**Title:** Fetal growth restriction alters chromatin access in 1 year old rats with metabolic syndrome

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**Background**: Fetal growth restriction (FGR) and a high fat diet (HFD) program metabolic syndrome. Physiologic changes resulting in metabolic syndrome occur by alteration in gene expression of numerous metabolic pathways in multiple tissues including visceral adipose tissue (VAT) and liver. Chromatin access determines gene expression; increased chromatin access allows for increased gene expression. A recently described genome-wide assay, called assay for transposase-accessible chromatin using sequencing (ATAC-Seq), directly measures chromatin access to provide a mechanism through which alterations in gene expression can occur. We previously reported FGR-induced increases in visceral adiposity, serum lipids, and serum glucoses on glucose tolerance testing in a rat model of FGR combined with a HFD. We hypothesized that FGR combined with a HFD would alter chromatic access around genes for lipid and glucose metabolism more than a HFD alone.

**Methods**: Adult female rats were fed a HFD prior to mating and through gestation and lactation. FGR was induced by uterine artery ligation at E19.5 of a 21 day gestation. At postnatal day (PND) 21 all offspring were weaned to a HFD through 1 year of age. At 1 year of age, genome-wide ATAC-Seq was performed on n=3 fasting female rat liver and visceral adipose tissues and data queried for chromatin access around genes involved in glucose and lipid metabolism.

**Results:** Compared to non-growth restricted female rats, FGR female rats had increased VAT chromatin access of lipid transcription factors Srebf1 and Srebf2, the low density lipoprotein receptor (Ldlr), fatty acid synthase (Fas), insulin receptor (Ir), and glucose transporters Glut4 and Glut2. Conversely, FGR decreased hepatic chromatin access of Srebf1, Ldlr, Fas, Ir, Glut4, and Glut2. Data analyzed by pairwise analysis with log2 ratios with a cutoff of greater than +/- 0.5-fold log2 change. An unexpected finding was that by 10 months of age, FGR increased mortality 2.5-fold over non-FGR rats consuming the same amount of the HFD (p=0.01).

**Conclusion/Speculation**: FGR altered tissue-specific chromatin access in genes involved in glucose and lipid metabolism in a model of metabolic syndrome with increased premature mortality. Increased VAT chromatin access suggests enhanced lipid biosynthesis and increased glucose and lipid uptake into the adipose tissue of FGR rats with metabolic syndrome.