ABSTRACTS COLLECTION

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e-Posters

EP01 Cancer Genetics

EP01.001 Relevance of the gene ITIH5 in vulvar diseases

Olga Rodenko[1], Anke Esber[1], Irina Cepraga[1], Stefanie Schütze[1], Lars Jansen[1], Mieczyslaw Romuald Gajda[2], Nikolaus Gaßler[2], Ingo B. Runnebaum[1], Matthias Dürst[1], Norman Häfner[1], **Claudia Backsch**[1]

[1]*Department of Gynecology and Reproductive Medicine, University Hospital Jena, Jena, Germany;* [2]*Section of Pathology, Institute of Legal Medicine, University Hospital Jena, Jena, Germany*

Background/Objectives: The number of vulvar cancers (VC) and their precancers has increased worldwide in recent decades. To date, molecular genetic markers have not played a role in the differential diagnosis of vulvar intraepithelial neoplasias (VIN) and VC. The gene *ITIH5* could be play a role as such a marker in vulvar carcinogenesis as like in other cancers. The aim of the present study is to determine the ITIH5 status on different vulvar patient material.

Methods: The copy number status of ITIH5 was analysed using fluorescence in situ hybridization in vulvar scrapes and vulvar tissues of patients with histologically confirmed VIN and VC and as well as Lichen sclerosus (LS) (scrapes n = 10, tissues n = 28). In parallel, promoter methylation was investigated by methylation specific PCR on vulvar scrapes and expression was determined using immunohistochemistry on paraffin embedded vulvar tissues.

Results: In vulvar scrapes, 60% of VIN and 60% of LS showed ITIH5 copy number loss and in 40% of VIN and in 20% of LS ITIH5 methylation were found. In paraffin sections, ITIH5 copy number losses were detected in 36.4% of VIN, in 40% of VC and in 14.3% of LS. Evaluation of ITIH5 expression in paraffin sections are still ongoing.

Conclusion: ITIH5 aberrations seems to be play a role in vulvar carcinogenesis. The use of ITIH5 as a molecular genetic marker could possibly enable a better treatment-relevant or prognostic differentiation of VIN, VC, LS and recurrences in the future.

Grants: Project is supported in part by the Brigitte and Dr. Konstanze Wegener Stiftung.

Conflict of Interest: None declared

EP01.002 Exploring the Impact of Secretome on Inflammation in Myeloproliferative Neoplasms (MPNs)

Selin Fulya Toprak Yalçın[1], *Esra Nur Demirtaş[1], Tugba Sarac-Sivrikoz[2], Selcuk Sözer Tokdemir[1]*

[1]*Istanbul University Aziz Sancar Experimental Medicine Research Institute, genetic, Istanbul, Türkyie;* [2]*Istanbul University Faculty of Medicine, Department of gynecology and obstetrics, Türkyie*

Background/Objectives: Myeloproliferative Neoplasms (MPNs) are characterized by a critical inflammatory component that exacerbates disease progression. This is believed to stem from alterations in the bone marrow milieu. Our research focuses on assessing the influence of the secretome, released by mutant cells, on the inflammatory processes in MPNs.

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EP07.061 Assessment of arrhythmia-related genes in patients prediagnosed with long QT syndrome

Feyza Altunbas Yalabik[1], *Aslı Toylu*[1], *Ibrahim Basarici*[2], *ercan mihci*[3], *banu nur*[3], *Fırat Kardelen*[4], *Özden Altıok Clark*[1]

[1]*Akdeniz University Faculty of Medicine, Medical Genetics, Antalya, Türkyie;* [2]*Akdeniz University Faculty of Medicine, Cardiology, Antalya, Türkyie;* [3]*Akdeniz University Faculty of Medicine, Pediatric Genetics, Antalya, Türkyie;* [4]*Akdeniz University Faculty of Medicine, Pediatric Cardiology, Antalya, Türkyie*

Background/Objectives: Long QT Syndrome (LQTS) is an inherited channelopathy characterized by varying degrees of prolongation of the corrected QT interval on the electrocardiogram (>450 ms) and associated with an increased susceptibility to life-threatening ventricular arrhythmias. Most LQTS cases are associated with pathogenic variants in the *KCNQ1*, *KCNH2*, and *SCN5A* genes. Several other genes encoding either ion channel subunits or proteins that regulate channel function have also been implicated in LQTS causality.

Methods: We investigated 10 cases that underwent genetic testing for diagnosis of LQTS. LQTS-associated target genes were analyzed by next-generation sequencing. Variants were classified according to ACMG guidelines.

Results: Previously reported pathogenic variants in *KCNQ1*, *KCNH2*, *SCN5A*, and *KCNE1* genes have been observed in seven patients. Variants with unknown clinical significance have been identified in *KCNQ1*, *SCN5A*, and *AKAP9* genes in three cases. Pathogenic variants were most frequently observed in the *KCNQ1* gene. Interestingly, we identified the c.1097G>A (p.Arg366Gln) *KCNQ1* variant in 3 unrelated patients.

Conclusion: Our results include known pathogenic variants reported in the literature and various variants whose clinical significance is yet to be understood. Our study is expected to contribute to the literature by emphasizing the significance of genetic diagnosis in LQTS cases.

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Conflict of Interest: None declared

EP07.062 Association of *C11orf58* gene, encoding chaperon "Hero", with the increased risk of ischemic stroke

Irina Shilenok[1;2], **Ksenia Kobzeva**[1;3], *Olga Bushueva*[1]

[1]*Kursk State Medical University, Laboratory of Genomic Research, Research Institute for Genetic and Molecular Epidemiology, Kursk;* [2]*Kursk Emergency Hospital, Division of Neurology, Kursk;* [3]*Kursk State University, Department of Biology and Ecology, Kursk*

Background/Objectives: Ischemic stroke (IS) holds a prominent position as a leading contributor to worldwide mortality and disability. While the involvement of chaperones in IS risk is well-established, the role of a recently discovered group of heat-resistant obscure proteins ("Hero" acronymically) with chaperone-like properties in the development of IS remains unexplored. This study aims to examine whether SNPs of *C11orf58*, a member of the "hero" proteins, are associated with the risk of IS development.

Methods: DNA samples from 2204 unrelated Russian subjects (917 IS patients, 1287 healthy controls) were genotyped for 14 common SNPs: rs6677, rs1846936, rs11024031, rs10766342, rs7928675, rs11024032, rs4757430, rs7951676, rs11826990, rs3203295, rs10832676, rs4757429, rs3802963, *C11orf58* using probe-based PCR, and rs10734249 *C11orf58* – using the MassARRAY-4 genetic analyzer.

Results: We observed an association between *C11orf58* SNPs and increased IS risk across the entire group: rs10766342 (risk allele A, $p = 0.02$), rs11024032 (risk allele T, $p = 0.014$), rs11826990 (risk allele G, $p = 0.0072$), rs3203295 (risk allele C, $p = 0.016$), rs10832676 (risk allele G, $p = 0.0056$), rs4757429 (risk allele T, $p = 0.023$). Associations of these SNPs were modified by environmental factors, specifically smoking and fruit/vegetable consumption. Moreover, the SNP rs11024030 (risk allele C) is linked to an increased risk of IS exclusively in smokers ($p = 0.032$) and in patients with low fruit/vegetable intake (Pbonf $= 0.032$).

Conclusion: Thus, polymorphisms in the *C11orf58* gene represent novel genetic markers of IS.

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EP07.063 Genetic findings of paediatric patients tested for long QT syndrome

Aurelija Kemezyte[1], *Raimonda Meskiene*[2], *Birutė Burnytė*[2]

[1]*Vilnius University, Faculty of Medicine, Vilnius, Lithuania;* [2]*Institute of Biomedical Sciences, Vilnius University, Faculty of Medicine, Vilnius, Lithuania*

Background/ Objectives: Long QT syndrome (LQTS) is a well renowned monogenic channelopathy, which clinical phenotype widely varies and largely depends on genetic penetrance and expressivity of phenomena. Study aim was to evaluate clinical and genetic data in patients referred for LQTS genetic diagnosis.

Methods: We performed a retrospective analysis of the virtual gene panel of hereditary cardiovascular diseases from whole exome sequencing data of the patients evaluated for LQTS between the years of 2021 and 2022.

Results: Clinical and genetic data from 92 unrelated patients (55%, 51/92 of females) were analysed. The mean age at time of testing was 10 ± 4.7SD years. Pathogenic or likely pathogenic variants were identified in 19% (17/92) of those patients. A total of 16 variants of unknown significance were identified in the study (7 absent in gnomAD). The most implicated gene was *KCNQ1*, with 65% (11/17) of the patients affected. Variants in *KCNH2* gene were found in 12% (2/17) of patients, while 24% (4/17) were distributed in other genes. Nearly a quarter of patients (24%, 4/17) had a first degree relative with clinical LQTS. Among the patients, mean Schwarz score and longest measured QTc interval were 3.4 ± 1SD and $497\text{ms} \pm 32$SD, respectively. More than half (59%, 10/17) were asymptomatic, diagnosed accidentally based on ECG findings and/or family history.

Conclusion: This study confirms the importance of genetic testing for LQTS patients showing 19% of them to benefit from genetic result that will guide their clinical management.

Grants:

Conflict of Interest: None declared

EP07.064 New variants identified in low evidence genes associated with pulmonary arterial hypertension development

Natalia Gallego[1;2;3], *Lucía Miranda-Alcaraz*[1;2;3], *Mónica Mora*[1;2;3], *Alejandro Cruz-Utrilla*[4;5], *Dra. María Jesús del Cerro*[6], *Manuel López Meseguer*[7], *Amparo Moya Bonora*[8], *Nuria Ochoa*[4;5], *alejandro parra*[1;2;3], *Patricia Pascual Vinagre*[1;2;3], *Mario Cazalla*[1;2;3], *cristina*