ORAL PRESENTATION ABSTRACTS

OP1- Whole genome characterization of probiotic *Latilactobacillus sakei* isolated from traditional Turkish pastrami: A functional genomics perspective on health-promoting bacteria

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Abstract

Probiotics are defined as live microorganisms that confer a documented health benefit on the host by interacting with gut microbiota and other host biological systems. Among them, lactic acid bacteria (LAB) play a significant role in promoting gastrointestinal and immune health and providing protection against pathogens. Fermented foods serve as natural reservoirs for LAB strains with potential probiotic properties. In this study, traditional Turkish pastrami, a fermented meat product typically consumed without heat treatment, was investigated as a source of beneficial LAB. A total of 49 LAB isolates were obtained from ready-to-eat pastrami samples collected from multiple production facilities in Kayseri. Initial screening was performed based on phenotypic and biochemical characteristics, followed by species-level identification using MALDI-TOF MS and 16S rRNA gene sequencing. Phylogenetic clustering was used to analyze the relationships among the isolates. Functional probiotic properties of the isolates were evaluated through *in vitro* experiments assessing resistance to simulated gastric and intestinal fluids, salt and acid tolerance, and adhesion capability to human colorectal adenocarcinoma cell lines (Caco-2). The whole genome sequencing was conducted on the most promising isolate, revealing genes associated with adhesion, acid and stress tolerance, antibiotic resistance, and antimicrobial peptide production. The findings demonstrated that certain *Latilactobacillus sakei* strains from pastrami possess significant probiotic potential at the molecular level. This study highlights the health-promoting potential of traditionally fermented meat products and supports their classification as functional foods. Integrating genomic and functional data aims to contribute to public health through evidence-based food choices.

Keywords: Healthy Nutrition, functional foods, next generation sequencing, adhesion assay.

OP2- A *de novo* pathogenic FOXG1 frameshift mutation associated with autosomal dominant congenital Rett Syndrome

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Abstract

Congenital Rett syndrome (OMIM #613454), an autosomal dominant ultra-rare neurodevelopment disorder that is characterised by the clinical presentation of early developmental delay, severe verbal impairment, and abnormal movement which shown in earlier onset in the first months of life. The case demonstrates the value of ruling out *FOXG1* mutations in a male neonate with marked neurodevelopment abnormality and epileptiform EEG findings shortly after birth, prompting referral for genetic investigation. The *FOXG1* gene encodes a transcriptional repressor which is essential for the early brain development, including telencephalon formation and maturation, and plays an essential role in neuronal proliferation, differentiation, and regional cerebral hemispheres patterning. The presented patient exhibited significant neurodevelopment delay, abnormal breathing patterns, atypical motor movements, and abnormal electroencephalographic findings, prompting referral for genetic evaluation. Therefore, Trio-WES analysis using third generation Oxford Nanopore sequencing technology has been done to patient and both parents which revealed a heterozygous c.459_460delGG (p.Glu154fs) frameshift variant in *FOXG1,* only in patient. This variant has been identified as pathogenic in ClinVar and further confirmed by in-silico predictors such as Varsome and Franklin, with expected functional consequences including premature truncation of the *FOXG1* protein with the congenital form of Rett syndrome. Additionally, parental analysis established that the mutation was *de novo*, and there was no family history of such characteristics. Despite immediate medical attention, the patient died within 24 hours of life. This case underscores the diagnostic value of NGS in detecting *de novo* pathogenic variants and highlights the importance of considering *FOXG1*

mutations in neonates with unexplained severe neurologica symptoms. In conclusion, the detection of such mutations ma explain cases of early postnatal sudden death; therefore, long read whole-exome sequencing and comprehensive family-base genetic analysis are recommended in similar presentations.
Keywords: FOXG1, Rett syndrome, ultra-rare genetic disease, neurodevelopment disorder

OP3- Tool combination via machine learning significantly improves CNV detection success in WGS

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Introduction: Despite the development of numerous tools to detect copy number variations (CNVs) utilizing next-generation sequencing (NGS) data, no single tool performs consistently well across all CNV types and datasets. To improve accuracy, studies suggest using multiple tools. However, how to combine different CNV detection tool outputs still remains a challenge, and interpreting combined results is yet to be explored.
Materials&Methods: 11 CNV detection tools (Breakdancer, CNVpytor, GATK gCNV, Canvas, Control-FREEC, cn.MOPS, CNVkit, Delly, Gridss, Manta, Lumpy) were selected based on literature and internal evaluation. The well-characterized NA12878 whole genome sequencing (WGS) dataset and its validated gold-standard CNV set were used for benchmarking and machine learning. Tool outputs were initially merged using the SURVIVOR tool. Later, we applied a custom genome-wide binning strategy to integrate results and used machine learning models (Random Forest, Logistic Regression, XGBoost) with 5-fold cross-validation for CNV detection. The performance of each method was evaluated using precision, recall, and F1-score against the gold standard.
Results: Among individual tools, Delly achieved the highest F1-score (0.35). All possible tool combinations with SURVIVOR produced F1-scores reaching up to 0.45. Our integration approach using Random Forest significantly improved performance, yielding F1-scores of 0.91 for deletions and 0.71 for duplications.
Discussion&Conclusion: This study shows that machine learning-based integration of CNV tools can greatly improve CNV detection success, reaching levels comparable to microarray platforms. Even low-performing tools add valuable data when intelligently combined. These findings highlight th promise of AI-supported CNV detection from NGS data.
Keywords: CNV, machine learning, random forest, NGS

OP4- Computational Analysis of Histone Lactylation Complex Genes and their Role in the Pathogenesis of AML

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Introduction: AML is an aggressive hematologic malignancy characterized by impaired differentiation and uncontrolled proliferation of immature hematopoietic precursors. Recent findings highlight the growing significance of epigenetic modifications, particularly histone lactylation, in cancer biology. The aim of study is to comprehensively identify mutations and expression profiles in the genes forming the lactylation complex using bioinformatics tools, with a focus on understanding the underlying mechanisms.
Material and Methods: Genomic sequences and expression profiles of AML cohort (n:872) were acquired from using tools and analyzed. PolyPhen-2, SIFT, Mutation Assessor, and AlphaMissense tools were utilized to forecast the pathogenic effects of mutations determined in target genes encoding subunits of the Lactylation modulation complex. Furthermore, m-RNA expression and survival profiles were also invastigated.
Results: 7 mutations were detected in 8 genes. 3 mutations were classified as pathogenic. A deletion leading to a homozygous loss of allele was discovered in *ALKBH5*. Mutations with function-altering effects were identified in the codes encoding the domains of the genes. The frameshift mutations p.S250Kfs*9 and p.T343Rfs*26 discovered in *WTAP* have the potential to cause the formation of transcripts with impaired function by altering the reading frame. The pathogenic p.C472Y mutation was detected in the C-terminal region of *FTO* and the pathogenic p.R693H mutation in the RRM region of the *RBM15* gene. A pathogenic p.Q28R was detected in the RNA methylase region of *METTL5* and a p.Y128H mutation was detected in the LDH1 domain of the *LDHB*. The results of our m-RNA expression profiling showed that the expression levels of *LDHA* and *LDHB* were down-regulated in AML samples and up-regulated in *FTO* compared to healthy subjects. ($p<0.01$). The effect of gene expression on survival was found to be significant with decreased *ALKH5*. ($p=0.017$).
Discussion: Targeting lactate-driven histone modifications or/and epitranscriptomic pathways in hematological malignancies such as acute myeloid leukemia may enhance the effectiveness of immunotherapies.
KeyWords: Acute myeloid leukemia; Epigenetics; Lactylation; Mutation; Expression

OP5- NIPT screening outcomes in Northern Cyprus

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Objectives:

This study aims to evaluate the clinical utility of Non-Invasive Prenatal Testing (NIPT) in detecting chromosomal abnormalities among pregnant women and to describe the demographic and biological parameters associated with the test results.

Materials and Methods:

A retrospective analysis was conducted on 282 pregnant women who underwent NIPT in Cyprus. Maternal age, gestational week at testing, fetal fraction levels, as well as presence/absence of Y chromosome were recorded. The NIPT assessed risk levels for common trisomies, including Trisomy 21, 18, and 13. Descriptive statistics and inferential analyses were performed using Jamovi software.

Results:

The average maternal age was 35.38 years (SD ±7.81), and the mean gestational age at testing was 11.86 weeks (SD ±2.84). The mean fetal fraction was 18.7% (SD ±8.18), ranging from 3.0% to 92.0%. Of the 282 cases analyzed, only 2 were reported as "very high risk" for Trisomy 21, while 280 (99.29%) were classified as "very low risk" for all screened trisomies. No high-risk cases were identified for Trisomy 18 or 13.

Sex chromosome analysis indicated that 141 samples (51.1%) showed the presence of a Y chromosome, while the remaining 48.9% did not. A one-way Welch's ANOVA was performed to evaluate the relationship between fetal fraction and the presence of the Y chromosome. The results showed no statistically significant difference in fetal fraction between groups ($F(1, 273) = 0.215$, $p = 0.643$). Group means were 0.212 (SD ±0.867) for the presence and 0.166 (SD ±0.785) for the absence of the Y chromosome. Additionally, a chi-square test assessing the association between fetal fraction and the presence of the Y chromosome showed no significant relationship ($p = 0.546$).

Conclusion:

NIPT proved to be a highly effective and non-invasive screening method for early detection of chromosomal abnormalities, with the majority of cases presenting as very low risk. Neither the presence of a Y chromosome nor the fetal fraction showed a significant statistical relationship, further supporting the robustness of NIPT across fetal sex. These findings support the routine use of NIPT in prenatal care, particularly for women of advanced maternal age, as a means to reduce reliance on invasive diagnostic procedures.

Keywords: NIPT, Prenatal Screening, Trisomy 21, Fetal DNA, Chromosomal Abnormalities, Fetal Fraction

OP6- Clinical and molecular features of a COXPD12 case with compound heterozygous variants in the EARS2 gene

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Introduction

EARS2 encodes mitochondrial glutamyl-tRNA synthetase, which is essential for mitochondrial protein synthesis. Biallelic pathogenic variants cause combined oxidative phosphorylation deficiency 12 (COXPD12, OMIM #614924), a rare autosomal recessive disorder characterised by infantile-onset hypotonic encephalopathy, psychomotor regression, basal ganglia involvement and lactic acidosis. In this report, we present a COXPD12 case carrying compound heterozygous variants in the *EARS2* gene with seizures, motor developmental delay and characteristic MRI findings.

Materials and Methods

A male patient presented at the age of 10 years with vomiting, diarrhoea and seizures. Neurological examination revealed microcephaly, brachycephaly, dysmetria, involuntary movements and motor delay. Brain MRI showed bilateral basal ganglia involvement and lactate peaks. Metabolic studies were unremarkable. Next-generation sequencing was performed using a targeted mitochondrial gene panel. Variant interpretation followed ACMG guidelines and in silico pathogenicity tools.

Results

Compound heterozygous variants in *EARS2* were identified: p.(Ala272Thr) [rs749912939], previously reported as likely pathogenic, and p.(Gly301Ala), classified as a variant of uncertain significance (VUS). The clinical phenotype was consistent with COXPD12, supporting the pathogenic relevance of the detected variants. The patient was treated with levetiracetam with good seizure control, although motor improvement remained limited.

Conclusions

This case highlights the importance of considering *EARS2* mutations in infants with early-onset seizures, microcephaly and basal ganglia involvement. Molecular diagnosis is crucial for the identification of COXPD12 and for appropriate genetic counselling. Phenotype-genotype correlation may help to clarify the clinical significance of rare or uncertain variants.

OP7- Prenatal diagnosis of Prader-Willi syndrome due to maternal mixed iso/hetero uniparental disomy

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Prader-Willi Syndrome (PWS) is a complex genetic disorder marked by neonatal hypotonia, poor feeding in infancy, later development of hyperphagia, obesity, cognitive deficits, behavioral abnormalities, and endocrine dysfunction, including hypogonadism and short stature. While the postnatal phenotype is well established, prenatal diagnosis remains challenging due to the absence of a consistent fetal presentation.

This case report presents a fetus diagnosed prenatally with PWS caused by maternal uniparental disomy of chromosome 15 (UPD15). Chromosomal microarray analysis (CMA) on amniotic fluid revealed a 35 Mb region of loss of heterozygosity (LOH) at 15q22.2q26.2. Combined with prior non-invasive prenatal testing (NIPT) results showing elevated risk for Trisomy 15, the findings suggested a trisomy rescue event. Further molecular karyotyping of both parents confirmed the maternal origin of both chromosome 15 copies in the fetus. Segmental analysis identified mixed heterodisomy and isodisomy, with the PWS-critical region (15q11.2–q13) located within the heterodisomic segment, confirming the genetic basis of PWS in this case. The family received genetic counseling regarding the expected clinical outcome and chose to terminate the pregnancy.

This case underscores the utility of integrated genomic technologies—NIPT, CMA, and parental studies—in identifying UPD-related syndromes. It also highlights the relevance of recognizing UPD15 as a pathogenic mechanism of PWS, enabling timely diagnosis and family-centered decision-making even in the absence of prenatal ultrasound findings.

Keywords: Prader-Willi Syndrome; Uniparental disomy; Prenatal diagnosis; Chromosome microarray

OP8- Chromosome 16q22 Fragility in a Male Patient with Azoospermia: A Case Report

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Abstract

Introduction:

Chromosomal abnormalities are a well-recognized cause of infertility, particularly structural rearrangements that affect key genomic regions. The 16q22 locus has been identified as a recurrent breakpoint in individuals with unexplained infertility, suggesting a potential role in reproductive dysfunction. However, the clinical significance and underlying mechanisms of this chromosomal fragility remain poorly understood.

Case Report:

A 44-year-old male was referred for azoospermia. He had one daughter and an eight-year history of secondary infertility. His history included significant weight gain, followed by bariatric surgery. Comorbidities included diabetes, hypertension, obstructive sleep apnea, and hypercholesterolemia. Family history revealed consanguinity and infertility among relatives. Physical examination noted deep-set eyes, long face, and seborrheic dermatitis. Hormonal evaluation showed normal FSH, borderline elevated LH, and prolactin. Scrotal and abdominal ultrasonography were unremarkable. Semen analysis confirmed azoospermia. Karyotype analysis identified chromosomal fragility at 16q22 in 10% of metaphases. Y-chromosome microdeletion testing was negative. Parental karyotyping was planned to explore potential inheritance.

Conclusion:

Although 16q22 is a common fragile site and may appear in otherwise healthy individuals, its presence has been associated with sperm anomalies and secondary infertility in the literature. This case supports the potential contribution of 16q22 fragility to male reproductive dysfunction and underscores the need for further studies to clarify its role in infertility. The detection of fragility in the parents, together with literature suggesting potential heritability, highlights the importance of clinically evaluating family members as part of a comprehensive assessment.

OP9- Severe Phenotype in Lodder-Merla Syndrome Linked to Homozygous *GNB5* c.863G>A Variant: A Case Report

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Background: Lodder-Merla syndrome is an autosomal recessive disorder caused by mutations in the *GNB5* gene, presenting with a broad clinical spectrum from mild neurodevelopmental delay to severe multisystemic involvement. We report a 12-year-old male, born to consanguineous parents, had hypotonia, non-verbal communication, developmental delay, epilepsy, and cerebral palsy. He had a history of neonatal hypotonia, feeding difficulties, and postnatal intensive care, cardiac arrest following a febrile seizure at age 4. MRI revealed leukomalacia, EEG showed abnormalities, and echocardiography indicated minimal aortic insufficiency.

Methods: Genomic alterations were investigated by conventional karyotyping and whole exome sequencing (WES).

Results: Karyotype analysis was normal; however, WES identified a homozygous missense variant in the *GNB5* gene (c.863G>A, p.Arg288Gln). This variant has previously been reported in a single case in a compound heterozygous state and is classified as pathogenic in the ClinVar database. Notably, the previously reported patient exhibited a milder phenotype, with developmental delay, visual and auditory impairments, episodic bradycardia requiring pacemaker implantation, and no documented seizures. In contrast, our patient presented with a significantly more severe clinical course, including early-onset hypotonia, developmental delay, epilepsy, cerebral palsy, and a history of cardiac arrest following febrile seizure.

Conclusions: Our findings suggest that the homozygous GNB5 c.863G>A variant may result in a more severe phenotype compared to the compound heterozygous case, likely due to zygosi-

ty differences and potential modifying factors, emphasizing the complexity of genotype–phenotype correlations and the importance of comprehensive clinical and molecular assessment in rare genetic disorders.

Keywords: Lodder-Merla Syndrome, GNB5 Mutation, Rare Diseases

OP10- Detection of de novo variants in CTNNB1 and NF1 genes in an infant conceived via in vitro fertilization: a case report

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The *CTNNB1* gene encodes β-catenin, which plays critical roles in both the Wnt/β-catenin signaling pathway and in cell-cell adhesion. As a key effector of the Wnt pathway, β-catenin is involved in processes such as embryogenesis, cell proliferation, and differentiation. Germline pathogenic variants in the *CTNNB1* gene have been associated with a neurodevelopmental disorder characterized by intellectual disability, hypotonia, visual defects, and spastic diplegia, and are most often identified as de novo. Moreover, somatic variants in this oncogene have been implicated in malignancies such as colorectal, hepatocellular, and ovarian cancers.

The *NF1* gene encodes neurofibromin, a tumor suppressor protein that negatively regulates the RAS/MAPK signaling pathway, thereby controlling cell proliferation and differentiation. Pathogenic variants in *NF1* are the primary cause of neurofibromatosis type 1, a disorder characterized by café-au-lait spots, neurofibromas, and an increased risk of malignancy. Affected individuals also frequently exhibit learning disabilities and other neurocognitive impairments. Notably, approximately 50% of cases are caused by de novo variants.

In this report, we present a 10-month-old female infant, conceived as a dizygotic twin via in vitro fertilization, in whom clinical exome sequencing revealed de novo variants in both *CTNNB1* and *NF1*. The patient has *NF1* c.3822_3823del p.Phe1275Profs*8 and *CTNNB1* c.1925_1926del p.Glu642Valfs*5 variants. Both variants were confirmed by Sanger sequencing in the parents and the patient. This exceedingly rare co-occurrence raises questions regarding whether in vitro fertilization and its effects on the embryo may contribute to an increased rate of de novo mutations.

Keywords: in vitro fertilization, exome sequencing, de novo, *CTNNB1*, *NF1*

OP11- Diagnostic utility of Oxford Nanopore-based whole exome sequencing in trio analysis for rare genetic disorders

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Abstract

Background: Whole Exome Sequencing (WES) in a trio format—simultaneously analyzing the proband and both biological parents—offers enhanced diagnostic yield in rare and undiagnosed genetic conditions by enabling the detection of *de novo*, inherited, and compound heterozygous mutations. Recent advancements in long-read sequencing, particularly using Oxford Nanopore Technology (ONT), have overcome many limitations of traditional short-read sequencing, especially in repetitive and complex genomic regions.

Material and Methods: This study focuses on nine WES-Trio analyses conducted between November 2024 and May 2025 at the Medical Genetic Diagnostic Laboratory of Near East University Hospital in Cyprus. Genomic DNA was isolated from peripheral blood samples of affected individuals and their parents. Library preparation and sequencing were performed using the WholEx Pro protocol (IVD-CE, 4Bases, Switzerland), optimized for ONT platforms. Long-read capabilities allowed for the detection of single nucleotide variants, insertions/deletions, and structural variants with high resolution.

Results: Pathogenic/ likely pathogenic/ *de novo* homozygous variants were identified in trios, offering direct insights into disease etiology. For example, a de novo *FOXG1* mutation was found in a patient with encephalopathy, consistent with congenital Rett syndrome. Similarly, compound heterozygous variants in *SUMF1* and *SLC3A1* were implicated in neurodegenerative and metabolic phenotypes. Trio analysis proved especially useful in distinguishing inherited versus *de novo* variants, aiding accurate clinical interpretation.

Conclusion: ONT-based WES-Trio analysis provides a powerful diagnostic tool for complex and rare genetic disorders. Its ability to resolve challenging genomic regions and provide real-time, high-throughput sequencing makes it especially valuable in clinical settings. The application of this approach in our cohort successfully identified causative variants in multiple patients, underscoring the clinical utility of combining LRS with trio-based WES.

Keywords: Whole Exome Sequencing, Trio Analysis, Oxford Nanopore Technology, Rare disease

OP12- Azoospermic Male Case with SRY-Positive 46,XX Testicular DSD

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Abstract:

46,XX testicular disorder of sex development (DSD) is a rare condition characterized by individuals with a female (XX) karyotype presenting with a male phenotype. Here, I present the genetic evaluation of a phenotypically male patient with infertility and a 46,XX karyotype, in whom the SRY gene was detected on the X chromosome.

A 26-year-old male patient presented with infertility. Physical examination revealed bilaterally small testes, with otherwise normal male secondary sexual characteristics. Semen analysis showed azoospermia. Conventional cytogenetic analysis demonstrated a 46,XX karyotype. Y chromosome microdeletion analysis revealed complete deletions in the AZF-a, AZF-b, and AZF-c regions, while the SRY gene was detected as positive. Further analysis using FISH showed localization of the SRY gene on the X chromosome. Based on these findings, the patient was diagnosed with SRY-positive 46,XX testicular DSD.
Patients with SRY-positive 46,XX testicular DSD may present with a normal male phenotype and are often diagnosed during infertility evaluations. This case highlights the importance of comprehensive genetic testing, including the assessment and localization of the SRY gene, in patients with discordance between phenotype and genotype.
Keywords:
46,XX male syndrome; SRY; testicular DSD; infertility; FISH

OP13- Effects of amniotic membrane-conditioned medium on pancreatic cancer cells

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Introduction
The amniotic membrane (AM), a thin layer lining the inner placenta, has gained attention for its unique biological properties, including anti-viral, anti-tumoral, anti-inflammatory, and anti-angiogenic effects. As a biomaterial free of ethical concerns, AM presents promising potential in cancer therapy. This study aims to evaluate the impact of human amniotic membrane-conditioned medium (hAM-CM) on pancreatic cancer (PANC-1) cells, a malignancy with high mortality and limited treatment options.
Materials and Methods
hAM-CM was prepared and applied to PANC-1 and HEK-293 cells. Cell proliferation was assessed using the XTT assay. Migration was evaluated via wound healing assay, while invasion was analyzed using Matrigel-coated inserts. Morphological changes were observed microscopically. Gene expression levels of IL1β, IL-6, IL-17, and HIF1α were measured by qRT-PCR. ELISA was used to quantify total and secreted protein levels of IL-17, HIF1α, and VEGF.
Discussion
hAM-CM significantly reduced the viability, migration, and invasion of PANC-1 cells, with no adverse effects on HEK-293 cells. Gene expression analysis indicated increased expression of inflammation- and hypoxia-related genes in PANC-1 cells post-treatment. ELISA revealed a complex regulation of cytokine and angiogenic protein secretion.
Conclusion
hAM-CM exerts anti-tumoral effects on PANC-1 cells by reducing proliferation, migration, and invasion. These findings suggest that hAM-CM could serve as a potential therapeutic tool in pancreatic cancer treatment, warranting further investigation.
Keywords: Amniotic membrane, gene expression, conditioning medium, pancreatic cancer

OP14- Utilization of RNAseq as a tool to identify the pathogenic nature of a genomic duplication in an individual with Diamond-Blackfan Anemia.

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Abstract
Background: Although the detection of CNVs has become more accessible with widespread usage of microarrays, interpreting their clinical significance remains challenging. One tool to gain further insight on clinically unknown CNVs is RNAseq. Diamond-Blackfan Anemia (DBA) is a ribosomopathy, where most disease-causing variants lead to loss-of-function in Ribosomal Protein (RP) genes. We previously identified an individual with DBA but no pathogenic RP gene variants. He had a *de novo* genomic duplication with unknown clinical significance encompassing chr1[hg38]:78,534,570-94,193,838. In this study, we utilized RNAseq to investigate the potential impact of this duplication on gene expression and identify its pathogenic nature.
Materials&Methods: RNAseq was performed using Illumina Stranded mRNA Prep kit from whole blood samples of unaffected parents and proband. Transcript counts were quantified using Salmon with a custom GENCODE v47 reference transcriptome excluding pseudogenes, differentially expressed genes were identified using DESeq2, and highly-variable immunoglobulin and T-cell receptor genes were removed. Gene set enrichment analyses (GSEA) were performed via DAVID.
Results: The cytoband-specific GSEA revealed a significant enrichment of 1p22.1 band within the duplicated region and it involved 7 genes including *RPL5*. The most significantly upregulated genes in GSEA for molecular function were ribosomal proteins owing to upregulation of 20 ribosome-related genes.
Discussion&Conclusion: RNAseq revealed that the duplicated region is significantly enriched within the upregulated genes, demonstrating the transcriptional consequence of this previously unknown CNV event. Our findings also provide biological insights into the disease pathogenesis demonstrating a significant compensatory upregulation of other ribosomal genes.

Keywords: Diamond-Blackfan Anemia, RNAseq, CNV

OP15- mRNA sequencing of AMPD2 gene proving transcript length change caused by c.353+11C>T novel intronic variant

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Background

A two-year-old female patient was referred to our clinic by her parents, due to speech and gait disturbances, vacant staring, pronounced truncal hypotonia, and spasticity in the extremities. The patient had a history of a complicated delivery resulting in perinatal asphyxia and brachial plexus injury. Electrocardiogram, echocardiogram, and abdominal ultrasound findings were reported as normal. Previously performed spinal muscular atrophy test, chromosomal microarray and karyotype analyses yielded normal results. On clinical examination, facial dysmorphic features included: prominently low-set ears, strabismus, downslanting palpebral fissures, micrognathia, and tapering fingers.

Methods:

Trio whole-exome sequencing (WES) was performed using DNA samples obtained from the patient and her parents. Analysis revealed a homozygous variant in the AMPD2 gene (NM_001368809.2) c.353+11C>T, with both parents identified as heterozygous carriers. The phenotype was found to be partially consistent with pontocerebellar hypoplasia type 9 (PCH9), a condition associated with AMPD2, which typically manifests more prominently at older ages. The variant was suspected to create a novel splicing site; therefore, blood samples were collected from the patient and her parents for RNA extraction. Subsequent cDNA analysis via gel electrophoresis and Sanger sequencing confirmed the presence of an alternative splicing event.

Conclusions:

This study designates the early-onset phenotype of PCH9 in a female patient carrying a splicing-altering variant in AMPD2. It also highlights the feasibility of functional studies in evaluating intronic variants. Functional validation of such variants, can provide insights for clinical decision-making for the patient and further reproductive planning for the family.

OP16- SCITUNA: Single-Cell data integration tool using network alignment

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Abstract

Background: As single-cell genomics experiments increase in complexity and scale, the need to integrate multiple datasets has grown. Such integration enhances cellular feature identification by leveraging larger data volumes.

However, batch effects—technical variations arising from differences in labs, times, or protocols—pose a significant challenge. Despite numerous proposed batch correction methods, many still have limitations, such as outputting only dimension-reduced data, relying on computationally intensive models, or results in overcorrection for batches with diverse cell type composition.

Results: We introduce a novel method for batch effect correction named SCITUNA, a Single-Cell data Integration Tool Using Network Alignment. We perform evaluations on 39 individual batches from four real datasets and a simulated dataset, which include both scRNA-seq and scATAC-seq datasets, spanning multiple organisms and tissues. A thorough comparison of existing batch correction methods using 13 metrics reveals that SCITUNA outperforms current approaches and is successful at preserving biological signals present in the original data. In particular, SCITUNA shows a better performance than the current methods in all the comparisons except for multiple batch integration of lung dataset where the difference is 0.004.

Conclusion: SCITUNA effectively removes batch effects while retaining the biological signals present in the data. Our extensive experiments reveal that SCITUNA will be a valuable tool for diverse integration tasks.

Keywords: Single-cell data integration, Batch effect, Rare cell types, Iterative correction.

Publication: Houdjedj, A., Marouf, Y., Myradov, M. et al. SCITUNA: single-cell data integration tool using network alignment. BMC Bioinformatics 26, 92 (2025). https://doi.org/10.1186/s12859-025-06087-3

OP17- Integrated Trio Phasing from BAM Files for Enhanced Clinical and Research Applications

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Introduction

Parent-of-origin haplotype reconstruction is vital in medical genetics—for diagnosing imprinting disorders, resolving compound heterozygosity, mapping runs of homozygosity (ROH) and copy-neutral loss of heterozygosity (CN-LOH)—and underlies allele-specific expression, population genetics, genotype imputation, pharmacogenomics, and preimplantation genetic testing.

Methods

A Python/C++ pipeline ingests aligned trio BAM files directly, converts them into a concise ".hap" format capturing consensus nucleotides and base qualities, and arranges data in a Trio Directory Structure. A single linear-time (O(n)) algorithm

then performs metadata parsing, high-confidence allele selection, contig ligation, trio inheritance assignment, and block assembly. Outputs are tab-delimited haplotype blocks annotated with coordinates and parent-of-origin.

Results

Applied to 15 Turkish clinical trios, the method fully reconstructed known maternal and paternal haplotypes across all targeted regions. In two probands with SNP-array–detected ROH, it matched reported intervals and unambiguously assigned parental origin. In two cases with CN-LOH, it correctly identified uniparental segments. Processing scaled linearly: human chromosome 1 (249 Mb) completed in 106 s, chromosomes 21 and 22 (~35 Mb each) in under 150 s.

Discussion

By eliminating VCF dependency, this BAM-centric approach reduces I/O and variant-calling biases. Unlike maximum-likelihood fragment assemblers requiring pre-called variants, it integrates mixed short- and long-read datasets without phase breaks and embeds parent-of-origin assignment within phasing. Rapid, modular outputs facilitate seamless integration into diagnostic and research workflows.

Conclusion

This direct BAM-driven trio phasing method delivers rapid, accurate, and lineage-aware haplotype reconstruction. Verified across 15 clinical trios, its linear scalability and clear outputs suit both medical genetics laboratories and genomic research.

Keywords: haplotype phasing • next-generation sequencing • trio analysis • runs of homozygosity • CN-LOH • clinical genetics

OP18- Expanding the Diagnostic Perspective on the 22q11.2 Critical Region: Analysis of a Case Series of Deletions and Duplications

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Introduction

The 22q11.2 region is a critical genomic area associated with a broad clinical spectrum, including DiGeorge/Velocardiofacial Syndrome (microdeletion) and 22q11.2 Microduplication Syndrome. This region's low copy repeats (LCRs) mediate deletions, duplications, and translocations by promoting genomic instability through non-allelic homologous recombination.

Although microdeletions in the 22q11.2 region are more commonly observed and reported, microduplications and Cat Eye Syndrome (CES) should also be considered in the differential diagnosis due to their phenotypic overlap with 22q11.2 deletion syndrome. These CNVs exhibit significant inter- and intrafamilial clinical variability.

Materials and Methods

This retrospective study includes 7 patients (4 with deletions and 3 with duplications) who underwent clinical and genetic evaluation. Diagnostic analysis involved both FISH and SNP-CMA, which can detect atypical CNVs often missed by conventional FISH probes limited to the LCR22A–B interval. Parental segregation studies were performed in all cases.

Discussion

The observed phenotypic heterogeneity underscores the complexity of 22q11.2 CNVs. Accurate diagnosis requires comprehensive methods capable of detecting atypical CNVs outside classical probe targets. While most CNVs arise de novo, familial inheritance with variable expressivity is not uncommon.This makes parental segregation analysis an indispensable tool for precise genetic counseling and accurate recurrence risk assessment.

Conclusion

Our findings support the need for comprehensive analysis of the 22q11.2 region using both microarray and parental segregation testing to ensure accurate diagnosis, personalized counseling, and effective clinical management, not only for deletions but also for duplications that may present with overlapping phenotypes.

Keywords: 22q11.2 region, LCR, CNV, microarray, FISH

OP19- Cleidocranial Dysplasia Due to *RUNX2* Gross Deletions: Clinical and Molecular Insights

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Abstract

Background:

Cleidocranial dysplasia (CCD) is a rare skeletal disorder characterized by hypoplastic or absent clavicles, delayed closure of cranial sutures, and various dental anomalies. Affected individuals commonly exhibit short stature, hypermobile shoulders, and narrow thorax, while cognitive development remains normal. CCD is mostly caused by single nucleotide variants in *RUNX2* gene. However, heterozygous deletions or duplications are reported rarely, in about 10% of all patients.

Methods:

The study included four patients from two unrelated families presenting clinical features compatible with CCD. Clinical exome sequencing-based copy number variation (CNV) analysis was employed to ascertain the genetic background.

Results:

The first family is included three affected patients. Proband is a 14-year-old male, presented with delayed fontanelle closure, hypoplastic clavicles, dental anomalies, and a family history of CCD. Imaging revealed aplastic clavicles, hypoplastic iliac bones, Erlenmeyer flask deformities of the long bones, and genu valgum. Chromosomal analysis was normal, and CNV analysis identified a heterozygous 16-kb deletion involving exons 3–5 of *RUNX2*.

The second family included only affected child. She was presented with clavicular and parietal bone hypoplasia at newborn. CNV analysis revealed a heterozygous 998 bp deletion covering exon 9 of *RUNX2*.

Conclusion:

In patients clinically diagnosed with CCD in whom no pathogenic variants are identified by standard sequence analysis, deletion/duplication analysis of the RUNX2 gene should be considered to detect exon-level or gross genomic alterations. NGS-based copy number analysis represents a valuable tool for identifying such CNVs and can enhance the diagnostic yield in suspected CCD cases with negative sequencing results.

OP20- CD90 knock-out modulates epithelial–mesenchymal traits and enhances drug response in U-CH1 chordoma cells

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Introduction

Chordoma is a rare and chemoresistant tumor with limited therapeutic options. CD90 (THY1), a glycophosphatidylinositol-anchored surface protein, has been linked to stemness and tumor progression in various cancers, but its function in chordoma remains undefined.

Methods

A CRISPR-Cas9 approach was employed to generate CD90 knockout (KO) U-CH1 chordoma cells, which were confirmed by flow cytometry. The expression of EMT markers was assessed by quantitative reverse transcription polymerase chain reaction (qRT-PCR). The migration and invasion properties of CD90-KO cells were evaluated in transwell assays. Cell cycle distribution and sphere formation were evaluated by flow cytometry and ultra-low attachment culture. Drug sensitivity to metformin, etoposide, cisplatin, and methotrexate was measured using MTS assays. Intracellular reactive oxygen species (ROS) levels and antioxidant gene expression were analyzed by DCFDA staining and qRT-PCR.

Results

The CD90 gene was successfully knocked out with CRISPR-Cas9 technology. The loss of CD90 triggered a spindle-shaped morphology, upregulated EMT transcription factors (SNAIL, SLUG, and TWIST), and enhanced invasiveness, indicating EMT activation. CD90 KO cells exhibited G1 arrest and reduced sphere formation despite increased OCT4 and SOX2 transcripts, suggesting non-canonical stem-like states. Dysregulated redox homeostasis, characterized by elevated basal ROS and differential antioxidant responses, likely underlies the enhanced sensitivity to metformin and etoposide.

Discussion

Collectively, these results demonstrate that CD90 depletion promotes an EMT phenotype with altered cell cycle dynamics and redox imbalance, thereby sensitizing chordoma cells to metformin- and etoposide-induced cytotoxicity. Targeting CD90 may overcome chemoresistance in chordoma.

Keywords: Chordoma; CD90; epithelial–mesenchymal transition; drug sensitivity

First report of germline mosaicism in *ZNF292*-related intellectual disability:

OP21- Expanding the clinical and molecular spectrum

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Background:

Heterozygous pathogenic variants in *ZNF292* are associated with intellectual developmental disorder 64 (#619188), frequently characterized with developmental delay and dysmorphic features. A limited number of cases have been documented, and none of them have indicated germline mosaicism. We aim to expand the clinical and molecular spectrum of the disorder by presenting a case with a novel variant and to report germline mosaicism associated with this gene for the first time, enabling appropriate genetic counseling regarding recurrence risk.

Methods:

This study includes the identification of a mosaic variant with a low allelic fraction in the asymptomatic mother's peripheral blood and buccal swab samples through segregation analysis of a case diagnosed with ZNF292-related intellectual disability using whole exome sequencing.

Results:

The proband is a 12-year-old male, born to non-consanguineous parents, referred due to a mild intellectual disability and dysmorphic facial features. Physical examination revealed hypertelorism, a broad nasal bridge, anteverted and prominent ears, retromicrognathia, and a long, triangular face. Karyotype, *FMR1* gene repeat analysis, and chromosomal microarray were all normal. Whole exome sequencing identified a heterozygous c.1531_1532del variant in *ZNF292* gene. Segregation analysis detected the variant in the unaffected mother with a 16% allelic fraction in both peripheral blood and buccal swab samples. The variant was not present in the healthy sister.

Conclusion:

This case expands the known phenotypic spectrum of *ZNF292*-related intellectual disability and represents the first reported instance of germline mosaicism in this condition. Recognition of mosaic parental transmission is crucial for ac-

curate recurrence risk assessment and genetic counseling.

OP22- Retrotransposon Profiling at CNV Breakpoints in Obese Patients Insights from a Single-Center Study

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Retrotransposons(LINEs,SINEs,LTRs) are mobile genetic elements that can lead to genomic instability by causing structural rearrangements through RNA-mediated retrotransposition. Several studies have shown that retrotransposons are associated with the breakpoints-of-CNVs.Obesity is a global health problem and a complex disease influenced by numerous genetic and environmental factors.There is evidence that retrotransposons,such as the methylation status of LINE-1,may be associated with various phenotypes of obesity and metabolic syndrome.This study aims to investigate the retrotransposon profiles at the breakpoints of CNVs detected in a single-center cohort of obese patients.In our centre,SNP-Microarray analysis was performed on 47 patients diagnosed with obesity.The detected CNVs were analysed for the presence of retrotransposons using the RepeatMasker track in the UCSC Genome Browser.126 CNVs were included as a result of CNV analyses performed in the obese patient cohort.Analysing the retrotransposon profiles at the breakpoints,it was observed that 40 CNVs(31.7%) contained the same type of retrotransposon at both breakpoints.The majority of these(87.5%) were associated with the LINE-1.Our findings suggest a significant proportion of CNVs seen in obese patients may be associated with retrotransposons.Furthermore,studies showing that epigenetic regulation of retrotransposons is associated with obesity that these elements not only contribute to structural variations but may also play a potential role in the complex pathogenesis of obesity.The findings of this study may represent an important step towards understanding genomic instability and structural variations in obesity.Further studies involving larger cohorts are needed to elucidate the mechanisms underlying this association,to clarify the specific role-of-retrotransposons in obesity-associated genomic alterations,to understand their potential implications in clinical genetics.

Keywords: CNV, Breakpoint, Obesity, Retrotransposon, LINE-1

OP23- A Previously Unreported Occurrence of an Ultra-Rare Disease: Intragenic Homozygous Deletion in the *AAAS* Gene

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Introduction: Structural variants of the human genome that are larger than 50 base pairs are defined as Copy-Number-Variants(CNVs). In routine practice, microarrays are often used as the primary technique for genome-wide CNV detection. Advances in microarray technology have improved resolution, enabling identification of previously undetectable CNVs.
Materials/Methods: An 8-year-old male patient, born to consanguineous parents, presenting with adrenal failure, seizures, and swallowing difficulties was referred to the medical genetics clinic. The onset of symptoms was 4 years ago and had been initially evaluated by pediatric gastroenterology and endocrinology with the preliminary diagnosis of Triple A/Allgrove syndrome(TAS). Upon examination, hyperpigmentation, gait disturbance and mild facial dysmorphism were observed. Previous laboratory tests revealed elevated ACTH and low cortisol levels, indicating adrenal insufficiency. Endoscopic, manometric and radiologic findings were consistent with achalasia, and Schirmer test revealed dry eyes. Considering the multiple anomalies, and to assess both loss-of-heterozygosity regions and the degree of consanguinity, SNP-microarray was performed.
Discussion: SNP-microarray detected a 6kb homozygous deletion in 12q13.13 with both breakpoints within *AAAS* gene, removing exons 3-7. Although the CNV appears to be in-frame, the lack of healthy population data, variant removing >10% of the protein, and the highly-specific phenotype increases the pathogenicity.
Conclusion: With an estimated prevalence of <1/1000000, Allgrove syndrome is an ultra-rare disorder. This case represents the first report of an intragenic homozygous deletion in *AAAS* gene, expanding the molecular spectrum of TAS and highlighting the utility of SNP-microarray in detecting small, clinically significant CNVs.

Keywords: Triple A/Allgrove Syndrome, AAAS, Microarray, CNV

OP24- Unraveling blended phenotypes: A pediatric case with dual *de novo* variants in *NSD1* and *TAB2*

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Introduction:

Dual molecular diagnoses, though rare, are increasingly recognized in pediatric genetics due to advances in next-generation sequencing (NGS). These cases often present with complex, overlapping phenotypes that do not compatible with a single syndrome. Here, we report a pediatric patient with a dual molecular diagnosis confirmed by whole exome sequencing (WES), highlighting the diagnostic power of NGS in elucidating blended phenotypes.

Methods:

Whole exome sequencing was performed in a pediatric patient presented with a complex clinical presentation. No single preliminary diagnosis could be considered via clinical evaluation before molecular analysis. Detected variants were evaluated based on ACMG/AMP guidelines, and familial segregation analysis was conducted to assess inheritance patterns.

Results:

A 5-month-old male, born to non-consanguineous parents, was referred from the neonatal intensive care unit due to cardiomyopathy and dysmorphic facial features. Physical examination revealed dolichocephaly, frontotemporal balding, frontal bossing, thin lips, large posteriorly rotated ears, inguinal hernia, velvety and lax skin, and joint hypermobility. Growth parameters were within normal limits, but he presented with marked hypotonia and global developmental delay. Echocardiography showed both ASD and VSD. Whole exome sequencing identified two *de novo* pathogenic variants: *NSD1*:c.4875_4878del, associated with Sotos syndrome, explaining the dysmorphic features and neurologic involvement; and *TAB2*:c.445del, associated with congenital heart defects, multiple types, 2, explaining the connective tissue abnormalities.

Conclusion:

This case illustrates the value of considering dual molecular diagnoses in patients with atypical or overlapping phenotypes. Comprehensive genomic analysis, such as WES, can uncover coexisting rare conditions, enabling accurate diagnosis and more informed clinical management.

OP25- A novel inframe CREBBP mutation in a cohort of three pa-tients with Rubinstein-Taybi syndrome

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Introduction:

Rubinstein-Taybi syndrome (RTS) is a rare genetic disorder characterized by intellectual disability, postna-tal growth retardation, microcephaly, distinctive facial dysmorphism, broad thumbs and toes. The genetic basis of the syndrome is largely attributed to mutations in the CREBBP gene, accounting for up to 55% of cases, while mutations in the EP300 gene are responsible for a smaller proportion (~8%).

Method:

After obtaining a comprehensive medical history, constructing a pedigree, and performing a thorough clini-cal evaluation, DNA was isolated from peripheral blood samples of the patients using Zeesan Lab-Aid 824s Blood Isolation Kit. The SOPHIATM Clinical Exome Solution (CES) V2 next generation sequencing kit cov-ering 5400 genes and Illumina NovaSeq system were used for DNA sequencing.

Case:

Of the three patients who presented with dysmorphic features, including broad thumbs and toes, polydac-tyly, and syndactyly, two were male and one was female. All three patients showed delayed motor mile-stones. Both male patients had cryptorchidism. Genetic analysis identified a novel in-frame c.3998_4006del (p.Arg1333_Gly1335del) variant located in exon 24 of the CREBBP gene, as well as the previously reported c.3832G>A (p.Glu1278Lys) and c.1943dupC (p.Ala649Serfs*39) variants, respectively. The patient carry-ing the c.3998_4006del variant had agenesis of the corpus callosum. The patient with the c.3832G>A vari-ant presented with growth retardation and persistent diarrhea during the first year of life.

Results:

In this study, the clinical features and genetic findings of three patients diagnosed with RTS were evaluated, and a novel mutation identified in one of the cases contributed to the existing literature.

Keywords: Rubinstein-Taybi syndrome (RTS), CREBBP, inframe novel mutation

OP26- ReNU Syndrome A Newly Discovered Prevalent Neurodevelopmental Disorder

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Introduction: ReNU syndrome (RS, *RNU4-2*-related neurodevelopmental disorder) is a recently defined monogenic

condition characterized by facial dysmorphism, microcephaly, hypotonia, global developmental delay (GDD), intellectual disability, epilepsy, and multisystem involvement. Pathogenic variants in the non-coding *RNU4-2* gene, encoding U4 small nuclear RNA (snRNA), a core spliceosomal component, have been identified in ~0.4% of individuals with undiagnosed neurodevelopmental disorders (NDDs). As these variants are not detectable by exome sequencing, phenotypic evaluation and targeted testing are warranted. We report a 3-year 3-month-old girl with features suggestive of RS, diagnosed through *RNU4-2* sequencing. This case underscores the diagnostic relevance of *RNU4-2* testing in unexplained NDDs. As the first confirmed case in our study, it is presented as a preliminary observation.
Materials and Methods: Phenotypic evaluation was performed through manual review of clinical records, focusing on features consistent with RS, using keyword-based screening. Given the phenotypic overlap with RS, *RNU4-2*-specific primers were designed, and Sanger sequencing was performed.

Results: A heterozygous pathogenic variant, *RNU4-2* (NR_003137.3):n.64_65insT, was identified in the patient, confirming the diagnosis of RS. The patient with GDD, microcephaly, hypotonia, facial dysmorphism, gastroesophageal reflux, acrocyanosis, constipation, feeding difficulties, and failure to thrive was retrospectively evaluated.
Discussion: This case represents one of the first confirmed RS diagnoses in Türkiye. As variants in such genes are only detectable by whole genome sequencing—a costly approach—targeted Sanger sequencing in *RNU4-2*–like cases may offer a cost- and labor-effective first step, followed by exome and genome sequencing if negative.
Keywords: GDD, ReNU syndrome, *RNU4-2*, Sanger sequencing

OP27- Angelman Syndrome: The Intersection of Genetic Mechanisms and Neurological Phenotype
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Angelman syndrome is a rare, well-characterized neurogenetic disorder with a defined genetic basis, presenting with developmental delay, speech impairment, ataxia, epilepsy, and a distinctively happy demeanor; additional clinical features include microcephaly, sleep disturbances, hyperactivity. The underlying cause of the syndrome is the loss of maternal expression of the UBE3A gene, located in the 15q11-q13 chromosomal region. This genetic anomaly can result from various mechanisms, including deletion, uniparental disomy, imprinting center defect, or UBE3A mutation.
Materials and Methods:
Data from 11 patients diagnosed with Angelman syndrome and followed at our clinic between 2014 and 2025 were retrospectively analyzed.
Results:
Seven patients (63.6%) were female. The median age at diagnosis was 18 months. All patients were referred due to developmental delay. EEG abnormalities and seizures were identified in 7 patients (63.6%), all of whom were receiving antiepileptic treatment. Diagnosis was established in 3 patients by FISH analysis, in 3 patients by array CGH, in 2 patients by MLPA, and in 3 patients through detection of mutations in the UBE3A gene.

Conclusion:
Most Angelman syndrome cases are diagnosed early due to developmental delay and seizures. Its molecular heterogeneity requires multiple genetic tests for confirmation. Early testing accelerates diagnosis, and identifying the specific genetic cause is key for management and counseling. The syndrome's complexity calls for a multidisciplinary approach.

OP28- All Roads Lead to CYLD: A Familial Brooke-Spiegler Syndrome Case
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The CYLD gene, located on chromosome 16q12.1 encodes a tumor suppressor enzyme that playing a vital role in cell proliferation and apoptosis. Disruption of this pathways can lead to various skin tumors, including cylindromas, trichoepitheliomas and spiroadenomas, commonly seen in Brooke Spiegler Syndrome(BBS).
We evaluated a multigenerational family through clinical assessment and genetic testing. Peripheral blood DNA was analyzed using Next Generation Sequencing(NGS) to detect CYLD gene variants
A 41-year-old female presented with multiple facial and scalp lesions beginning in adolescence. Family history revealed similar findings in her daughter, three sisters and mother. Notably, her brother died of lung cancer at the age of 26 and another daughter was diagnosed with Noonan Syndrome. Genetic testing identified a heterozygous c.850C>T (p.Gln284*) nonsense variant in exon 8 of the CYLD gene and classified as pathogenic according to ACMG guidelines. Segregation analysis confirmed the presence of this variant in other affected family members.
This case highlights the classical triad of Brooke Spiegler Syndrome, with familial clustering and clearly pathogenic variant. While BBS typically manifests with skin tumors the brother's

early-onset lung canser may varrant further investigation of non cutaneous cancer risks .Genetic counseling and dermatological surveillance remain critical for affected families.

Keywords: Brooke Spiegler Sydrome, CYLD gene, Cylindroma, Trichoepithelioma, Familial skin tumors, Lung Cancer

OP29- Detection of Intron 22 Inversion in the F8 Gene Using Oxford Nanopore Long-Read Sequencing

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Abstract:

Intron 22 inversion (Inv22) of the F8 gene is the most common genetic cause of severe Hemophilia A, typically diagnosed using Inverse Shifting-PCR. Comprehensive molecular diagnosis for Hemophilia A currently requires a combination of methods, including PCR for Inv22, MLPA for large deletions/duplications, and either Sanger or next-generation sequencing (NGS) for point mutations. However, this multi-step approach is time-consuming, costly, and often cannot be fully performed at a single center—potentially delaying diagnosis and increasing healthcare burden.

In this early-stage study, we assessed the feasibility of detecting Inv22 using Oxford Nanopore long-read sequencing. Genomic DNA from a single male patient with a known Inv22 was sequenced at low coverage (4–5 reads). Despite the limited read depth, the inversion was clearly detected through long-read alignment. Specifically, soft-clipped reads aligning to intron 22 were observed in IGV, suggesting a breakpoint, and supporting the presence of a structural inversion.

Although not yet ready for routine diagnostics, this result highlights the potential of long-read sequencing to streamline F8 genotyping. A single, scalable assay could detect inversions, deletions, point mutations, and deep intronic variants—many of which are missed by conventional methods. If further optimized for cost, coverage, and analysis pipelines, this approach may offer a comprehensive and accessible alternative for Hemophilia A diagnosis, reducing the need for multiple specialized referrals. These advantages may also extend to other rare diseases with similar mutation profiles, where structural variants play a key pathogenic role.

OP30- Identification of Novel Variants in the Ultra-Rare Hardikar Syndrome: A Case Report

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Introduction

The *MED12* gene is associated with Lujan-Fryns, Ohdo, Opitz-Kaveggia, and Hardikar syndromes (HS). HS is a rare condition with X-linked dominant inheritance. It may include anomalies of the biliary tract, the genitourinary system and congenital heart defects, and distinctive craniofacial features. We report a patient with HS who had a novel intronic deletion and frameshift mutation in the *MED12*.

Case Presentation

She was born to a 20-year-old G1P1 mother at 36 weeks and 4 days of gestation via cesarean section due to bradycardia. Birth weight was 2520 grams. Prenatal ultrasonography (USG) revealed tricuspid valve dysplasia, coarctation of the aorta, cleft palate-lip, single umbilical artery, increased echogenicity in the small intestine, and absence of the gallbladder. In the postnatal period, bilateral hydronephrosis, megaureter and anterior ectopic anus were detected. Liver biopsy revealed cholestatic type injury findings and fibrotic enlargement in portal areas. Postnatal USG findings were compatible with biliary atresia. It was learned that she died at the age of 2.5 months after Kasai operation and subsequent liver transplantation from a living donor.

Whole exome sequencing and segregation analysis revealed a de novo *MED12* frameshift mutation, c.1758_1759insTAG (p.Glu587*), and an intronic deletion, c.1745-13_1754del. Visualization in IGV confirmed that the variants were located in cis.

Discussion

Our case, which presented with features of HS and carried two novel variants in the MED12 gene, differed from other reported cases by exhibiting early mortality due to liver failure. In disorders where the same gene is affected can show variable phenotypes, the documentation of novel variants and their clinical consequences plays critical role in refining genotype-phenotype correlations.

Keywords: Hardikar Syndrome, MED12, Biliary atresia

OP31- Coffin-Siris syndrome with clinical and genetic features: case series

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Key Words: Coffin Siris Syndrome, Intellectual disability, ARID1B

Introduction: Coffin-Siris syndrome (CSS) is a congenital syndrome characterised by growth retardation, coarse face, aplasia/hypoplasia of the distal phalanx or nail, hirsutism/hypertrichosis and hypotonia. Approximately 200 patients with molecularly confirmed diagnosis have been reported. Heterozygous pathogenic variants in ARID1A, ARID1B, ARID2, BICRA, DPF2, SMARCA4, SMARCB1, SMARCC2, SMARCD1, SMARCE1, SOX11 and SOX4 genes have been associated with CSS. We aimed to present the clinical and genetic features of six cases with pathogenic variants in ARID1A, ARID1B, DPF2 and SMARCC2 genes.
Method: In this study, after isolation of DNA from peripheral blood for genetic testing from patients with CSS ,sequencing was performed with the next generation sequencing method (Illumina, NovaSeq) using QIAseq human exome and SOPHIA TM Clinical Exome Solution(CES) V3 kit.
Results: Of the six patients included in this study, four were boys and two were girls and their ages ranged between 5-20 years. Six different variations were found in the cases, three of which were novel (ARID1B c.1719_1720insA, ARID1B c.5704A>T, ARID1A c.3540-1G>C) and three of which were previously associated with CSS (SMARCC2 c.574C>T, ARID1B c.6880C>T, DPF2 c.1067G>C).
Discussion: CSS is a rare congenital syndrome with high heterogeneity in both genotype and phenotype and the clinical course may be highly variable. Molecular genetic diagnosis is important for the patient and family to receive genetic counselling and clinical management. This study is presented because it contributes to the literature in terms of genotype-phenotype correlation by expanding the genotypic spectrum with new variants.

OP32- Regulation of miRNA in high fat diet induced obesity hypoventilation syndrome

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Obesity has become a major public health problem in recent years. In addition to metabolic diseases resulting from obesity, conditions affecting ventilation due to obesity have also increased. The most important of these is obesity hypoventilation syndrome (OHS), which is associated with insufficient oxygen supply to tissues. Expressions in hypoxia-induced factors (HIFs) are the precursor genes for this condition. HIFs are key molecules that regulate how cells respond to inflammation and low oxygen. Evidence suggests that they also play a role in obesity and metabolic diseases. HIF-1α is crucial for maintaining oxygen homeostasis and regulating biological processes, including protein translation, gene transcription, glucose, and energy metabolism. This study aimed to identify HIF-1α-regulated miRNAs in OHS. Recent studies have demonstrated the critical roles of endogenous microRNAs (miRNAs) in regulating gene expression in response to hypoxia. In our study, C57BL/6 mice were divided into HFD (high-fat diet) and ND (normal diet). These groups were divided into the control and adenosine 2A receptor antagonist (istradefylline (IST)) groups. The medulla oblongata tissues of these groups were analyzed by real-time PCR analysis for miR-421 and miR-101a targeting the HIF-1α gene. As a result, miR-101a expression was significantly increased in the HFD_IST group compared to the ND_CON group. The present data support the idea that miRNA might play an important role in obesity and hypoxia.
Keywords: Obesity, Hypoxia, miRNA

OP33- Uncovering inherited hyperlipidemia: The role of genetic testing in early diagnosis and cardiovascular risk reduction

Esra Çelik, Mehmet Kocabey, Ayfer Ülgenalp, Ahmet Okay Çağlayan

Introduction-Aim: Hyperlipidemia is a major risk factor for atherosclerotic cardiovascular disease and the early diagnosis of genetically inherited forms is crucial for reducing morbidity and improving clinical outcomes. This study aimed to evaluate the diagnostic yield and clinical implications of genetic screening in patients diagnosed with hyperlipidemia.
Materials-Methods: Between 2018 and 2025, a targeted next-generation sequencing (NGS) panel encompassing 18 genes associated with lipid metabolism was performed on 106 patients diagnosed with hyperlipidemia who presented to our center. Identified variants were classified in accordance with the American College of Medical Genetics and Genomics (ACMG) guidelines. Clinical data were retrospectively reviewed from patient records.
Results: Pathogenic or likely pathogenic variants were detected in 47 patients (44.3%). The distribution of these variants was as follows: *LDLR* (n=33), *LPL* (n=5), *APOB* (n=4), *APOE* (n=3), *PCSK9* (n=1) and *APOC2* (n=1). Notably, 21 of the variant-positive individuals were under 18 years of age, underscoring the critical importance of early genetic diagnosis in pediatric cases.
Conclusion: Our study highlights the dominant role of the *LDLR* gene in the etiology of hyperlipidemia, while also demonstrating that panel-based genetic screening can uncover rare genetic causes. These findings emphasize the importance of genetic evaluation for early diagnosis and family screening, especially in pediatric patients.
Keywords: Hyperlipidemia, NGS, ACMG, *LDLR*, *APOB*

OP34- Prevalence and spectrum of multiple pathogenic variants identified through hereditary cancer panel testing in a cohort of 1,977 patients

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From 2018 to 2025, hereditary cancer panel testing was performed on patients (n=1977) referred to our clinic for various clinical indications. Multiple pathogenic variants were identified in 29 (1.4%) of these individuals.

Heterozygous pathogenic variants were detected regardless of the indication for testing. The most frequently affected genes were *MUTYH* (n=11), *CHEK2* (n=8), *BRCA1* (n=6), and *BRCA2* (n=6). Less frequently, variants were detected in *PALB2, NBN, ATM, RAD51D, BRIP1, NF1, MSH2, MLH1, MSH6, RAD50, TP53, BLM, MPL, BARD1, NTHL1*, and *STK11.*

The most common indications for referral included breast cancer, ovarian cancer, and a positive family history of cancer. Less frequently, patients were referred due to preliminary diagnoses such as neurofibromatosis, colorectal cancer, prostate cancer, gastric cancer, endometrial cancer, lung cancer, and Peutz-Jeghers syndrome.

These findings indicate that the co-occurrence of multiple pathogenic variants in hereditary cancer screening may be more frequent than previously recognized, in line with recent studies reporting dual or multilocus variants carriage in up to 2–5% of patients undergoing multigene panel testing.

Importantly, the identification of multiple genetic etiologies within a single patient highlights the complexity and heterogeneity of hereditary cancer syndromes. This supports the need for a comprehensive, multidisciplinary approach encompassing clinical genetics, molecular diagnostics, risk assessment, and genetic counseling to ensure accurate interpretation and appropriate clinical management.

In conclusion, these results underscore the clinical relevance of extended multigene panel testing and the importance of considering combinatorial genetic risk in the evaluation of patients with hereditary cancer predisposition.

Keywords: cancer, multiple, *MUTYH, CHEK2, BRCA1*

OP35- A case suspected of KBG syndrome, a novel pathogenic variant detected in SETD5

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Introduction: SETD5 is a methyltransferase that targets histone H3K36 for trimethylation and thereby is involved in development of neural progenitors and their derivatives. SETD5-related neurodevelopmental disorder is an autosomal dominant disorder that includes facial dysmorphism, impaired moderate to severe intellectual development and predisposition to moyamoya disease. This study reveals a novel SETD5 pathogenic variant in a KBG syndrome suspected case.

Materials and Methods: Whole exome sequencing (WES) utilized by Next Generation Sequencing (NGS). Family segregation analysis of the identified variant was performed using Sanger sequencing.

Results: Our patient was a 5 years old male. He was born to nonconsanguineous parents and no similar cases were reported in the family. On physical examination short stature, triangular face, prominent nasal bridge, hypertelorism, long and flat philtrum, thin vermilion of the upper lip, retrognathia, macrodontia, crowded teeth, preauricular skin tag, mild brachidactyly, single palmar crease of both hands, unilateral operated polydactyly scar, proximally placed thumbs were detected. Cerebral venous malformation was detected in cranial MRI. Karyotype and array analyses were normal. Based on dysmorphic facial features, KBG syndrome was suspected. However, no pathogenic variants were found in ANKRD11 gene. Eventually we detected SETD5 c.2120G>A (p.Trp707*) pathogenic novel variant in WES analysis. Family segregation analysis confirmed that the variant occurred de novo.

Discussion: This study highlights the need to consider SETD5 mutations in patients with KBG-like facial features but without ANKRD11 variants, and underlines distinguishing clinical signs between SETD5-related neurodevelopmental disorder and KBG syndrome.

Keywords: SETD5, Neurodevelopmental disorder, Dysmorphism, KBG syndrome

OP36- A novel splicing variant in *RORB* in a patient with epilepsy

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Introduction: RAR-related orphan receptor beta is a nuclear receptor and a transcription factor encoded by *RORB*. *RORB* is predominantly expressed in central nervous system, particularly in regions related with circadian rhythm. Pathogenic variants in *RORB* have recently been associated with susceptibility to idiopathic generalized epilepsy. In the largest available cohort of cases with RORB related disorder, the most common seizure type is absence seizure. More than half of the patients also have variable degrees of intellectual disability.

Case presentation: We report a 14 year-old male patient with epilepsy. His first seizure was at 2 years old. The patient's early developmental milestones were according to his age and he had no major congenital anomalies, dysmorphic features, or intellectual disability. His father's grandmother and his mother's cousin had history of seizures. EEG studies revealed epileptiform abnormalities. Patient's seizures were mostly generalized tonic-clonic type. The seizures were resistant to levatiracetam and were controlled with valproic acid.

We performed whole exome sequencing to enlighten the molecular etiology behind the seizures. We identified c.93+1G>T variant in *RORB* at heterozygous state (NM_006914.4). The variant was absent in healthy controls and is expected to disrupt splicing. We classified the variant as likely pathogenic according to the ACMG criteria.

Conclusion: We report a novel variant in *RORB*, an ultra rare cause of epilepsy, highlighting the importance of exome sequencing. Our case also represents a relatively uncommon presentation of RORB related disorder regarding the seizure type and normal intellectual development.

Keywords: RORB, epilepsy, next-generation sequencing

OP37- A novel variant in the *COASY* Gene: A case with arthrogryposis and pontocerebellar hypoplasia

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The *COASY* gene encodes an enzyme involved in the biosynthesis of coenzyme A. Biallelic pathogenic variants in this gene are responsible for two distinct phenotypes: COASY protein-associated neurodegeneration(CoPAN) and pontocerebellar hypoplasia type 12(PCH12). PCH12 is characterized by neonatal respiratory failure, microcephaly, arthrogryposis, and pontocerebellar hypoplasia. Here, we present a case with a novel homozygous variant in the *COASY* gene associated with PCH12; a rare, perinatal-lethal neurodegenerative disorder.

A week-old female patient was referred to the Medical Genetics department with findings of dysmorphic features, respiratory distress, and multiple joint contractures. Clinical evaluation revealed microcephaly, hypertelorism, broad nasal bridge, clubfoot, and arthrogryposis. She also had lissencephaly and cerebellar hypoplasia. The parents were consanguineous and had previously lost a child with skeletal malformations. The patient's karyogram, SNP-array analysis, and FISH testing for Miller-Dieker syndrome were normal. A comprehensive NGS panel(KAPA HyperCap Heredity) was performed and revealed a homozygous missense variation in the *COASY* gene(ENST00000590958, c.1177A>C). Both parents were observed to harbour the same variant, heterozygously. The proband was deceased in 10 months.

Detected missense change was not reported in the literature before. It was not found in population databases(ACMG criteria PM2). *In silico* tools predicted the variant to disrupt the protein structure and/or function(PP3). The clinical features of the proband were found to be fully compatible with the *COASY*-related phenotype(PP4). Only a few patients with PCH12 have been reported, making this case clinically noteworthy. Since pontocerebellar hypoplasia is genetically heterogeneous, evaluation with comprehensive molecular panels is crucial in establishing a definitive diagnosis.

Keywords: *COASY*, Coenzyme A Synthase, pontocerebellar hypoplasia, arthrogryposis

OP38- Targeted effects of Intronistat B on PLD1 and PLD2: an in silico and in vitro approach in glioblastoma cells

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Introduction: Glioblastoma multiforme (GBM) is the most aggressive primary brain tumor, characterized by its invasive nature and resistance to conventional therapies. HIF1A and PLD2 from the phospholipase family play critical roles in glioblastoma progression. According to Protein Atlas data, the expression of these genes is increased in glioblastoma cells, supporting their survival, metastasis, and angiogenesis capabilities.

Materials and Methods: This study aimed to evaluate the binding potential of Intronistat B to HIF1A and PLD2 via in silico docking, guiding subsequent in vitro validation in GBM models. For protein targets, PDB structures 3KCX for HIF1A and 6OHP for PLD2 were utilized. Active sites were defined as pocket ID:1 (volume: 1068 $Å^3$) and the catalytic domain, respectively. The 3D structure and SMILES code of Intronistat B were obtained from the PubChem database. In docking analyses performed using the CB-Dock2 platform, binding scores of -8.5 kcal/mol for HIF1A (3KCX) and > -7.0 kcal/mol for PLD2 (6OHP) were obtained.

Discussion: Docking analyses revealed that Intronistat B exhibited high binding affinity to both target proteins. The binding pockets overlapped with functionally active regions, indicating a probable inhibitory effect. These findings suggest that Intronistat B may interact with residues critical for enzymatic or transcriptional activity, potentially altering tumor progression pathways.

Conclusion: Computer-aided analyses of Intronistat B indicate its potential to exert antitumor effects in glioblastoma cells by suppressing HIF1A and PLD2. If validated by laboratory tests,

this molecule could emerge as a promising drug candidate for glioblastoma treatment.

Keywords: Intronistat B, HIF1A, PLD2, Glioblastoma, Docking

OP39- Homozygous Null Variation in the KIFBP gene: A rare case of Goldberg-Shprintzen Syndrome

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Goldberg-Shprintzen syndrome (GOSHS) is a rare multisystemic genetic disorder characterized by delayed motor and cognitive milestones, distinctive craniofacial dysmorphisms, cardiovascular anomalies, and various musculoskeletal abnormalities. Here, we present a case with a homozygous *KIFBP* gene variant, aiming to underscore the utility of comprehensive genetic panels in diagnosing complex multisystemic disorders.

A 17-year-old female was referred to the Department of Medical Genetics due to dysmorphic facial features, delayed motor milestones, and skeletal abnormalities including scoliosis, pectus excavatum, kyphosis, developmental hip dysplasia, and pes cavus. In the neonatal period, she underwent surgical correction for an atrial septal defect and Hirschsprung disease. Clinical evaluation revealed a failure to thrive, microcephaly, and dysmorphic facial appearance with a flat forehead, high-arched eyebrows, upslanting palpebral fissures, blue sclera, convex nasal bridge, and prominent long nose. A comprehensive NGS panel (KAPA HyperCap Heredity) was performed and identified a homozygous variant in the *KIFBP* gene (ENST00000361983, c.169G>T), establishing the diagnosis of Goldberg-Shprintzen syndrome. The variant was a null change resulting in a premature stop codon. It was not found in population databases and has not been previously reported. According to the ACMG criteria, the variant was interpreted as likely pathogenic (PVS1, PM2).

This case with GOSHS enriches the limited literature on this rare condition by broadening its phenotypic spectrum and highlights the critical role of molecular diagnostics in the evaluation of complex multisystemic disorders. Reporting such cases aims to raise clinical awareness and facilitate early and accurate diagnosis for affected individuals.

Keywords: Goldberg-Shprintzen syndrome, GOSHS, *KIPBP*, NGS

OP40- OncoSemScore: Integrative Semantic Scoring of Multigenic Co-Occurrences in Hereditary Cancer

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Introduction: Hereditary cancers are among the primary focuses of genetic research and clinical practice. While some of these cancers follow a monogenic inheritance pattern, many exhibit a complex multigenic architecture. However, current algorithms are insufficient to fully explain this intricate genetic structure. Therefore, there is a pressing need for novel mathematical and computational approaches to more accurately analyze hereditary cancer susceptibility.

Material-Methods: We obtained data on 4302 hereditary cancer patients between 2023 and 2025. First, we selected 59 genes among the 5000 that may be associated with hereditary cancer. In the second stage, we identified genes that appear together. We classified them according to the five semantic similarity algorithms. We adapted integrative classifier algorithms developed by Alay MT into classifying semantic similarity algorithms and found a new scoring system.

Results: The co-occurrence probability for both BRCA2–FANCA and ATM–BRCA2 gene pairs was calculated at 18,56%, indicating a comparable frequency of joint occurrence. This similarity reflects their collaborative roles in DNA repair pathways, with BRCA2 and FANCA participating in homologous recombination and the Fanconi anemia pathway, and ATM functioning as a kinase that activates BRCA2 in response to DNA damage.

Discussion: Algorithms on harmony of coexistence of multiple genes are very limited, and the use of new methods developed in cancers with multi-genic inheritance may fulfill a significant need in understanding the co-occurrence rates of genes.

Keywords: Hereditary cancers, semantic similarities, integrative classifier

OP41- A case of Jackson-Weiss syndrome with FGFR1 p.(Pro252Arg) variant: expanding the phenotypic spectrum

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Abstract:

Jackson-Weiss syndrome (JWS) is a rare autosomal dominant disorder characterized by craniosynostosis and foot anomalies, caused by pathogenic variants in the FGFR1 gene. In this case we present a 4-year-old male referred for genetic evaluation due to bilateral toe syndactyly, macrodactyly of the thumbs, and rocker-bottom feet. The patient also had a history of pyloric stenosis that required surgery. Prenatally, polyhydramnios and maternal use of metoclopramide between the 12th and 16th gestational weeks were noted. Postnatal findings included neonatal hypoglycemia and cyanosis. Dysmorphic features included downslanting palpebral fissures, long eyelashes, prominent ears with notched helix, high-arched palate, and syndactyly of the second and third toes. Family history

revealed syndactyly and hearing loss on the paternal side, suggesting autosomal dominant inheritance. Next-generation sequencing identified a heterozygous missense variant in FGFR1: NM_023110.2:c.755C>G (p.Pro252Arg), previously reported as pathogenic. No additional cardiac, auditory, or visual abnormalities were detected.

This case reinforces the clinical relevance of the FGFR1 p.(Pro252Arg) variant and contributes to the growing phenotypic spectrum of JWS. The presence of gastrointestinal findings and detailed family history highlights the importance of considering FGFR1-related syndromes in patients with digital anomalies, even in the absence of craniosynostosis.

Keywords: FGFR1, Jackson-Weiss syndrome, syndactyly, macrodactyly, dysmorphic features

OP42- A case of Jackson-Weiss syndrome with FGFR1 p.(Pro252Arg) variant: expanding the phenotypic spectrum

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Abstract:
Jackson-Weiss syndrome (JWS) is a rare autosomal dominant disorder characterized by craniosynostosis and foot anomalies, caused by pathogenic variants in the FGFR1 gene. In this case we present a 4-year-old male referred for genetic evaluation due to bilateral toe syndactyly, macrodactyly of the thumbs, and rocker-bottom feet. The patient also had a history of pyloric stenosis that required surgery. Prenatally, polyhydramnios and maternal use of metoclopramide between the 12th and 16th gestational weeks were noted. Postnatal findings included neonatal hypoglycemia and cyanosis. Dysmorphic features included downslanting palpebral fissures, long eyelashes, prominent ears with notched helix, high-arched palate, and syndactyly of the second and third toes. Family history revealed syndactyly and hearing loss on the paternal side, suggesting autosomal dominant inheritance. Next-generation sequencing identified a heterozygous missense variant in FGFR1: NM_023110.2:c.755C>G (p.Pro252Arg), previously reported as pathogenic. No additional cardiac, auditory, or visual abnormalities were detected.

This case reinforces the clinical relevance of the FGFR1 p.(kPro252Arg) variant and contributes to the growing phenotypic spectrum of JWS. The presence of gastrointestinal findings and detailed family history highlights the importance of considering FGFR1-related syndromes in patients with digital anomalies, even in the absence of craniosynostosis.

Keywords: FGFR1, Jackson-Weiss syndrome, syndactyly, macrodactyly, dysmorphic features

OP43- A case of 3M syndrome type 2 with a homozygous pathogenic OBSL1 variant: clinical and genetic findings

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Abstract:
3M syndrome is a rare autosomal recessive growth disorder characterized by pre- and postnatal growth retardation, distinctive craniofacial features, and skeletal anomalies. Three genes—**OBSL1**, **CUL7**, and **CCDC8**—have been associated with types 2, 1, and 3, respectively. Here, we report a 15-year-old male with clinical and radiological features consistent with 3M syndrome type 2.

The patient was referred for genetic evaluation due to proportionate short stature and facial dysmorphism. Prenatal ultrasonography showed microcephaly and suspected cerebral anomalies. Postnatal brain MRI revealed polymicrogyria and agenesis of the corpus callosum. Despite normal intelligence (IQ 78), the patient had poor academic performance. Physical findings included triangular face, prominent forehead, deep-set eyes, upslanting palpebral fissures, infraorbital hollowness, zygomatic hypoplasia, and beaked nose. Anthropometric parameters were below the 3rd percentile. Trio-based next-generation sequencing revealed a homozygous frameshift variant in the OBSL1 gene: **c.1273dup (p.Thr425AsnfsTer40)**. Both parents were confirmed as heterozygous carriers.

This case confirms the typical clinical phenotype of 3M syndrome and expands the mutational spectrum of **OBSL1**-related cases. Our findings emphasize the role of targeted genetic testing in patients with syndromic short stature and the importance of integrating clinical, radiological, and genetic data for accurate diagnosis.

Keywords: 3M syndrome, OBSL1, short stature, frameshift mutation, skeletal dysplasia

OP44- Family case report of the m.9185T>C *MT-ATP6* variant highlighting variable expressivity

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Introduction: Mitochondrial disorders frequently demonstrate variable expressivity and incomplete penetrance due to heteroplasmy and tissue-specific vulnerabilities. We report a family carrying the m.9185T>C (p.Leu220Pro) *MT-ATP6* variant with strikingly variable clinical manifestations.

Materials and Methods: The proband is a 16-year-old male

with mild intellectual disability, pes cavus, and EMG-confirmed axonal peripheral neuropathy. Brain MRI and metabolic screenings, including lactate levels were normal. Whole exome sequencing (WES) trio analysis was performed for the proband, which identified the m.9185T>C variant in the *MT-ATP6* gene. This was confirmed by a mitochondrial DNA panel and segregation analysis within the family. His mother exhibited only mild pes cavus without other neurological findings. His maternal uncle presented with progressive axonal and autonomic neuropathy requiring wheelchair dependency, despite no definitive diagnosis after extensive evaluations. The maternal aunt reported mild exercise intolerance, and the maternal grandmother remained completely asymptomatic.

Results: Genetic testing revealed the m.9185T>C (p.Leu220Pro) variant in the *MT-ATP6* gene, as homoplasmic in the proband, his mother, and maternal uncle, while it was heteroplasmic in the maternal aunt (25.5%) and maternal grandmother (58.1%). All family members had normal lactate and blood gas levels.

Discussion: This family illustrates the clinical heterogeneity associated with the m.9185T>C variant in *MT-ATP6*. While the maternal uncle developed severe neuropathy, other carriers, including the homoplasmic mother, remained minimally or entirely asymptomatic. These findings highlight the limited predictive value of heteroplasmy levels alone in mitochondrial diseases.

Conclusion: This case expands the understanding of the m.9185T>C *MT-ATP6* variant, demonstrating variable expressivity and emphasizing the challenges of clinical interpretation in mitochondrial neuropathies.

Keywords: mitochondrial disease, *MT-ATP6*, m.9185T>C, peripheral neuropathy, heteroplasmy, homoplasmy

OP45- A novel variant associated with spastic paraplegia with neurodevelopmental disorder

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Hereditary spastic paraplegia (HSP) is an inherited disorder of the Central Nervous System mainly characterized by gradual spasticity and weakness of the lower limbs. Spastic Paraplegia 56 (SPG56) is a rare autosomal recessive early onset form of HSP. Symptoms include delayed motor development, spastic paraplegia, unsteady gait, and toe walking. Other features are hyperreflexia, and rarely, dystonic posturing or mild cognitive impairment. SPG56 is caused by biallelic pathogenic variants in the CYP2U1 gene, encoding cytochrome P450, family 2, subfamily U, polypeptide 1. In this study, we present a case in which a loss of function variant was detected in the CYP2U1 gene. The proband, a 2-year-old girl, presented with neurodevelopmental delay, inability to walk, hyperactive deep tendon reflexes, and spasticity. She could walk on her tiptoes with assistance, and her speech development was delayed, with an inability to form two-word sentences. In the genetic testing a novel NM_183075 c.615del p.(Tyr205Ter) frameshift homozygous likely pathogenic variant was detected in the CYP2U1 gene (Exon 2). The findings were consistent with Hereditary Spastic Paraplegia. This study presents a novel variant of this rare syndrome.

Keywords: CYP2U1, Spastic Paraplegia 56, autosomal recessive.

OP46- Frank-Ter Haar Syndrome: An uncommon diagnosis revealed by sequencing

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Introduction:

Frank-Ter Haar syndrome (FTHS) is a remarkably rare autosomal recessive disorder characterized by craniofacial dysmorphism, skeletal anomalies, and cardiovascular involvement. It is associated with biallelic pathogenic variants in *SH3PXD2B* gene, which encodes a protein involved in podosome formation, cell adhesion, and migration.

Case Report:

A female neonate born to consanguineous parents was referred to our medical genetics clinic within the first 24 hours of life due to multiple dysmorphic features. Examination revealed hallmark craniofacial anomalies including mild bitemporal narrowing, a wide anterior fontanel (5×2 cm), hypertelorism, low-set ears, nasal bridge hypoplasia, bilateral sandal gaps, and a simian crease on the right palm. Chromosomal microarray analysis was performed as a first-tier diagnostic test and yielded normal results. Subsequent karyotype and next-generation sequencing (NGS) analyses revealed a homozygous c.127C>T (p.Arg43Trp) missense variant in *SH3PXD2B*, confirming the diagnosis of FTHS. The phenotypic findings were consistent with previously described features of the syndrome.

Conclusion:

FTHS is an uncommon genetic condition, with a gradually expanding clinical description based on reported cases. In this case, comprehensive NGS enabled a definitive diagnosis after initial microarray and karyotype analyses yielded inconclusive results. This report highlights the utility of broad NGS panels in evaluating patients with complex phenotypes, particularly in consanguineous populations, and aims to contribute to the limited literature on FTHS.

Keywords: Frank-Ter Haar Syndrome, SH3PXD2B, Next-Generation Sequencing (NGS), Craniofacial Dysmorphism.

OP47- A Case of CTNNB1-Related Neurodevelopmental

Disorder

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Introduction:

The *CTNNB1* gene encodes β-catenin, a protein involved in cell–cell adhesion. β-catenin also plays a crucial role in cell proliferation, differentiation, and developmental processes via the Wnt signaling pathways. While somatic *CTNNB1* variants have been associated with various tumors, in recent years, germline pathogenic variants—particularly de novo truncating and splice-site alterations—have been implicated in a neurodevelopmental disorder known as NEDSDV (MIM 615075). NEDSDV is characterized by microcephaly, intellectual disability, speech impairment, spasticity, and ocular findings. Here, we present a patient referred for neurodevelopmental delay in whom a frameshift variant in the *CTNNB1* gene was detected, leading to a diagnosis of NEDSDV.

Case report:

A 7-year-old female was evaluated for microcephaly, developmental delay, and features of autism spectrum disorder. She exhibited profound developmental delays: head control was achieved at 2 years, independent sitting at 4 years, with no acquisition of walking or speech. Physical examination revealed microcephaly, dysmorphic facial features, spasticity in the lower extremities, and stereotypic movements. Cranial MRI showed delayed myelination; aside from this, no significant pathology was identified in other investigations. Karyotype and chromosomal microarray analyses were normal. Clinical exome sequencing revealed a heterozygous *CTNNB1* c.760del p.(Tyr254Metfs*22) frameshift variant in exon 6, classified as likely pathogenic.

Conclusion:

CTNNB1-related neurodevelopmental disorder was first described in 2012. Since then, over 20 loss-of-function mutations have been reported. We describe a novel, previously unreported frameshift variant predicted to result in protein truncation. The patient's phenotype aligns with known *CTNNB1*-related disorders, contributing to the expanding mutational and clinical spectrum of NEDSDV.

Keywords: *CTNNB1*, NEDSDV, Neurodevelopmental delay.

OP48- A Case of Verloes Bourguignon Syndrome Diagnosed in the Infantile Period

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Introduction

Verloes Bourguignon Syndrome is a rare autosomal recessive genetic disorder caused by homozygous or compound heterozygous mutations in the *LTBP3* gene located on chromosome 11q13. The syndrome is characterized by short stature, amelogenesis imperfecta, maxillary hypoplasia, mandibular prognathism, cardiovascular anomalies, and various skeletal abnormalities. This case report presents a patient with Verloes Bourguignon Syndrome exhibiting distinct clinical features.

Case Report

A 19-month-old male patient was referred to our clinic with a preliminary diagnosis of congenital myasthenia due to prominent unilateral ptosis. Medical history revealed that the patient was born at 41+2 weeks via spontaneous vaginal delivery, with a birth weight of 3050 grams. Notable ptosis of the left eye was observed at birth. The parents were first-degree cousins. Anthropometric measurements included a height of 80 cm (-1.43 SD) and weight of 10 kg (-1.25 SD). Physical examination revealed significant left eyelid ptosis, bilateral puffy upper eyelids, maxillary hypoplasia, Stahl's ear deformity, sparse hair and eyebrows, and yellowish teeth indicative of amelogenesis imperfecta due to enamel absence. Visual tests were normal. Echocardiography (ECHO), electromyography (EMG), and visual evoked potential (VEP) assessments were unremarkable, and cranial MRI and CT showed no abnormalities. Based on these findings, a neuromuscular disease panel was performed.

Results

DNA was extracted from the patient's peripheral blood, and sequencing was performed using the TWIST Custom Select Panel kit on the MGI DNBSEQ-G400 platform. Analysis revealed a homozygous c.3427G>T variant in the *LTBP3* gene, classified as pathogenic according to ACMG guidelines. Based on these findings, the patient was diagnosed with Verloes Bourguignon Syndrome. Parental segregation analysis was planned.

Discussion

This case is noteworthy as a rare presentation of Verloes Bourguignon Syndrome, reflecting its clinical and genetic characteristics. The patient's presentation with ptosis and diagnosis in the infantile period, prior to the development of cardiovascular and dental anomalies, highlights the importance of early diagnosis and follow-up to manage potential complications. This case contributes to the literature by emphasizing the need for early monitoring and appropriate management of this rare syndrome.

Keywords: Verloes Bourguignon Syndrome, *LTBP3*, amelogenesis imperfecta

OP49- A rare case of adult-onset neurodegeneration due to a pathogenic IRF2BPL variant

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Introduction

Neurodevelopmental disorders associated with the IRF2BPL (Interferon Regulatory Factor 2 Binding Protein-Like) gene

are typically characterized by childhood-onset epilepsy, ataxia, speech delay, and motor regression. While pathogenic variants in this gene often present clinically at an early age, adult-onset cases are rare. In this presentation, we report a case of adult-onset neurological decline associated with a stop-gain variant in the IRF2BPL gene.

Materials and Methods

Our case is a 29-year-old male patient referred to us from the neurology outpatient clinic with complaints of progressive walking disturbance and speech slowing over the past 1–2 years.

Initial clinical manifestations began at the age of 24 with a nocturnal seizure, tongue biting, and urinary incontinence, and the patient was diagnosed with epilepsy. Since the age of 26, he developed progressive gait difficulties, speech slowing, and stereotypic movements in the extremities.

For genetic analysis, the Comprehensive Hereditary Panel including the ataxia panel was performed using the KAPA HyperCap Hereditary Panel. Next-generation sequencing (NGS) identified a heterozygous stop-gain variant in the IRF2BPL gene: c.358C>T (p.Arg120*). The variant was classified as pathogenic according to ACMG guidelines and was confirmed by Sanger sequencing. Screening for SCA (spinocerebellar ataxia) trinucleotide repeat expansions yielded normal results.

Discussion

A review of the current literature suggests that heterozygous pathogenic variants in the *IRF2BPL* gene are rare. To date, only 34 such cases have been reported through whole-exome sequencing (WES). Despite the limited number of cases, the associated clinical phenotypes demonstrate considerable variability. These variants are most frequently linked to childhood-onset neurodevelopmental regression. In contrast, the case presented here exhibits a distinct clinical profile, characterized by adult-onset neurological symptoms. This report aims to contribute to the understanding of the phenotypic spectrum associated with pathogenic *IRF2BPL* variants.

Keywords: IRF2BPL, adult onset, ataxia, epilepsy

OP50- KBG Syndrome: A Rare Neurodevelopmental Disorder Characterized by ANKRD11 Loss-of-Function Variants

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Introduction: KBG syndrome is a rare neurodevelopmental syndrome that occurs as a result of loss-of-function variants or deletions involving this region in the ANKRD11 gene located on chromosome 16. ANKRD11 encodes the chromatin coregulator Ankyrin Repeat Domain-Containing Protein 11, which regulates transcription by binding to nuclear receptor complexes in neurons and glial cells. Loss of function of the gene has been associated with phenotypic features such as macrodontia of maxillary central incisors, triangular face, synophrys, hypertelorism, short stature, skeletal anomalies, and brain malformations. The clinical picture is mostly accompanied by feeding problems in infancy, seizures, attention deficit hyperactivity disorder, and learning disabilities.

Case Report: A 10-year-old gril patient was referred to our medical genetics clinic due to attention deficit hyperactivity disorder, heart defect and dysmorphic appearance. As a result of the examination, triangular face, synophrys, brachydactyly was detected in the patient. Karyotype analysis, microarray and NGS analyses were planned for the patient.

Results: Karyotype analysis and microarray results were reported as normal. Next-generation DNA sequencing identified a heterozygous frameshift variant at the c.4411_4412del position in the ANKRD11 gene. According to ACMG guidelines, this variant was classified as Likely Pathogenic, confirming the diagnosis of KBG syndrome (PVS1,PM2).

Conclusion: KBG syndrome is a very rare syndrome and it is important to apply comprehensive gene panels with NGS method in its diagnosis. It is aimed to contribute to the literature in terms of genotype-genotype correlation of KBG syndrome.

Keywords: KBG syndrome, NGS, Macrodontia

OP51- Rare copy number variants of 8p23 gene region and their association with neurodevelopmental disorders

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Introduction: The *8p23* gene region has been implicated in neurodevelopmental disorders (NDDs), yet the clinical significance of rare copy number variants (CNVs) in this region remains poorly understood. This study aims to characterize CNVs in *8p23* and identify novel candidate genes associated with NDDs.

Methods: We analyzed chromosomal microarray data from patients with neuropsychiatric disorders to detect CNVs in the *8p23* region. Clinical findings were correlated with genetic results.

Results: We presented detailed clinical findings of cases carrying heterozygous *8p23* copy number variants. In addition, we identified three novel candidate gene variants of these disorder, following as *TDRP, FAM90A10* and *FAM90A7* genes.

Discussion/Conclusion: Our findings highlight the clinical relevance of *8p23* CNVs in NDDs and propose *TDRP*, *FAM90A10*, and *FAM90A7* as novel candidate genes requiring further investigation. This study underscores the importance of comprehensive CNV analysis for understanding NDD pathogenesis.

Keywords: TDRP, FAM90A10, FAM90A7, 8p23, autism spectrum disorder, intellectual disability

OP52- Single-Center Experience: A Retrospective Evaluation of Prenatal Genetic Counseling and Diagnostic Approach Between January and March 2025

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Background:

Prenatal diagnosis refers to genetic testing used to determine whether a fetus at increased risk for a genetic disorder is affected. This risk may stem from a previous child with a genetic condition, familial disease history, parental carrier status, or high-risk findings in screening.

Prenatal genetic counseling is crucial for early anomaly detection and effective clinical management. Timely, well-indicated testing enhances both clinical outcomes and personalized decision-making.

Material and methods:

This study aimed to evaluate the clinical management of pregnant individuals who underwent invasive prenatal diagnostic testing following referral to our clinic for genetic counseling between January and March 2025. Clinical histories, types of diagnostic tests performed, genetic findings,
and pregnancy outcomes were reviewed using patient records.

Results:

All 33 patients received comprehensive genetic counseling, and non-invasive and/or invasive diagnostic tests were recommended based on case-specific indications. Chromosomal aneuploidy was identified in three cases, and microdeletion/duplication syndromes in three others. Seven patients exhibited copy number variations (CNVs) deemed potentially clinically relevant. One patient was found to carry a familial chromosomal translocation. Additionally, whole-exome sequencing (WES) identified single-gene variants potentially related to the clinical presentation in three cases. Sixteen patients had normal genetic test results. Four pregnancies were electively terminated, while the remaining 29 continued with follow-up or resulted in delivery.

Conclusion:

Our study highlights the critical role of prenatal genetic counseling in multidisciplinary management and the importance of applying diagnostic tests with the correct indications. This comprehensive approach, conducted independently of the referral indication, improves quality and patient compliance in the prenatal diagnosis process and serves as a reference as a single-center experience. As the results of ongoing cases are completed, diagnostic performance will be evaluated through further analysis.

OP53- The effect of early radiotherapy effects on A549 lung cancer stem cell population

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Introduction: Radiotherapy is a commonly used method in the treatment of lung cancer; however, the presence of therapy-resistant cell populations limits its effectiveness. Cancer stem cells (CSC) play a critical role in both tumor recurrence and resistance. This study aimed to investigate the effects of radiotherapy on CSC subpopulations and migration ability in A549 cells.

Material and Methods: A549 cells were irradiated with 0, 2, 4, 6, and 8 Gy. CSC populations were analyzed by flow cytometry at 24 and 48 hours using CD44 and CD24 markers. Cell migration was assessed via scratch assay.

Discussion: Our findings indicate that radiotherapy effect both cell viability and the proportion of cancer stem-like cells in A549 cells in a dose-dependent manner. The most notable reductions were observed at 6 Gy, suggesting this dose may target resistant subpopulation. Decreased migration capacity at higher doses points to a potential anti-metastatic effect of radiation. These results support the therapeutic value of radiotherapy in limiting CSC-related relapses and metastasis.

Results: A significant decrease in cell viability was observed in A549 cells 24 hours after exposure to 2 Gy of radiation, as determined by the MTS assay. Flow cytometric analysis of cancer stem cell populations at 24 and 48 hours revealed dose-dependent variations in the proportions of $CD44^+$ and $CD24^-$ cells. In the 6 Gy group at 24 hours, a significant reduction was detected in both $CD24^-$ (0.54%) and $CD24^-CD44^+$ (2%) cell populations. The migratory capacity of cells was reduced in all groups.

Keywords: Stem cell, radiotherapy, cancer

OP54- Analysis of miRNA Expression Profile by Small RNA Sequencing in Schizophrenia Patients

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Introductıon: This study aimed to analyze miRNA expression profiles and identify potential disease-related biomarkers in schizophrenia patients treated with paliperidone palmitate, a long-acting injectable antipsychotic, using small RNA se-

quencing in peripheral blood.

Materials and Methods: Our study included 20 individuals diagnosed with schizophrenia, 20 individuals diagnosed with schizophrenia and treated with paliperidone palmitate, and 20 healthy control individuals. RNA was isolated from peripheral blood samples collected in EDTA tubes. Following quality and quantity analyses, small RNA sequencing was conducted. For the sequencing process, samples from 3 individuals with schizophrenia, 2 individuals with schizophrenia treated with paliperidone palmitate, and 3 healthy controls were selected. In the bioinformatic analysis, significantly differentially expressed miRNAs were identified based on LogFC, p-value, and FDR (<0.05) criteria.

Discussion: Our results indicate that miRNA expression in peripheral blood is significantly altered in schizophrenia patients. miRNAs such as miR-486 and miR-451a have previously been associated with neuroinflammation, synaptic function, and neuronal plasticity. Although the effect of paliperidone palmitate on these expression profiles is not yet fully understood, the observed changes may be attributed to both disease pathophysiology and treatment effects. Our findings are promising for the discovery of potential diagnostic and prognostic peripheral blood biomarkers in schizophrenia. However, the results need to be validated in larger patient cohorts.

Conclusıon: A total of 15 miRNAs were found to be significantly downregulated in schizophrenia patients compared to the control group. In particular, hsa-miR-486-1/2, hsa-miR-92a-1/2, hsa-miR-451a, and hsa-miR-4732 were found to be noteworthy.

Keywords: Schizophrenia, miRNA, small RNA sequencing, paliperidone palmitate

OP55- Blended RASopathy and autoinflammatory phenotype due to coexisting NF1, RAF1, and MEFV variants: a father–daughter case report

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The RAS/MAPK signaling pathway is a conserved mechanism that regulates cellular responses to growth factors and extracellular stimuli. Genetic alterations in this pathway lead to a group of syndromes known as RASopathies. Among them, Neurofibromatosis type 1 (NF1) is one of the most common autosomal dominant neurocutaneous disorders and is usually caused by pathogenic variants in the NF1 gene.

RAF1 is another gene within this pathway. The co-occurrence of NF1 and RAF1 variants in a single individual is rare and may indicate a genetic interaction or modifying effect on phenotype.

Here, we present a proband with a blended phenotype carrying a pathogenic stop-gain NF1 c.4078T>C (p.Gln1360Ter) variant, a stop-gain RAF1 c.874C>T (p.Arg292Ter) variant classified as a variant of uncertain significance (VUS), and a pathogenic missense MEFV c.2177T>C (p.Val726Ala) variant. Clinically, the proband exhibited café-au-lait macules, axillary and inguinal freckling, along with recurrent headaches, dizziness, nausea, and abnormal brain MRI findings. Her father, who was diagnosed following the evaluation of his daughter, showed similar pigmentary findings in addition to multiple neurofibromas.

This case contributes to the understanding of blended phenotypes involving both RASopathy-related and autoinflammatory gene variants. It highlights the importance of comprehensive genetic testing in patients with complex or atypical features. Early and accurate molecular diagnosis is essential for elucidating the underlying genetic etiology, guiding individualized management, preventing potential complications, and enabling long-term follow-up in RASopathies and related conditions.

Keywords: Neurofibromatosis type 1, NF1 gene, RAF1 gene, whole exome sequencing

OP56- Genealogy and ethics after advances in artificial fertilization techniques

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Developments in genetic science and artificial fertilization techniques have brought about many ethical debates. Among these, issues such as cloning, anonymous gamete donation (sperm banking, egg freezing and donation), surrogacy are bioethical issues that also concern biological ties. With these developments, many things about the traditional family structure have changed and the importance of the concept of genealogy/biological ties has been questioned more and more.

Genealogy refers to the biological bond between a person and his/her descendants and ascendants. In Islam, the protection of genealogy, which is referred to as "neseb" in Arabic, has been emphasized and for this reason, it is forbidden for a woman whose husband has died or whose husband has separated from her to marry another man during the 4-month period of iddat to determine whether she is pregnant from her deceased husband. In the Turkish Civil Code, this period is 300 days, except in special cases.

Recently, some researchers have focused on the importance of biological ties in the development of a coherent and positive sense of identity, arguing that an ongoing bond with biological parents is important for self-knowledge and self-formation, and that it is morally wrong to deprive someone of this. This

raises ethically important questions such as whether it is important to know one's biological parents and what kind of value should be attributed to biological ties/ancestry.
This study aims to evaluate the importance of the concept of geneslogy and bioethical issues related to genetics in this context.
Key words: Genealogy, Bioethics, Artificial fertilization.

OP57- A Rare Genetic Cause of Early Infantile Onset Epilepsy: CSNK2B

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Introduction: Poirier-Bienvenu Neurodevelopmental Syndrome (PBNS) is a rare autosomal dominant genetic disorder caused by mutations in the *CSNK2B* gene. This gene encodes the beta subunit of casein kinase 2 (CK2), an eosinophilic serine/threonine kinase involved in processes such as apoptosis, cell proliferation, DNA damage response, neuronal development, signal transduction, metabolic processes, replication, transcription, and translation. *CSNK2B* is abundantly expressed in the brain, particularly in neurons and neuroepithelial cells, and plays a critical role in neuronal development. The syndrome is characterized by various findings such as neurodevelopmental disorder, intellectual disability, developmental delay, epileptic seizures, and, in some cases, hypotonia.
Case Presentation: In this study, we present a 2.5-month-old male patient affected by PBNS. The patient was referred to pediatric neurology with a preliminary diagnosis of epileptic seizures. His parents were not consanguineous. His measurements were: weight 6.2 kg (-0.08 SDS), height 62.0 cm (0.44 SDS), and head circumference 39.5 cm (-1.03 SDS). Physical examination revealed slanted eyes, prominent ears, thick eyebrows, a 0.5×0.5 cm hyperpigmented lesion on the back, and a Mongolian spot on the gluteus maximus. EEG reported multifocal medium-to-high amplitude sharp slow-wave discharges in the left hemisphere. No pathology was detected in the brain MRI. WES, conducted under the preliminary diagnosis of epilepsy, revealed a heterozygous likely pathogenic frameshift variant, c.438del p.Lys147SerfsTer80, in the *CSNK2B* gene.
Conclusion: There are a limited number of reported cases of PBNS in the literature. We report the first case from Turkey. This study contributes to the clinical and genetic diversity and expands the variant spectrum of PBNS. The identified variant in this case supports loss of function as a common molecular mechanism.
Keywords: *CSNK2B*; Epilepsy; Next-Generation Sequencing; Rare Diseases; Poirier-Bienvenu Neurodevelopmental Syndrome

OP58- The role of clinical and genetic findings in the diagnostic process of disorders of sex development: a current overview with single center experience

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Introduction
Disorders of sex development (DSD) are conditions where chromosomal, gonadal, or anatomical sex is atypical. This study aims to retrospectively evaluate the demographic, clinical, laboratory, and genetic features of patients diagnosed with DSD over the last 15 years in a tertiary pediatric endocrinology center.
Materials and Methods
Patients diagnosed with DSD at Erciyes University Pediatric Endocrinology Department between 2010 and 2025 were included. Data were categorized based on the Chicago Consensus
as sex chromosome DSD, 46 XX DSD, and 46 XY DSD.
Results
A total of 241 patients were included (58.9% female). The most common etiologic group was 46 XY DSD (42.3%), followed by sex chromosome DSD (29.5%) and 46 XX DSD (28.2%). Common presentation symptoms were ambiguous genitalia (22%), short stature (19.5%) and hypospadias (12%). In the 46 XX DSD group, 21-hydroxylase deficiency was the most common diagnosis (64.1%). In 46 XY DSD, androgen receptor mutations, SRD5A2, CYP17A1, and PMKS defects were identified. Turner syndrome was the most frequent sex chromosome anomaly (84.5%).
Discussion and Conclusion
This single-center experience emphasizes the complex and heterogeneous nature of DSD. Contrary to some reports, 46 XY DSD was the most prevalent group. Comprehensive clinical, hormonal, imaging, and genetic evaluations are essential for accurate diagnosis and optimal management of DSD patients.
Keywords: disorders of sex development, clinical findings, genetics

OP59- A New Translocation: t(3;6)(q13.3;q27) in a Case of Recurrent Pregnancy Loss (RPL)

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Introduction: Recurrent pregnancy loss (RPL) is when a woman has three or more consecutive miscarriages. Chromoso-

mal abnormalities are frequently seen in RPL cases.
Material Method: In this case report, a female patient who applied to Erciyes University Medical Genetics Department with the indication of RPL was examined with a chromosome analysis for cytogenetic purposes and a thrombophilia panel for molecular genetics.
Result: As a result of the chromosome analysis, a balanced t(3;6)(q13.3;q27) translocation was detected in the female patient. As a result of the thrombophilia panel, it was determined that she had a homozygous mutation for MTHFR C677T and a heterozygous mutation for PAI-1 4G-5G Variant1. The female patient's father was examined in terms of family segregation and it was observed that her father also had a balanced t(3;6)(q13.3;q27) translocation.
Discussion: Balanced translocation is a type of chromosomal anomaly in which two chromosomes exchange parts but the total amount of genetic material remains the same. Balanced translocations are generally harmless to the carrier. This explains why a woman continues her life as a carrier even though a balanced translocation is transferred from the father to the affected individual. However, when the chromosomes are transferred to the child unbalanced, it can cause RPL. Thrombophilia, or a coagulation disorder, is also seen as one of the most important causes of recurrent miscarriages. It is seen that the genetic anomalies we detected in the patient explain the RPL clinic seen in the patient.
Conclusion: This case report shows the importance of examining the clinic thoroughly and conducting cytogenetic and molecular genetic studies together. Our study makes a new contribution to the literature by detecting the t(3;6)(q13.3;q27) translocation, which has not been reported in the literature.

OP60- From ICD Codes to Rare Disease Genetic Counselling

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Background
Timely genetic-counselling referral remains a bottleneck in diagnosing rare diseases. We asked whether a lightweight model derived solely from routinely entered ICD-10 codes could serve as an instant, high-precision triage tool at the moment a molecular test is ordered.
Methods
The dataset is from Erciyes University Hospitals Health Application and Research Center. Covering all genetic-test accessions at a tertiary pediatric hospital between January 2015 and August 2021 (N = 112 314) were linked to encounter-day M800-M899, D50-D89, C00-C97, U00-U49, Q80-Q99) who also had genetic procedure codes (681*), age and sex. A lasso-penalised logistic regression converted the full code universe (~70 000 strings) into a sparse indicator matrix. The penalty parameter was selected by five-fold cross-validation on 2015-2019 data and temporally validated on 2020-2021 encounters. The primary outcome was the presence of a rare-disease code (Q00–Q99 or D81–D89). Counselling impact was simulated by mapping alerts to existing referral slots.
Results
The lasso retained just 22 non-zero coefficients—18 positive and 4 negative. On the 17 321-encounter validation set the model achieved:
– AUROC = 0.9998 (95 % CI 0.9996–1.000)
– Sensitivity = 0.982, Specificity = 0.960
– Positive predictive value = 0.964, Negative predictive value = 0.998
Prospective implementation would trigger a median 1.8 alerts per clinic day, capturing 98 % of encounters that ultimately returned a pathogenic or likely-pathogenic result while increasing counsellor workload by only 4 %. Large positive weights mapped to primary immunodeficiencies (e.g. D84.9, $\beta = +11.3$) and congenital malformation syndromes (Q87.8, $\beta = +7.8$); acute leukaemia codes carried the strongest negative weights (C91.0, $\beta = -5.7$).
Conclusion
A transparent, 22-term ICD-10 rule transforms routine billing data into real-time counselling action, fast-tracking high-probability rare-disease cases without overwhelming limited genetics resources. External validation and a prospective implementation trial are warranted to confirm generalisability and patient-level benefit.
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