ABSTRACTS COLLECTION

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Presenting author names **are bold** in the contributor lists.

e-Posters

EP01 Reproductive Genetics

EP01.001 Correlations between cytogenetic findings and spermatogenic failure in Bulgarian infertile men

Svetlana Yovinska[1], *Kalina Belemezova*[2], *Mariela Hristova-Savova*[2], *Tanya Milachich*[2], *Petya Andreeva*[2], *Yuri Buchvarov*[2], *Maria Yunakova*[2], *Tanya Timeva*[2], *Atanas Shterev*[2], *Ivanka Dimova*[3]

[1]*Medical University - Sofia, Department of Pharmacology and Toxicology, Sofia, Bulgaria;* [2]*SAGBAL "Dr. Shterev", Sofia, Bulgaria;* [3]*Medical University - Sofia, Department of Medical Genetics, Sofia, Bulgaria.*

Background/Objectives: Chromosomal aberrations have a great impact on spermatogenesis, semen quality, and successful conception. The objective of our study was to determine the type and frequency of chromosomal aberrations and polymorphisms in men with different degrees of spermatogenic failure in comparison to men with normozoospermia, in order to find some correlations between cytogenetic findings and the abnormal results of semen analysis.

Methods: In our study, we have performed cytogenetic analysis in 901 infertile men, divided into 5 groups according to semen analysis—normozoospermia, asthenozoospermia, oligoasthenozoospermia, severe male factor and azoospermia.

Results: The frequency of polymorphisms was similar in all groups (11–16%, without significant differences). The frequency of numerical and structural aberrations increases with the degree of the spermatogenic failure (3.5% in normozoospermia, 5.6% in asthenozoospermia, 9.8% in oligoasthenozoospermia, 9% in severe male factor and 13.5% in azoospermia). We have found significantly higher incidence of numerical chromosome aberrations in severe male factor (7%) and azoospermia (9.3%). Oligoasthenozoospermia was associated with chromosomal translocations, as it occurs in 45% of cases with translocation, compared to 20% in the group with normal karyotype.

Conclusion: We revealed that chromosomal translocations are significantly associated with oligoasthenozoospermia, whereas numerical chromosomal aberrations—with severe male factor and azoospermia. These are important aspects of genetic counseling for those cytogenetic findings. Chromosome polymorphisms don't seem to disturb significantly spermatogenesis and their impact should be studied in regard to unsuccessful pregnancy achievement, even in patients with normozoospermia.

References:

Grants:

Conflict of Interest: None declared.

EP01.002 Comparison of carrier status among patients with or without family history of disease using targeted and expanded panels

Karen Phaik Har Lim[1], *Bridgette Meyers*[1], *Ezen Choo*[1], *Trevor Smart*[1], *Sindhu Arun*[1], *Nina Sanapareddy*[1], *Dianne Keen-Kim*[1]

[1]*Natera Inc., San Carlos, United States.*

Background/Objectives: Inflammation plays a key role in the pathogenesis of atherosclerosis. However, the role of genetic variability on inflammation after treatment with proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors remains to be elucidated. For the first time, we examined the influence of polymorphisms in *CRP*, *TNF-α*, and *IL6* genes on plasma levels of hsCRP, TNF-α, and IL6 at baseline and after treatment with PCSK9 inhibitors.

Methods: A total of 69 patients with stable coronary artery disease after a premature myocardial infarction were included in the study. All patients had extremely elevated lipoprotein(a) levels and received a PCSK9 inhibitor. Genotyping for *CRP* rs1800947, *TNF-α* rs1800629, and *IL6* rs1800795 was performed.

Results: Our results showed no significant association between single nucleotide polymorphisms in *CRP*, *TNF-α*, and *IL6* and plasma levels of hsCRP, TNF-α, and IL6, respectively. Consistent with previous studies, no significant change in levels of inflammatory biomarkers was observed after 6 months of treatment with PCSK9 inhibitors. Moreover, genetic variability in selected genes was not significantly associated with the change in plasma levels of corresponding inflammatory markers.

Conclusion: Genetic variability did not affect plasma levels of inflammatory markers, which could be due to background therapy with statins or extremely elevated lipoprotein(a) levels, because lipoprotein(a) itself contributes to inflammation. Further studies are needed to clarify which factors contribute most to the modulation of inflammation in high-risk patients.

References: Ruscica et al., Atherosclerosis, 2019.

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Conflict of Interest: None declared.

EP06.015 Circulating microRNAs as biomarkers for pulmonary arterial hypertension

*Mauro Lago-Docampo[1], **Jesús Eduardo Martín-Salazar**[1], Ainhoa Iglesias-López[1], Isabel Blanco[2], Adolfo Baloira Villar[3], Joan Albert Barbera[2], Diana Valverde Pérez[1]*

[1]CINBIO, Universidade de Vigo, Vigo, Spain; [2]Hospital Clínic de Barcelona, Barcelona, Spain; [3]Complexo Hospitalario Universitario de Pontevedra, Universidad de Vigo, Pontevedra, Spain.

Background/Objectives: Pulmonary Arterial Hypertension (PAH) is a rare disease where the thickening of the precapillary pulmonary arteries ends up inducing right heart failure. The prognosis of PAH patients depends on multiple factors, being the time of diagnosis a critical one. Currently, diagnosis is complicated and usually delayed until performing right-heart catheterization.

Methods: We perform small RNA sequencing in plasma of idiopathic PAH patients and controls. We used classification models to analyse the potential of the microRNAs, that we found differentially expressed, as PAH predictors. Also, we use miRBase to predict the targets for the dysregulated miRNAs we detected. Finally, we performed functional assays based on qPCR and western blotting to confirm our results.

Results: We were able to find 29 differentially expressed microRNAs and validate 7 of them in a nationwide cohort (let-7a-5p, let-7b-5p, let-7c-5p, let-7f-5p, miR-9-5p, miR-31-5p, miR-3168). In our cohort, we obtained a model with an AUC of 0.738. Also, we identified miR-3168 as a novel upregulated miRNA in PAH patients. We demonstrate that it targets the Bone Morphogenetic Protein Receptor type 2 (BMPR2), as validated at mRNA and protein levels. Preliminary results show that miR-3168 overexpression increases resistance to apoptosis and enhanced angiogenesis.

Conclusion: We found novel downregulated and upregulated microRNAs in idiopathic PAH patients. We were able to develop a 3-microRNA signature for diagnosis and functionally characterized in vitro the effect of miR-3168 as a possible modulator of the disease.

References:

Grants:

Conflict of Interest: None declared.

EP06.016 22q11.2 microdeletion is the most common genomic abnormality in Serbian newborns with critical congenital heart disease and could be rapidly detected by Multiplex ligation probe amplification analysis

*Aleksandra Miletic[1], **Goran Cuturilo**[1;2], Jelena Ruml Stojanovic[1], Danijela Drakulic[3], Marija Mijovic[1], Brankica Bosankic[1], Hristina Petrovic[1], Milena Stevanovic[3;4;5]*

[1]University Children's Hospital, Belgrade, Department of Clinical Genetics, Belgrade, Serbia; [2]Faculty of Medicine, University of Belgrade, Belgrade, Serbia; [3]Institute of Molecular Genetics and Genetic Engineering, University of Belgrade, Belgrade, Serbia; [4]Faculty of Biology, University of Belgrade, Belgrade, Serbia; [5]Serbian Academy of Sciences and Arts, Belgrade, Serbia.

Background/Objectives: Genetic tests may facilitate rapid and effective diagnostics but unfortunately their high costs usually limit their application in all patients (1). We aimed to investigate the utility of rapid, cost effective and high sensitive Multiplex ligation probe amplification analysis (MLPA) for detection copy number variants (CNV) in newborns with critical CHD, admitted to the Neonatal Intensive Care Unit (NICU).

Methods: Study included 100 consecutive newborns admitted to the NICU, University Children's Hospital in Belgrade from August 2014 to September 2019. Patients with viable trisomies (21, 18 and 13) were excluded. All participants were tested by MLPA analysis using SALSA MLPA P250-B2 Di George and SALSA MLPA P311-B1 Congenital Heart Disease probemixes (MRC Holland, The Netherland).

Results: Pathogenic CNVs were identified in ten (10%) patients. Nine of them had 22q11.2 deletion detected by both kits while one patient had 3p25 deletion detected by P311 kit.

Conclusion: Genetic evaluation of all newborns with critical CHD admitted to the NICU by rapid and inexpensive MLPA analysis using combination P250 and P311 SALSA probemixes could contribute to high detection rate of pathogenic variants.

References: 1. Monteiro RA, Freitas ML, Vianna GS et al. (2017) Major contribution of genomic copy number variation in syndromic congenital herat disease: the use of MLPA as the first genetic test. Mol Syndromol 8: 227-23.

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Conflict of Interest: None declared.

EP06.017 Is the phenotype for ARVC caused by TMEM43 (p.S358L) becoming more severe in women over time?

*Ashley Baker[1], Stephen Duffett[2], Fiona Curtis[3], Emily Bonnell[3], Susan Stuckless[4], Sean Connors[2], Fred Paulin[2], Lesley Turner[3], Terry-Lynn Young[5], **Kathy Hodgkinson**[4]*

[1]Memorial University of Newfoundland, St. John's, Canada; [2]Memorial University of Newfoundland, Division Of Cardiology, St. John's, Canada; [3]Eastern Health, Provincial Medical Genetics Program, St. John's, Canada; [4]Memorial University of Newfoundland, Unit of Clinical Epidemiology, St. John's, Canada; [5]Memorial University of Newfoundland, Faculty of Medicine, St. John's, Canada.