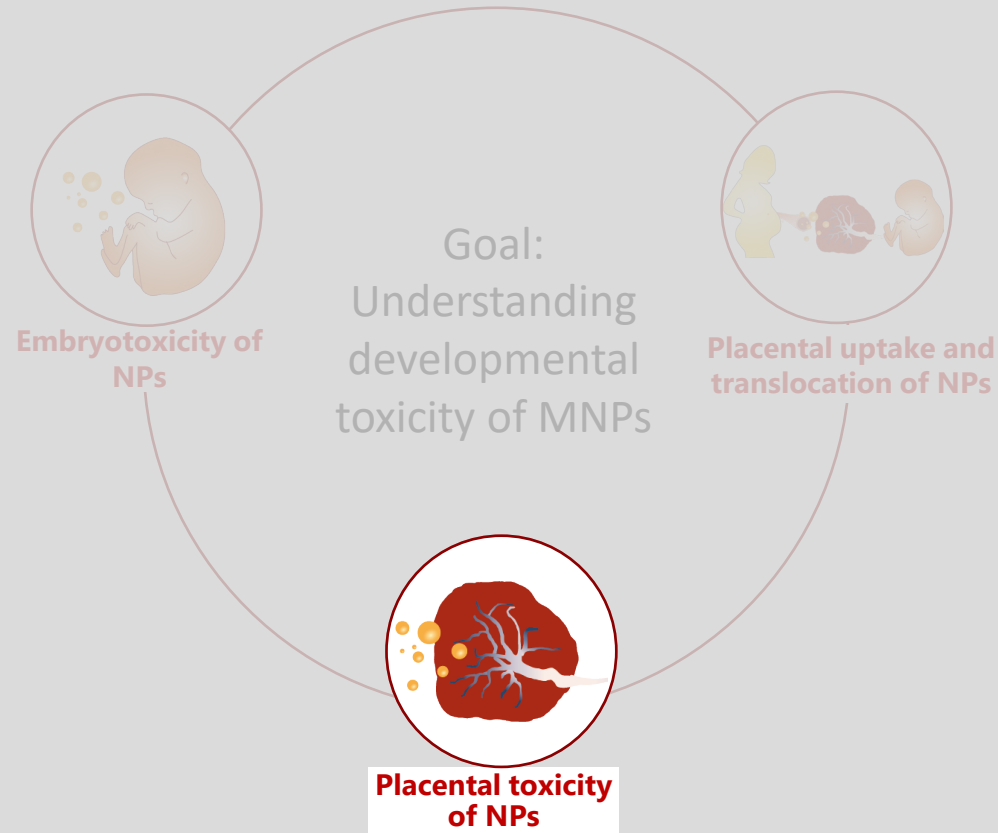
CARRY STRONG®



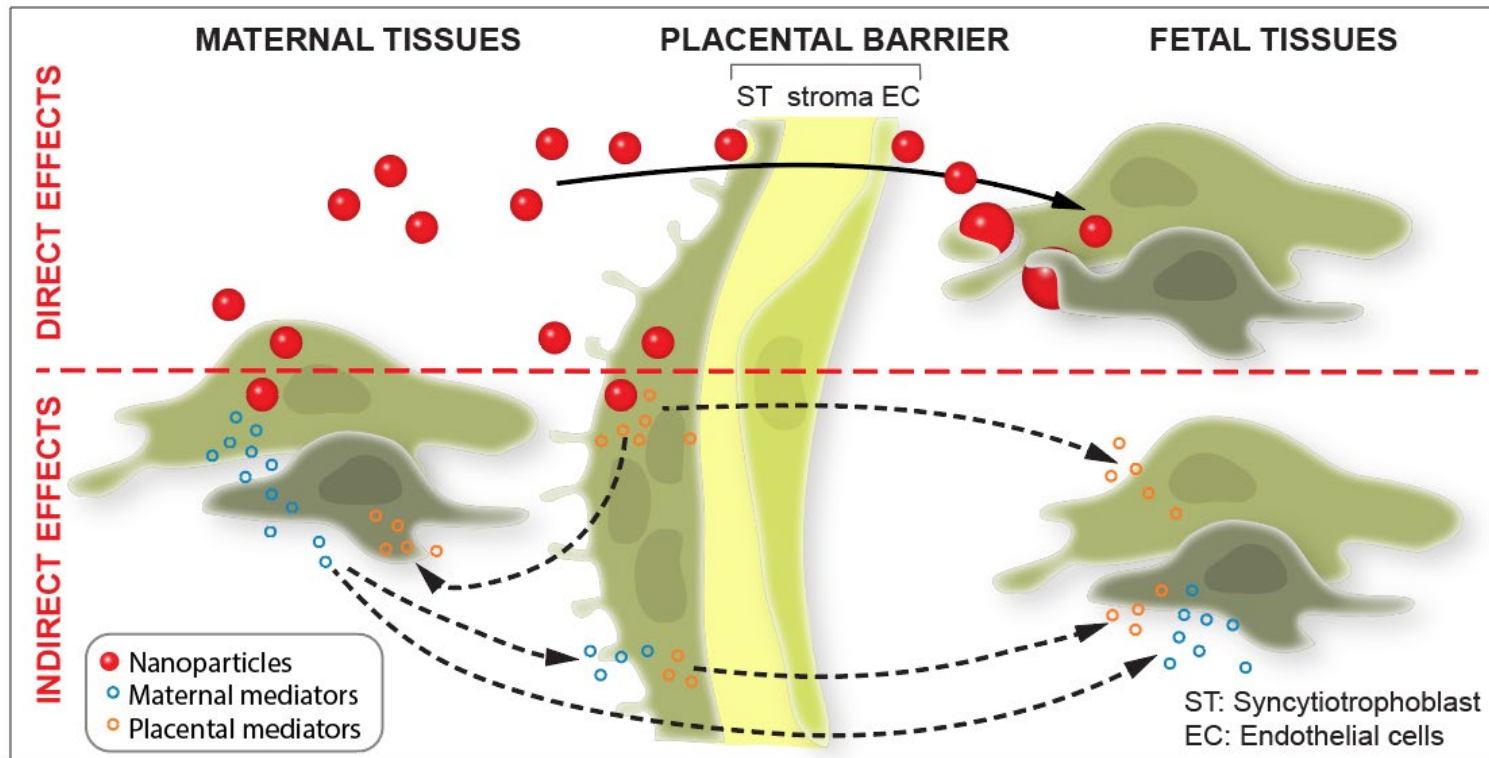
"Evidence of microplastics in human breastmilk, coupled with the previous discovery of these microparticles in the human placenta represents a great concern since it impacts the extremely vulnerable population of infants."

L'ORÉAL
PARIS

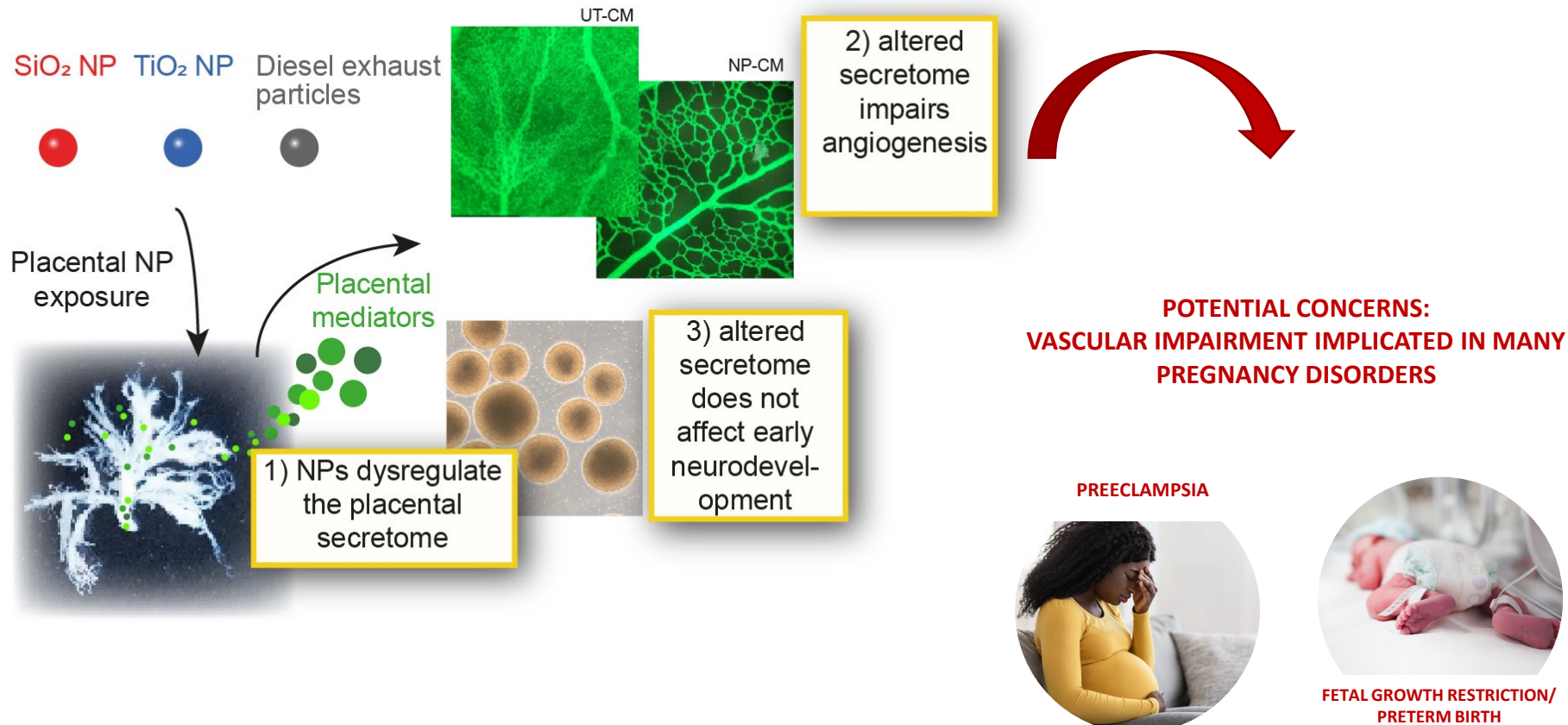
WWW.PLASTICENTA.COM



Developmental toxicity mechanisms of NPs



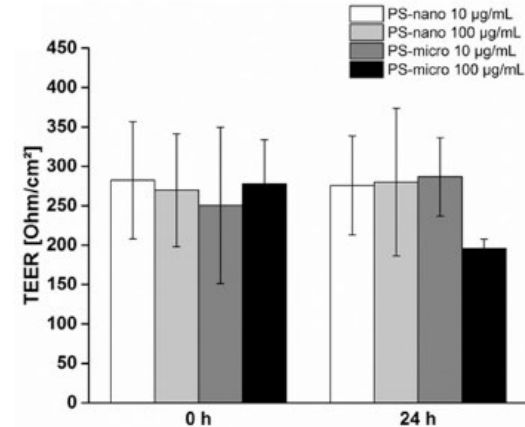
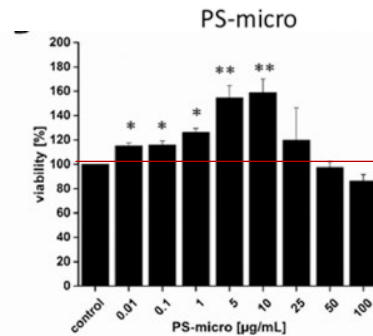
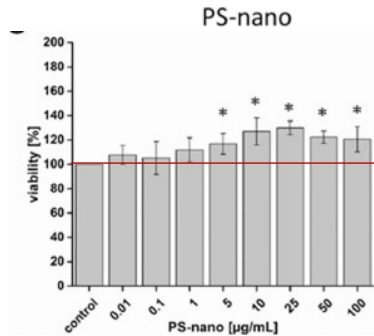
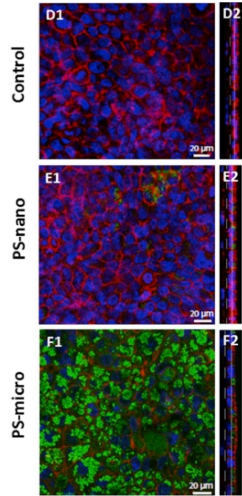
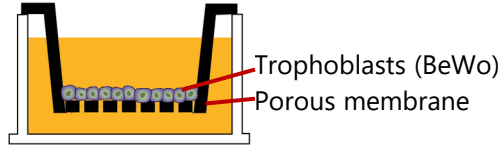
Indirect effects matter!



Effects of MNPs on placenta viability and function



COOH-PS MNPs (50 nm, 5 μ m)
48 h

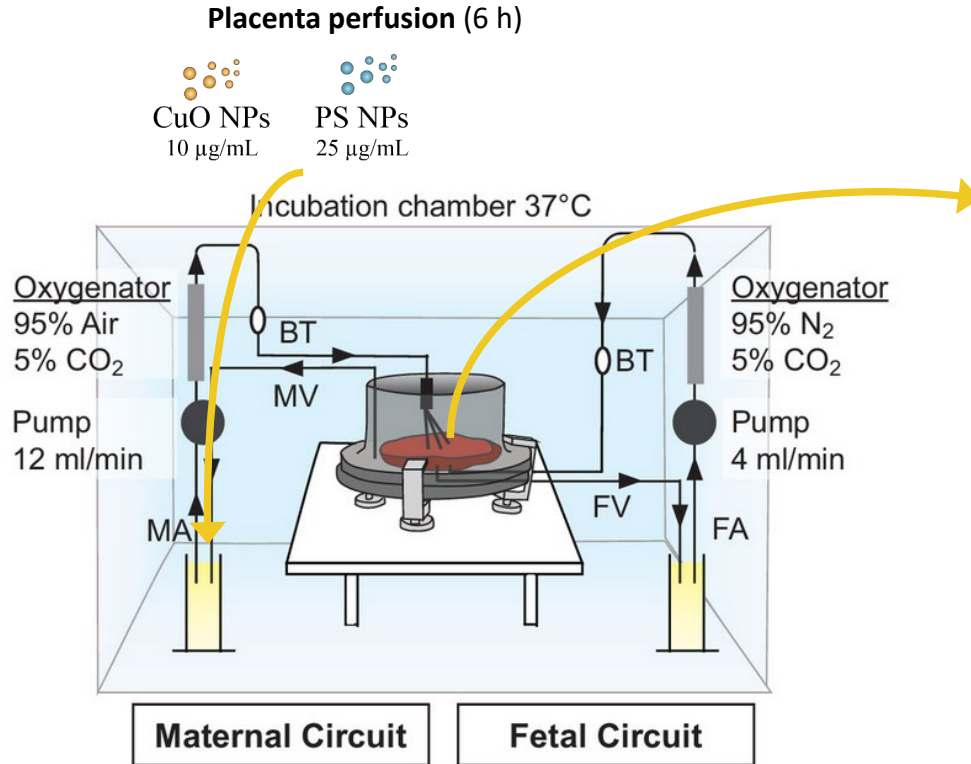


➡ no translocation but intracellular accumulation

➡ no effect on cell viability (MTS; 48 h)

➡ no effect on barrier integrity (TEER; 48 h)

Effects of PS NPs on placental gene expression



Transkriptomics /Bioinformatik

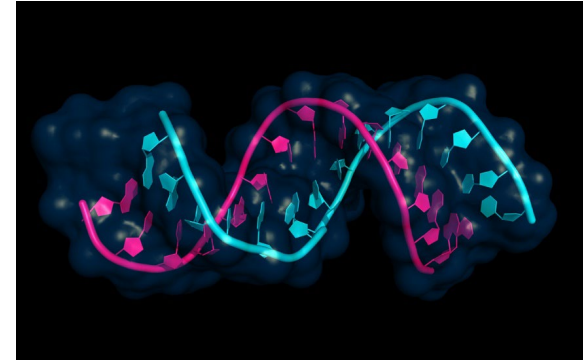
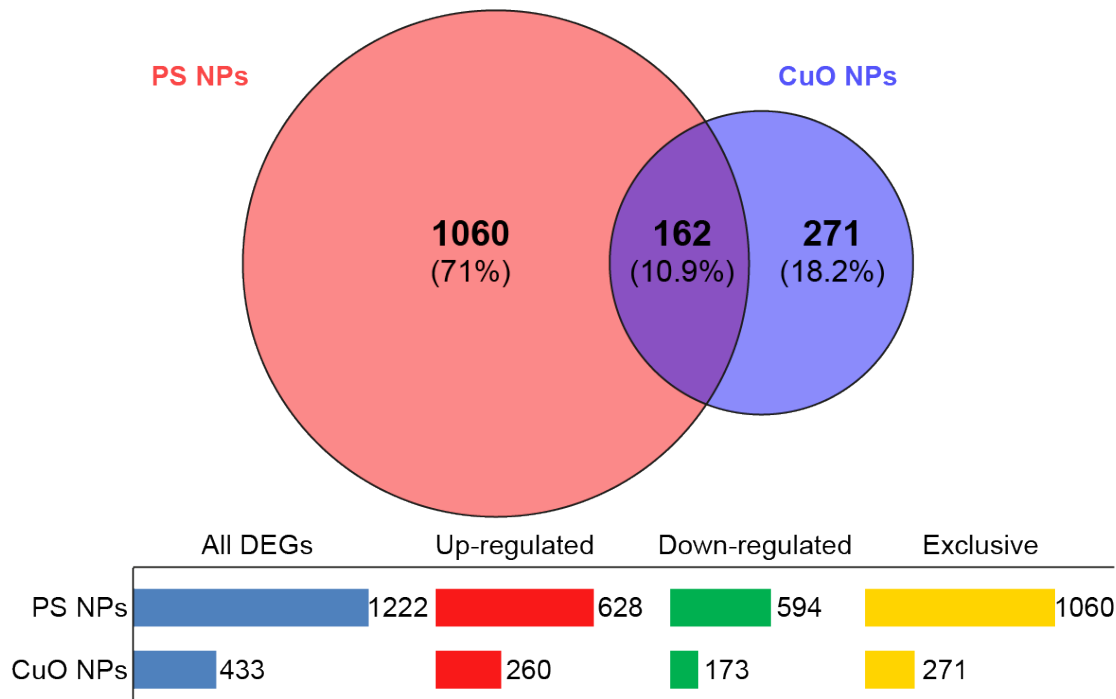
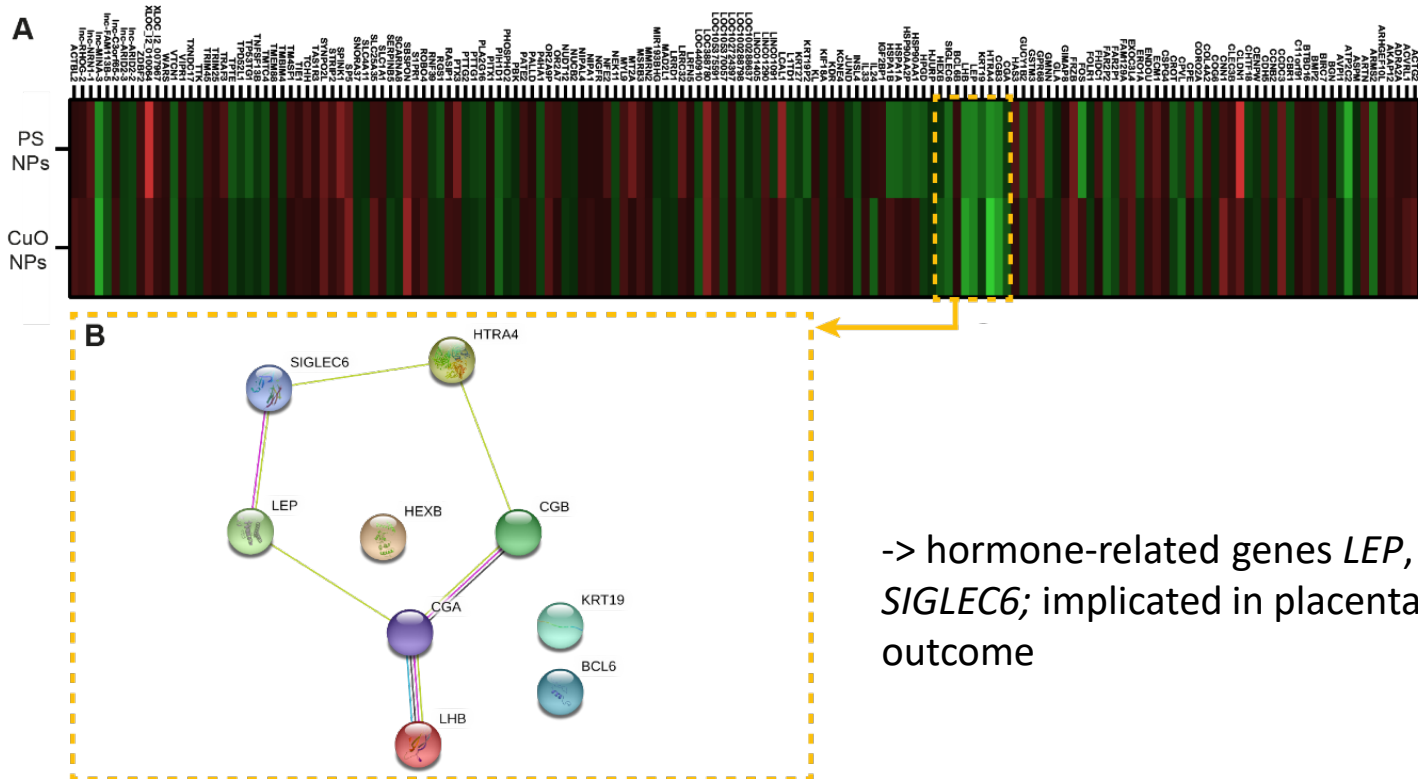


ILLUSTRATION: © PETARG/SHUTTERSTOCK.COM

Material-specific alterations of gene expression

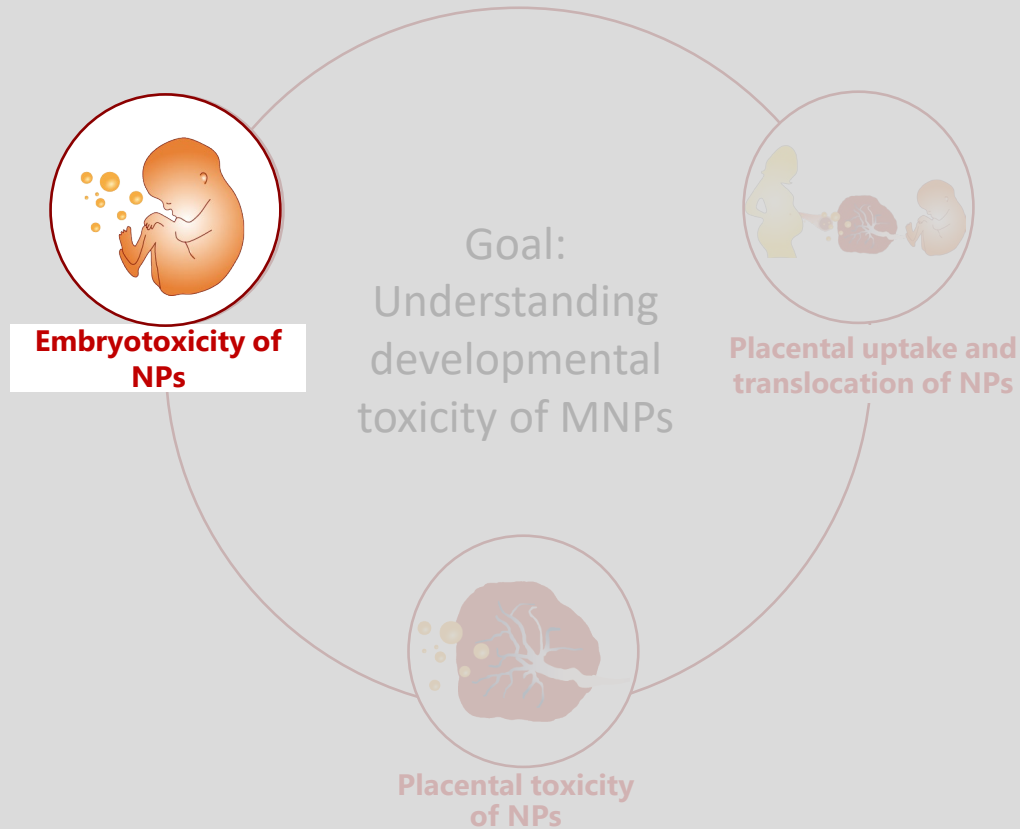


Common DEGs: hormone metabolic processes



-> hormone-related genes *LEP*, *LHB*, *CGA*, *CGB*, *HTRA4*, *SIGLEC6*; implicated in placental function and pregnancy outcome

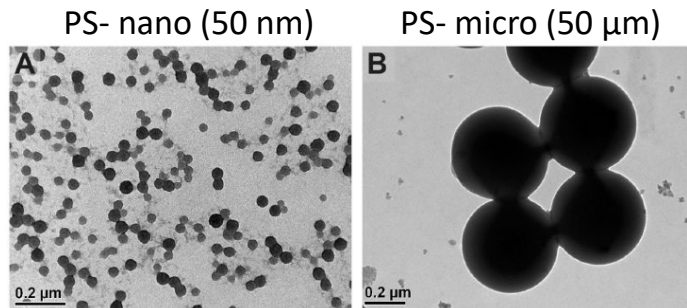
LEP: Leptin
CGA/B: human chorionic gonadotropin
LHB: Luteinizing hormone
SIGLEC-6: potential leptin receptor in PE



Embryotoxicity of COOH-PS MNPs



Mouse embryonic stem cell test
(EST, ECVAM validated):



1. Cytotoxicity to fibroblasts
2. Cytotoxicity to ES cells
3. Inhibition of differentiation
(contracting myocardial cells)

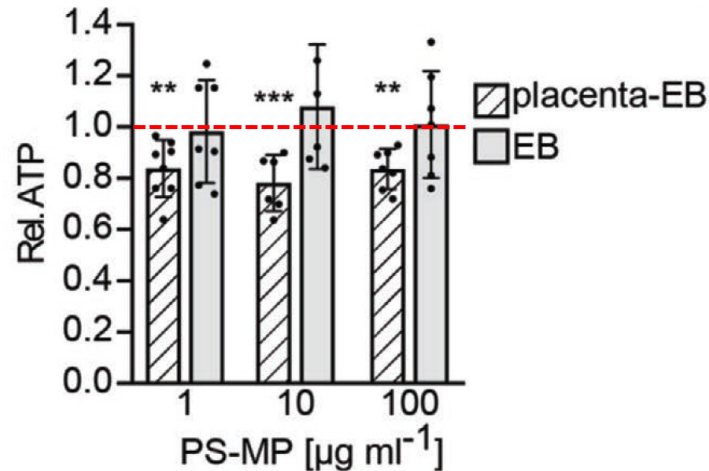
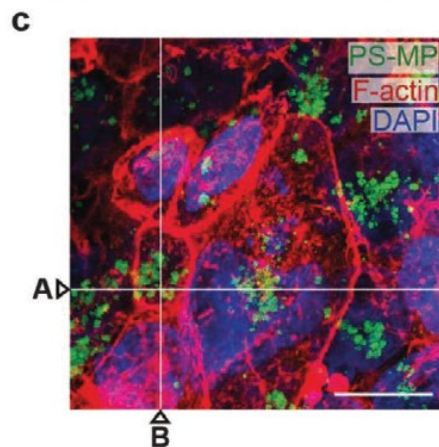
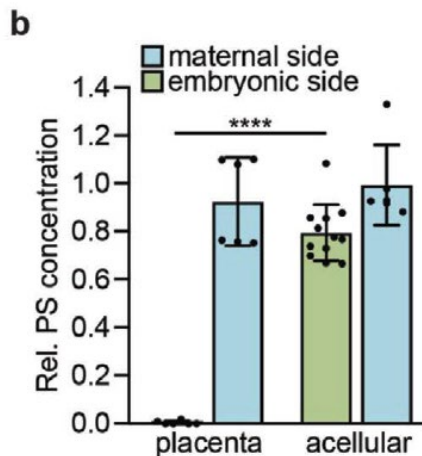
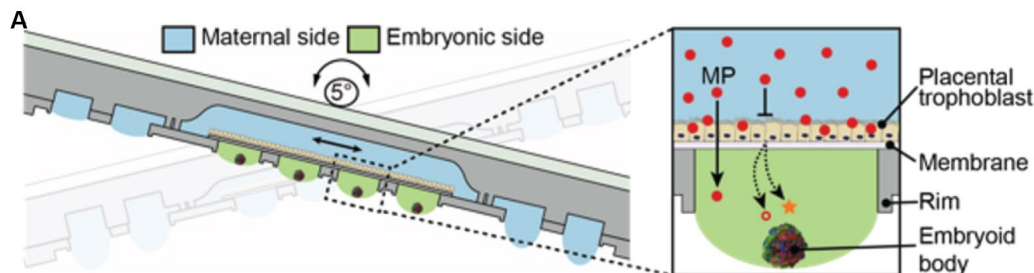
	PS- nano	PS- micro
IC ₅₀ NIH/3T3	> 100 μ g/mL	12.6 μ g/mL
IC ₅₀ mESC-D3	> 100 μ g/mL	12.6 μ g/mL
ID ₅₀	89.9 μ g/mL	0.1 μ g/mL
Classification	weak embryotoxic	weak embryotoxic

Adapted from Seiler et al. Methods Mol Biol. 2006

Hints for indirect embryotoxicity of MNPs

Placenta-embryo chip:

Capture systemic responses including short lived intermediates



→ **placental uptake but no translocation** of PS-MPs (500 nm)

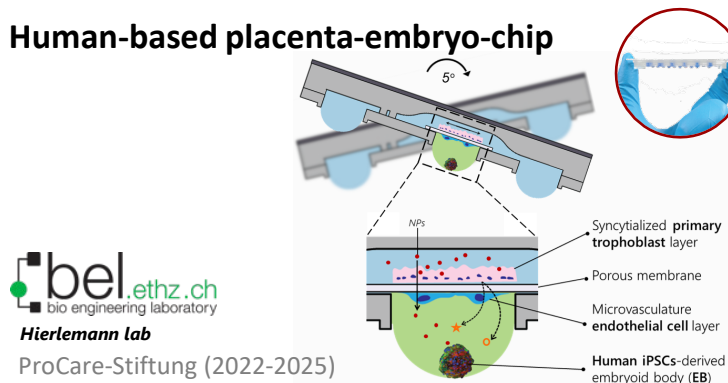
→ **Viability of the EBs decreased** only in presence of the placental barrier

Conclusions and Outlook



- 1) MNPs accumulate in the placenta and can cross to the embryo (dep. on physico-chem. properties)
- 2) MNPs can induce sub-lethal effects at the maternal-fetal interface (direct and indirect mechanisms) -> long-term consequences?

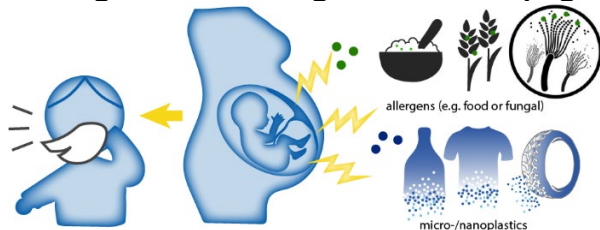
Outlook Human-based placenta-embryo-chip



bel.ethz.ch
bio engineering laboratory
Hierlemann lab

ProCare-Stiftung (2022-2025)

Priming of immunological diseases (e.g. allergies)

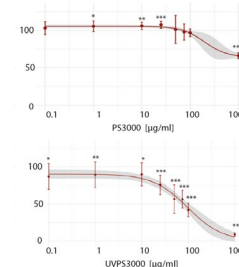
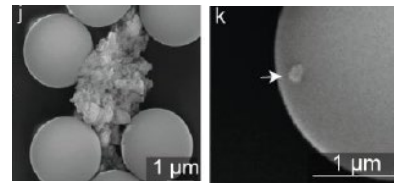


Heuberg Stiftung / Eduard Aeberhardt-Stiftung (2024-2027)

Production and assessment of more realistic MNPs

Grinding/milling/abrasion of real-life plastics

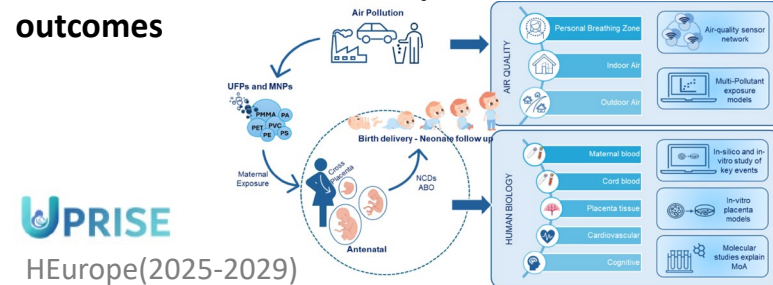
UV-exposure



role of additives/env. contaminants?

Englert et al, Env SciNano, 2021

Correlation of UFP/MNP exposure with adverse birth outcomes



Uprise

HEurope(2025-2029)

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Thank you for your attention!