ABSTRACT BOOK OF THE INTERNATIONAL COURSE

“Pre- and perinatal determinants of health in child- and adulthood”

April 23-24, 2015
Tartu, Centre of Genetics and Biotechnology Omicum, Riia 23b lecture hall 105

Estonia, Tartu 2015
Supported by:
Doctoral School of Clinical Medicine
Graduate School in Biomedicine and Biotechnology
Project HAPPY PREGNANCY

Organized by:
Doctoral School of Clinical Medicine

Dr Kristiina Rull, PhD
Prof Maris Laan, PhD
Programme of the international course

“Pre- and perinatal determinants of health in child- and adulthood”

April 23, 2015 Thursday
(hosted by Doctoral School of Clinical Medicine)

Session I: Intrauterine and early childhood determinants of individual’s health

9.00 - 9.55 Prof. Johan Gunnar Eriksson (Finland): Importance of early life for later health outcomes--findings from the Helsinki Birth Cohort Study

9.55 - 10.50 Prof. Maria Christina Jenmalm (Sweden): Intrauterine and early infancy determinants of allergy development

10.50 - 11.40 Coffee and poster session

11.40 - 12.35 Prof. Rebecca Reynolds (UK): Endocrine communication in maternal-fetal programming and long-term offspring outcomes

12.35 -13.35 Kadi Jairus (Estonia): Chorionic villus direct method in everyday diagnostic practice – use the benefits, but know the risks

Laura Kasak (Estonia): Extensive load of somatic CNVs in the human placenta

Mariann Koel (Estonia): The effect of TGFbeta and FGF2 inhibitors on BMP4-initiated differentiation from human embryonic stem cells

13.35 - 14.30 Lunch break

14.30 - 15.00 Zilvinas Venclovas (Lithuania): One year DHEAS concentration-axed search for dehidroepiandrosteronism (dehism) and dehidroepiandrosteroma (dehoma)

Jelena Meiniilä (Finland): Nutrient intake in pre-pregnant and pregnant women at high risk of gestational diabetes

Session II: Nutritional modifiers of pregnancy course and offspring health

15.00 - 15.55 Prof. Régine P.M. Steegers -Theunissen (Netherland): Periconceptional nutritional care: Should we care?

15.55 - 16.50 Dr. Nicholas Harvey (UK): Vitamin D in pregnancy: implications for maternal and offspring health
April 24, 2015 Friday

Session III: Pregnancy disorders: link to maternal and offspring long-term health complications (hosted by HAPPY PREGNANCY project)

9.00 - 9.55 Prof. Christopher Redman (UK): Placental stress and preeclampsia, in relation to future maternal health

9.55 - 10.50 Prof. Anne Cathrine Staff (Norway): Long-term maternal cardiovascular disease after pregnancy hypertension and placental dysfunction: possible mechanisms and how to follow up women at risk?

10.50 - 11.30 Coffee and poster session

11.30 - 12.25 Prof. Peter Damm (Denmark): Gestational diabetes - short and long-term consequences for mother and offspring

12.25 - 13.30 Kristiina Rönö (Finland): Gestational diabetes can be prevented by lifestyle intervention The Finnish gestational diabetes prevention study (RADIEL) - a randomized controlled trial

Ele Hanson (Estonia): Clinical characteristics of patients with pregnancy related hypertensive disorders in Happy Pregnancy study: pilot data

Nora Grotenfeld (Finland): Gestational weight gain does not associate with incidence of gestational diabetes mellitus in women with high risk for GDM

13.30 -14.30 Lunch break

Session IV: Genetic and exocrine determinants of fertility and fetal programming (hosted by Graduate School in Biomedicine and Biotechnology)

14.30 - 15.25 Prof. Richard Sharpe (UK): Impacts of common fetal exposures on reproductive development and function in both sexes and their long-term impacts

15.25 - 16.20 Dr. Rachel Freathy (UK): Using genetics to understand how the intrauterine environment influences fetal growth
Oral presentations
Chorionic villus direct method in everyday diagnostic practice – use the benefits, but know the risks

Kadi Jairus¹, Kirsi Piippo², Nina Horelli-Kuitunen²

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Introduction

Chorionic villus sampling (CVS) is an invasive procedure used for first-trimester prenatal diagnosis. Depending on the part of chorionic villi used for karyotyping, two methods are distinguished: (1) direct method is based on the rapidly multiplying cytotrophoblast cells and (2) culture method is based on the long-term cultivation of the cells from the inner mesodermal core. Current cytogenetic guidelines suggest the parallel use of both methods, but culture method is preferred and more common. With the current study we show how these two methods complement each other in everyday diagnostic practice. The goals of this study were to (1) detect the factors affecting the success of the methods and (2) suggest the best laboratory practice based on the benefits and awareness of the possible risks.

Materials and Methods

The study involves 143 patients referred to CVS for prenatal diagnosis. For each sample two cultures were established, direct method was used when there was enough villus material left. Three indicators were used to quantify the success of the methods: (1) the amount of analysed good-quality direct mitotic cells, (2) growing time of the culture and (3) reporting time of the final karyotype. Spearman’s R correlation test and repeated measures GLM were performed using STATISTICA.

Results

In 96% of all samples enough chorionic villus tissue for both methods was available. The failure rate of the methods was similar, 2%, but not concurrent. The success of the direct method was significantly lower in case of higher gestational age. However, this did not affect the reporting time, which was dependent of the growth of the culture. Direct method enabled to get the karyotype on average 11 days earlier. In 97% of cases both methods resulted in the same karyotype, but also a false negative result and placental mosaicism were detected.

Conclusions

Using only one method adds the risk of misdiagnosis due to placental mosaicism, uniparental disomy or maternal cell contamination. We suggest using both methods to reduce the risk of false-negative reports. Direct method should preferably be used along with culture method to report normal karyotype. However, the direct karyotype provides valuable information and enables to report abnormal karyotypes faster, even if culture method or molecular analyses are still needed for confirmation. In the era of vast advancement of molecular diagnostic methods the benefits of preliminary karyotype from direct method should not be forgotten.
Extensive load of somatic CNVs in the human placenta

Laura Kasak¹, Kristiina Rull¹,²,³, Pille Vaas²,³, Pille Teesalu²,³ & Maris Laan¹

¹Human Molecular Genetics Research Group, Institute of Molecular and Cell Biology, University of Tartu, Riia St. 23, Tartu 51010, Estonia, ²Department of Obstetrics and Gynaecology, University of Tartu, Puusepa St. 8, Tartu 51014, Estonia, ³Women’s Clinic of Tartu University Hospital, Puusepa St. 8, Tartu 51014, Estonia.

Placenta is a central organ in mammalian pregnancy. Presenting highly invasive properties similarly to tumours, it enables effective implantation via trophoblast cell proliferation and migration and guarantees successful progression of pregnancy.

We hypothesized that comparably to cancer, somatic genomic rearrangements are promoted in the course of placental development. Here we present the first study describing copy number variations (CNVs) in human placental genomes, showing an extensive load of somatic CNVs, especially duplications and suggesting that this phenomenon may be critical for normal gestation.

Placental somatic duplications were significantly enriched in genes involved in cell adhesion, immunity and embryonic development, deletions on the other hand in cell cycle and mitosis. Somatic duplications encompassed a great deal of imprinted genes which suggests that amplified gene copies may represent an alternative mechanism to support parent-of-origin specific gene expression. Placentas from complicated pregnancies exhibited significantly altered CNV profile compared to normal gestations, suggestive of several clinical implications of the study.
The effect of TGF beta and FGF2 inhibitors on BMP4 initiated trophoblast differentiation from human embryonic stem cells

Mariann Koel 1,2, Kaarel Krjutškov 1,3 Viljar Jaks 2, Andres Salumets 1,4,5

1 Competence Centre on Health Technologies, Estonia 2 Institute of Molecular and Cell Biology, University of Tartu, Estonia 3 Department of Biosciences and Nutrition, Karolinska Institutet, Stockholm, Sweden 4 Institute of Biomedicine and Translational Medicine, University of Tartu, Estonia 5 Chair of Obstetrics and Gynecology, University of Tartu, Estonia

Introduction

The first cell-fate decision in mammalian development is the segregation of the blastocyst trophectoderm and inner cell mass. During human embryo implantation, the outer trophectoderm layer attaches to endometrial epithelial cells and continues to differentiate into syncytiotrophoblasts. Over the last decade, several laboratories have demonstrated that human embryonic stem cells (hESC) can be directed to differentiate into trophoblast cells, if exposed to TGF-β superfamily member, bone morphogenic protein 4 (BMP4). To prevent the formation of other cell lines, FGF-2 and TGF-β/Activin signaling have been inhibited in addition to BMP4 treatment. The goals of this study are to analyse the effect of different combinations of inhibitors to trophoblast differentiation and to find most optimal combination among them.

Methods

Pluripotent hESCs, line H9, were grown on matrigel and maintained in the StemPro medium. For trophectoderm directed differentiation, hESC were splitted and StemPro were replaced by the N2B27 supplemented with BMP4 (10 ng/ml) and/or 0.1 μM FGFR1 inhibitor PD173074 and/or 1 μM TGFβR1 inhibitor A83-01. Every other day, during 12 days, 2 plates (35 mm) of cells were dissociated for RNA extraction and cell culture medium was gathered. RNA were sequenced by single-cell tagged reverse transcription (STRT) gene expression analysis pipeline using Illumina Platform. The presence of total hCG and hCGh were confirmed by ELISA-based quantification of media supernatants.

Results

We showed that 10 days of FGFR inhibition leads to up-regulation of several syncytiotrophoblast specific genes (CGA, CGB, CYP11A1 and HOPX). Both FGF and TGF-β inhibition caused significant up-regulation of ECM–receptor interaction, focal adhesion and tight junction KEGG pathways which are known to be involved in embryo implantation. However, inhibition of TGFβR alone caused down-regulation of syncytiotrophoblast marker genes, early trophoblast specific genes (CALB1 and DLX3) and genes expressed in extravillous trophoblasts (MMP2 and TIMP1). Immunocytochemical based staining for the pan-trophoblast marker cytokeratin-7 (KRT7) at day 5 revealed that FGF2 inhibition rendered nearly all visible cells KRT7 positive. Additionally we screened the supernatant of the cells for the marker of fully differentiated syncytiotrophoblast - hCG and hyper-glycosylated hCG (hCGh), produced by poorly differentiated or invasive trophoblast cells. We demonstrated that hCG and hCGh were produced by the cells where either FGF2 or both FGF2 and TGF-β were inhibited.

Conclusion

We performed RNA sequencing to understand global scale changes in the transcriptome during the differentiation of hESCs in the trophoblast lineage. Transcriptome profile and hCG secretion indicates that, in addition to BMP4, only FGF2 inhibition is sufficient to formation of early trophoblast cells. However, TGF-β/Activin pathway inhibition slowed the differentiation significantly. Our results suggest that TGF-β/Activin signalling inhibition is not essential for generating trophoblast cells.
ONE YEAR DHEAS CONCENTRATION-AXED SEARCH FOR DEHIDROEPIANDROSTERONISM (DEHISM) AND DEHIDROEPIANDROSTEROMA (DEHOMA)

Valentinas Matulevicius ¹, Rytas Ostrauskas¹, Tomas Kurakovas¹, Zilvinas Venclovas¹, Ilona Banisauskaite¹, Justina Jureviciute¹, Gintare Placinskaite¹, Rasa Verkauskiene¹, Vaidotas Urbanavicius ².

1. Institute of Endocrinology, Lithuanian University of Health Sciences, Kaunas, Lithuania
2. Vilnius University, Vilnius, Lithuania

Former and recent investigations show the possibility of hypersecretion of dehydroepiandrosterone sulfate (DHEAS) in women. In attempt to find more such cases, we analyzed results of DHEAS determinations in 2 university hospitals of Lithuania (Vilnius and Kaunas) during 1 year – 2014. We checked 1215 DHEAS results of 18-50-year-old woman to investigate our hypothesis. Increased DHEAS was considered when patient’s DHEAS concentration was higher than maximal value of DHEAS indicated in the assay kit (Ratio DHEAS patient/DHEAS maximal value, R/DHEAS) -11.76%. Mild increase was in 87.4 %, moderate increase – in 9.8 % and high increased - in 2.8 %. These results confirm that mild increase of DHEAS is frequent (DEHISM). High increase of DHEAS was very rare- found only in 4 patients (DEHOMA).

We managed to analyze outpatient files of 56 patients, that have R/ DHEAS >1. Results of age, height, weight, BMI and DHEAS in the whole group are shown in the table 1, and results of patients with R/DHEAS > 1, 3 are shown in the table 2.

Table 1

<table>
<thead>
<tr>
<th>R/DHEAS &gt;1</th>
<th>Age</th>
<th>Height</th>
<th>Weight</th>
<th>BMI</th>
<th>DHEAS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>26,32</td>
<td>168,55</td>
<td>80,38</td>
<td>27,87</td>
<td>15,14</td>
</tr>
<tr>
<td>Median</td>
<td>24</td>
<td>168,25</td>
<td>77</td>
<td>26,35</td>
<td>14,55</td>
</tr>
<tr>
<td>Standard Deviation</td>
<td>6,12</td>
<td>5,76</td>
<td>21,08</td>
<td>7,18</td>
<td>3,02</td>
</tr>
<tr>
<td>Minimum</td>
<td>18</td>
<td>153</td>
<td>47</td>
<td>17,5</td>
<td>9,9</td>
</tr>
<tr>
<td>Maximum</td>
<td>44</td>
<td>180</td>
<td>130</td>
<td>42,2</td>
<td>28,1</td>
</tr>
<tr>
<td>Count</td>
<td>56</td>
<td>56</td>
<td>56</td>
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</tbody>
</table>

Table 2

<table>
<thead>
<tr>
<th>R/DHEAS &gt;1,3</th>
<th>Age</th>
<th>Height</th>
<th>Weight</th>
<th>BMI</th>
<th>DHEAS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>24,37</td>
<td>167,03</td>
<td>77,09</td>
<td>26,82</td>
<td>1,52</td>
</tr>
<tr>
<td>Median</td>
<td>23</td>
<td>166</td>
<td>75</td>
<td>25,82</td>
<td>1,5</td>
</tr>
<tr>
<td>Standard Deviation</td>
<td>4,30</td>
<td>5,02</td>
<td>19,70</td>
<td>6,57</td>
<td>0,21</td>
</tr>
<tr>
<td>Minimum</td>
<td>20</td>
<td>160</td>
<td>55</td>
<td>18,1</td>
<td>1,30</td>
</tr>
<tr>
<td>Maximum</td>
<td>37</td>
<td>178</td>
<td>130</td>
<td>41</td>
<td>2,23</td>
</tr>
<tr>
<td>Count</td>
<td>16</td>
<td>16</td>
<td>16</td>
<td>16</td>
<td>16</td>
</tr>
</tbody>
</table>

These results are the first attempt to describe phenotype of women with increased DHEAS.
Nutrient intake in pre-pregnant and pregnant women at high risk of gestational diabetes

Meinilä J1,2, Koivusalo SB3, Valkama A2,4, Erkkola M5, Kautiainen H2,6,7, Eriksson JG1,4,8,9

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2 Unit of General Practice and Primary Health Care, University of Helsinki and Helsinki University Hospital, Finland.
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4 Folkhälso Research Centre, Helsinki, Finland
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8 National Institute for Health and Welfare, Department of Chronic Disease Prevention, Helsinki, Finland

Objectives: The objective was to study the nutrient intake and its’ adequacy among women at elevated risk of gestational diabetes (GDM). Design and methods: Subjects were 394 Finnish women either planning pregnancy or at ≤ 20 weeks of pregnancy at baseline, and either obese or had a history of GDM. Nutrient intake was assessed from 3-day food records. Statistical significance for the hypotheses was evaluated by using generalized linear models with appropriate distribution and link function, median regression models (least-absolute-value), and chi-square test.

Results and interpretation: The pre-pregnant and the pregnant women had a mean fat intake of 33 E% (SD 7 and SD 6), and SFA 12 E% (SD 3). The pre-pregnant women had carbohydrate intake of 44 E% (SD 8) and the pregnant of 46 E%, respectively (SD 6). Sucrose intake among pregnant women with a history of GDM was 7 E% (SD 3) which was different from the other pregnant women’s 10 E% (SD 4) (p<0.001). The pre-pregnant women less frequently used dietary supplements than the pregnant (53% vs. 77%, p<0.001), and had median folic acid intake below the national recommendation. Both, the pre-pregnant and the pregnant women had intake of vitamin A below the recommendation. The observed non-optimal dietary composition of macronutrients among women at high risk of GDM may further increase their risk of GDM. A history of GDM, however, seems to reduce sucrose intake in a future pregnancy. Women planning pregnancy and pregnant women seem to have insufficient amounts of vitamin D and folate from food and thus need supplementation. Adequacy of intake of vitamin A in Finnish pregnant women needs further studying.
Gestational diabetes can be prevented by lifestyle intervention. The Finnish gestational diabetes prevention study (RADIEL) - a randomized controlled trial

Kristiina Röno, Saila B Koivusalo, Risto P Roine, Hannu Kautiainen, Johan G Eriksson, Beata Stach-Lempinen, on behalf of RADIEL study group

Department of Obstetrics and Gynecology, University of Helsinki and Helsinki University Hospital, Helsinki, Finland; Department of Health and Social Management, University of Eastern Finland and Kuopio University Hospital, Kuopio, Finland; Helsinki and Uusimaa Hospital District; Department of General Practice and Primary Health Care, University of Helsinki and Helsinki University Hospital, Finland; Department of General Practice and Primary Health Care, University of Eastern Finland, Kuopio, Finland; Folkhälsan Research Centre, Helsinki, Finland; Department of Obstetrics and Gynecology, South Karelia Central Hospital

Study objective: To assess the effect of moderate lifestyle intervention in prevention of gestational diabetes mellitus (GDM) in pregnant women at high risk for the disease.

Design and setting: A randomized controlled trial conducted between 2008 and 2014 in four maternity hospitals in South Finland.

Methods: 293 women with a history of GDM and/or a pre-pregnancy body mass index ≥ 30 kg/m², and with no type 1 or type 2 diabetes were enrolled at less than 20 weeks of gestation (mean 13 weeks) and randomized to intervention (n=155) and control group (n=138). Women in intervention group received individualized counseling on diet, physical activity, and weight control from trained study nurses and had one group session with dietitian. The control group received standard antenatal care. Participants visited the study nurse once in each trimester during pregnancy.

The main outcome was incidence of GDM, defined as one or more pathological glucose value in a 75 g two-hour oral glucose tolerance test according to American Diabetes Association 2008 criteria.

Results: 269 women (intervention n=144; control n=125) were included in the final analyses. The incidence of GDM was 13.9 % in the intervention group and 21.6% in the control group (RR 0.61, 95% CI: 0.40 to 0.98, p=0.044 after adjustment for age, pre-pregnancy BMI, previous GDM status, and weeks of gestation). Gestational weight gain was lower in the intervention group (-0.58 kg 95% CI: -1.12 to -0.04, adjusted p=0.037).

The dietary index score improved 0.7 points (95% CI: 0.3 to 1.1) in the intervention group and 0.3 points (95% CI: -0.1 to 0.7) in the control group, with the adjusted mean difference of 0.5 (95% CI: 0.0 to 1.1, p=0.049, adjusted for age, baseline BMI, previous GDM status and baseline values). Women in the intervention group increased their self-reported median weekly leisure time physical activity by 15 minutes (95% CI: 1 to 29), while no change was seen in the control group (p=0.035, adjusted age, baseline BMI, previous GDM status and baseline values). There were no differences across groups in the other maternal pregnancy or birth outcomes assessed.

Conclusions: Among high-risk pregnant women a moderate individualized lifestyle intervention reduced the incidence of GDM by 39%, a finding that may have major health consequences for both the mother and the offspring.

Trial registration: clinicaltrials.gov Identifier: NCT01698385.
Clinical characteristics of patients with pregnancy related hypertensive disorders in Happy Pregnancy study: pilot data

Ele Hanson¹, Kristiina Rull¹²

¹Women’s Clinic of Tartu University Hospital, Estonia; Dept. of Obstetric and Gynecology University of Tartu; ²Human Molecular Genetics Research Group, Institute of Molecular and Cell Biology, University of Tartu, Estonia

Study objective: The purpose of the study was to characterise the patients who developed hypertensive disorders during the pregnancy using pilot data from Happy Pregnancy Study.

Design and methods: In the frame of the ongoing prospective Happy Pregnancy study we are collecting longitudinal anthropometric, epidemiological (life-style, parity, etc) clinical data and biological material through the pregnancy and at delivery in Women’s Clinic of Tartu University Hospital in Estonia. Only patients who delivered after 24 weeks and had available outcome data were included into pilot study.

Results: Study population consisted of 523 women including 5 patients (1%) with early preeclampsia (PE, delivery <34 gestational weeks), 21 patients (4%) with late preeclampsia and 10 patients (2%) with gestational hypertension (GH).

<table>
<thead>
<tr>
<th>Maternal characteristics</th>
<th>Controls (n=487)</th>
<th>Early PE (n=5)</th>
<th>Late PE (n=21)</th>
<th>GH (n=10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal age in years, median (min-max)</td>
<td>29 (16-45)</td>
<td>26 (22-32)</td>
<td>27 (22-39)</td>
<td>30 (22-37)</td>
</tr>
<tr>
<td>BMI in kg/m², median (min-max)</td>
<td>22.3 (15.5-53.3)</td>
<td>26.8 (23.0-45.7)*</td>
<td>25.2 (18.0-42.8)*</td>
<td>30.8 (22.1-34.1)*</td>
</tr>
<tr>
<td>Nulliparity, n (%)</td>
<td>221 (45%)</td>
<td>5 (100)*</td>
<td>16 (76%)*</td>
<td>6 (60%)</td>
</tr>
<tr>
<td>GD during the pregnancy n (%)</td>
<td>22 (5.4%)</td>
<td>0</td>
<td>2 (10%)*</td>
<td>4 (40%)*</td>
</tr>
<tr>
<td>Newborns with growth restriction n (%)</td>
<td>14 (2.9%)</td>
<td>1 (20%)</td>
<td>6 (29%)*</td>
<td>0</td>
</tr>
</tbody>
</table>

*p<0.05 compared to controls. Student’s t-test; chi² test or Fisher exact;
BMI, body mass index; GD, gestational diabetes, PE, preeclampsia, GH, gestational hypertension

There was no difference between the groups regarding maternal age, smoking status and history of predisposing diseases (hypertension, diabetes, renal and autoimmune diseases). Mean BMI was significantly higher in all groups with pregnancy related hypertension compared to control group. Among patients with PE (both early and late) there were more nulliparous women than in controls. Fetal growth restriction occurred more frequently in late PE cases. In GH group four patients (40%) were diagnosed gestational diabetes compared 22 cases among control group (5,4%). No fetal macrosomia occurred in any cases of hypertensive diseases.

Interpretation: Risk factors of preeclampsia were higher BMI, first delivery and for parous women - pregnancy related hypertension in their medical history. The finding are consistent with the results of other studies. Patients with gestational hypertension had higher BMI and were more often diagnosed GD, their blood pressure rise during pregnancy might be part of metabolic syndrome revealed by pregnancy.

Limitation of the study is the low number of patients with pregnancy related hypertensive diseases. The overall sample size is expected to quadruple during the ongoing Happy Pregnancy study.

FUNDING: European Regional Development Fund (project 3.2.0701.12-0047).
Gestational weight gain does not associate with incidence of gestational diabetes mellitus in women with high risk for GDM

Grotenfelt Nora E MD¹, Huvinen Emilia MD², Prof Eriksson Johan G MD³, Rönö Kristiina MD³, Valkama Anita MSc⁴, Meinilä Jelena MSc⁴, Kautiainen Hannu MSc PhD⁴, Stach-Lempinen Beata MD PhD⁵, Koivusalo Salla B MD PhD² on behalf of the RADIEL group.

¹Folkhälsan Research Centre, Helsinki, University of Helsinki, Finland, ²Department of Obstetrics and Gynecology, Helsinki University Central Hospital, Finland, ³Unit of General Practice, Helsinki University Central Hospital, Finland, ⁴Department of General Practice and Primary Health Care, University of Helsinki, Finland, ⁵Department of Obstetrics and Gynecology, South-Karelia Central Hospital, Lappeenranta, Finland.

Objective: To study the incidence of GDM in relation to gestational weight gain taking into account baseline phenotypic characteristics of women at high risk for GDM.

Design and setting: A randomized controlled trial conducted between 2008 and 2014 in four maternity hospitals in Southern Finland.

Methods: 293 women with a history of GDM and/or a pre-pregnancy body mass index ≥ 30 kg/m2, and with no overt diabetes at baseline were enrolled at less than 20 weeks of gestation (mean 13 weeks) and randomized into an intervention group receiving lifestyle counseling and a control group receiving standard antenatal care. The main outcome was incidence of GDM, defined as one or more pathological glucose value in a 75 g two-hour oral glucose tolerance test. In total, 269 women (intervention n=144; control n=125) were included in the final analyses. We further divided the participants into four groups according to parity, BMI and previous history of GDM and adjusted for age, years of education, family history of diabetes and the plausible effects of the intervention. Group A included 113 primiparous women with a pre-pregnancy BMI > 30 kg/m2. The 68 women without GDM in previous pregnancies and a BMI > 30 kg/m2 formed Group B. The participants with a previous history of GDM were divided according to BMI under (group C, N=64) or over (group D, N=24) 30 kg/m2.

Results: At baseline the women with previous GDM and BMI <30 kg/m2 had a healthier metabolic profile. There was a significant difference in incidence of GDM between the groups: The incidence for group A was 9,7%, for group B 11,8%, for group C 35,9% and for group D 20,8%, respectively (p< 0,001).

There were significant differences in gestational weight gain (GWG) between the groups. The mean GWG for group A was 3,7 kg, for group B 3,1 kg, group C 6,3 kg and D 4,5 kg, respectively (p<0,001). The figure shows the GWG as a percentage of pre-pregnancy weight according to group and GDM outcome. There was no significant difference in GWG between the non-diabetic women and the women diagnosed with GDM. This finding was similar in all the groups as shown in the figure. There was no association between GWG and GDM outcome in any of the groups.

Conclusions: Despite the healthier metabolic profile at baseline the non-obese women with previous GDM displayed a markedly higher cumulative incidence of GDM. They also gained more weight during pregnancy. GWG was not associated with GDM occurrence in this study of women with high risk for GDM.
Poster presentations
STRUCTURE OF SEXUAL FUNCTION OF 26 – 36 YEAR-OLD LITHUANIAN MEN,
FUNCTION OF ESTONIAN, LATVIAN YOUNG MALES”

Ilona Banisauskaite*, Valentinienas Matulevicius*, Rasa Verkauskiene*, Vaidotas Urbanavicius#, Rytas Ostrauskas*, Indre Matuleviciute*

*Institute of Endocrinology, Lithuanian University of Health Sciences, Kaunas, Lithuania
#Vilnius University, Vilnius, Lithuania

Introduction. Comprehensive investigation of young men's reproductive health, including hormones and genes, was performed in 2003/2004 in Nordic and Baltic countries. However the sexual function analysis was beyond the scope of this research.


Patients and methods. Eighty two KELLY men aged 26-36 years were recruited from the list of study participants. 129 T1D patients were randomly selected from Lithuanian register of diabetes. All the 211 individuals completed EMAS – SFQ. Descriptive statistical data analysis and all the calculations were performed as the EMAS group calculations.

Results and interpretation. In KELLY men overall sexual functioning (OSF) was 11-27 scores (85%), when the possible score ranged from 0 to 33. Sexual-function-related distress (SFD) 1-5 scores (the possible score range 0 to 20), Masturbation score (M) was high (≥ once per week 45% and once to 2-3 times per month 30%, altogether 75%), when the possible score range 0 to 7. In T1D males M is lower than in KELLY men from the beginning of disease (disease duration 0-4 years). SFD becomes significantly higher in patients with disease duration 5 +, and OSF – significantly lower in 10 +. Capacity to achieve and maintain erections was statistically higher in KELLY than in D T1D males: 79 (97,5%) and 114 (81,4 %) respectively, p<0,001. More than 4 morning awaking erections per week were observed in 23 (28, 4 %) KELLY men in contrary to the findings in T1D males 28 (19, 9 %). Absence of morning erections was reported in 4 (4,9%) of KELLY males and in 24 (17,1%) of T1D. No statistically significant differences (p>0,05) were observed between the capacity of erection maintaining and morning erection frequency comparing T1D patients with different duration of disease. Changes of sexual activity during the 1 year were not observed. When compared with EMAS study, KELLY sexuality is similar with EMAS 40-49 –year men, but higher as compared with other age participants in the EMAS.

Sexuality of KELLY males after 9-10 years of investigation of their reproductive health is excellent in comparison with presumably disturbed sexuality of patients (T1D). Early appearance of M disturbance and increase of SFD in T1D in comparison with KELLY males is surprising, since appearing of “diabetic complication”needs some time. On the other hand, so far not all the diabetic patients suffer from sexuality disturbances even after a long duration of diabetes.
CAG and GGN repeats in AR gene exert combinatorial effects on reproductive parameters in Baltic young male cohort

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Objectives: The androgen receptor (AR) mediating androgen action is primarily involved in sexual differentiation during embryogenesis, growth of accessory sex organs as well as normal sperm production. Androgen receptor gene (AR) harbours two polymorphic polyglutamine (CAG) and polyglycine (GGN) repeat motifs. We aimed to study individual and combinatorial effect of CAG and GGN repeats on hormonal and testicular parameters in Baltic male cohort.

Material and methods: Baltic young male cohort (n=974, 20.1±2.0 yrs, sperm conc. 81.6±73.0 mln/mL; genotyping of CAG and GGN repeats by fluorescently-labelled PCR; linear regression (CAG and GGN repeat lengths as continuous variables), one-way analysis of covariance (ANCOVA, CAG and GGN trichotomised as short, medium, and long (i.e., CAG≤21, 22≤CAG≤24, CAG≥25; GGN≤22, GGN=23, GGN≥24), and treated as categorical variables), adjustment for confounders; Mann-Whitney U- (M-W) and Kruskal-Wallis (K-W) tests in the groups of trichotomised CAG and GGN lengths as well as in nine groups of the combinations of short (s), medium (m), and long (l) CAG and GGN repeats (i.e., ICAG=sGGN = long CAG—short GGN, etc.).

Results and Conclusion: The median (range) of CAG and GGN repeat length were 23 (13-33) and 23 (9-28), respectively. Significant positive correlation was identified between CAG and GGN repeats (Pearson's r=0.142, p<0.0001). Men with longer CAG repeat length had significantly lower serum FSH (linear model p=0.002, β=-0.056 IU/L; sCAG vs ICAG, mean(median), 3.24(2.92) vs 2.94(2.53) IU/L, M-W p=0.014) accompanied with non-significantly lower sperm concentration (sCAG vs ICAG, 89.0(71.6) vs 80.0 (62.9) mln/mL, M-W p=0.061). Longer GGN repeats were significantly associated with lower sperm concentration (sGGN vs lGGN, 91.3(68.4) vs 76.2 (60.2) mln/mL, M-W p=0.027). Individuals carrying the combination of long CAG and short GGN (ICAG—sGGN, n=13, 1.33%) exhibited significantly lower total testosterone (ICAG—sGGN vs others, M-W p=0.01), as well as trends for lower serum LH, free testosterone, estradiol, Inhibin B, and total testes volume. Men with combination of long CAG and long GGN (ICAG—lGGN, n=76, 7.8%) expressed with the lowest sperm counts (ICAG—lGGN vs others, sperm concentration, M-W p=0.001; total sperm count, M-W p=0.02) and lower FSH level. Median sperm concentration and total sperm count numbers in ICAG—lGGN group (concentration, 49.0 mill/mL; count, 165.1 mill/ejaculate) were 26.2 and 24.1% lower when compared to the joint group of other CAG-GGN combinations (concentration, 66.3 mill/mL; count, 217.5 mill/ejaculate).

The current study demonstrates for the first time that CAG and GGN repeats in the AR gene affect male reproductive parameters in a combinatorial way.
GENETICS OF GLYCOPROTEIN STANNIOCALCIN-1

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Study background: The STC1 gene coding for glycoprotein hormone Stanniocalcin-1 has been previously identified by our research group as a gene exhibiting aberrantly high placental expression level in term placentae from complicated pregnancies. Parallel analysis of human post-partum maternal plasma samples revealed significantly elevated level of circulating STC1 in pregnancies complicated with preeclampsia (PE) (n=16) compared to non-PE controls (n=40) (Uusküla et al. 2012).

Aims of the study: 1. To replicate the initial findings of the discovery study by measuring STC1 concentrations in all remaining REPROMETA individuals. 2. To investigate the genetic variation of the STC1 gene and identify SNPs that could potentially modulate STC1 hormone levels in maternal post-partum plasma samples which in turn may be associated with maternal predisposition to PE.

Methods: Study samples originate from Estonian REPROgrammed fetal and/or maternal METAbolism (REPROMETA) sample collection project that includes clinical, biological and phenotype materials from pregnancies at term (gestational weeks 36-42). For the current study we genotyped 13 tag-SNPs from the STC1 genomic region in 366 REPROMETA maternal samples and measured their post-partum plasma STC1 levels using ELISA. The obtained dataset was then used for the quantitative association analysis of STC1 concentration as well as for case-control analysis between REPROMETA PE (n=50) and non-PE (n=316) subgroups. For the replication of the REPROMETA case-control analysis the matched subset of individuals (547 PE and 568 non-PE) from Finnish PE cohort FINNPEC (Finnish Genetics of Preeclampsia Consortium) was also genotyped. Genotyping of both sample sets was performed using Sequenom MassARRAY Analyzer. Subsequent genetic association analysis was done using PLINK genetic analysis toolset. Statistical tests were adjusted by relevant co-variables including maternal BMI, gestational age and type of delivery for the STC1 hormone analysis and maternal age, BMI, sex of the new-born and parity for the PE case-control analysis.

Results: We confirmed our initial results in full REPRPMETA sample set (n=366) by observing significantly higher maternal post-partum STC1 concentrations in pregnancies complicated with PE (n=50) compared to non-PE (n=316) pregnancies (P<0.01). A quantitative association analysis indicated several significant (P<0.05) SNP associations with STC1 level in maternal post-partum plasma. The detected associations were then alternatively tested with case-control analysis and at least one of the SNPs associated with STC1 concentration was also associated with PE in REPROMETA samples. The data analysis of the FINNEPC replication samples is currently in progress.

Conclusion: Despite a modest sample size in this analysis, we identified SNPs that are associated with circulating STC1 hormone levels in maternal blood. Maternal predisposition to preeclampsia and other pregnancy complications may be related to differences in circulating STC1 during pregnancy, which may be influenced by polymorphisms in the STC1 gene.

Finding eQTLs from RNA sequencing data of placental transcriptome

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Background: Expression quantitative trait loci (eQTL) are SNPs, both in cis and trans positions, that can determine or alter the expression of certain genes, both in cis and trans positions; often the effect can be tissue-specific. As the gene expression changes, it can also affect the phenotype of an individual. It has been shown that in preeclampsia and other pregnancy complications, there are several changes in gene expression of placenta [1, 2]. Therefore it would be very important to determine the eQTLs in placenta which has not been done yet.

Aims of this study: Firstly, to establish a pipeline for finding eQTLs in placental RNAseq data by focusing on cis-eQTLs of genes that were differentially expressed in term pregnancy complications (preeclampsia, gestational diabetes, small and large for gestational age babies). Secondly, to conduct the whole genome screen with an aim to identify placental cis- and trans-eQTLs.

Methods: We utilized two datasets generated from term placentas: a) RNA transcriptome data sequenced in cooperation with Institute for Molecular Medicine Finland, University of Helsinki, on a Illumina Hiseq 2000 platform [1], b) SNP genotyping data using Illumina HumanOmniExpress-12-v1, genotyped by in-house institutional core facility (n=40). Cis-eQTLs were defined by us as SNPs 10kB up- or downstream from the gene. For validating chosen SNPs we used Taqman RT-qPCR with expanded samples (n=72). For analysing cis-eQTLs and screening whole genome for eQTLs we have used linear regression with PLINK 1.07 software [3]

Results: From first part of our study, I have determined 29 SNPs with a p-value <0.05 before FDR correction. For the downstream analysis we five SNPs were selected, considering p-values and genomic context of the SNP. We were able to validate two SNPs with Taqman RT-qPCR: rs11697869 (p-value = 2.76E-06) and rs216259 (0.001743) were significantly associated with gene expression of TMEM74B and FAM65B, respectively. From the pilot whole genome analysis we have determined 125 SNPs (FDR p-values range 1.73·10^-14 -2.69·10^-8) that are associated with the placental expression of 23 genes.

Conclusions: For the first time we have conducted a placental eQTL study and we were able to observe signifi-cantly associated SNPs across genome. In perspective these eQTLs may be developed further as molecular diagnostics markers for predicting risks of pregnancy complications.


3. S Purcell, B Neale, K Todd-Brown, L Thomas, MAR Ferreira, D Bender, J Maller, P Sklar, PIW de Bakker, MJ Daly, PC Sham, 2007; PLINK: a toolset for whole-genome association and population-based linkage analysis. American Journal of Human Genetics, 81.
Gestational diabetes mellitus (GDM) is a disorder of carbohydrate metabolism that occurs during pregnancy. Early diagnosis of the disease reduces the incidence of perinatal problems (birth traumas, the need for caesarean section) and helps to identify mothers who have a higher risk of developing type 2 diabetes in later life.

**Objectives:** The aim of the study was to analyse the frequency of gestational diabetes and its risk factors at Women's Clinic of Tartu University Hospital, and the predictive value of the different factors in assessment of the risk for GDM.

**Methods:** We analysed the clinical data and medical history of women (n=1073) who received antenatal care at Women's Clinic of Tartu University Hospital in 2012-2013. GDM was diagnosed based on the antenatal care guideline approved by the Estonian Gynecologists’ Society in 2011. The criteria for diagnosis of GDM follow on the recommendations of International Association of Diabetes in Pregnancy Group: 75 g oral glucose tolerance test (OGTT) that resulted in at least one abnormal value of plasma glucose level: ≥5.1 mmol/l (fasting), ≥10 mmol/l (1h), and/or ≥8.5 mmol/l (2h)

**Results:** 46% of pregnant women (n=495) had one or more risk factors for GDM. The most common risk factor was overweight (18.5% of the women, BMI 25.0-30kg/m²), obesity (8.6%, BMI ≥30kg/m²). GDM in a previous pregnancy, large birth weight baby (>4.5kg), and elevated fasting blood glucose levels during the current pregnancy were the significantly related to the likelihood of developing GDM (p<0.0002, OR>10).

867 pregnant women (81%) were monitored according to the antenatal care guideline. GDM was diagnosed in 52 (6%) cases using OGTT: in 36 (4.2%) cases at 24-28 gestational weeks and in 16 cases (1.8%) already during the first trimester.

In addition to dietary treatment, 7 patients needed additional metformin and 5 patients insulin (23% of patients with GDM).

Pregnant women with GDM had a higher frequency of fetal macrosomia and premature labor (p<0.05, OR= 4.8 and 2.9, respectively).

**Conclusions.** The frequency of gestational diabetes has increased after implementing the new guidelines. The most important risk factor for GDM is maternal overweight (BMI >25 kg/m² before the pregnancy. It is necessary to develop a strategy for postpartum monitoring of mothers with GDM to decrease the risk for development of type II diabetes mellitus.
TRANSLATION OF EUROPEAN MALE AGEING STUDY SEXUAL FUNCTION QUESTIONNAIRE (EMAS-SFQ) FROM ENGLISH TO RUSSIAN AND UKRAINIAN

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EMAS – SFQ is recently available instrument, validated and proved valid in multicentre European study of more than 3000 elderly men (O’Connor DB, Corona G, Forti G et EMAS group, 2008). This questionnaire assesses male sexual functions rather than only erection disturbances.

The aim of this study was to perform translation of EMAS – SFQ from English to Russian and Ukrainian languages.

Design and methods. Permission for translation was kindly offered by I.Huhtaniemi, D.Lee and J.Finn as well as detailed procedure when having the questionnaire translated to Russian and Ukrainian.

Two pairs of translation – backtranslation for each language were used with subsequent evaluation of independent experts.

Results and interpretation. Translation – backtranslation work together with expert evaluation resulted in optimal Russian and Ukrainian versions of EMAS-SFQ.

These questionnaires are presented in this poster.

Model of translation using 2 pairs of translators – backtranslators plus expert evaluation elucidates coincidences and differences in translation and permits the emission of final optimal version of it.
Incidence of cryptorchidism in boys born at Tartu University Hospital in 2012-2014

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Introduction: Undescended testicles is one of the most frequent malformations of the urogenital system in boys. The incidence of cryptorchidism varies in different countries between 1.6-9.0%. Postnatal spontaneous descent of the testicles has been reported even in up to 78% of boys with cryptorchidism.

The aim of the study was to analyse the incidence of cryptorchidism and postnatal descent of the testicles in boys born at Tartu University Hospital in 2012-2014 and the prevalence of known risk factors among the boys with cryptorchidism and controls.

Material and Methods: All 3727 boys, born at Tartu University Hospital in 2012-2014, were investigated for cryptorchidism. Cases where a testicle was located in the lower part of the scrotum, or could be lowered freely into this position and remained there, were considered normal. Undescended testicles were diagnosed in 46 newborn boys. One patient was excluded from further study due to left-sided perineal testicular ectopia. The position of the testicles in boys born in 2012-2013 (n=31) was checked at the age of 6 months. The prevalence of known risk factors and other epidemiological data were assessed by the maternal questionnaire among 45 cases with cryptorchidism and 251 controls descended testicles. The control group was extracted from the ongoing prospective HAPPY PREGNANCY1 cohort consisting unselected pregnancies that resulted with birth of boys with normal testicles.

Results: The incidence of cryptorchidism among the boys born in 2012-2014 was 1.2%. Right-sided cryptorchidism occurred in 23 (51.1%) cases, left-sided in 16 (35.6%) cases and bilateral cryptorchidism in 6 (13.3%) cases. In 8 (17.7%) cases the baby was preterm (<37 gestational weeks), 4 (8.8%) babies had birth weight <2500g and 2 (4.4%) babies were small weight for gestational age (SGA). The incidence of cryptorchidism among preterm boys was higher compared to term boys: 2.2% vs 1.2% respectively (p=0.069). Among of SGA boys, cryptorchidism occurred more frequently compared with normal weight term boys (5.7% vs 1.2%, p=0.066). At the age of 6 months the testicles had descended into the scrotum in 11 (35.4%) boys out of 31 patients (11 testicles out of 34 testicles, 32.3%). Surgical treatment was indicated in the remaining cases. The boys with cryptorchidism were born more frequently from in vitro fertilization (IVF) pregnancies compared with control group (13.1% vs 4.4%, p=0.045). There was found no significant association with parental age or body mass index, tobacco smoking, and maternal drinking of alcohol or cola-like beverages during pregnancy.

Conclusion: The incidence of cryptorchidism in boys born at Tartu University Hospital was 1.2%. It is lower than expected regarding relevant published data. Postnatal descent of the testicles occurred in 35% of boys, that is also lower compared to corresponding data published elsewhere. Cryptorchidism occurs more frequently in preterm boys and in boys with SGA. IVF pregnancy proved to be significantly more common among boys with undescended testis.

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1 HAPPY PREGNANCY – the full name of the project (3.2.0701.12-0047): Development of novel non-invasive biomarkers for fertility and healthy pregnancy (2013-2015); supported by European Regional Development Fund, www.happypregnancy.ut.ee
Epsilon gamma delta beta thalassemia diagnosed by chromosomal microarray in critically ill neonate

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BACKGROUND: Epsilon gamma delta beta thalassemias represent a group of rare autosomal dominant haemoglobinopathies caused by deletions of the β-globin gene cluster. The most prominent clinical feature is ante- or neonatal anaemia, which might lead to severe complications. The severe anaemia resolves in a couple of months after birth. Here we describe a familial case of (εγδβ)-thalassemia caused by a novel 11p15.4 microdeletion, which is the first reported case from North-Eastern Europe.

CASE REPORT: The proband is a girl born with severe non-immune haemolytic anaemia complicated by persistent pulmonary hypertension of the newborn. The baby required blood transfusions, mechanical ventilation and extracorporeal membrane oxygenation due to critical condition. At the age of 2 months the outcome is favourable, although she remains mildly anaemic. The family history was remarkable as her older brother, father, paternal grandfather, aunt and cousin have had anaemia-related health problems of variable severity.

METHODS AND RESULTS: As a first-tier genetic test, chromosomal microarray analysis (CMA) from DNA sample of the proband was performed using Illumina HumanCytoSNP-12 array. CMA revealed a 115 kb deletion (arr[hg19] 11p15.4(5,228,708-5,343,533)x1). The deletion was found also in other five affected family members. The deleted region covers the whole β-globin gene cluster encompassing genes HBB, HBD, HGB1, HBG2, and HBE1.

CONCLUSIONS: Firstly, this case demonstrates that CMA could serve as a useful first-tier genetic test for severe life-threatening neonatal anaemia. Secondly, the detected 11p15.4 deletion is clearly pathogenic and has a size that is just slightly above the resolution limit of arrays routinely used in clinical diagnostics. Thirdly, we would like to emphasize that some rarer forms of thalassemia may also be present in Northern-European population and should be included in differential diagnosis of severe neonatal anaemia.
Serum Biomarkers for Predicting and Characterization of Preeclampsia

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Preeclampsia (PE) is a multisystem disorder of pregnancy of which there can be problems both to the mother and foetus. Clear symptoms to PE are mother’s hypertension and proteinuria with onset following the 20th week on pregnancy that brings foetus into high risk (eg retarder growth or mortality) (Wagner, 2001). No certain biomarker test is introduced to predict PE in advance.

The ultimate cause of the diseases is still unknown, and the only cure is delivery of the foetus and placenta. Various agents and variables have been investigated to see if they influence the development of PE. Peptides related to angiogenesis, especially vascular endothelial growth factor (VEGF) and placental growth factor (PIGF) have shown great correlation with the disease and are the most studied (Verlohren et al., 2010). Further more there are many recent gene expression level based studies that introduces new markers involved in pregnancy complications (Rull et al., 2013; Uusküla et al., 2012).

Our research group purpose is to gain more information about different serum markers from mother’s blood. Combining protein based biomarkers with maternal characteristics is a key to successful medical diagnostics. We have selected ca 20 protein based markers both from published articles and unpublished works. Luminex xMAP® platform is being used to develop method for simultaneous detection of selected markers from participants in Happy Pregnancy project. Risk assessment and prospective studies will be performed for potential diagnostic purpose.

First multiplex assay with eight analytes has been introduced. Analytical parameters from trial experiments confirm suitability of set-up reagents and selected platform. Reference values and dynamics is to be set for non problematic pregnancy outcome and this will be compared to PE cases. New markers are still in validation for expanded selection and novelty.


RNA-seq analysis of placental transcriptional landscape in normal and complicated pregnancies

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Approximately one in five pregnancies suffer from complications of varying severity, and prenatal conditions are increasingly recognized as major determinants in infant, adolescent and recently also adult health. We performed an extensive study of the placental transcriptome using RNA sequencing, the most powerful and contemporary method for gene expression analysis. Our samples (n=40) cover placentas representing normal gestation (n=8), preeclampsia (n=8), gestational diabetes (n=8), as well as aberrations in fetal growth defined as small- (n=8) and large-for-gestational-age (n=8) newborns. The generated dataset is the largest of its kind generated to date and covers the widest range of pregnancy outcomes. Sequencing yielded ~3.4 Billion 46 + 46 bp paired end reads (Mean: 84.4 M reads per sample; range: 48.4M – 145.2M). Of the total 164 billion sequenced bases 121 billion (73.5%) were successfully mapped to the human genome after quality control, filtering and alignment steps (49.2% mapped to known mRNAs). We observed a clear distinction in the severity of transcriptional disturbances in preeclampsia (215 differentially expressed genes) compared to other pregnancy complications which only exhibit differential expression in a few genes. A limited number of transcription factors including LRF, SP1 and AP2 are implicated as drivers of these changes. Our results also provide support to the hypothesis of shared placental responses to pregnancy complications as we observe substantial overlap of gene expression alterations in different pregnancy complications. Our data provide a rich resource for identification of potential biomarkers and therapeutic targets involved in gestational disturbances.
The effect of dietary counselling on food intake in pregnant women at high risk for gestational diabetes – results from a randomized controlled trial RADIEL

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The prevalence of gestational diabetes (GDM) is increasing worldwide. GDM might be prevented by improving diet of pregnant women. The objective of the study was to evaluate the effect of dietary counselling on diet in pregnant women at increased GDM risk. This study was a randomized controlled trial in which pregnant women with previous GDM or BMI ≥30 kg/m² were allocated into two groups. The control group received standard antenatal dietary counselling according to national recommendations. The intervention group participated, in addition, in one individual dietary counselling session and one group dietary counselling session. Food intake was assessed using a food frequency questionnaire (FFQ). The follow-up of the present study was conducted from the first to the second trimester of pregnancy, and included 242 participants. Bootstrap type analysis of covariance indicated that the intake of low-fat cheese increased in the intervention group and decreased in the control group (baseline adjusted means 0.09 times/day and -0.14 times/day; \( P = 0.040 \)). Also, the intake of fish increased more in the intervention group compared to the control group (baseline adjusted means 0.28 times/day and 0.06 times/day; \( P = 0.011 \)). The present study showed that dietary counselling in early pregnancy can improve diet of pregnant women at increased GDM risk.
Supporters:
Doctoral School of Clinical Medicine

Duration: 01.09.2009 – 31.08.2015, coordinated by Archimedes Foundation. European Social Fund, measure “Promoting PhD study and internationalization”

The Doctoral School of Clinical Medicine is a collaborative project between University of Tartu, Tartu University Hospital and University of Helsinki. The main goal of this project is to organize doctoral studies more effectively and to enhance the quality of the studies.

The activities of the Doctoral School are:

1. Preparing and conducting Winter- and Summer Schools, intensive courses and practical trainings, seminars etc events addressed to doctoral students.

2. Including foreign lecturers, scientists, (co)instructors or doctorate students in events conducted in Estonia.

3. Preparing and conducting interdisciplinary research projects for doctorate students.

4. Including foreign (co)instructors and doctorate students and instructors in short-term non-international and international visitations to see (co)instructors or participate in conferences.

5. Organising trainings for lecturers and instructors in order to enhance their competence in teaching and instructing.

6. Evolving new courses or developing the existing ones in doctoral study curriculums (including inviting foreign lecturers).

7. Popularise science and doctorate schools, including the publishing of articles which introduce doctoral papers.

8. Preparation of events that develop the collaboration between universities and private and public sectors (collective seminars).

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Graduate School in Biomedicine and Biotechnology

Duration: 01.09.2009 – 31.08.2015, coordinated by Archimedes Foundation.

European Social Fund, measure “Promoting PhD study and internationalization”

Graduate school is an exclusive/special project for developing academic cooperation including universities or other relevant institutions. It aims to develop existing doctoral programs through various activities and projects attracting different supplementary resources. The Graduate School does not offer Ph.D. degrees nor conduct independent research.

Graduate School in Biomedicine and Biotechnology is established under the Faculty of Science and Technology in the University of Tartu, in collaboration with partners - Estonian University of Life Sciences and Tallinn University of Technology.

The Graduate School is managed by the Head of Graduate School and advised by the Academic Board consisting of representatives from associated partner institutions and foreign partner universities. The management team including project manager and two coordinators provides administrative support to the Head of the School.

The overall goal of the Doctoral School in Biomedicine and Biotechnology is to increase the competencies in the field of biomedicine and biotechnology in Estonia by strengthening appropriate education.

The specific objectives of the Doctoral School are:

- To raise the efficiency of doctoral studies through better planning, financing and organization of PhD courses and research
- To shorten study time and offer better quality of supervisors, involving underexploited competencies and resources to doctoral studies Sponsors and funding
- To tighten the international research networks by offering additional mobility measures to graduate students.

Graduate School in Biomedicine and Biotechnology is focusing on the following activities:

- Providing financial support to the Ph.D. students enrolled in the Graduate School
- Organizing regular research seminars and doctoral courses
- Organizing international workshops and conferences
- Mobility grants for Ph.D. students for research or training at the foreign partner institutions; and participation in the international conferences
- Involving guest Ph.D. students in order to promote the creation of cross-national/international research groups
- Recruitment of foreign experts to teach doctoral courses and seminars and to supervise theses.

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**Project HAPPY PREGNANCY**

The full name of the project: "Development of novel non-invasive biomarkers for fertility and healthy pregnancy"

Duration: 01.09.2012 – 31.08.2015

Funding: European Regional Development Fund, measure “Supporting Biotechnological Research and Development”, coordinated by Archimedes Foundation

HAPPY PREGNANCY project represents applied translational research in reproductive biomedicine from the lab to the implementors in clinic and private sector.

The main aims of the project are:

- to test and evaluate the clinical relevance of novel DNA polymorphisms and copy number variations discovered by researchers and to translate these genetic biomarkers to the routine application in molecular diagnostics in reproductive medicine; to prepare for their potential future assessments in pharmacogenetics.
- to test and evaluate the clinical prognostic potential of novel maternal blood serum biomarkers in pregnancy complications identified by researchers, as well as to evaluate the clinical performance of blood serum biomarkers suggested in scientific literature, but not yet applied in Estonian patients;
- to develop together with the private partner a multi-marker test of these biomarkers for the routine application in clinic.

The research groups comprise basic scientists (reproductive genetics; University of Tartu), clinicians (andrology; obstetrics and gynecology; Tartu University Hospital;) and project implementing partners from public (Department of Genetics, United Laboratories, Tartu University Hospital) and private sectors (Quattromed HTI Laborid OÜ). The project represents a joint effort by a novel academia-clinic-commercial partner consortium.

Recent publications:


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