Presentation number: PP42 Abstract number: 9-ISABS-2026

PHYSICAL ACTIVITY AND IgG N-GLYCOMIC PROFILE: A CROSS-SECTIONAL STUDY AMONG MEDICAL STUDENTS

Vidović Stipe[1,2], Maduna Ivanka[1,7], Mešin Marko[1], Fančović Matko[3], Hanić Maja[3], Heffer Marija[1,4], Lauc Gordan[3], Zibar Lada[1,5,6]

[1]Faculty of Medicine Osijek, Josip Juraj Strossmayer University of Osijek, Osijek, Croatia; [2]Clinic for Eye Diseases, University Hospital Centre Osijek, Osijek, Croatia; [3]Genos Glycoscience Research Laboratory, Zagreb, Croatia; [4]Department of Medical Biology and Genetics, Faculty of Medicine Osijek, Josip Juraj Strossmayer University of Osijek, Osijek, Croatia; [5]Department of Pathophysiology, Faculty of Medicine Osijek, Josip Juraj Strossmayer University of Osijek, Osijek, Croatia; [6]Department of Nephrology, University Hospital Merkur, Zagreb, Croatia; [7]Health Center of Osijek-Baranja County, Osijek, Croatia

stipevidovic1@gmail.com

The aim of this study was to examine physical activity (PA) among medical students, to measure their IgG N-glycan composition and determine differences in the IgG N-glycan profile according to PA category, and to explore associations between specific types of PA and IgG N-glycan traits. This cross-sectional study was conducted in December 2023 among first- and second-year medical students at the University of Osijek, Croatia. PA was assessed using the International Physical Activity Questionnaire - Short Form (IPAQ-SF) questionnaire. IgG was isolated from plasma, and its N-glycan composition was analyzed by capillary gel electrophoresis (27 IgG N-glycan peaks, and eight derived glycan traits representing shared structural features). Results: A total of 79 students (23 males), median age 20 years (interquartile range 19 – 20), completed the questionnaire. According to the IPAQ-SF, 23 participants were classified as health-enhancing physical activity (HEPA)-active, while 56 were categorized as non–HEPA-active. After Benjamini–Hochberg false discovery rate (FDR) correction, no significant differences were found in IgG N- glycan peaks or traits between groups. Initial correlations were observed between vigorous PA and monogalactosylated glycan traits (G1) ($\rho = -0.24$, $P = 0.034$), total PA and digalactosylated glycan traits (G2) ($\rho = -0.31$, $P = 0.005$) and G1 ($\rho = 0.25$, $P = 0.024$), and walking and G2 ($\rho = -0.23$, $P = 0.046$), but none remained significant after FDR correction ($P \geq 0.218$). PA in medical students was not prevalent. No significant differences or associations between PA and the IgG N-glycan profile were identified after multiple testing correction in this young, homogeneous population. Larger longitudinal and interventional studies with objective PA assessment are needed. In this context, artificial intelligence–based multi-omics integration may help identify complex PA–IgG glycosylation interactions.

Keywords: glycomics, immunoglobulin G, medical students, N-glycans, physical activity

AI IN PRECISION ONCOLOGY

Presentation number: PP43 Abstract number: 18-ISABS-2026

CIRCULATING TUMOR DNA AND MULTIPARAMETRIC MRI BIOMARKERS FOR MONITORING RESPONSE TO STEREOTACTIC RADIOTHERAPY IN RENAL CELL CARCINOMA: A REVIEW OF EVIDENCE AND PERSPECTIVES

Bebek Marko[1], Katalinić Darko[2,3], Škrlec Ivana[2], Brlek Petar[3,4,5], Bulić Luka[3,4,6], Primorac Dragan[2,3,4,7,8,9,10,11,12,13,14]

[1]UPMC Hillman Cancer Center Hrvatska, Zabok, Bracak 8, Croatia; [2]Faculty of Dental Medicine and Health, Josip Juraj Strossmayer University of Osijek, Osijek, Croatia; [3]School of Medicine, Josip Juraj Strossmayer University of Osijek, Osijek, Croatia; [4]St. Catherine Specialty Hospital, Zagreb, Croatia; [5]Department of Molecular Biology, Faculty of Science, University of Zagreb, Zagreb, Croatia; [6]Algebra Bernays University, Zagreb, Croatia; [7]International Center for Applied Biological Research, Zagreb, Croatia; [8]Eberly College of Science, The Pennsylvania State University, State College, PA, United States of America; [9]School of Medicine, University of Split, Split, Croatia; [10]The Henry C. Lee College of Criminal Justice and Forensic Sciences, University of New Haven, New Haven, CT, United States of America; [11]Sana Kliniken Oberfranken, Coburg, Germany; [12]School of Medicine, University of Rijeka, Rijeka, Croatia; [13]School of Medicine, University of Pittsburgh, Pittsburgh, PA, United States of America; [14]Gandhinagar Campus, National Forensic Sciences University, Gandhinagar, India

bebekm@upmc.hr

This review synthesizes current evidence on circulating tumor DNA (ctDNA) and multiparametric MRI biomarkers (ADC, K^trans, perfusion/excretion parameters) for assessing response and monitoring patients with renal cell carcinoma (RCC) after stereotactic body radiotherapy (SBRT). It also highlights opportunities for integrating these biomarkers to enable earlier detection of progression, with emphasis on the limitations of existing literature, particularly for ctDNA, where data are heterogeneous and mostly derived from small or extrapolated cohorts. A systematic search of PubMed, EMBASE, and Web of Science identified studies evaluating ctDNA and MRI biomarkers in RCC after SBRT. Key aspects reviewed include ctDNA detection approaches (tumor informed vs. tumor agnostic), detectability and temporal association with imaging findings, correlations of diffusion and perfusion MRI parameters with volumetric response and clinical outcomes, and concepts for combining ctDNA and MRI signals in predictive models. Due to methodological variability and few studies evaluating both biomarker types concurrently, a qualitative synthesis was performed. Ultrasensitive ctDNA assays detect molecular residual disease (MRD) in ~60% of oligometastatic RCC patients, predicting progression with a lead time of 13 to 14 weeks. DCE MRI parameters show strong correlations with volumetric response at 12–24 months, while volumetry outperforms RECIST and transient enlargement occurs in ~20% of cases. Integrating ctDNA and MRI biomarkers improves prognostic accuracy: serial ctDNA negativity with favorable MRI parameters identifies low risk patients, whereas persistent ctDNA positivity indicates need for earlier intervention. Combined ctDNA–MRI assessment represents a promising strategy for personalized post SBRT monitoring, though prospective studies are needed to standardize integration protocols and define robust biomarker thresholds.

Keywords: precision oncology, multiparametric MRI, circulating tumor DNA, stereotactic radiotherapy, renal cell carcinoma

Presentation number: PP44 Abstract number: 14-ISABS-2026

CLINICAL UTILITY OF TUMOR MOLECULAR PROFILING IN BILATERAL CLEAR CELL RENAL CELL CARCINOMA

Čačija Dominik[1], **Ćuk Roko**[1], Brenner Eva[2], Bulić Luka[2,3,4], Brlek Petar[2,3,5], Primorac Dragan[2,3,6,7,8,9,10,11,12,13,14]

[1]School of Medicine, University of Zagreb, Zagreb, Croatia; [2]St. Catherine Specialty Hospital, Zagreb, Croatia; [3]School of Medicine, Josip Juraj Strossmayer University of Osijek, Osijek, Croatia; [4]Algebra Bernays University, Zagreb, Croatia; [5]Department of Molecular Biology, Faculty of Science, University of Zagreb, Zagreb, Croatia; [6]International Center for Applied Biological Research, Zagreb, Croatia; [7]Faculty of Dental Medicine and Health, Josip Juraj Strossmayer University of Osijek, Osijek, Croatia; [8]Eberly College of Science, The Pennsylvania State University, State College, PA, United States of America; [9]School of Medicine, University of Split, Split, Croatia; [10]The Henry C. Lee College of Criminal Justice and Forensic Sciences, University of New Haven, New Haven, CT, United States of America; [11]Sana Kliniken Oberfranken, Coburg, Germany; [12]School of Medicine, University of Rijeka, Rijeka, Croatia; [13]School of Medicine, University of Pittsburgh, Pittsburgh, PA, United States of America; [14]Gandhinagar Campus, National Forensic Sciences University, Gandhinagar, India

dominik.cacija@gmail.com; rokocuk2411@gmail.com

The Von Hippel-Lindau (VHL) protein is an E3 ligase that functions as a tumor suppressor, clinically associated with clear-cell renal cell carcinoma (ccRCC). Loss of VHL function leads to activation of hypoxia-inducible transcription factors (HIF), which can promote tumorigenesis. Inactivation of the *VHL* gene, located on chromosome 3p25, is the most common abnormality in ccRCC. This case report aims to highlight the importance of tumor molecular profiling in identifying actionable mutations and enabling the initiation of targeted therapy in patients with ccRCC. We present a 51-year-old male patient with bilateral ccRCC detected during routine ultrasound examination. Imaging revealed a mass in the upper pole of the left kidney measuring 27 x 26 x 22 mm and a smaller mass of 12 mm in the upper pole of the right kidney. MSCT confirmed hypervascular lesions suspicious of RCC. The patient underwent surgical resection of the left renal tumor and histopathological examination confirmed ccRCC. Tumor molecular profiling was subsequently performed using next-generation sequencing to identify potential actionable genomic alterations. Tumor molecular profiling identified a pathogenic *VHL G144** mutation, with a variant allele frequency of 30.03%. Copy number analysis additionally revealed 3p and 3q chromosome deletions. The identified alteration represents a potential therapeutic target, as inhibitors targeting vascular endothelial growth factor receptors and HIF proteins may be efficient in treating tumors with *VHL* alterations. Belzutifan is a HIF-2 alpha inhibitor approved for the treatment of adult patients with ccRCC associated with *VHL* mutation, which could therefore be considered as a potential therapeutic option in this case. This case highlights the clinical value of tumor molecular profiling in RCC. Identification of actionable mutations can facilitate personalized treatment strategies and expand therapeutic options in patients with ccRCC.

Keywords: renal cell carcinoma, next-generation sequencing, targeted molecular therapy, Von Hippel- Lindau, precision oncology

Presentation number: PP45 Abstract number: 3-ISABS-2026

PROGRAMMABLE DNA ORIGAMI BIOSENSORS FOR RAPID MICRORNA-BASED CANCER BIOMARKER DETECTION IN PRECISION ONCOLOGY

Domljanovic Ivana[1], Kocabey Samet[1], Acuna Guillermo P.[1], Ruegg Curzio[1]

[1]University of Fribourg, Fribourg, Switzerland

ivana.domljanovic@unifr.ch

Rapid and accurate detection of cancer-associated biomarkers is essential for precision oncology, particularly for early detection, diagnosis, therapy monitoring, and relapse. Circulating microRNAs (miRNAs) are powerful liquid-biopsy biomarkers, but their clinical utility is limited by detection technologies that require amplification, centralized laboratories, and complex workflows.Therefore, there is a critical need for rapid, low-cost, and highly sensitive detection. We introduce a DNA-origami "book" biosensor that detects breast cancer–associated miRNAs in biological fluids. It features a reconfigurable DNA nanostructure that opens upon miRNA binding, producing an optical signal. Readouts based on FRET and fluorescence quenching rely on optimized donor–acceptor fluorophore pairs for robust, high–dynamic- range detection. To enhance sensitivity in biofluids, the lock mechanism was optimized using fluorine- modified bases and locked nucleic acids, while diethylene glycol improved stability and target accessibility. These features enable specific miRNA detection in buffer, human serum, and plasma. Using breast cancer–associated miR-21, we achieve detection limits of 0.69 pM in biofluids within 10 min. The platform is validated using plasma samples from primary and metastatic breast cancer patients and benchmarked against qPCR. Multiplexed detection is demonstrated by measuring miR-21 and miR-7a in plasma samples. In parallel, a qPCR-validated miRNA expression database from breast cancer patients is being developed to train artificial intelligence models for miRNA signature discovery. This AI-based framework identifies miRNA patterns linked to cancer subtype, stage, and metastasis, enabling data-driven patient stratification. The integration of DNA nanotechnology and AI establishes a new paradigm for precision oncology through rapid, amplification-free liquid biopsies, improving early detection, relapse prediction, therapy monitoring, and personalized care via tests.

Keywords: miRNA, DNA origami, AI, breast cancer, biosensing

Presentation number: PP46 Abstract number: 19-ISABS-2026

MOLECULAR CHARACTERIZATION OF COLON ADENOCARCINOMA USING WES/WTS TO GUIDE TARGETED TREATMENT STRATEGIES

Horvat Magda[1], Kovačić Jelena[1], Ivanović Tomislav[1], Bulić Luka[2,3,4], Brlek Petar[2,3,5], Primorac Dragan[2,3,6,7,8,9,10,11,12,13,14]

[1]School of Medicine, University of Zagreb, Zagreb, Croatia; [2]St. Catherine Specialty Hospital, Zagreb, Croatia; [3]School of Medicine, Josip Juraj Strossmayer University of Osijek, Osijek, Croatia; [4]Algebra Bernays University, Zagreb, Croatia; [5]Department of Molecular Biology, Faculty of Science, University of Zagreb, Zagreb, Croatia; [6]International Center for Applied Biological Research, Zagreb, Croatia; [7]Faculty of Dental Medicine and Health, Josip Juraj Strossmayer University of Osijek, Osijek, Croatia; [8]Eberly College of Science, The Pennsylvania State University, State College, University Park, Pennsylvania, PA, United States of America; [9]School of Medicine, University of Split, Split, Croatia; [10]The Henry C. Lee College of Criminal Justice and Forensic Sciences, University of New Haven, New Haven, CT, United States of America; [11]Sana Kliniken Oberfranken, Coburg, Germany; [12]School of Medicine, University of Rijeka, Rijeka, Croatia; [13]School of Medicine, University of Pittsburgh, Pittsburgh, PA, United States of America; [14]Gandhinagar Campus, National Forensic Sciences University, Gandhinagar, India

magdahorvat5@gmail.com

In the era of precision medicine, oncology is increasingly based on the understanding of molecular tumor traits, enabling the use of targeted therapies directed at specific genetic alterations. This is made possible by advances in medical genetics and next-generation sequencing (NGS). The aim of this abstract is to highlight the importance of tumor molecular profiling in order to enable effective targeted therapy with minimal adverse effects. A 60-year-old woman with a diagnosis of medium grade mucinous colon adenocarcinoma o(pT3N1b, G II), without extramural vascular invasion, presented to the St. Catherine Hospital for molecular tumor profiling. The analysis was performed using whole exome sequencing (WES) and whole transcriptome sequencing (WTS), taking into account 1190 clinically relevant genes linked to approved therapies. A *KRAS G13D* mutation was identified, which is associated with treatment options using MEK- or ERK-targeted inhibitors such as Binimetinib, Cobimetinib, and Trametinib. Additionally, sequencing identified a *PIK3CA E545K* mutation, which may respond to selective PI3K inhibitors. A third alteration was found in the tumor suppressor gene *FBXW7*. Several promising clinical studies support the use of the PKMYT1 inhibitor Lunresertib in combination with the ATR inhibitor Camonsertib in patients with *FBXW7*-mutated solid tumors. For the alterations detected in the *SMAD2* and *APC* genes, there were currently no FDA-approved therapies or NCCN-compendium-listed treatment options. In summary, close and effective collaboration between oncology and medical genetics holds the potential for targeted therapy application and improved treatment outcomes for patients with malignancies. Genetic counseling is crucial, as it places sequencing results into a clinical context and guides the selection of targeted therapy based on identified molecular alterations.

Keywords: colon adenocarcinoma, genetic counseling, gene expression profiling, molecular targeted therapy, precision oncology

Presentation number: PP47 Abstract number: 70-ISABS-2026

MULTI-MODAL GENOMIC PROFILING IN CANCER DIAGNOSTICS: INTEGRATING GERMLINE AND LIQUID BIOPSY FINDINGS IN OVARIAN CANCER

Hrvatin Nenad[1,2], Bulić Luka[2,3,4], Brlek Petar[2,3,5], Dulibić Mario[15], Primorac Dragan[2,3,6-14]

[1]Department of Genomic Medicine, University Hospital Centre Rijeka, Rijeka, Croatia; [2]St. Catherine Specialty Hospital, Zagreb, Croatia; [3]School of Medicine, Josip Juraj Strossmayer University of Osijek, Osijek, Croatia; [4]Algebra Bernays University, Zagreb, Croatia; [5]Department of Molecular Biology, Faculty of Science, University of Zagreb, Zagreb, Croatia; [6]International Center for Applied Biological Research, Zagreb, Croatia; [7]Faculty of Dental Medicine and Health, Josip Juraj Strossmayer University of Osijek, Osijek, Croatia; [8]Eberly College of Science, The Pennsylvania State University, State College, PA, United States of America; [9]School of Medicine, University of Split, Split, Croatia; [10]The Henry C. Lee College of Criminal Justice and Forensic Sciences, University of New Haven, New Haven, CT, United States of America; [11]Sana Kliniken Oberfranken, Coburg, Germany; [12]School of Medicine, University of Rijeka, Rijeka, Croatia; [13]School of Medicine, University of Pittsburgh, Pittsburgh, PA, United States of America; [14]Gandhinagar Campus, National Forensic Sciences University, Gandhinagar, India; [15]School of Medicine, University of Zagreb , Zagreb, Croatia

nenad.hrvatin@svkatarina.hr

Comprehensive genomic profiling is increasingly transforming the management of cancer. By integrating data from germline and somatic genomic profiles, physicians are offered a more complete understanding of tumor biology, enabling risk assessment and targeted treatment. We present the case of a 50-year-old female patient diagnosed with ovarian cancer who underwent a comprehensive genomic evaluation, including liquid biopsy, whole genome sequencing (WGS), as well as pharmacogenomic and nutrigenomic testing to support a personalized approach to care. Initial liquid biopsy identified two pathogenic variants: a frameshift variant in the *BRCA1* gene (c.1938_1947del; p.Ser646ArgfsTer2) with a variant allele frequency (VAF) of 45.30%, and a splice-site variant in the *RB1* gene (c.607+1G>C, VAF 2.27%). The *BRCA1* alteration is associated with homologous recombination deficiency and has therapeutic implications, including eligibility for PARP inhibitor therapy. Subsequent germline WGS analysis from peripheral blood, targeting hereditary cancer, cardiometabolic, and carrier screening panels confirmed the presence of a heterozygous pathogenic *BRCA1* variant, despite variable representation in circulating tumor DNA. Additional findings included carrier status for pathogenic variants in the *SBDS, MYO7A, UGT1A1* and *HFE* genes, as well as a likely pathogenic variant in the *HAVCR2* gene. This case underscores the clinical value of combining liquid biopsy with germline WGS to distinguish somatic versus inherited variants and to refine risk assessment. Furthermore, integration of pharmacogenetic and nutrigenetic profiling enabled a personalized approach to patient management. Genetic counseling and targeted therapeutic recommendations, including consideration of PARP inhibitors, were provided based on the comprehensive genomic findings.

Keywords: ovarian cancer, *BRCA1* gene, liquid biopsy, whole-genome sequencing, precision oncology

Presentation number: PP48 Abstract number: 20-ISABS-2026

SMARCB1 LOSS GUIDES TARGETED THERAPY IN PEDIATRIC DEDIFFERENTIATED CHORDOMA

Ivanović Tomislav[1], Horvat Magda[1], Kovačić Jelena[1], Bulić Luka[2,3,4], Brlek Petar[2,3,5], Primorac Dragan[2,3,6,7,8,9,10,11,12,13,14]

[1]School of Medicine, University of Zagreb, Zagreb, Croatia; [2]St. Catherine Specialty Hospital, Zagreb, Croatia; [3]School of Medicine, Josip Juraj Strossmayer University of Osijek, Osijek, Croatia; [4]Algebra Bernays University, Zagreb, Croatia; [5]Department of Molecular Biology, Faculty of Science, University of Zagreb, Zagreb, Croatia; [6]International Center for Applied Biological Research, Zagreb, Croatia; [7]Faculty of Dental Medicine and Health, Josip Juraj Strossmayer University of Osijek, Osijek, Croatia; [8]Eberly College of Science, The Pennsylvania State University, State College, PA, United States of America; [9]School of Medicine, University of Split, Split, Croatia; [10]The Henry C. Lee College of Criminal Justice and Forensic Sciences, University of New Haven, New Haven, CT, United States of America; [11]Sana Kliniken Oberfranken, Coburg, Germany; [12]School of Medicine, University of Rijeka, Rijeka, Croatia; [13]School of Medicine, University of Pittsburgh, Pittsburgh, PA, United States of America; [14]Gandhinagar Campus, National Forensic Sciences University, Gandhinagar, India

tomislavivanovic2@gmail.com

Chordoma is a rare primary malignant bone tumor of the axial skeleton that arises from remnants of the fetal notochord. The World Health Organization (WHO) classifies chordomas into three subtypes: conventional, dedifferentiated, and poorly differentiated, which all differ in histopathology and prognosis. A six-year-old girl diagnosed with dedifferentiated chordoma was referred for molecular tumor profiling to identify potential mutations for targeted therapy. She initially presented to her physician with persistent coccygeal pain following trauma that occurred five months earlier. A comprehensive diagnostic workup was performed, including ultrasound, magnetic resonance imaging, and biopsy. Biopsy confirmed the diagnosis of chordoma and showed both dedifferentiated and conventional components. The disease was classified as stage IV with suspected pulmonary metastases. Molecular analysis showed low tumor mutational burden, a *TERT* promoter mutation (c.-124C>T), and a *SMARCB1* deletion (exons 1–7). The tumor was *BRAF* wild-type, microsatellite stable, and negative for homologous recombination deficiency signature (HRDsig). Although no standard actionable genomic alterations were identified, the *SMARCB1* loss suggested potential sensitivity to EZH2 inhibition. Based on these findings, a multidisciplinary tumor board recommended surgical resection followed by adjuvant radiotherapy, with evaluation of pulmonary lesions. In parallel, systemic therapy with an EZH2 inhibitor was proposed as a targeted approach informed by the molecular profile. This case demonstrates that molecular tumor profiling can uncover biologically actionable vulnerabilities even in the absence of canonical targetable mutations. Specifically, *SMARCB1* deletion may serve as a predictive biomarker for EZH2 inhibition, highlighting the clinical value of comprehensive genomic profiling in guiding precision oncology strategies for rare pediatric tumors.

Keywords: chordoma, EZH2, molecular profiling, precision oncology, *SMARCB1*

Presentation number: PP49 Abstract number: 13-ISABS-2026

PCDH9 EXPRESSION AND PROGNOSTIC SIGNIFICANCE IN CLEAR CELL RENAL CELL CARCINOMA

Kelam Nela[1,3], Smoljo Lara[1], Mateljak Tonka[1], Racetin Anita[1,3], Todorović Petar[1,3], Bajt Patricija[1,3], Pavlović Nikola[1,3], Rakić Tomislav[1,3], Vukojević Katarina[1,2,3], Komić Jelena[5], Komić Luka[5], Đolonga Petar[4], Grubišić Danijel Antonio[4], Mardešić Snježana[1,3], Kostić Sandra[1,3]

[1]Department of Anatomy, Histology and Embryology, University of Split School of Medicine, Split, Croatia; [2]Mediterranean Institute for Life Sciences, Split, Croatia; [3]Center for Translational Research in Biomedicine, School of Medicine, University of Split, Split, Croatia, Split, Croatia; [4]Department of Pathology, Forensic Medicine and Cytology, University Hospital of Split, Split, Croatia; [5]Department of Family Medicine, Split-Dalmatia County Health Center, Split, Croatia

nelakelam6@gmail.com

Clear cell renal cell carcinoma (ccRCC) is the most prevalent subtype of renal cancer, frequently diagnosed at advanced stages and associated with poor prognosis. Protocadherin 9 (PCDH9) is an emerging tumor suppressor increasingly recognized across multiple malignancies, yet its role in ccRCC and its relationship with epithelial-mesenchymal transition (EMT) remain poorly characterized. This study aimed to investigate PCDH9 expression, its co-regulation with epithelial adhesion molecules, and its prognostic significance in ccRCC. Immunofluorescence analysis was performed on FFPE tissue sections from 48 ccRCC patients (31 low-grade, 17 high-grade) and adjacent normal renal cortex, and findings were validated using the TCGA-KIRC dataset via GEPIA2/GEPIA3. PCDH9 mRNA was significantly downregulated in ccRCC tumors compared to normal kidney tissue. At the protein level, a strong trend toward reduced PCDH9 immunoexpression was observed in tumor tissue. A strong positive correlation between PCDH9 and CDH1 (E-cadherin) present in normal kidney was completely lost in ccRCC, indicating disruption of epithelial adhesion molecule co-regulation during tumorigenesis. PCDH9 downregulation may be mechanistically linked to VHL inactivation, which occurs in the majority of sporadic ccRCC cases. Unexpectedly, PCDH9 showed positive correlations with EMT-inducing transcription factors in tumor tissue, supporting a partial rather than classical EMT phenotype in ccRCC. In univariate survival analysis, high PCDH9 expression was significantly associated with improved overall survival, though this association was lost in multivariate analysis, likely reflecting its co-regulation with β-catenin. These findings collectively support a tumor-suppressive role for PCDH9 in ccRCC and suggest its potential utility as a prognostic biomarker, warranting further functional and prospective clinical validation.

Keywords: PCDH9, ccRCC, EMT, prognostic biomarker, clear cell renal cell carcinoma

Presentation number: PP50 Abstract number: 12-ISABS-2026

MOLECULAR PROFILING IN ENDOMETRIAL SARCOMAS: IDENTIFYING POTENTIAL THERAPEUTIC TARGETS

Skejić Lucija[1], Krišto Anđela[1], Bulić Luka[2,3,4], Brlek Petar[2,3,5], Primorac Dragan[1,2,3,6,7,8,9,10,11,12,13]

[1]University of Split, School of Medicine, Split, Croatia; [2]St. Catherine Specialty Hospital, Zagreb, Croatia; [3]School of Medicine, Josip Juraj Strossmayer University of Osijek, Osijek, Croatia; [4]Algebra Bernays University, Zagreb, Croatia; [5]Department of Molecular Biology, Faculty of Science, University of Zagreb, Zagreb, Croatia; [6]International Center for Applied Biological Research, Zagreb, Croatia; [7]Faculty of Dental Medicine and Health, Josip Juraj Strossmayer University of Osijek, Osijek, Croatia; [8]Gandhinagar Campus, National Forensic Sciences University, Gandhinagar, India; [9]Eberly College of Science, The Pennsylvania State University, State College, United States of America; [10]The Henry C. Lee College of Criminal Justice and Forensic Sciences, University of New Haven, New Haven, United States of America; [11]Sana Kliniken Oberfranken, Coburg, Germany; [12]School of Medicine, University of Rijeka, Rijeka, Croatia; [13]School of Medicine, University of Pittsburgh, Pittsburgh, United States of America

skejiclucija@gmail.com

Next-generation sequencing (NGS) is a modern technology for parallel DNA and RNA sequencing that enables detailed molecular profiling of malignant tumors. It provides key information for personalized therapy particularly in rare, aggressive tumors such as endometrial stromal sarcoma (ESS). We present the case of a 53-year-old woman who was diagnosed with high-grade ESS, confirmed by pathohistological findings after hysterectomy and bilateral adnexectomy. Chemotherapy included six cycles of the AI protocol but PET/CT demonstrated progression so second-line treatment with trabectedin via an elastomeric pump was initiated. Tumor genetic profiling using NGS was performed (whole exome and whole transcriptome sequencing), which revealed an oncogenic variant in the *PTEN* gene (c.402_404del, p.Met-134del), a homozygous deletion of *CDKN2A/B*, and *ZC3H7B::BCOR* gene fusion. Considering that chemotherapy/radiotherapy do not demonstrate improved survival rates and overall survival ranging 9-24 months, a new approach is needed. Although therapies targeting *PTEN* mutations are approved in breast cancer, their applicability in ESS is unknown. Laboratory data suggest that beta isoform-selective PI3K/mTOR inhibitors may be effective against *PTEN*-mutant ESS. Considering BCOR fusions have been identified in ESS and BCOR is involved in epigenetic regulation, it is possible that epigenetic inhibitors (EZH2/HDAC inhibitors) could be a therapeutic option but there is no clinical evidence to support this. *CDKN2A* deletion is common and cells harboring this deletion could potentially be sensitive to CDK4/6 inhibitors (palbociclib/ribociclib/abemaciclib). We highlight the importance of tumor molecular profiling and precision oncology, especially in patients diagnosed with aggressive tumors with high mortality. With the relevant genetic mutations known, future research should focus on exploring potential therapies to address the gap in clinical evidence for targeted therapy application.

Keywords: tumor molecular profiling, high-grade endometrial stromal sarcoma, next-generation sequencing, precision oncology, targeted tumor therapy

Presentation number: PP51 Abstract number: 74-ISABS-2026

MOLECULAR PROFILING IDENTIFIES TARGETABLE *CHEK2* MUTATION IN A METACHRONOUS DUCTAL CARCINOMA IN SITU

Škoprc Tonia[1], Žaja Sara[1], Bulić Luka[2,3,4], Brlek Petar[2,3,5], Primorac Dragan[1,2,3,6,7,8,9,10,11,12,13]

[1]University of Split School of Medicine, Split, Croatia; [2]St. Catherine Specialty Hospital, Zagreb, Croatia; [3]School of Medicine, Josip Juraj Strossmayer University of Osijek, Osijek, Croatia; [4]Algebra Bernays University, Zagreb, Croatia; [5]Department of Molecular Biology, Faculty of Science, University of Zagreb, Zagreb, Croatia; [6]International Center for Applied Biological Research, Zagreb, Croatia; [7]Faculty of Dental Medicine and Health, Josip Juraj Strossmayer University of Osijek, Osijek, Croatia; [8]Eberly College of Science, The Pennsylvania State University, State College, PA, USA, State College, PA, United States of America; [9]The Henry C. Lee College of Criminal Justice and Forensic Sciences, University of New Haven, New Haven, CT, USA, New Haven, CT, United States of America; [10]Sana Kliniken Oberfranken, Coburg, Germany; [11]School of Medicine, University of Rijeka, Rijeka, Croatia; [12]School of Medicine, University of Pittsburgh, Pittsburgh, PA, USA, Pittsburgh, PA, United States of America; [13]Gandhinagar Campus, National Forensic Sciences University, Gandhinagar, India, Gandhinagar, India

toniaskoprc56@gmail.com

Ductal carcinoma in situ (DCIS) is the most common form of non-invasive breast cancer and is typically identified through mammographic screening programmes. Despite multiple therapeutic options, there is a significant over-treatment risk. Genomic profiling using next-generation sequencing (NGS) has become increasingly utilized in clinical oncology, detecting target mutations and creating personalized treatment strategies. We present a case of a 53-year-old woman diagnosed with DCIS in her right breast. The patient underwent skin-sparing mastectomy followed by endocrine therapy (ET) (tamoxifen, letrozole, exemestane and anastrozole). Three years after her initial diagnosis, she underwent prophylactic contralateral skin- and nipple-sparing mastectomy with histopathological examination identifying subsequent DCIS. Due to metachronous disease, molecular profiling using next- generation sequencing (Illumina NovaSeq/NextSeq platform) was performed, enabling the detection of key solid tumor genetic variants. Profiling identified a likely pathogenic mutation in the *CHEK2* gene, a checkpoint kinase responsible for DNA repair. This finding provided biological justification for the use of olaparib or talazoparib, PARP inhibitors currently indicated as targeted therapy in other malignancies. This case highlights the potential for expanding therapeutic strategies in DCIS treatment, suggesting possible wider implementation of personalized medicine through genomic profiling in clinical decision-making.

Keywords: ductal carcinoma in situ, next-generation sequencing (NGS), *CHEK2* mutation, personalized oncology, PARP inhibitors

Presentation number: PP52 Abstract number: 85-ISABS-2026

USING DEEP LEARNING TO PREDICT DUSP1 EXPRESSION DYNAMICS IN GEFITINIB-SENSITIVE AND -RESISTANT LUNG CANCER CELLS: TOWARD PRECISION ONCOLOGY

Vitlov Nina[1]

[1]School of Medicine, University of Split, Split, Croatia

nina.vitlov7@gmail.com

The goal of this study was to investigate dynamic gene expression patterns of DUSP1, a stress response gene implicated in drug resistance, in gefitinib-sensitive PC9 and gefitinib-resistant PC9GRM2 lung cancer cells and to evaluate deep learning models for predicting temporal expression trends. The data were obtained from the Gene Expression Omnibus (GSE34228), focusing on cells treated with Epidermal Growth Factor (EGF) and a combination of EGF and an EGFR inhibitor (IRS) over 24 hours. Data for DUSP1 were extracted and filtered to create subsets for specific cell line and treatment conditions (PC9 + EGF, PC9 + EGF + IRS, PC9GRM2 + EGF, PC9GRM2 + EGF + IRS). Two models were compared: Long Short-Term Memory (LSTM) network with an input window of 8 and a Transformer with an input window of 20, optimized on the volatile PC9_EGF_IRS dataset. Hyperparameter tuning showed that the optimal Transformer configuration used a learning rate of 0.001 and four attention heads. Data were split 80/20 for training and testing. Results showed that sensitive PC9 cells exhibited more dynamic and volatile DUSP1 expression than resistant PC9GRM2 cells, suggesting distinct cellular responses. Combined EGF+IRS treatment induced sharper fluctuations than EGF alone. LSTM models captured general trends, but struggled with sharp peaks, showing overfitting in volatile PC9 datasets. The tuned Transformer provided smoother and more accurate predictions while still struggling with the timing and magnitude of sharp DUSP1 changes, reflecting biological complexity. On less variable PC9GRM2 data, both models performed comparably. In conclusion, our ability to predict DUSP1 expression dynamics, even with some limitations, represents a meaningful step toward applying gene expression trajectories as predictive tools. DUSP1 not only reflects cellular states under treatment and resistance, but also shows promise as a biomarker for anticipating therapeutic response in precision oncology.

Keywords: DUSP1, lung cancer, gefitinib resistance, deep learning, precision oncology

Presentation number: PP53 Abstract number: 73-ISABS-2026

MOLECULAR PROFILING IDENTIFIES ACTIONABLE *PTEN* MUTATION IN RECURRENT UTERINE LEIOMYOSARCOMA: A CASE REPORT SUPPORTING TARGETED THERAPY APPROACH

Žaja Sara[1], Škoprc Tonia[1], Bulić Luka[2,3,4], Brlek Petar[2,3,5], Primorac Dragan[2,3,6,7,8,1,9,10,11,12,13]

[1]School of Medicine, University of Split, Split, Croatia; [2]St. Catherine Specialty Hospital, Zagreb, Croatia; [3]School of Medicine, Josip Juraj Strossmayer University of Osijek, Osijek, Croatia; [4]Algebra Bernays University, Zagreb, Croatia; [5]Department of Molecular Biology, Faculty of Science, University of Zagreb, Zagreb, Croatia; [6]International Center for Applied Biological Research , Zagreb, Croatia; [7]Faculty of Dental Medicine and Health, Josip Juraj Strossmayer University of Osijek , Osijek, Croatia; [8]Eberly College of Science, The Pennsylvania State University, State College, University Park, PA, United States of America; [9]The Henry C. Lee College of Criminal Justice and Forensic Sciences, University of New Haven, New Haven, CT, United States of America; [10]Sana Kliniken Oberfranken, Coburg, Germany; [11]School of Medicine, University of Rijeka, Rijeka, Croatia; [12]School of Medicine, University of Pittsburgh, Pittsburgh, PA, United States of America; [13]Gandhinagar Campus, National Forensic Sciences University, Gandhinagar, India

sara01zaja@gmail.com

Uterine leiomyosarcoma is a rare and highly aggressive malignancy with limited treatment options in the recurrent setting. Comprehensive genomic profiling using next-generation sequencing (NGS) is increasingly used to identify actionable mutations and guide precision oncology. We present a 47-year-old female patient diagnosed with uterine leiomyosarcoma (FIGO stage IC) in October 2022. The patient underwent multiple surgical procedures, including myomectomy followed by hysterectomy with bilateral adnexectomy and repeated cytoreductive surgeries due to recurrent disease. Systemic treatment included adjuvant chemotherapy (AI protocol), gemcitabine due to hypersensitivity to docetaxel, and subsequent targeted therapy with pazopanib. Despite treatment, the disease progressed with a pelvic recurrence measuring 29 × 29 × 37 mm. Due to further progression, molecular profiling was performed using hybrid- capture-based NGS (Illumina NovaSeq platform), enabling simultaneous DNA and RNA analysis from metastatic tissue. Molecular profiling results identified a pathogenic mutation in the *PTEN* gene, a key regulator of the PI3K/AKT signaling pathway. This finding provided a biologically rational therapeutic option using targeted therapy with the AKT inhibitor capivasertib in combination with fulvestrant. This case demonstrates the clinical value of repeat molecular profiling in advanced uterine leiomyosarcoma. Genomic analysis may significantly influence treatment decisions and represents an important step toward precision oncology in rare gynecologic malignancies.

Keywords: uterine leiomyosarcoma, next-generation sequencing (NGS), *PTEN* gene mutation, precision oncology, capivasertib therapy

AI IN DRUG DISCOVERY AND DEVELOPMENT