Differentially expressed microRNAs in maternal plasma and preimplantation embryos of diabetic rabbits

Context: Placental dysfunction is a common complication of diabetic pregnancies with potentially long-lasting effects on offsprings' health. We hypothesize that placental dysfunction begins during trophoblast differentiation and may be identified by the expression of specific trophoblastic microRNAs (miRNAs).

Objective: To determine the effects of diabetes mellitus type 1 during early pregnancy on maternal and embryonic microRNA expression.

Methods: Experimental insulin-dependent diabetes (expIDD) was induced in female non-pregnant rabbits by alloxan treatment. Rabbits were held in diabetic conditions with blood glucose concentrations of >14 mmol/l by regular insulin supplementation 3 times per day. Six days after mating the maternal blood samples were collected, embryos recovered and RNA extracted. In vitro culture with 17nM insulin for 2 or 4 hours was performed with day 6 blastocysts from healthy rabbits. The relative expression of miRNA-27b, -141, -191, -222 and -433 was determined by RT-qPCR in maternal plasma and day 6 blastocysts (blastocyst cavity fluid, embryoblast and trophoblast cells).

Animal model: New Zealand White rabbits and rabbit blastocysts

Intervention: Quantitative real-time PCR

Main Outcome Measure: MicroRNA expression profile

Results: MiR-27b, -141, -191, -222 and -433 were found in maternal plasma, embryoblast and trophoblast cells and blastocyst cavity fluid. ExpIDD led to an altered expression pattern of these miRNAs in maternal plasma and in preimplantation embryos. In vitro culture with 17nM insulin had no influence on miRNA expression.

Conclusions: Maternal diabetes mellitus leads to distinct changes of miRNA expression in the mother and in blastocysts. Furthermore, our results show for the first time the incidence of miRNAs in blastocyst cavity fluid, indicating that they might serve as communicator between embryoblast and trophoblast cells.