Mice exposed to maternal androgen excess and diet-induced obesity have altered phosphorylation of catechol-O-methyltransferase in the placenta and fetal liver

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Background/objectives: Maternal obesity together with androgen excess in mice negatively affects placental function and maternal and fetal liver function as demonstrated by increased triglyceride content with dysfunctional expression of enzymes and transcription factors involved in de novo lipogenesis and fat storage. To identify changes in molecular pathways that might promote diseases in adulthood, we performed a global proteomic analysis using a liquid-chromatography/mass-spectrometry system to investigate total and phosphorylated proteins in the placenta and fetal liver in a mouse model that combines maternal obesity with maternal androgen excess. Methods: After ten weeks on a control diet (CD) or high fat/high sugar-diet, dams were mated with males fed the CD. Between gestational day (GD) 16.5 and GD 18.5, mice were injected with vehicle or dihydrotestosterone (DHT) and sacrificed at GD 18.5 prior to dissection of the placentas and fetal livers. Four pools of female placentas and fetal livers were subjected to a

global proteomic analysis. Total and phosphorylated proteins were filtered by ANOVA $q < 0.05$, and this was followed by two-way ANOVA to determine the effect of maternal obesity and/or androgen exposure. Results: In placenta, phosphorylated ATP-citrate synthase was decreased due to maternal obesity, and phosphorylated catechol-O-methyltransferase (COMT) was differentially expressed due to the interaction between maternal diet and DHT exposure. In fetal liver, five total proteins and 48 proteins phosphorylated in one or more sites, were differentially expressed due to maternal obesity or androgen excess. In fetal liver, phosphorylated COMT expression was higher in fetus exposed to maternal obesity. Conclusion: These results suggest a common regulatory mechanism of catecholamine metabolism in the placenta and the fetal liver as demonstrated by higher phosphorylated COMT expression in the placenta and fetal liver from animals exposed to diet-induced maternal obesity and lower expression of phosphorylated COMT in animals exposed to maternal androgen excess.