associated with an increase of cMND (odds ratio 1.197 (95% confidence interval 1.031–1.389).

CONCLUSION: Ovarian hyperstimulation, the in vitro procedure, the combination of both and a history of subfertility are not associated with worse neurological outcome in 4-year-olds, while increased TTP is, suggesting that rather the severity of subfertility than its presence is associated with minor neurological dysfunction.

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O-483 Wednesday, October 16, 2013 04:30 PM

MATERNAL AGE AFFECTS INSULIN SIGNALING PATHWAY AND ANGIOGENIC FACTORS OF HUMAN CUMULUS CELLS: IMPORTANCE OF MIR-21 AND MIR-140. T. Al Edani, S. Assou, A. Gala, O. Ait-Ahmed, H. Dechaud, S. Hamamah. Université Montpellier 1, CHU Montpellier, Institute for Research in Biotherapy, Inserm U1040, Montpellier, Herault, France.

OBJECTIVE: To evaluate the impact of maternal aging on the gene expression profile of human cumulus cells (CCs) and to characterize the biological relationships between miRNAs and the CC-genes according to maternal age.

DESIGN: This study includes 43 CCs isolated from mature MII oocytes collected from patients aged <30 years (24-29 years) and 42 CCs from patients aged ≥30 years (30-42 years).

MATERIALS AND METHODS: CCs from each MII oocyte were analyzed individually using whole genome U133 Plus 2 GeneChip Affymetrix microarrays. Significance analysis of microarray was used to analyze the data according to age of patients with 1.5 fold cut-off and false discovery rate <5%. Using deep-sequencing technology, we dissected the microRNome of pooled CCs (n=20). The correlation between miRNAs and their corresponding mRNA targets was analyzed using in silico prediction algorithms. Validation was performed by qPCR.

RESULTS: 370 genes were differentially expressed (FC ≥1.5, FDR <0.05) between the two groups according to age. In CCs collected from patients > 30 years, the angiogenic factors that are known to play an important role in the human pre-ovulatory and oocyte competence, including SPP1 (4.2, p= 0.0001) and chemokine genes CCL2 (2.9, p= 0.003), CCL20 (2.3, p= 0.009) which is regulated by MIR-21, were down-regulated. Conversely, genes related to insulin signaling pathway were up-regulated such as INSR (2.3, p= 0.0001), IGFBP3 (1.8, p= 0.0001) and IGFBP5 (1.7, p= 0.0001) which is regulated by MIR-140. Interestingly, a set of transcriptional genes involved in particular stress responses were preferentially expressed in CCs-collected from patients > 30 years. Among these genes MSRB3 (1.8, FDR=0.0001) plays a protective role during oxidative stress.

CONCLUSION: This study reveals that the expression of genes and miRNAs involved in angiogenesis and insulin signaling pathway are affected in CCs with maternal age and probably explain why there is an increase in oocyte aneuploidy with age due to oxidative stress.

Supported by: Ferring and Genevrier companies.

O-484 Wednesday, October 16, 2013 04:45 PM

TOWARDS UTERINE FIBROIDS GENE THERAPY: FIBROID-TARGETED ADENOVIRUS (AD-SSTR-RGD-TK/GCV) DEMONSTRATES ENHANCED INHIBITION OF TUMOR GROWTH IN NUDE MICE. S. Nair,[a] D. Curiel,[b] C. Sharan,[a] A. Al-Hendy.[a] [a]CWHR, Ob Gyn, Meharry Medical College, Nashville, TN; [b]Radiation Oncology, Washington University School of Medicine, St. Louis, MO.

OBJECTIVE: Uterine fibroid is a major indication for hysterectomy due to limited non-surgical treatment options.Our previous work showed that classical adenoviral vectors optimally transduced rat uterine leiomyoma cells and reduced fibroid volume (Hassan M et al., 2009). We also showed that modification of adenovirus vector by adding a RGD-4C (arginine-glycine-aspartic acid) motif to make it CAR (Coxsackie adenovirus receptor) independent, leads to increased transduction affinity towards human leiomyoma cells. Our aim was to assess the efficacy of Ad-SSTR-RGD-TK vector in a fibroid mouse model and compare with untargeted adenovirus thymidine kinase vector (Ad-TK) /Ganciclovir (GCV).

DESIGN: In vivo study.

MATERIALS AND METHODS: Nude mice (16) implanted with estrogen pellets, were subcutaneously injected with rat ELT3 leiomyoma cells (10 million/mouse) in the right flank.A single intra tumor injection of Ad-SSTR-RGD-TK, Ad-TK, or Ad-LacZ (Adenovirus βgalactosidase) was given followed by GCV intraperitoneal for 10 days. Mice were evaluated regularly and tumors measured weekly.Analysis of apoptosis and proliferation markers in the tissues are ongoing in our laboratory.Statistical analysis was done using Student's T test.

RESULTS: Ad-SSTR-RGD-TK/GCV showed a significant reduction in the size of tumor volume by 16±0.66% of the pretreatment volume and Ad-TK/GCV showed a reduction by 10±0.52% of the pretreatment tumor volume (P<0.05).Both vectors showed a significant reduction in tumor size when compared with Ad-LacZ (P<0.05), however Ad-SSTR-RGD-TK/GCV showed a superior reduction (P<0.05).Long term evaluation of Ad-SSTR-RGD-TK/GCV treatment is underway and will be presented at the meeting.

CONCLUSION: Specific modification of adenovirus vector Ad-TK to Ad-SSTR-RGD-TK enhances the targeting ability towards tumors in nude mice model.Ad-SSTR-RGD-TK/GCV gene therapy approach with Fibroid/ON-normal tissue/OFF design could provide a potential non-surgical treatment alternative for symptomatic uterine fibroids.

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O-485 Wednesday, October 16, 2013 05:00 PM

1H NMR BASED METABOLITE PROFILING FOR UNDERSTANDING THE COMPLEX RELATIONSHIP CONNECTING OXIDATIVE STRESS WITH ENDOMETRIOSIS. K. Chaudhury,[a] S. K. Jana,[a] M. Dutta,[a] M. Joshi,[b] S. Srivastava,[b] B. Chakravarty.[c] [a]School of Medical Science and Technology, Indian Institute of Technology, Kharagpur, West Bengal, India; [b]National Facility for High-field NMR, Tata Institute of Fundamental Research, Mumbai, Maharashtra, India; [c]Reproductive Biology, Institute of Reproductive Medicine, Kolkata, Kolkata, West Bengal, India.

OBJECTIVE: Oxidative stress and metabolite imbalances are interlinked and may have a role in the pathogenesis of endometriosis.

DESIGN: Serum samples were collected from 75 women (24-40 years, BMI<25) with endometriosis confirmed by diagnostic laparoscopy and biopsy, and 60 women with controls (tubal factor infertility). These women were reporting at the Institute of Reproductive Medicine, Salt Lake, Kolkata, India for infertility treatment during Aug 2009 - Sep 2012.

MATERIALS AND METHODS: ROS and TAC were measured by chemiluminescence assay and LPO, superoxide dismutase (SOD), catalase, glutathione (GSH), and advanced oxidation protein products (AOPP) were determined using spectrophotometry. Metabolites were identified using 1H NMR and analyzed by multivariate statistical analysis software.

RESULTS: ROS, LPO and AOPP were significantly higher whereas TAC, SOD, catalase and GSH levels were significantly less in endometriosis women as compared to controls, thereby confirming the association of OS with endometriosis. Further, several amino acids, organic acids and other molecules were identified in serum of these patients using 1H NMR metabolic profiling. Principle Component Analysis (PCA) and Partial least squares Discriminant Analysis (PLS-DA) of the metabolites obtained from 50 recorded spectra showed very good discrimination between endometriosis and controls. Metabolites with high VIP scores including lactate, l-alanine, glycerophosphatidylcholine, glucose, l-leucine, l -lysine, creatine, l-Arginine, succinic acid, adipic acid, lipid, pyruvate, 2-hydroxybutyrate, l-isoleucine, l-Asparagine were considered as significantly changed.

CONCLUSION: It is suggested that increased glucose metabolism and defects in the mitochondrial respiratory system are possible sources of excessive ROS generation. Targeting pathways related to these altered processes could be of therapeutic benefit to women with endometriosis.

O-486 Wednesday, October 16, 2013 05:15 PM

TRANSMEN AS FATHERS THANKS TO DSI: A 12 YEAR FOLLOW-UP STUDY OF THEIR CHILDREN. J. P. Wolf,[a] A.-M. Clouet,[b] B. Golse,[b] M. Guinot,[b] C. Chiland.[a] [a]Histology, Embryology, Biology of Reproduction – CECOS, Cochin Hospital, AP-HP, University Paris Descartes, Paris, France; [b]Child and Adolescent Psychiatry, Necker Hospital-Enfants Malades, AP-HP, University Paris Descartes, Paris, France.

OBJECTIVE: Couples in which the man is a female-to-male transsexual need a donor sperm insemination (DSI) to achieve pregnancy. In France, they can apply for DSI in the sperm banks called CECOS. Because of