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# Review of reports of the IFPA annual meeting «Placenta: Back to the Basics» (September 13-16, 2016, Portland, USA)

September 13-16, 2016, Portland (Oregon, USA) hosted a scientific meeting of International Federation of Placenta Associations (IFPA) titled «Placenta: Back to the Basics». The conference was organized by the Oregon Health & Science University (OHSU) and the Placenta Association of the Americas (PAA).

Placenta as a rich source of various populations of stem cells and unique biologically active substances in recent years has been attracting considerable attention of scientists worldwide. A number of biobanks in the developed world launched the service of cryopreservation of placental stem cells, and placental tissue is increasingly used for the manufacturing of a wide range of cell products and cosmetics.

The scientific program of the conference included reports on the modern view of the role of placenta in the maintenance of pregnancy and fetal life, biology and pathology of trophoblast, subpopulations of placental stem cells, placental genes expression, molecular and cellular interactions in the placental tissue, and new methods of diagnostic imaging of the placenta. Significant attention was also paid at the problem of preeclampsia, which is a leading cause of maternity and perinatal mortality in the world and as of today there is no effective treatment for this severe pregnancy complication. A number of presented reports were focused on the approaches to creation of the experimental models of preeclampsia, included 3D bioengineered placenta and microengineered model of the human placental barrier for the investigation of preeclampsia pathogenesis and testing of the new therapies. Placental molecular markers of genetically mediated diseases as well morphological features of chorion and placental microvessels in the early detection of autism spectrum disorders were also widely discussed.

At the meeting the Human Placenta Project as a social and scientific initiative aimed at revolutionizing understanding of the human placenta was presented. The budget of Human Placenta Project is more than 50 million USD to support the human placenta research, awarding 19 grants to researchers inside and outside USA.

Since placenta is a complex organ in which distinct regulatory programs must be activated at specific times and locations during development, *R. Starks et al.* in a report «**Integrating multi-dimensional genomics data to build regulatory maps of placental development**» aimed to predict transcriptional regulatory modules during placental development using a systems level approach. This group of scientists suggested that *Plagl1* (Pleiomorphic Adenoma Gene-Like 1) and *Pparg* (Peroxisome Proliferator Activated Receptor Gamma) may work together and regulate metabolic genes in the placenta and integration of multidimensional data can be used to predict regulatory modules on a genome-wide scale. Following the development of refined computational pipeline the scientists plan to test the functionality of their predictions in placental cell lines.

A number of reports were devoted to the biochemical, i.e. amino acid composition of the placenta in health and disease, peculiarities of placental metabolism and its role in the development of fetus and fetal complications, in particular intrauterine growth restriction syndrome.

Thus, *A. Ganguly et al.* in a report «**Distinct molecular mechanisms regulate mammalian placental glucose and leucine transporter induced**

**transport in response to varying degrees of maternal calorie restriction**» tested the hypothesis that molecular mechanisms regulating placental glucose and amino acid transport contribute towards fetal growth restriction induced by maternal calories restriction. In experimental studies on mice with created mild and moderated reduced food intake it was shown that maternal calorie restriction evoked differential molecular mechanisms to regulate placental *Glut3* (glucose transporter 3) and *LAT2* (L-amino acid transporter-2). The scientists suggest that future diagnostics and therapeutics may target these identified uniquely molecular pathways to detect and intervene based on the degree of intrauterine growth restriction encountered.

The topic on amino acid turnover in placenta was also discussed in the study of *M. Blomhoff Holm et al.* «**Is the placenta the source of fetal glycine and glutamine? A human *in vivo* study**». The ovine fetus receives glycine and glutamine from the placenta after conversion of serine and glutamic acid respectively. The activity of serine hydroxymethyl transferase is low in human placenta whereas glutamine synthetase appears active. The group of scientists hypothesized that in human fetus placental conversion of serine is not an important source of glycine, while placental conversion of glutamic acid provides a net supply of glutamine. Based on the investigations of blood samples of 178 healthy women from uterine vein, radial artery, umbilical vein and artery, collected at planned cesarean section, it was shown that the term human fetus does not receive a net supply of glycine from the placenta, implying endogenous synthesis of glycine. For glutamine, however, the placenta appears to mediate a net provision to the fetus apparently after intraplacental conversion of glutamic acid. *K. McIntyre et al.* in another study showed that placental transfer (clearance) of glutamine is dependent upon placental size in mice.

The importance of choline supplementation during pregnancy was shown by *Sze Ting (Cecilia) Kwan et al.* in the study «**Maternal choline supplementation during pregnancy improves placental vascularization and modulates placental nutrient supply in a sexually dimorphic manner**». Fetus growth is impacted by placental nutrient supply and choline is known as essential macronutrient, precursor for three metabolites, crucial for gene expression, brain development and cell membrane formation. In this report maternal choline supplementation was proved to impact placental nutrient supply by modulating placental perfusion, nutrient transport and metabolism in sex-dependent manner. Interestingly, more endothelial cells were detected in female placentas labyrinth as well as *Glut3* protein and *Gys1* (glycogen synthase 1) transcript were also increased in female placentas under conditions of choline supplementation. The authors suggested that sex differences in placenta development may contribute to different birth outcome and disease susceptibilities between males and females.

*N. Cureton et al.* in the report «**Targeted nanoparticle delivery of a novel nitric oxide donor increased fetal weight in a mouse model of fetal growth restriction**» presented the coupled to liposomes novel uteroplacental specific targeting peptide SE175, which is a nitric oxide donor. SE175 has previously been shown to induce vasorelaxation in isolated rat aorta. In this study the scientists examined the outcome of liposomal delivery

of SE175 in the endothelial nitric oxide synthase knockout mice, a well characterized model for fetal growth restriction and drew a conclusion that novel uteroplacental specific targeting peptides can be utilized for the selective delivery of SE175 to the uterus and placenta. The treatment with SE175 improved fetal weight and placental efficiency and may therefore provide a novel treatment for fetal growth restriction.

*E. M. Price et al.* in a report «**Transcriptomic profiling of sncRNA in placenta by RNAseq**» discussed small noncoding RNAs (sncRNAs) as increasingly recognized important modifiers of gene expression. sncRNAs with tissue or condition specific expression are attractive noninvasive biomarkers of health and disease. During pregnancy secretion and shedding of trophoblast is known to result in release of placental sncRNAs into maternal circulation. Based on analysis of sncRNAs transcriptome from 26 healthy placentas, novel transcripts and sequencing of both piRNAs and miRNAs were detected.

*Hanna Huebner et al.* in a report «**Impaired gene-expression and epigenetic regulation of Retinoic Acid Receptor Responder 1 in preeclampsia and choriocarcinoma**» studied the expression and regulation of retinoic acid receptor responder 1 (RARRES1) in preeclampsia, intrauterine growth restriction and choriocarcinoma and confirmed the hypothesis that RARRES1 expression is dysregulated in placental diseases. Human placental development is known to resemble tumorigenesis in its invasive and proliferative capacity. But in contrast to cancer, these features are tightly regulated. Disturbances within this regulation are thought to contribute to gestational diseases like choriocarcinoma, preeclampsia and intrauterine growth restriction. Retinoic acid receptor responder 1 is a recognized tumor suppressor. Conducted research showed hypermethylation of retinoic acid receptor responder 1 promotor, accompanied by significant reduced gene expression in choriocarcinoma. In analogy, DNA derived from choriocarcinoma tissue showed a higher retinoic acid receptor responder 1 methylation compared to healthy placentas of the 1st trimester.

Human fetoplacental endothelial cells from growth restricted fetuses with abnormal umbilical artery Doppler velocimetry (FGRadv) were

reported to have impaired angiogenesis. These cells also demonstrate defects in migration and adherence. *K. Mestan et al.* in the report «**Vascular endothelial growth factor A administration rescues fetoplacental endothelial cell defects seen in severe fetal growth restriction**» presented results of *in vitro* studies, aimed at elucidation whether vasculoendothelial growth factor A is lower *in vivo* in FGRadv endotheliocytes and whether administration of VEGF-A would rescue endotheliocytes migration and adherence defects. 36 preterm infants from 23-36 weeks gestational age were investigated. Cord blood plasma vasculoendothelial growth factor A concentration was shown to be decreased significantly in fetuses with growth restriction and impaired endotheliocytes migration was rescued by VEGF-A treatment *in vitro*.

*Che-Ying Kuo et al.* in the report «**3D printed, bioengineered placenta model incorporating decellularized placental extracellular matrix and primary trophoblasts**» presented the first *in vitro* bioengineered placenta model, containing spiral pattern chemoattractants and placenta-derived extracellular matrix which may be used for the investigation of placental biology and especially preeclampsia. As it was mentioned above, preeclampsia is a major and poorly understood cause of maternal and perinatal morbidity and lack of experimental models detains scientific advances in this direction.

*C. Blundell et al.* developed and characterized microphysiological model of the human placental barrier and results of studies presented in a report «**A microengineered model of the human placental barrier**». Placental barrier mediates material transfer between mother and fetus *in vivo*. This placenta-on-a-chip platform has the potential to be used as innovative tool for *in vitro* investigation of human placental function.

Ukraine on the IFPA annual meeting was represented by the Institute of Cell Therapy in the person of *Volodymyr Shabliy*, PhD, the deputy director of cryobank, who presented a report «**Placenta-derived multipotent cells shared the expression of several trophoblast-related genes**».

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