## Crosstalk between the mother, placenta and fetus in health and disease

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The placenta is a multifunctional organ that orchestrates maternal adaptations to pregnancy, provides gaseous, nutritional and waste exchange between the maternal and fetal circulations and mediates fetal signalling to the mother. Placental function is determined by fetal genetics but also responds to maternal genetics, maternal health, nutrition, lifestyle and environmental exposures. The complexity of its multiple functions and the myriad factors that influence it have made it difficult to understand the mechanisms by which the placenta programs the fetus. We recruited a large cohort of pregnant nulliparous women and aimed to identify factors in early pregnancy that contribute to risk for pregnancy complications namely preeclampsia, preterm birth, IUGR and gestational diabetes. Fetal genetics including genes on the sex chromosomes contribute to differences in pregnancy outcomes. Males are more likely to be born spontaneously preterm than females while females are more likely to be delivered early by doctor initiated interventions due to preterm preeclampsia. Our meta-analysis of the transcriptome from 303 placentas showed that 142 genes are differentially expressed in the normal term singleton male *versus* female placenta. In our recent analysis of DNA methylation in the placenta from 8-42 weeks gestation we have identified 62 CpG sites for which the dynamically changing profile reflects the gestation at sampling. Interestingly, DNA methylation age is accelerated in placentas from early onset preeclampsia cases but not in term preeclampsia. Other factors that contribute to adverse pregnancy outcomes include maternal micronutrient status, particularly deficiencies in zinc, folate and vitamin D. We have data from both mouse and human studies that show that maternal deficiencies in these important micronutrients associate with oxidative stress in the placenta and with small for gestational age and preterm babies. Ongoing work is focused on whether these deficiencies also alter placental epigenetic state.