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Placenta perfusion system: a human ex vivo model system to study the maternal – fetal barrier capacity for nanosized materials

Background: Humans have been exposed to nanosized particles (NPs; < 100 nm) throughout their evolutionary stages. Exposure changed dramatically since the industrial revolution. Additionally the emerging field of nanotechnology led to the fact that engineered NPs, i.e. nanoparticulate materials with novel physical and chemical properties and commercial expectations in different manufacturing sectors were used.

Reviews summarizing several in vitro and in vivo studies with special focus on biopersistent and bioavailable NPs show the potential toxic effects of these particles to human health. The main translocation routes for the uptake of NPs are the respiratory tract (by air), the gastrointestinal tract (GI) (by food, water) and the skin (by air and water). When inhaled, NPs are efficiently deposited in all regions of the respiratory tract; they may evade specific defense mechanisms and can translocate via different pathways (endocytosis or transcytosis) into the blood system.

One important barrier was not yet taken into consideration so far: the human placenta which is responsible for the nutrients, gas and waste exchange between fetal and maternal blood. Because of the unique anatomy of the human placenta no equivalent animal system is available. The ex vivo dual perfusion system can address therefore the questions of pharmacokinetics of endogenous substances, xenobiotics and nanoparticles in maternal/fetal circulation.

Objective: To establish and validate the placenta perfusion system for studying the translocation and accumulation of NPs and potential changes of the placental tissues after perfusion.

Methods: Intact placentas were obtained from uncomplicated pregnancies either after vaginal or cesarean section. To perfuse the placenta, the arteries and veins of a suitable cotyledon were cannulated resulting in two independent perfusion circuits (Figure 1). Polystyrene beads of varying size (50 – 500 nm) were added to the perfusion system and perfusion was run for up to 6 hours. The concentration of nanoparticles was determined by fluorescence analysis. Viability and function parameters of the placenta were determined by measuring the glucose consumption, the production of lactate and two placental hormones (human chorionic gonadotropin (hCG) and leptin) as well as the ¹⁴C]antipyrine concentration (indicator for placental permeability) from the perfused media. Histological investigations of the placental tissue and biochemical analysis of the perfusion solution were made to assess the viability of the placenta during the perfusion period.

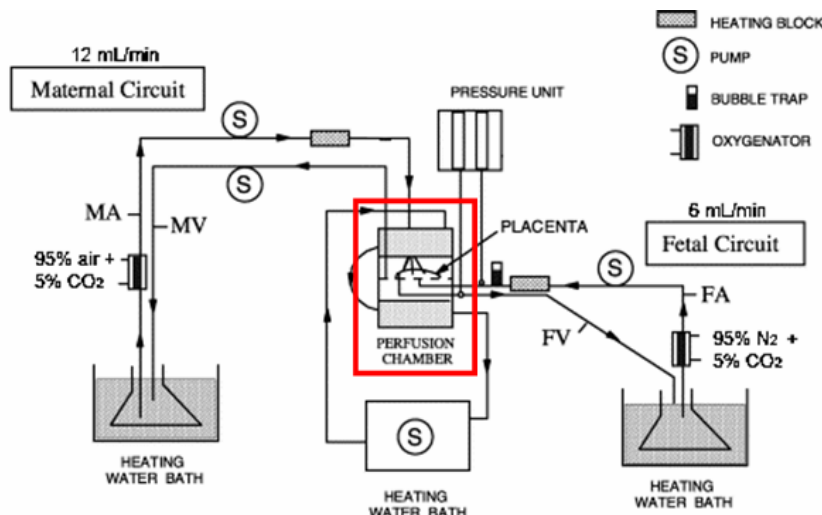


Figure 1: The human placenta perfusion model. FA: fetal artery; FV: fetal vein; MA: maternal artery; MV: maternal vein (from Malek A et al., 2003).