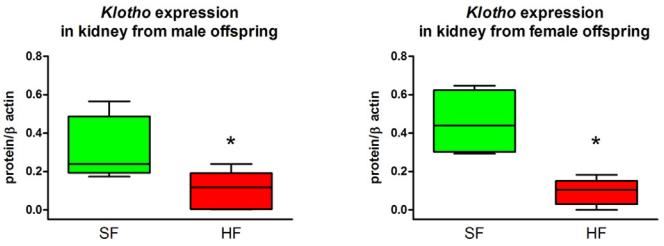
CONCLUSION: Offspring born to obese mice demonstrate an accelerated aging process. These modifications were tissue- specific. Our data demonstrates for the first time that maternal pre-pregnancy obesity resulting from high fat diet programs the offspring for the development of accelerated aging.



Box plot: median, 25th-ile, 75th-ile, max and min values. *p<0.05. SF: pups born to mothers fed standard chow, HF: pups born to mothers fed high fat diet.

46 Lipopolysaccharide (LPS)-induced perinatal inflammation increases postnatal airway reactivity

Arij Faksh[1], Rodney Britt[3], Elizabeth Vogel[3], Elizabeth Baldwin[1], Mari Charisse Trinidad[1], Wendy White[1], Brian Brost[1], Norman Davies[1], Carl Rose[1], Kristi Borowski[1], Christina Pabelick[2], Ys Prakash[2]

[1]Mayo Clinic College of Medicine, Maternal Fetal Medicine, Rochester, MN, [2]Mayo Clinic College of Medicine, Anesthesiology, Rochester, MN, [3]Mayo Clinic College of Medicine, Physiology & Biomedical Engineering, Rochester, MN

OBJECTIVE: Antenatal inflammation can impair pulmonary maturation and potentially promote development of postnatal chronic lung disease. The purpose of our investigation is to evaluate how in utero exposure to maternal inflammation influences neonatal pulmonary function in a murine model. Our hypothesis was that inflammation leads to structural and functional airway changes that contribute to chronic diseases such as asthma.

STUDY DESIGN: Breeding colonies of C57/BL6 wild-type mice were established. On embryonic day 16 pregnant dams underwent intraperitoneal injections with sterile saline or with different concentrations of LPS (E. coli 055:B5) to induce maternal inflammation: 50 ug/kg, 200 ug/kg, 400 ug/kg. Dams spontaneously delivered and pups were monitored until postnatal day 21 when pulmonary function testing was performed using a SciReq FlexiVent system. Airway resistance, compliance and inspiratory capacity were assessed at baseline and in response to increasing concentrations of the bronchoconstrictor methacholine.

RESULTS: Intra-peritoneal LPS did not adversely influence maternal or neonatal mortality, or maternal failure to thrive during pregnancy. Neonatal pups were of comparable weight across groups. At postnatal day 21, LPS pups showed lower weight compared to controls, but there were no significant differences between the three different LPS dose groups. Airway resistance was increased with LPS, and importantly, LPS pups showed decreased airway compliance and inspiratory lung capacity compared to saline controls.

CONCLUSION: In this model of LPS-induced maternal inflammation, pulmonary function of the progeny is detrimentally impacted in terms of increased airway resistance, decreased airway compliance, and decreased inspiratory capacity. These changes represent characteristics of inflammatory reactive airway disease such as asthma. Future studies are needed to determine how antenatal inflammation alters neonatal pulmonary structure and airway function with the aim of developing novel therapeutic avenues.

47 Differential expression of Rac1 in common aneuploidies: a model for altered placentation

Jason Farrell[1], Hannah Tilden[1], Yan Zhou[2], Susan Fisher[1], Katherine Bianco[1]

[1]University of California, San Francisco, Division of Maternal-Fetal Medicine, Department of Obstetrics, Gynecology, and Reproductive Sciences, San Francisco, CA, [2]University of California, San Francisco, Department of Obstetrics, Gynecology, and Reproductive Sciences, San Francisco, CA

OBJECTIVE: Inadequate formation and regeneration of the placenta contribute to several pregnancy syndromes such as IUGR & preeclampsia, which may lead to iatrogenic preterm delivery with the goal of preventing fetal death and maternal complications. We investigated the effects of commonly occurring aneuploidies (Trisomy 21,18, and 13; T21,T18 and T13, respectively) on placentation. Specifically, we focused on the role of Rac1, which our microarray data showed was upregulated in all three trisomies.

STUDY DESIGN: We collected second trimester samples of the maternal-fetal (decidua-placental) interface: 20 trisomy cases (T21, n=10; T18, n=6; T13, n=4) and 4 gestational age-matched, euploid controls (14-22 weeks). Fluorescent in situ hybridization was used to confirm ploidy. Microarray approach enabled global transcriptional profiling in trisomies vs. controls. For immunolocalization, samples were fixed in 3% paraformaldehyde and embedded in OCT. Cryosections were stained with an antibody specific for Rac1 to validate its differential expression at the protein level.

RESULTS: Microarray analyses revealed upregulation of RAC1 mRNA in the trisomies that were studied (T13, T18, T21). Rac1, a small G protein, is involved in a wide variety of signaling pathways and in the migration of extravillous trophoblasts. We observed a marked increase in staining intensity for the Rac1 protein in trisomic placental biopsies as compared to control. RAC1 localized primarily to the mesenchymal cores of floating/anchoring chorionic villi, with expression generally absent from the basal plate and invasive trophoblasts (Fig 1.).

CONCLUSION: Our findings showed altered expression, in trisomy-affected pregnancies, of a protein that is involved in normal placental development. These pregnancies have increased rates of miscarriage and adverse pregnancy outcomes. Overexpression of Rac1 could explain these problems and points to the possible role of the mesenchymal compartment in the placental defects that are associated with these aneuploidies.