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

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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

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Results: Overall MR was 10.21% (5.74% CDKN2A). Sporadic multiple primary melanoma (spoMPM) with 2 CMs had the lowest overall MR ($p = 0.02$), and >60 was the age category with the lowest CDKN2A MR ($p < 0.01$). ≥3CM cases, spoMPM with ≥3CMs, PC and region were predictive of CDKN2A likely/pathogenic variants (OR = 5.14, 4.97, 3.25 and 4.45, $p < 0.05$), whereas age >60 was a negative predictor (OR = 0.16, $p = 0.014$). In particular, MR was nearly 19% when CMs and PC clustered together.

Conclusion: Our results suggest that a revision of national genetic testing criteria for melanoma should be considered, especially regarding age cut-off and number of CM in absence of familial history. The use of telecounseling in our clinical practice allowed us to have a nationwide picture of the differences between CDKN2A and non-CDKN2A MRs in different regions.

References:

Grants:

Conflict of Interest: None declared.

EP13.012 Analysis of transcripts from alternative PRKAR1B gene promoters in colorectal cancer

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Background/Objectives: The transcriptional regulation of *PRKAR1B* is controlled by alternative promoters, and previous in silico analysis has indicated their differential activity in colon and rectal cancer tissue in comparison to normal gut mucosa. The aim of this study was to investigate *PRKAR1B* promoters and transcripts potentially involved in cancer.

Methods: The sequences of *PRKAR1B* alternative promoters were retrieved from Ensembl database: promoter A 752209 and promoter B 767287 bases upstream from the translation start site. Bioinformatic tools Alggen, AliBaba, CiiiDER, and TFBIND were used to predict binding of transcriptional regulators. Primer extension assay was performed on RNA isolated from malignant colon cell lines using an oligonucleotide probe binding to the sequence at the exon2/exon3 junction common for all *PRKAR1B* transcripts.

Results: Based on analyzed elements, both *PRKAR1B* promoters were found to have atypical structure. According to the prediction, promoter A that encodes transcript PRKAR1B-201 binds several factors involved in cell proliferation, while promoter B that encodes transcript PRKAR1B-203 binds mostly pro-apoptotic factors. In primer extension experiments, a single signal corresponding to the transcript PRKAR1B-212 was observed in malignant cells.

Conclusion: The differential activity of alternative *PRKAR1B* promoters in colorectal cancer can be explained by in silico results, predicting that promoter sequences bind sets of transcriptional regulators with opposing roles. However, experiments point to the transcript unrelated to either of the investigated promoters as potential cancer biomarker and it should be further characterized.

References:

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Conflict of Interest: None declared.

EP13.015 Frequency and spectrum of non-founder clinically actionable BRCA1/2 mutations in Russian patients with breast cancer: a series from one institution

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Background/Objectives: Most common mutations in *BRCA1* (5382insC, 185delAG, 4153delAG, T300G) and *BRCA2* (6174delT) genes account for 6-8% breast cancer (BC) patients of Slavic origin and are major targets for routine testing. But many BC cases with family history remain unsolved. The aim was to estimate the frequency and spectrum of non-founder *BRCA1/2* mutations in a large group of BC patients treated in our clinic.

Methods: A total, 560 women diagnosed with BC, which did not carry any of 5 BRCA1/2 Russian founder mutations, were enrolled. Age ranged from 18 to 83 years, mean age 49,3 years. Target sequencing was performed using multi-gene panel, including all exons of *BRCA1* and *BRCA2* genes.

Results: Clinically actionable non-founder genetic variants in coding regions of *BRCA1/2* genes were found in 35 from 560 (6,3%) patients. *BRCA2* mutations prevailed (22 cases or 62%), while *BRCA1* mutations explained 13 cases (38%). The 28/35 (80%) of mutations were frameshift deletions/insertions leading to premature stop codon, 6/35 (17%) mutations were missense and 1/35 (3%) mutation was from splice site. The majority of mutations was unique in this study, but previously described as pathogenic variants in BC patients from different populations. The recurrent mutations were BRCA2 c.7879A>T (rs80359014) in 3/35 (8,5%), BRCA2 c.9253del (rs80359752) in 2/35 (5,7%) and BRCA1 c.1303_1309del (rs886039941) in 2/35 (5,7%) BC cases.

Conclusion: The contribution of founder and non-founder mutations to the disease was compatible in our study population. The analysis of all *BRCA1/2* coding regions may double the number of identified *BRCA1/2* cases in Russian BC patients.

References:

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Conflict of Interest: None declared.

EP13.016 Germinal mutations in POLE and POLD1 genes

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Background/Objectives: Germline mutations in the exonuclease domain of POLE and POLD1 repair polymerases affect their proofreading capacity and have been described to confer a high risk for multiple colorectal adenomas and carcinoma. Other tumours were also associated with the syndrome: breast, brain, ovaries, pancreas, stomach uterus and skin.

Methods: An NGS multi-gene hereditary cancer panel called CZECANCA was used according to SeqCap or KAPA HyperCap Workflow (Roche) for the analysis of 3000 adult patients indicated by clinical geneticist for suspected hereditary cancer predisposition: 49% breast and/or ovarian cancers patients; 6.5% polyposis, non-polyposis colorectal or endometrial cancer; 21% with other type of solid cancers; remaining 23.5% were healthy individuals with high risk family history of hereditary cancer syndromes.

Results: Germinal deleterious (FS, N) mutations in the POLE gene have been detected so far only in breast cancer patients in 3 families without family history of CRC. Several potentially significant missense variants were detected in highly conserved amino acids of the exonuclease domains of POLE and POLD1 genes, but even in these cases, breast cancer was predominant.

Conclusion: Cancer patients with POLE/POLD1 mutations were described to respond well to immune checkpoint inhibition. Could