**THE EFFECT OF MATERNAL OBESITY ON THE EXPRESSION AND FUNCTIONALITY OF PLACENTAL P-GLYCOPROTEIN: IMPLICATIONS IN THE INDIVIDUALIZED TRANSPLACENTAL DIGOXIN TREATMENT FOR FETAL HEART FAILURE**

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*Introduction*: Placental P-glycoprotein (P-gp) plays a significant role in controlling digoxin transplacental rate. Investigations on P-gp regulation in placenta of women with different pregnant pathology are of great significance to the individualized transplacental digoxin treatment for fetal heart failure (FHF). This study aimed to explore the effect of maternal obesity on the expression and functionality of placental P-gp both in human and in mice.

*Methods*: Placenta tissues from obese and lean women were collected. Female C57BL mice were fed with either a normal chow diet or a high-fat diet for 12 weeks before mating and throughout pregnancy. Maternal plasma glucose, HDL-C, LDL-C, TC, TGs, insulin, IL-1β, IL-6 and TNF-α concentrations was detected. Placental *ABCB1/abcb1a/abcb1b/IL-1β/IL-6/TNF-α* mRNA and P-gp/IL-1β/IL-6/TNF-α protein expression were determined by real-time quantitative PCR and western-blot, respectively. Maternal plasma and fetal-unit digoxin concentrations were detected by a commercial kit assay.

*Results*: Both *ABCB1* gene mRNA and protein expression of obesity group was significantly lower than that of control group in human. The high-fat dietary intervention resulted in an overweight phenotype, a significant increased Lee’s index, higher levels of plasma glucose, HDL-C, LDL-C, insulin and TGs, increased peri-renal and peri-reproductive gland adipose tissue weight and larger size of adipose cell. Compared with control group at the same gestational day (E12.5, E15.5, E17.5), placental *Abcb1a* mRNA and P-gp expression of obese group were significantly decreased in mice, while digoxin transplacental rates were significantly increased. Higher maternal plasma IL-1β/TNF-α concentrations and placental IL-1β/TNF-α expression were observed in obesity groups in comparison with control group at the same gestational age.

*Conclusions*: Maternal obesity could inhibit placental P-gp expression and its functionality both in human and in mice, which might be resulted from a heightened inflammatory response.