from the electron transport chain on to molecular oxygen. The ROS generated can cause indiscriminate damage to any biomolecules in their immediate vicinity, but reduced levels of ATP and disruption of calcium homeostasis can also perturb endoplasmic reticulum function and other cell activities.
Opportunities to intervene include boosting antioxidant defences with vitamins C and E or mitochondrial targeted compounds, and dietary supplementation with endoplasmic reticulum chaperone proteins, hydrogen sulphide donors and fish oils. Although highly effective with cells and tissue explants *in vitro* and in animal model systems, these approaches have produced disappointing results in clinical trials. The reasons for the lack of success will be explored, and new approaches for intervention will be considered.

http://dx.doi.org/10.1016/j.placenta.2017.07.067

S11.4.
PLACENTAL MITOCHONDRIAL ADAPTION OVER GESTATION AND IN PREECLAMPSIA

Olivia J. Holland, Anna Alvsaker, Georgia McEnroe, Anthony V. Perkins. *School of Medical Science, Menzies Health Institute Queensland, Griffith University, Gold Coast, Queensland, Australia*

Placenta oxygen exposure changes over gestation with alterations in blood flow to the placenta. Blood flow is also restricted by preeclampsia. Given the importance of mitochondrial function in placental disorders, we investigated mitochondria over early gestation, and in healthy and preeclamptic term pregnancies.
Placental tissue was obtained from first trimester pregnancies, and healthy and preeclamptic term pregnancies. Mitochondrial content was determined by qPCR. Respiratory states were assessed by respirometry. Western blot was used to determine levels of NRF1 and BCL2 in whole lysate, and complex IV and HSP-60 in syncytiotrophoblast- or cytotrophoblast-enriched mitochondrial fractions. Protein carbonyls were measured by ELISA. Healthy term tissue was subjected to hypoxia/reoxygenation in vitro, and respiration and reactive oxygen species (ROS) monitored.
Mitochondrial content was increased at 12–13 relative to 7–10 weeks. Respiration decreased at 11 weeks compared to earlier gestations, and increased from 12 weeks. In term placentae, total capacity of the respiratory system was higher compared to first trimester. Preeclamptic mitochondrial content and respiration were increased, and reserve respiratory capacity was reduced relative to healthy tissue. No change was found in BCL2, NRF1, or protein carbonyls. Complex IV and HSP-60 levels were increased in preeclamptic cytotrophoblast-enriched mitochondrial fractions, and HSP-60 was reduced in syncytiotrophoblast-enriched mitochondrial fractions. In vitro hypoxia/reoxygenation led to a decrease in respiration and no change in ROS.
Mitochondria adapt over gestation and in preeclampsia. Changes at 11 weeks may relate to onset of maternal blood flow. Increased mitochondrial content, respiration, and decreased respiratory reserve capacity in preeclampsia may represent adaptation to ischaemia-reperfusion, although no overt oxidative stress was detected. Changes in mitochondrial proteins in different enriched mitochondrial fractions but not whole tissue suggest that the mitochondria of different trophoblast linages are differentially affected in preeclampsia. Hypoxia/reoxygenation increased respiration, providing a potential mechanism for mitochondrial adaptation in preeclampsia.

http://dx.doi.org/10.1016/j.placenta.2017.07.068

S11.5.
NOVEL INSIGHT INTO INSULIN-DEPENDENT CHANGES IN MITOCHONDRIAL DYNAMICS IN GESTATIONAL DIABETES MELLITUS

Joelcio Abbade [1,2], Andrea Tagliaferro [2], Leonardo Ermini [2], Martin Post [4], Isabella Caniggia [2,3]. [1] *Department of Obstetrics & Gynecology, Botucatu Medical School, São Paulo State University (UNESP), Botucatu, Brazil;* [2] *Lunenfeld-Tanenbaum Research Institute, Mount Sinai Hospital, Toronto, Canada;* [3] *Departments of Obstetrics & Gynecology and Physiology, University of Toronto, Toronto, Canada;* [4] *Program in Physiology and Experimental Medicine, Peter Gilgan Centre for Research and Learning, Hospital for Sick Children, Toronto, Canada*

Objectives: Mounting evidence highlights the importance of mitochondrial dynamics (MD), namely mitochondrial fusion and fission, in the genesis of a variety of human pathologies. To date, the contribution of these processes in disorders of pregnancy including gestational diabetes mellitus (GDM) remains elusive. Our aim was to decipher the involvement of MD in GDM. Furthermore, we sought to delineate whether changes in MD were affected by either diet (GDM-D) or insulin treatment (GMD-I), both currently used in the clinical management of GDM.
Methods: Expression of mitochondrial markers of fusion (OPA1) and fission (DRP1 and pDRP1) were examined in GDM-D/GDM-I and controls by western blotting (WB) and transmission electron microscopy (TEM). To mimic GDM, JEG3 choriocarcinoma cells were treated with insulin (I), glucose (G), or both, and expression of fusion/fission markers was examined. Immunofluorescence was used to establish subcellular distribution of OPA1 in JEG3 cells following the aforementioned hindrances. JEG3 cells were treated with genistein, an inhibitor of insulin mediated glucose uptake, and fusion/fission markers were analysed.
Results: OPA1 expression in placenta from GDM-D and GDM-I was significantly increased compared with AMC, and this was associated with decreased pDRP1 expression. In line with our tissue findings, treatment of JEG3 cells with I/GI resulted in elevated OPA1 while decreasing pDRP1 levels. Furthermore, genistein treatment abrogated the expression of OPA1 in JEG-3 cells treated with I/GI. IF analysis showed an accumulation of OPA1 in the mitochondria of JEG3 cells treated with insulin relative to control. TEM analysis revealed increased mitrochondrial fusion as shown by changes in mitochondrial number, surface area, perimeter and main diameter in cytotrophoblastic cells (CT) of GDM-I and GDM-D when compared to AMC.
Conclusion: Our data indicates that in pregnancies complicated by GDM, mitochondrial dynamics shift towards fusion and this is in part dependent on altered insulin signalling.
Supported by CIHR

http://dx.doi.org/10.1016/j.placenta.2017.07.069

S12.1.
BLASTOCYSTS FROM ADVANCED MATERNAL AGE MICE AND POSTNATAL CONSEQUENCES

Miguel A. Velazquez. *Newcastle University, Newcastle, UK*

Several epidemiological studies in humans have suggested that advanced maternal age (AMA) can affect the postnatal health of the offspring. However, long-term effects of (AMA) in experimental settings are largely unexplored, and given the increasing use of assisted reproductive technologies (ART) to alleviate infertility in women of AMA, it is pivotal to develop experimental ART-AMA models. In this study, mice were used to examine the effects of AMA on the postnatal development of offspring under an ART-derived procedure (i.e. embryo transfer). Blastocyst from old (34-39 weeks) or young (8-9 weeks) females mated with young males (13-15 weeks) were transferred into young surrogates (8-9 weeks) to produce young (Young-ET) and old embryo-derived (Old-ET) offspring. All animals were fed with standard chow. Blood pressure was measured at postnatal weeks 9, 15 and 21. At postnatal week 30 a glucose tolerance test (GTT) was performed. Two days after GTT organ weight was collected. Data were analysed with a multilevel random effects regression model. Weekly body weight did not differ in males, but an increase in weight from week 13 onwards was observed in Old-ET female offspring. Blood pressure was increased in Old-ET male offspring at weeks 9 and 15. Old-ET female offspring also showed increased blood pressure but only in week 15. GTT response and organ allometry was not affected in Old-ET male offspring. In contrast, Old-ET female offspring showed a greater peak glucose concentration at 30 min during the GTT and their spleen weight and several