

THE ANNUAL PATHOLOGY CONFERENCE OF THE `VICTOR BABEŞ` INSTITUTE BUCHAREST



November 12 – 14, 2025

Splaiul Independenței 99-101, Bucharest, România



ANNUAL CONFERENCE OF THE VICTOR BABES NATIONAL INSTITUTE OF PATHOLOGY
BUCHAREST, ROMANIA
12-14 NOVEMBER, 2025

PROGRAM ȘTIINȚIFIC

Miercuri 12 noiembrie 2025 / Wednesday, 12 November 2025 Amfiteatrul Victor Babeș	
09:00-09:45	Înregistrare
09:45-10:00	Deschidere
10:00-11:00	Sesiunea 1: Institutul Victor Babeș - Noutăți (Amf. Mare) Moderator: Mihail Eugen Hinescu <ul style="list-style-type: none">- Mihaela Gherghiceanu – Patologie Ultrastructurală- Laura Ceafalan – Biologie Celulară, Neuroștiințe și Miologie Experimentală- Sorina Papuc – Genetică Medicală- Andrei Niculae - Histopatologie și Imunohistochimie- Monica Neagu - Imunologie- Elena Codrici – Biochimie și Proteomică- Gina Manda - Radiobiologie- Gina Isvoranu – Biobază și modele experimentale
11:00-11:15	Pauză de cafea
11:15-13.30	Sesiunea 2: Noi tehnici de cercetare și diagnostic Moderator: Ana Maria Enciu, Mihaela Gherghiceanu <ul style="list-style-type: none">- Redefinirea imagisticii 2D/3D: noul microscop electronic 120kV / Redefining 2D/3D imaging: Introducing new 120kV TEM. Diego Cordero, Business Development Manager Thermo Fisher Scientific, Ronexprim- Puterea PCR-ului digital – avansarea științei, salvarea de vieți / The power of Digital PCR– advancing science, saving lives. Alexandra Livescu, Dialab Solutions- Dezvoltarea de bio/imunosenzori cu aplicații în diagnosticul uman în cadrul DDS Diagnostic / Development of bio/immunosensors with applications in human diagnostics within DDS Diagnostic. Dana Stan, DDS Diagnostics- Sinergie pentru succes: Conectarea institutelor naționale de cercetare cu mediul economic/Synergy for success: Linking national research institutes with economic agents. Justinian-Andrei Tomescu – Hofigal S.A- GeneTrustChain – Platformă securizată de analiză și partajare a datelor genetice / GeneTrustChain – Secure Genetic Data Analysis and Sharing Platform. Mihai Butolo, MBM Software- De la anticorpi himeric la SignalStar TM: Soulile inovatoare ale CST pentru biologie spațială / From Chimeric Antibodies to SignalStarTM: CST's Innovative Solutions for Spatial Biology, Flora Guarnotta, Cell Signaling Technology, Biomedica Medizinprodukte Romania
13:30-14:30	Pauză de masă
14:30-15:30	Workshop PNRR-CNCC – Patologie Digitală & AI Moderator: Laura Cristina Ceafalan, Mihaela Gherghiceanu <ul style="list-style-type: none">- Patologia computațională- de la concept la practica clinică/ Computational pathology – from concept to clinical use. Filip Mureșan, UMF Carol Davila București



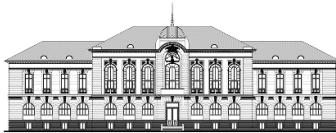
ANNUAL CONFERENCE OF THE VICTOR BABES NATIONAL INSTITUTE OF PATHOLOGY
BUCHAREST, ROMANIA
12-14 NOVEMBER, 2025

Miercuri 12 noiembrie 2025 / Wednesday, 12 November 2025
Amfiteatrul Victor Babeș

	<ul style="list-style-type: none">- Provocări în implementarea pe scară largă a inteligenței artificiale în histopatologia digitală / Challenges in large scale deployment of AI for digital histopathology. <i>Mihai Trăscău</i>, Universitatea Politehnica din București- Identificarea automată bazată pe inteligența artificială a factorilor de prognostic morfologic în carcinomul urotelial / Artificial intelligence-based automatic identification of morphological prognostic factors in urothelial carcinoma. <i>Sabina Zurac</i>, Spitalul Clinic Universitar Colentina, București- Diagnosticul histopatologic convențional și asistat de AI în cancerul colorectal/ Conventional and AI-assisted histopathological diagnosis in colorectal cancer. <i>Vlad Herlea</i>, Institutul Clinic Fundeni, București <p>Discuții libere</p>
15:30-16:00	Pauză de cafea
16:00-18:00	<p>Sesiunea 3: Nefropatologie</p> <p>Moderator: Mihaela Gherghiceanu</p> <ul style="list-style-type: none">- Spectrul diagnosticului histopatologic în biopsiile de grefă renală: analiza preliminară a datelor din Centrul de Transplant Renal I.C. Fundeni / Spectrum of histopathological diagnosis in renal graft biopsies: preliminary data from Fundeni Clinical Institute. <i>Bogdan Sorohan</i> - Institutul Clinic Fundeni București- Capilarita peritubulară nu înseamnă întotdeauna rejet: prezentare de caz / Peritubular capillaritis doesn't always mean rejection: case report. <i>George Terinte-Balcan</i> - Hôpital Universitaire Necker, Paris, France- Nefrologie pediatrică – prezentare de caz / Case report – pediatric nephrology. <i>George Claudiu Costea</i>. Institutul Clinic Fundeni București- Experiența Institutului Clinic Fundeni în managementul nefritei lupice./ The experience of Fundeni Clinical Institute in lupus nephritis management. <i>Bogdan Obrișă</i>. Institutul Clinic Fundeni București- Inflamația ascunsă: de ce contează încă biopsia renală în nefrita lupică silentioasă / Hidden Inflammation: Why Renal Biopsy Still Matters in Pediatric Silent Lupus Nephritis. <i>Adrian Cătălin Lungu</i>. Institutul Clinic Fundeni București- Imunofluorescența ca tehnică rapidă de diagnostic pentru personalizarea terapiei în bolile glomerulare / Immunofluorescence as a rapid diagnostic technique for personalizing therapy in glomerular diseases. <i>Mihaela Gherghiceanu</i>, Institutul Victor Babeș, București
17:30-19:30	<p>Sesiune de postere:</p> <p>Chairs: Ana-Maria Enciu, Emanuel Tudor Fertig</p>

Joi 13, noiembrie 2025 / Thursday, 13 November 2025
Amfiteatrul Ioan Morar

09:30-11:15	<p>Sesiunea 4: Modele <i>in vitro</i> pentru studiul mecanismelor patologice și medicină personalizată</p> <p>Moderator: Laura Cristina Ceafalan, Elena Codrici</p>
-------------	---

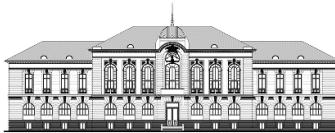


ANNUAL CONFERENCE OF THE VICTOR BABES NATIONAL INSTITUTE OF PATHOLOGY
BUCHAREST, ROMANIA
12-14 NOVEMBER, 2025

Joi 13, noiembrie 2025 / Thursday, 13 November 2025

Amfiteatrul Ioan Morar

	<ul style="list-style-type: none">- Modele neurale pentru instabilitatea genică / Neural models for diseases with gene instability, Roxana Deleanu, Institutul de Neuranatomie, Universitatea de medicina, Innsbruck- Evaluarea răspunsului la terapia punctelor de control imun cu ajutorul unor teste alternative inovatoare / Evaluating Immune Checkpoint Therapy Responses with Novel Alternative Assays, Mihaela Chivu Economescu, Institutul de Virusologie Ștefan Nicolau- A Complementary Strategy for TNBC: Herbal extract Plus NOS inhibitor Suppresses Survival Pathways and Promotes Apoptosis, Gayane Petrosyan, Research Institute of Biology, Yerevan, Armenia- Generarea unei linii celulare CD36 Knockout de cancer mamar / Generation of a CD36 Knockout Cell Line of Breast Cancer, Maria Dudău, Institutul Victor Babeș- Caracterizarea unui model de organoid vascular / Characterization of a vascular organoid model, Emanuel Tudor Fertig, Institutul Victor Babeș, UMF "Carol Davila"- Bioactivitatea extractelor de ulei din semințe presate la rece evaluată pe modele in vitro de celule hepatice / Bioactivity of cold press-seed oil extracts evaluated on in vitro models of hepatic cells, Sevinci Pop, Institutul Victor Babeș
11:15-11:30	Pauză de cafea
11:30-13:30	<p>Sesiunea 5: Cercetare biomedicală – scurte comunicări</p> <p>Moderator: Gina Manda, Gheorghita Isvoranu</p> <ul style="list-style-type: none">- Repoziționarea medicamentului aprobat de FDA ca modulator al inflamației induse de IL-1β / FDA approved drug repositioning as modulator of IL-1β-driven inflammation - Marioara Chiritoiu-Butnaru, Institute of Biochemistry of the Romanian Academy, Bucharest, Romania- Dezvoltarea de produse biologice de la nivel de laborator până la nivel pilot / Development of biological products from laboratory level to pilot area, Crina Stăvaru, „Cantacuzino” Medical Military National Research and Development Institute, Bucharest, Romania- Simptome psihiatrice in boala inflamatorie intestinală: rezultate preliminare asupra rolului microbiomului intestinal / Psychiatric symptoms in Inflammatory Bowel Diseases: preliminary results on the role of the gut microbiome. Elena Milanesi, „Victor Babeș” National Institute of Pathology, Bucharest, Romania- Progrese recente în diagnosticul și evaluarea prognostică a cancerului oral / Recent advances in the diagnosis and prognostic assessment of oral cancer, Costin Căruntu, UMF „Carol Davila”, Bucharest, Romania- Dezvăluirea mecanismelor epigenetice bazate pe metilarea histonei în ateroscleroză: noi oportunități pentru diagnostic, prognostic și tratament personalizat / Unveiling histone methylation-based epigenetic mechanisms in atherosclerosis: new opportunities for diagnosis, prognosis and personalized treatment, Adrian Manea, Institute of Cellular Biology and Pathology „Nicolae Simionescu”, Bucharest, Romania- Hypoxia-Linked Alterations in Arginine Metabolism and Oxidative Stress in the Bone Marrow during Breast Cancer Progression and Treatment, Hayarpi Javrushyan, Research Institute of Biology, Yerevan, Armenia



ANNUAL CONFERENCE OF THE VICTOR BABES NATIONAL INSTITUTE OF PATHOLOGY
BUCHAREST, ROMANIA
12-14 NOVEMBER, 2025

Joi 13, noiembrie 2025 / Thursday, 13 November 2025

Amfiteatrul Ioan Morar

	<ul style="list-style-type: none">- Confruntarea cu noi provocări în materie de sănătate legate de epuizarea stratului de ozon și expunerea crescută la UVB și raze cosmice secundare: perspective din cadrul proiectului BIOSPHERE. / Facing New Health Challenges Related to Ozone Depletion and Increased Exposure to UVB and Secondary Cosmic Rays: Insights from the BIOSPHERE Project. Gina Manda, „Victor Babeș” National Institute of Pathology, Bucharest, Romania- Efecte citotoxice induse de emisiile de radioizotopi de cupru în radioterapia țintită asupra cancerului de colon / Cytotoxic effects induced by copper radioisotopes emissions in colon cancer targeted radiotherapy, Radu Șerban, IFIN Horia Hulubei Magurele, Romania
13:30-14:30	Pauză de Masă
14:30-15.15	Raluca Nicoli , Previous Translational Biomedical Scientist at National Human Genome Research Institute, National Institutes of Health Bethesda, USA, RRUDWG GRDI, Romania; UDNI, Low- and Middle Income Countries Working Group Representative De la laborator la patul pacientului: accelerarea științei translatională în România prin studiul bolilor nediagnosticate / From Bench to Bedside: Accelerating Translational Science in Romania Through the Study of Undiagnosed Diseases.
15:15-16.00	Dr Maryna Panamarova – Wellcome Sanger Institute, UK Dezvoltarea și validarea testelor de înaltă performanță în modele 3D / High-throughput assay development and validation in 3D models.
16:00-16.15	Pauză de cafea
16:15-18:00	Sesiunea 6: Histopatologie Moderator: Gabriel Becheanu, Andrei Marian Niculae <ul style="list-style-type: none">- Testarea expresiei PD-L1 în cancerul pulmonar fără celule mici (NSCLC). Andrei M. Niculae, „Victor Babeș” National Institute of Pathology, Bucharest, Romania- Possible elemente patologice identificabile pe biopsiile colonice ale pacienților cu diaree cronică / What to expect on colonic biopsies from patients with chronic diarrhea. Florina Almarii, UMF „Carol Davila”, Bucharest, Romania
18:00-19:00	Discuții libere Cocktail (Biblioteca Institutului Victor Babeș) Concert: Andreea Robu & Bogdana Cocîrlea

Vineri, 14 noiembrie 2025 / Friday, 14 November 2025

Amfiteatrul Victor Babeș

09:00-13:00	Registration
13:00-13:20	Welcome Remarks Monica Neagu , President, SIR & Bojan Bolic , President, EFIS

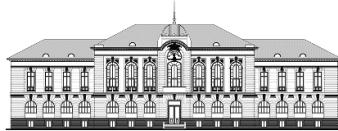


ANNUAL CONFERENCE OF THE VICTOR BABES NATIONAL INSTITUTE OF PATHOLOGY
BUCHAREST, ROMANIA
12-14 NOVEMBER, 2025

Vineri, 14 noiembrie 2025 / Friday, 14 November 2025
Amfiteatrul Victor Babeș

13:20 – 15:00	<p>Session 1 - Cancer and Molecular Immunology</p> <p>Moderator/Chair: Monica Neagu, Președinte Societatea Română de Imunologie, Institutul Victor Babeș, București; Bojan Bolic, University of Rijeka</p> <ul style="list-style-type: none">- MicroARN-uri și profilul celulelor imune: descoperirea de noi straturi ale imunobiologiei cancerului pulmonar / MicroRNAs and Immune Cell Profiling: Uncovering New Layers of Lung Cancer Immunobiology, Ioana Berindan-Neagoe, UMF Iuliu Hatieganu Cluj Napoca- Macrofage asociate lipidelor în cancer / Lipid-associated macrophages in cancer. Elena Timperi, Università Cattolica del Sacro Cuore- Investigarea impactului complexului ESCRT-0 asupra traficului, semnalizării și funcției receptorilor de imunoglobulină G / Investigating the impact of ESCRT-0 complex on traffic, signaling and function of Immunoglobulin G receptors, Elena Georgiana Dobre, bursier EFIS, Institutul Victor Babeș- Reglarea citotoxicității celulelor Natural Killer / Regulation of Natural Killer cell Cytotoxicity. Carsten Watzl, Dortmund University- Q&A session
15:00-15:30	Coffee Break
15:30-17:10	<p>Session 2 Immune Regulation, Infection and Clinical Immunology</p> <p>Chairs: Marieke van Ham, Sanquin, Carolina Constantin, "Victor Babes" National Institute of Pathology</p> <ul style="list-style-type: none">- Dinamica imunității umorale și celulară a SARS-CoV-2 la doi ani după vaccinare / Dynamics of SARS-CoV-2 Humoral and Cellular Immunity over Two Years post-vaccination. Carmen Diaconu, Institutul de Virologie „Ștefan S. Nicolau” București- Dezvoltarea vaccinurilor în Institutul Cantacuzino / Vaccine development in Cantacuzino Institute, Cătălin Tucureanu, INCD MM Cantacuzino, București- Innate lymphoid cells in asthma and atopic dermatitis Günnur Deniz, Istanbul University- Imunogenetica transplantului și nu numai / Immunogenetics of Transplantation and beyond, Ileana Constantinescu, UMF Carol Davila București <p>Q & A and Closing</p>

Ateliere de lucru	Data	Nr. locuri
Imunofluorescența pentru biopsiile renale / Immunofluorescence of Renal Biopsy Coordonator: Mihaela Gherghiceanu	Joi, 13 noiembrie 2025 14.00-18.00	5
Electroforeza proteinelor și western-blot / Protein electrophoresis and western blot hands-on Coordonator: Ana-Maria Enciu	Vineri, 14 noiembrie 2025 09.00-13.00	6



**ANNUAL CONFERENCE OF THE VICTOR BABES NATIONAL INSTITUTE OF PATHOLOGY
BUCHAREST, ROMANIA
12-14 NOVEMBER, 2025**

Tehnica PCR / hands-on PCR Coordonator: Gisela Găină	Vineri, 14 noiembrie 2025 9.00-13.00	6
--	---	----------

COMITET ȘTIINȚIFIC

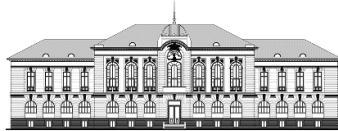
Președinte: Mihail Eugen Hinescu
Vice-Președinte: Mihaela Gherghiceanu

Membri:

Gabriel Becheanu
Laura Cristina Ceafalan
Elena Codrici
Carolina Constantin
Ana-Maria Enciu
Gheorghița Isvoranu
Gina Manda
Monica Neagu
Sorina Papuc
Bogdan O. Popescu
Cristiana Tănase

COMITET DE ORGANIZARE

Liliana Ionica Ion
Aurora Arghir
Tudor Emanuel Fertig
Andrei Niculai
Daniela-Ionela Popescu
Cezar Petrescu

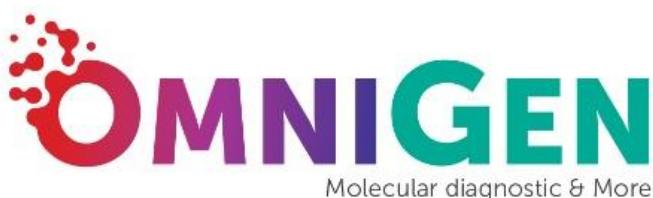


ANNUAL CONFERENCE OF THE VICTOR BABES NATIONAL INSTITUTE OF PATHOLOGY
BUCHAREST, ROMANIA
12-14 NOVEMBER, 2025

SPONSORS



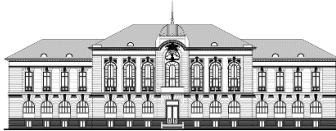
Dialab Solutions®



RONEXPRIM
WE DELIVER PERFORMANCE



 **MEDIST**
Delivering Trust



ANNUAL CONFERENCE OF THE VICTOR BABES NATIONAL INSTITUTE OF PATHOLOGY
BUCHAREST, ROMANIA
12-14 NOVEMBER, 2025

Plenary 1

Scaling Up Complex Organoid Models: Challenges and Solutions

Maryna Panamarova^{1*}, Chloe Admane², Hema Lingala¹, Amy Yeung¹ and Muzlifah Haniffa²

¹ *Cellular Operations, Wellcome Sanger Institute, Cambridge, United Kingdom*

² *Cellular Genomics, Wellcome Sanger Institute, Cambridge, United Kingdom*

*presenting author – correspondence: mp35@sanger.ac.uk

Keywords: Modelling approaches • Modelling complex organ tissues • Qualification & validation • Automation

Background

Despite rapid advances in developing complex organoid models that integrate multiple cell or organoid types, scalability and reproducibility remain major challenges. These limitations restrict the use of advanced organoid systems in clinical applications such as therapeutic screening and disease modelling.

Materials and methods

Vascularised, hair-bearing skin organoids supplemented with macrophages were used as a case study to investigate the challenges associated with scaling complex disease models.

Results

Through iterative optimisation of differentiation workflows, automation of culture steps, and implementation of quantitative quality control, we developed strategies to improve reproducibility and throughput of vascularised skin organoids that mimic the complexity of human skin.

Conclusions

These findings highlight common bottlenecks in scaling advanced organoid systems and demonstrate practical solutions that can be applied to other complex cellular models to enhance consistency and scalability.

Acknowledgements: Cameron Collins and Amelia Potter

References

1. Lee, J., Rabbani, C.C., Gao, H. et al. Hair-bearing human skin generated entirely from pluripotent stem cells. *Nature* 582, 399–404 (2020). <https://doi.org/10.1038/s41586-020-2352-3>
2. Lee, J., van der Valk, W.H., Serdy, S.A. et al. Generation and characterization of hair-bearing skin organoids from human pluripotent stem cells. *Nat Protoc* 17, 1266–1305 (2022). <https://doi.org/10.1038/s41596-022-00681-y>
3. Gopee, N.H., Winheim, E., Olabi, B. et al. A prenatal skin atlas reveals immune regulation of human skin morphogenesis. *Nature* 635, 679–689 (2024). <https://doi.org/10.1038/s41586-024-08002-x>



ANNUAL CONFERENCE OF THE VICTOR BABES NATIONAL INSTITUTE OF PATHOLOGY
BUCHAREST, ROMANIA
12-14 NOVEMBER, 2025

Plenary 2

**From Bench to Bedside: Accelerating Translational Science in Romania
Through the Study of Undiagnosed Diseases**

Elena-Raluca Nicoli^{1,2,3,*}, **Dana-Cristina Craiu**^{1,2,4}, **Madalina-Doina Antonescu**^{1,2}, **Corina-Silvia Pop**^{1,2,3}, **Ruxandra Oana Jurcut**^{1,2,5}, **Horia Bumbea**^{1,2,3}, **Diana Barca**^{1,2,4}, **Ana-Maria Enciu**¹, **Vlad Buica**^{1,2}, **George Pescaru**^{1,2,4}, **Dragoș-Claudiu Popescu**^{1,3}, **Anisia-Cristiana Vasiliniuc**^{1,2}, **Patricia Maria Perdun**¹, **Octavian Bucur**^{1,2}

¹*Carol Davila University of Medicine and Pharmacy, Bucharest, Romania;*

²*Genomics Research and Development Institute, Bucharest, Romania;*

³*Emergency University Hospital Bucharest, Carol Davila University of Medicine and Pharmacy, Bucharest, Romania;*

⁴*Center of Expertise of Rare Pediatric Neurological Disorders Obregia Clinical Hospital, Bucharest, Romania;*

⁵*Prof. Dr. C. C. Iliescu Emergency Institute for Cardiovascular Diseases, Bucharest, Romania;*

*Elena-Raluca Nicoli – raluca.nicoli@umfcd.ro

Keywords: undiagnosed diseases, translational science, genomics, Romania, rare disease, precision medicine

Undiagnosed diseases remain one of the most challenging areas in modern medicine, often revealing the limits of current diagnostic frameworks while offering opportunities for discovery. Advances in genomic sequencing and molecular diagnostics have opened new paths for identifying the underlying causes of complex and rare disorders, yet the translation of these findings into clinical care requires coordinated efforts across research and healthcare systems. In Romania, initiatives focused on undiagnosed diseases are helping to bridge this gap, fostering collaboration between clinicians, geneticists, and researchers to move discoveries from the laboratory to patient care.

We present three representative cases that exemplify this approach. Case 1: a 3-year-old patient with autism spectrum disorder, with molecular karyotype results of uncertain significance and discordant results from two exome sequencing tests, which remains undiagnosed. Case 2: a 42-year-old patient with multisystemic fibrosis carrying variants of uncertain significance in KCP gene, suggesting a possible novel mechanism in connective tissue pathology. Case 3: a 1-year-6-month-old patient with global developmental delay, epilepsy, and brain atrophy associated with variants of uncertain significance in TRRAP gene, variant discordant with the severity of the patient's phenotype.

These 3 cases illustrate that there are situations in which elaborate genomic analyses and functional tests are necessary to elucidate rare disease mechanisms, refine diagnosis, and inform potential therapeutic directions. Strengthening Romania's translational research infrastructure will be key to accelerating the journey from bench to bedside and providing answers for patients long left without a diagnosis.



**ANNUAL CONFERENCE OF THE VICTOR BABES NATIONAL INSTITUTE OF PATHOLOGY
BUCHAREST, ROMANIA
12-14 NOVEMBER, 2025**

Acknowledgement: We would like to express our sincere gratitude to all the scientists and trainees who contributed their time, expertise, and clinical research insights to this work. We also extend our heartfelt thanks to the patients and their families for their invaluable participation and willingness to share their experiences, which made this project and collaborations possible.



O1: Natural Killer cell adoptive transfer therapy for metastatic melanoma

Gheorghita Isvoranu^{1*}, Valeriu Cișmașiu¹, Emanuel Fertig¹, Mihaela Surcel¹, Ana-Maria Enciu¹, Elena Codrici¹, Daniela Popescu¹, Andrei Niculae¹, Marioara Chiritoiu-Butnaru^{1,2}, Gabriela Chiritoiu^{1,2}, Cristian Munteanu^{1,2}, Livia Sima², Mihaela Gherghiceanu¹

¹ Victor Babeș National Institute of Pathology, 050096 Bucharest, Romania.

² Institute of Biochemistry of the Romanian Academy, 060031, Bucharest, Romania.

* Gheorghita Isvoranu: gina_isvoranu@yahoo.com

Keywords: NK cells, cytokines, TGF- β , melanoma

Background

Despite the innate ability of Natural Killer (NK) cells to kill tumor cell without prior sensitization, NK cell-based immunotherapies have several limitations, mainly due to suppressive effects of the tumor microenvironment and poor cell persistence and trafficking. Here, our objective was to investigate the effects of two different cytokine combinations on NK cell phenotype and function *in vitro* and their persistence *in vivo*, in a mouse model of lung metastasis.

Materials and methods

NK cells isolated from mouse spleens were cultured overnight with two cytokine combinations, IL-12/18/15 and IL-12/15/21. The phenotype and function of the pre-activated NK cells were investigated *in vitro* by flow cytometry. For *in vivo* investigations, mice were injected intravenously with B16-F10 cells on day 0, subsequently receiving adoptive transfer of cytokine pre-activated or freshly-isolated NK cells on days 8 and 15 after tumor cell inoculation. The NK cell persistence was evaluated at 48h, 3 and 6 days.

Results

Pre-activation of NK cells with IL-12/15/18 cytokines induced the highest expression of activating receptors and IFN- γ production, while the pre-activation with IL-12/15/21 enhanced production of perforin and granzyme B. Addition of transforming growth factor β (TGF- β) downregulated the expression of activating receptors and reduced the function of cytokine-activated NK cells. Pre-activation of NK cells with cytokines, especially with IL-12/18/15, increased their persistence in mice with pulmonary metastases.

Conclusions

The two cytokine combinations differently modified the NK cell phenotype and functionality, and NK cell functionality was affected by the presence of TGF- β . Cytokine-activated NK cells exhibited enhanced persistence in mice with lung metastases, the persistence being crucial for cell-based therapies.

Acknowledgement

This work was funded by Ministry of Education and Research, projects PN 23.16.02.02/2023 and PN-IV-P2-2.1-TE-2023-1169.



ANNUAL CONFERENCE OF THE VICTOR BABES NATIONAL INSTITUTE OF PATHOLOGY
BUCHAREST, ROMANIA
12-14 NOVEMBER, 2025

O2: GeneTrustChain – Secure Genetic Data Analysis and Sharing Platform

Author: Mihai Constantin Butolo

Affiliation: Universitatea Politehnica Bucureşti, Romania

Presenting author – correspondence: [institutional email not provided]

Keywords:* blockchain, genetic data, privacy, dynamic consent, cybersecurity, Hyperledger Fabric

Background

Currently, integrating genomic sequencing into healthcare raises major challenges related to data ownership, privacy, and secure sharing of genetic information. Traditional data management approaches struggle to give patients control over their genomic data and ensure secure, consent-based sharing across institutions.

Materials and Methods

GeneTrustChain, a secure blockchain-based platform, was developed to extend existing genomic data solutions and address these issues. It leverages Hyperledger Fabric to enable efficient genomic data storage, analysis, and controlled sharing in a private consortium network where multiple institutions act as nodes. This architecture ensures data integrity, immutability, and robust access control via cryptographic mechanisms. GeneTrustChain also incorporates tools for direct on-chain genomic analysis and a dynamic consent module implemented through smart contracts. These features grant patients granular control over their genetic data, allowing selective sharing with authorized entities and ensuring transparency and full traceability of data access.

Results

We developed a GeneTrustChain prototype using Hyperledger Fabric to demonstrate the system's feasibility. Preliminary results show that the platform supports secure querying and sharing of genomic data among participating nodes in the network.

Conclusions

These findings highlight the platform's promise in fostering a trustworthy, privacy-preserving ecosystem for multi-institutional genomic data analysis and sharing.



ANNUAL CONFERENCE OF THE VICTOR BABES NATIONAL INSTITUTE OF PATHOLOGY
BUCHAREST, ROMANIA
12-14 NOVEMBER, 2025

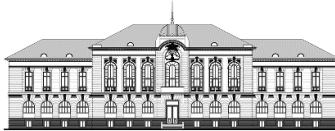
O3: Hidden Inflammation: Why Renal Biopsy Still Matters in Pediatric Silent Lupus Nephritis

Adrian Lungu – Pediatric Nephrology, Fundeni Clinical Institute, ERKNet Center, Bucharest, Romania

Lupus nephritis (LN) represents one of the most serious complications of systemic lupus erythematosus (SLE), particularly in the pediatric population. This presentation emphasizes the pivotal role of kidney biopsy in the diagnosis and classification of LN, even in the absence of overt renal manifestations. Silent lupus nephritis (SLN), characterized by biopsy-confirmed nephritis without clinical or biochemical evidence of renal involvement, underscores the limitations of relying solely on traditional markers for renal evaluation.

Case discussions illustrate the variability of LN presentation—from normal urine sediment to class III or IV histological findings—and demonstrate how complement levels, especially C3 and C4, can serve as more reliable predictors of proliferative LN than traditional autoantibody markers like anti-dsDNA. Notably, decreased complement levels were significantly associated with severe nephritis, although potential confounding due to primary complement deficiencies was acknowledged.

In conclusion, early and routine kidney biopsy in pediatric SLE patients with high disease activity, regardless of renal symptoms, may lead to earlier detection and treatment of LN, ultimately improving outcomes. This reinforces the notion that histopathology remains the gold standard for LN diagnosis and management.



O4: Gastric Cancer Image Analysis – from conventional pathologic approach to computer vision assisted diagnosis by Artificial Intelligence

Vlad Herlea^{1,3}, Florina Almarii^{1,3}, Corina-Elena Minciuna^{2,3}, Stefan Tudor^{2,3}, Mihai Tanase^{4,5}, Dragos Stan⁶, Alex Micu^{2,3}, Ovidiu Bitere², Catalin Pechianu¹, Simona O. Dima^{2,3}, Catalin Vasilescu^{2,3}

1. Department of Pathology, Fundeni Clinical Institute, 022328 Bucharest, Romania
2. General Surgery Department, Fundeni Clinical Institute, Romania
3. Carol Davila University of Medicine and Pharmacy, Romania
4. Department of Automatic Control and Computers, Politehnica University of Bucharest, Bucharest, Romania
5. University of Bucharest, Bucharest, Romania
6. Businessdata Systems / Net Brinel, Bucharest, Romania

Background: Gastric cancer (GC), for which the first steps for image based-analysis were developed, is a leading cause of cancer-related death worldwide. Nowadays we have an important ally: artificial intelligence (AI).

Method: First, we began with the process of image acquisition at high resolution using the Aperio scanner after the H&E slides were reviewed by two expert pathologists. The whole-slide images for 465 patients were obtained from Fundeni Clinical Institute.

Results: Each image was processed for the AI as listed below:

A. Black-Box Approach Using Vision Transformers:

- **Process:** Neural Network models, specifically vision transformers, are used to classify the slide tiles
- **Procedure:** Each slide is segmented into 640x640 pixel, which are fed into the vision transformer model for class prediction.
- **Visualization:** A color-coded map representing the predictions is created, with each tile color corresponding to the predicted class
- **Accuracy:** The model's accuracy is assessed by comparing its predictions with manually annotated slides, crucial for calculating accuracy and constructing a confusion matrix.

B. Structural Approach via Segmentation and Statistical Analysis:

- **Segmentation:** Basic segmentation is achieved using color clustering techniques on a rescaled image.
- **Nuclei Identification:** The Difference of Gaussian filters is utilized to locate potential nuclei
- **Further Exploration:** After identifying nuclei, their size, shape, and distribution are analyzed and statistically correlated with the tile label.

Conclusion: We believe that AI is the key to understand the relationship between genotype and phenotype and to reduce the work burden of pathologists. This method needs to be validated through clinical studies, but is the first step towards a tumor-specific tailored treatment.

Acknowledgment: This work has been supported by the project PN-III-P4-PCE-2021-1068.



O5: Generation of a CD36 Edited Cell Line of Breast Cancer

Dudău Maria^{1*}, Maria Savoiaia², Zahiu-Ioan Teodor², Cârloanță Teodor², Diaconeasa Alexandru², Ana-Maria Enciu^{1,3}, Cristiana Tănase^{1,4}, Ionela-Daniela Popescu¹, Codrici Elena^{1,3}

¹*Laboratory of Biochemistry, Victor Babes National Institute of Pathology, Bucharest, Romania*

²*Carol Davila University of Medicine and Pharmacy, Bucharest, Romania*

³*Department of Cell Biology and Histology, Carol Davila University of Medicine and Pharmacy, Bucharest, Romania*

⁴*Department of Clinical Biochemistry, Faculty of Medicine, Titu Maiorescu University, Bucharest, Romania*

*presenting author – correspondence: maria.dudau@ivb.ro

Keywords: breast cancer, gene editing, CD36, fatty acids

Background: CD36, a multifunctional membrane glycoprotein involved in fatty acid uptake and metastasis, has been involved in the aggressiveness of breast cancer subtypes. To assess its functional contribution, we performed CRISPR/Cas9-mediated editing of CD36 in two epithelial breast cancer cell lines of distinct phenotypes: MCF-7 (HTB-22), an estrogen- and progesterone-receptor-positive, slow-proliferating line, and MDA-MB-231 (HTB-26), a highly aggressive triple-negative model.

Material and method: Cells were transfected with either Cas9–RNP complexes or plasmids encoding Cas9 and guide RNAs targeting various exons of CD36. Following GFP-based sorting, several edited pools and individual clones were isolated, including combinations of single-guides (AA, AB, AC) and triple-guide (ABC) edits. Edited populations were validated by Sanger sequencing to confirm CRISPR-induced indels and guide-specific editing events.

Results: Both plasmid and Cas9-RNP complexes induced gene-editing with various genetic outcomes. Proliferation assessment showed that not all edits induced a significant effect, when compared to wild-type. Furthermore, the cell phenotype was determinant for the functional outcome. CD36 gene-editing did not significantly influence fatty-acid uptake, showing that tumour cells rely on multiple mechanisms for metabolic rewiring.

Conclusion: These findings highlight the context-dependent role of CD36 in breast cancer cell behavior and demonstrate the utility of CRISPR/Cas9-mediated gene editing—validated by Sanger sequencing and coupled with functional and biochemical assays—to dissect lipid metabolism-linked pathways driving metastatic progression

Acknowledgement: This work was supported by the Core Program within the National Research, Development and Innovation Plan, 2022–2027, with the support of MCID, project no. 10N/01.01.2023, PN 23.16.02.03.



O6: *Hypericum alpestre* Extract and L-NAME Suppress PI3K/Akt Pathway and Induce Apoptosis in MDA-MB-231 Triple-Negative Breast Cancer Cells

Gayane Petrosyan¹, Nikolay Avtandilyan¹, Mikayel Ginovyan¹, Hayarpi Javrushyan¹,

¹ Research Institute of Biology, Laboratory of Fundamental and Pathological Biochemistry, Yerevan State University, Yerevan, Armenia

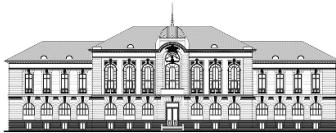
Keywords: PI3K/Akt, apoptosis, breast cancer, inflammation, metastasis.

Triple-negative breast cancer (TNBC) is an aggressive subtype characterized by high metastasis rates and resistance to targeted therapies. The PI3K/Akt signaling pathway plays a crucial role in TNBC progression by regulating survival, inflammation, angiogenesis, and apoptosis resistance. Identifying novel therapeutic strategies that modulate this pathway is essential for improving treatment outcomes. *Hypericum alpestre* (HA), a medicinal plant with bioactive polyphenols, has demonstrated cytotoxic potential against cancer cells. In combination with L-NAME, a nitric oxide synthase (NOS) inhibitor, its effects on TNBC cells were evaluated. This study aimed to assess the impact of HA extract and L-NAME on the PI3K/Akt pathway and downstream molecular targets, including TNF α , VEGF α , COX-2, and MMP-2, in MDA-MB-231 triple-negative breast cancer cells.

Cytotoxicity was evaluated using MTT assays. ELISA and Western blot analyses were performed to measure the expression levels of PI3K, Akt, TNF α , VEGF α , COX-2, and MMP-2. Apoptosis was assessed through Caspase-3 activation and nuclear staining with Hoechst 33258 dye.

HA extract effectively suppressed PI3K/Akt signaling in MDA-MB-231 cells, reducing the levels of TNF α and VEGF α , thereby decreasing inflammation and angiogenesis. Additionally, HA combined with L-NAME further downregulated COX-2 and MMP-2, which are critical regulators of tumor invasion and metastasis. The combination treatment significantly increased Caspase-3 activation and apoptotic cell death compared to either agent alone. Importantly, HA+L-NAME demonstrated stronger cytotoxic effects than 5-FU, suggesting its potential as a superior therapeutic approach.

HA extract, particularly in combination with L-NAME, significantly inhibits tumor-promoting pathways and enhances apoptosis in MDA-MB-231 cells. These findings suggest that HA+L-NAME could serve as a promising complementary strategy for TNBC treatment, supporting further preclinical validation.



O7: Human neural models for genetic instability-related diseases

Roxana Deleanu ^{1*}

¹ Institute for Neuroanatomy, Medical University of Innsbruck, Müllerstr. 59, 6020 Innsbruck, Austria

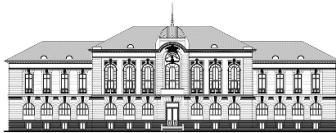
* correspondence: Irina-Roxana.Deleanu@i-med.ac.at

Keywords: neural genetic diseases; tandem repeat expansion; genetic instability; neuronal mosaicism; cell-type-specific vulnerability; single-nucleus transcriptomics; iPSC-derived neurons; neurogenesis; forced ageing.

Several genetic diseases affecting the human nervous system are incurable and poorly understood. Some affected genes are unstable, mainly due to inherited nucleotide repeat expansions. In most patients, these diseases progress over decades, leading to severe movement incoordination and/or cognitive dysfunction, often accompanied or followed by neurodegeneration. Although inherited genes with tandem- repeat expansions have been identified for several decades, the neuronal- type- specific pathologies and their long pre-symptomatic latency remain underexplored. Recent advances in single- nucleus transcriptomic detection, combined with analysis of tandem repeat lengths in post- mortem Huntington's disease (HD) brains, have revealed high neuronal mosaicism and very elongated repeats that cause transcriptional dysregulation and cell death in specific projection neurons (1). To understand the pathological process, several well-established animal models are available, and patient iPSC-derived neurons and neural organoids are also being studied, all with several limitations. While human iPSC-derived models are limited in their ability to reach cellular maturity, various genetic and epigenetic approaches have shown that neurons can acquire an "aged" phenotype in culture (2, 3). My approach involves differentiating and "ageing" patient iPSC-derived neurons for modelling Friedreich ataxia and several polyQ diseases, including HD and various spinocerebellar ataxias. This includes, for now, neocortical, striatal, nigral, cerebellar, medullary/spinal motor, and peripheral sensory neurons. The next challenge is to identify dynamic changes in tandem repeat length and their effects on these disease-vulnerable neurons at single-cell resolution. This will establish a platform for pinpointing pathological events in vulnerable long projection neurons and for developing targeted therapies for tandem-repeat expansions affecting these neurons, thereby enhancing understanding and treatment of neuronal genetic instability across multiple human diseases.

References

1. Handsaker RE, Kashin S, Reed NM, Tan S, Lee WS, McDonald TM, et al. Long somatic DNA-repeat expansion drives neurodegeneration in Huntington's disease. *Cell*. 2025;188(3):623-39.e19.
2. Cohen-Carmon D, Sorek M, Lerner V, Divya MS, Nissim-Rafinia M, Yarom Y, Meshorer E. Progerin-Induced Transcriptional Changes in Huntington's Disease Human Pluripotent Stem Cell-Derived Neurons. *Mol Neurobiol*. 2020 Mar;57(3):1768-1777.
3. Zhang C, Saurat N, Cornacchia D, Chung SY, Sikder T, Nemchik A et al. Identifying Age-Modulating Compounds Using a Novel Computational Framework for Evaluating Transcriptional Age. *Aging Cell*. 2025 Jul;24(7):e70075.



O8: Cytotoxic effects induced by copper radioisotopes in colon cancer targeted radiotherapy

Radu Serban¹, Dragos Niculae², Diana Cocioaba¹, Roxana Tudoroiu-Cornoiu¹, Radu Leonte¹, Mihaela Temelie¹, Ionela Neagoe³, Andrei Necsoiu¹, Gina Manda³, Dana Niculae¹

¹*Horia Hulubei National Institute for Physics and Nuclear Engineering, 30 Reactorului street, 077125 Magurele, Ilfov, Romania*

²*University of Medicine and Pharmacy Carol Davila, Faculty of Pharmacy, 37 Dionisie Lupu street, 020021, Bucharest, Romania*

³*National Institute of Pathology Victor Babeș, 99-101 Splaiul Independenței, Bucharest, Romania*

*presenting author – correspondence: radu.serban@nipne.ro

Keywords: radiotoxicity, radiotherapy, radiolabelling, Auger-electrons

Background

The radiotherapy using internalized radioisotopes with high linear energy transfer (LET) emissions benefits from enhanced delivery mechanisms and high specificity, boosting the treatment's efficacy. The use of biocompatible molecules to ensure improvements in the dose delivered to target cells increases the cellular damage caused by radiation and triggers specific cell death mechanisms, all the while having a lesser impact to surrounding healthy tissue. Low-energy Auger electrons (~2 keV), with short-range penetration limited to the cell interior, can damage sensitive structures like DNA in cancer cells through direct interactions or inducing oxidative stress. Copper-64 was selected for study given its role as a cofactor in DNA replication, cell division, and metabolism.

Materials and methods

The in vitro effects of ⁶⁴Cu emissions on carcinoma cell lines were investigated, using the isotope both in the form of chloride and chelated with peptides. The cellular viability was investigated using the MTS and LDH assays; genotoxicity using comet assay, and the gene expression profiles changes were investigated for the cells incubated with [⁶⁴Cu]CuCl₂.

Results

According to the in vitro investigations, cells with a higher proliferation rate are more vulnerable to Auger electron toxicity. Also, the use of radiolabelled peptides reduced the impact to normal cell lines, compared to cancerous ones.

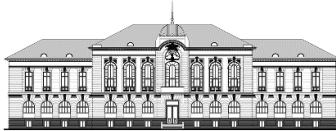
Conclusions

Understanding the cell death mechanism triggered as response to the stress induced by such radiations and improvements to delivery systems via radiolabelled peptides contributes to developing therapeutic strategies for tumour treatment.

Acknowledgement This work was supported by a grant from the Romania Ministry of Research, Innovation and Digitalization project number PN23210201 and IOSIN-Accelerator Ciclotron TR19.



**ANNUAL CONFERENCE OF THE VICTOR BABES NATIONAL INSTITUTE OF PATHOLOGY
BUCHAREST, ROMANIA
12-14 NOVEMBER, 2025**



ANNUAL CONFERENCE OF THE VICTOR BABES NATIONAL INSTITUTE OF PATHOLOGY
BUCHAREST, ROMANIA
12-14 NOVEMBER, 2025

O9: Facing New Health Challenges Related to Ozone Depletion and Increased Exposure to UVB and Secondary Cosmic Rays: Insights from the BIOSPHERE Project

Gina Manda^{1*}, Ionela-Victoria Neagoe¹, Elena Mihaela Dragnea¹, Maria Dobre¹, Angeliki Gkikoudi^{2,3}, Christina Beinke⁴, Ulrich Giesen⁵, Amer Al-Qaaod⁵, Viviane Pierrard^{6,7}, Georgia I. Terzoudi³, Faton Krasniqi⁵, Mastaneh Zadehrafhi⁸, Alexandros G. Georgakilas²

¹ Radiobiology Laboratory, “Victor Babeș” National Institute of Pathology (IVB), 99-101 Splaiul Independentei, Bucharest, Romania

² DNA Damage Laboratory, Physics Department, School of Applied Mathematical and Physical Sciences, National Technical University of Athens (NTUA), Leof. Alimou Katechaki, Zografou Campus, 15780 Athens, Greece

³ Laboratory of Health Physics, Radiobiology & Cytogenetics, Institute of Nuclear & Radiological Sciences & Technology, Energy & Safety, National Centre for Scientific Research “Demokritos”, 15341 Agia Paraskevi, Athens, Greece

⁴ Radiobiology Laboratory, Bundeswehr Institute of Radiobiology, University of Ulm, Neuherbergstraße 11, Munich, Germany

⁵ Physikalisch-Technische Bundesanstalt (PTB), Bundesallee 100, Braunschweig, Germany

⁶ Solar wind division, Royal Belgian Institute for Space Aeronomy, Ringlaan 3 Avenue Circulaire, Brussels, Belgium

⁷ Earth and Life Institute – Climate Sciences (ELI-C), Université Catholique de Louvain, Pl. de l'Université 1, Ottignies-Louvain-la-Neuve, Belgium

⁸ Radioisotopes and Radiation Metrology, „Horia Hulubei“ National Institute of Physics and Nuclear Engineering (IFIN-HH), Strada Reactorului 30, Magurele, Romania

Keywords: ozone layer, muons, UVB, DNA damage, gene expression, NRF2

Background

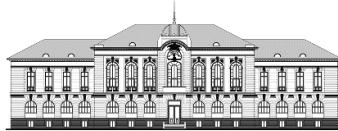
Stratospheric ozone depletion and solar-driven secondary cosmic rays jointly enhance terrestrial exposure to ionizing particles and UVB radiation, raising concerns about the potential health consequences of this combined exposure.

Materials and methods

Human non-cancerous skin and blood cell lines were exposed to 0.5 Gy energetic protons (mimicking secondary muons) or to 1-2 Gy γ rays, and thereafter to 50 J/m² UVB. Cellular viability, DNA damage (γ H2AX immunofluorescence and dicentric chromosomes), and the expression changes of 84 stress genes were investigated at various time points after exposure. Cells were also exposed to a low radiation background in the IFIN-HH laboratory (Unirea Salt Mine, Slanic, Romania).

Results

The co-exposure of normal cells to ionizing radiation and UVB drove synergistic DNA damage and chromosomal instability, accompanied by a pro-inflammatory shift, oxidative and hypoxic stress responses [1]. Two waves of stress responses were evidenced, indicating a long-lasting damage inflicted in co-exposed cells. Even the natural radiation background triggered a cellular stress response when compared to cells exposed to a very low-radiation



**ANNUAL CONFERENCE OF THE VICTOR BABES NATIONAL INSTITUTE OF PATHOLOGY
BUCHAREST, ROMANIA
12-14 NOVEMBER, 2025**

background, suggesting the broad sensitivity and adaptability of normal cells to ionizing radiation.

Conclusions

The emerging health issues arising from progressive ozone depletion and solar events need mechanistic investigations to design protective medical measures such as the pharmacological activation of the cytoprotective transcription factor NRF2.

Acknowledgement All authors acknowledge funding from the BIOSPHERE project (21GRD02, European Partnership on Metrology, co-financed by Horizon Europe and Participating States). Additional funding was obtained from the Nucleu grant PN 23.16.02.01 (Romanian Ministry of Education).

References

1. Gkikoudi A, Manda G, Beinke C, et al. Synergistic Effects of UVB and Ionizing Radiation on Human Non-Malignant Cells: Implications for Ozone Depletion and Secondary Cosmic Radiation Exposure. *Biomolecules* 2025;15(4):536.



O10: Bioactive Effects of Cold-Pressed Seed Oil Extracts: In Vitro Analysis Using Hepatic Cell Models

Sevinci Pop^{1*}, Valeriu B. Cismasiu¹, Maria Dudau², Radu M. Marinescu¹, Antonia M. Stroe¹, Georgeta Alexandru³, Justinian A. Tomescu³, Mihaela Neagu³

¹ Department of Cell Biology, Neuroscience and Experimental Myology, "Victor Babes" National Institute of Pathology and Biomedical Sciences, Splaiul Independentei 99-101, 050096, Bucharest, Romania

² Department of Biochemistry-Proteomics, "Victor Babes" National Institute of Pathology and Biomedical Sciences, Splaiul Independentei 99-101, 050096, Bucharest, Romania

³ Research Department, SC Hofigal Export-Import SA, Intrarea Serelor nr. 2, 042124, Bucharest, Romania

* spop@ivb.ro

Keywords: liver epithelial cells, *S. Marianum* seed oil, cellular antioxidant activity, proliferation, oxidative stress, polyunsaturated fatty acids

Cold-pressed seed oil extracts have shown promising health benefits, mainly through their antioxidant and anti-inflammatory potential. Seed oil extracts have been used for centuries in traditional medicine, especially to maintain hepatic health, in addition to their high nutritional value. The seeds of *Silybum Marianum* are rich in polyunsaturated fatty acids and flavonolignans, demonstrating significant pharmaceutical potential.

This study aimed to characterize the components of *S. Marianum* seed oil and assess their effects on cellular processes—including viability, proliferation, and oxidative stress—in both tumor and normal liver cells. The oil was extracted using cold-pressing method to preserve molecular structure of the bioactive compounds. Gas chromatography-mass spectrometry analysis revealed an enriched fatty acid composition, with linoleic (54.7 \pm 0.8%) and oleic (28.79 \pm 0.25%) acids present in the highest amounts. The antioxidant capacity was evaluated by measuring ferric reducing antioxidant power and total phenolic content.

Biological effects were tested on human hepatocarcinoma (HepG2) and normal liver epithelial (THLE-2) cell lines. Cytotoxicity was evaluated using endpoint assays (MTS and LDH), while real-time cell proliferation was monitored with the xCELLigence system. Additionally, cellular antioxidant activity was assessed in both liver cell types.

Results showed that the oil induced cytotoxic and anti-proliferative effects on hepatocarcinoma cells in a time- and dose-dependent manner, with minimal impact on normal cells under the same conditions. The bioactive constituents from the oil effectively attenuated intracellular accumulation of reactive oxygen species and mitigated lipid peroxidation.

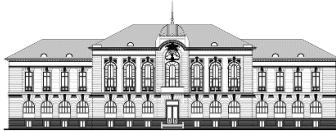
Overall, this study indicates that cold-pressed milk thistle seed oil may exert an anti-tumor effect by selectively targeting hepatocarcinoma cells, decreasing their proliferation and viability. Moreover, pre-treatment with the oil conferred protection to hepatic epithelial cells against oxidative damage. Further studies are necessary to elucidate the molecular mechanisms underlying the bioactivity of *S. Marianum* seed oil and validate its therapeutic potential.

Acknowledgement: This work was funded by a grant of the Romanian Ministry of Education and Research - UEFISCDI, project number PN-IV-P7-7.1-PED-2024-2526 within



**ANNUAL CONFERENCE OF THE VICTOR BABES NATIONAL INSTITUTE OF PATHOLOGY
BUCHAREST, ROMANIA
12-14 NOVEMBER, 2025**

PNCDI IV (Contract nr. 137PED/2025) and by the National Program 1N/2023/ PN 23.16.01.02.



O11: Hypoxia-Linked Alterations in Arginine Metabolism and Oxidative Stress in the Bone Marrow during Breast Cancer Progression and Treatment

Hayarpi Javrushyan^{1*}, Edita Nadiryan ¹, Svetlana Hovhannisyan ¹, Nikolay Avtandilyan ²

¹ Research Institute of Biology, Yerevan State University, 1 Alex Manoogian, 0025, Yerevan, Armenia

² Laboratory of Fundamental and Pathological Biochemistry, Department of Biochemistry, Microbiology and Biotechnology, Yerevan State University

*Hayarpi Javrushyan – correspondence: institutional email: hg.javrushyan@ysu.am

Keywords: Breast cancer; Bone marrow microenvironment; Arginine metabolism; Oxidative stress; Hypoxia; Herbal extracts

Background: The bone marrow microenvironment plays a critical yet understudied role in breast cancer progression, influencing metastatic dissemination, angiogenesis, and resistance to therapy. This study aimed to investigate how breast cancer and its treatment affect the bone marrow niche, focusing on hypoxia-induced molecular changes, arginine metabolism, and oxidative stress.

Materials and Methods: A DMBA-induced breast cancer rat model was used to evaluate bone marrow alterations following chemotherapy and combined treatments with herbal plant extracts. Colorimetric assays were performed to determine arginase activity, nitric oxide (NO) levels (measured as nitrite ions), and malondialdehyde (MDA) concentrations as markers of lipid peroxidation and oxidative stress. In addition, immunocytochemistry (ICC) was applied to assess HIFCOX-2 and MMP-2 expression levels in bone marrow cells, and Western blotting was performed to analyze the protein expression of key molecular markers involved in hypoxia-associated signaling pathways.

Results: Untreated cancer-bearing rats showed elevated arginase activity and MDA levels, accompanied by reduced nitrite ion concentrations, indicating enhanced oxidative stress and impaired NO bioavailability. Treatment with *Inula helenium* extract, especially in combination with the arginase inhibitor nor-NOHA, significantly decreased lipid peroxidation and restored NO levels. In contrast, NOS inhibition with L-NAME and *Alchemilla smirnovii* Juz. extract increased MDA, suggesting exacerbated oxidative damage.

Conclusions: The findings demonstrate that breast cancer and its treatment profoundly alter bone marrow homeostasis through dysregulation of arginine metabolism and oxidative balance. These processes may be linked to hypoxia-driven mechanisms involving PI3K/Akt and HIF-1 α signaling pathways. Moreover, certain herbal extracts show therapeutic potential as adjuncts to conventional therapy to protect bone marrow integrity and improve treatment outcomes.

References

1. Wilkinson, L. and Gathani, T. (2022) Understanding breast cancer as a global health concern. *British Journal of Radiology* 95.
2. Siegel, R. L., Miller, K. D., Wagle, N. S., and Jemal, A. (2023) Cancer statistics, 2023. *CA Cancer J Clin* 73, 17–48.
3. Yip, R. K. H., Rimes, J. S., Capaldo, B. D., et al. (2021) Mammary tumour cells remodel the bone marrow vascular microenvironment to support metastasis. *Nat Commun* 12.



**ANNUAL CONFERENCE OF THE VICTOR BABES NATIONAL INSTITUTE OF PATHOLOGY
BUCHAREST, ROMANIA
12-14 NOVEMBER, 2025**

4. Avtandilyan, N., Javrushyan, H., Petrosyan, G., and Trchounian, A. (2018) The Involvement of Arginase and Nitric Oxide Synthase in Breast Cancer Development: Arginase and NO Synthase as Therapeutic Targets in Cancer. *Biomed Res Int* 2018, 1–9.
5. Ginovyan, M., Javrushyan, H., Petrosyan, G., et al. (2023) Anti-cancer effect of Rumex obtusifolius in combination with arginase/nitric oxide synthase inhibitors via downregulation of oxidative stress, inflammation, and polyamine synthesis. *Int J Biochem Cell Biol* 158.
6. Semenza, G. L. (2012) Hypoxia-inducible factors: Mediators of cancer progression and targets for cancer therapy. *Trends Pharmacol Sci* 33, 207–214.
7. Chetty, C., Lakka, S. S., Bhoopathi, P., and Rao, J. S. (2010) MMP-2 alters VEGF expression via α V β 3 integrin-mediated PI3K/AKT signaling in A549 lung cancer cells. *Int J Cancer* 127, 1081–1095.



O12: Psychiatric symptoms in Inflammatory Bowel Diseases: preliminary results on the role of the gut microbiome

Elena Milanesi^{1,2*}, Iulia Andreea Pelisenco¹, Teodora Ecaterina Manuc^{2,3}, Mircea Manuc^{2,3}, Ioan-Costin Matei⁴, Alexia-Cătălina Mihai², Naida Babic Jordamovic⁵, Sarah Ahmetovski⁶, Silvano Piazza⁵, Maria Dobre¹

¹ Victor Babeș National Institute of Pathology, 050096 Bucharest, Romania.

² Faculty of Medicine, Carol Davila University of Medicine and Pharmacy, 050474 Bucharest, Romania.

³ Fundeni Clinical Institute, 022328 Bucharest, Romania.

⁴ Nutrimed Clinic, 020625 Bucharest, Romania.

⁵ International Centre for Genetic Engineering and Biotechnology (ICGEB), Trieste, Italy

⁶ Faculty of Natural Sciences and Mathematics, University of Sarajevo, Bosnia and Herzegovina

* Elena Milanesi: elena.k.milanesi@gmail.com

Keywords: inflammatory bowel diseases, depressive disorder, gut microbiome, brain-gut interaction

Background

In inflammatory bowel diseases (IBD), a wide range of outcomes are negatively impacted by psychiatric symptoms, especially stress, anxiety, and depression (SAD). Alterations in gut microbiome composition have been demonstrated both in IBD and SAD. However, no study has identified a specific enterotype pattern underlying the crosstalk between IBD and SAD.

Materials and methods

We included 39 IBD patients, 20 patients with depressive disorder as primary diagnosis, and 22 controls (CTRL). Following a psychiatric evaluation, the IBD patients were divided into IBD patients with SAD (IBD+SAD) and IBD patients without SAD (IBD). The stool samples have been collected.

The enterotypes of each group were characterized by analyzing the V3-V4 variable regions of the 16S ribosomal RNA gene amplicon libraries. SILVA v138.1 was used for the Taxonomic Assignment. Seven α -diversity metrics determined the diversity across the main groups, while difference in abundance was evaluated by LEfSe (LDA score ≥ 2.0) and Wilcoxon/Kruskal-Wallis with FDR correction.

Results

Compared to the CTRL group, *Faecalibacterium* (LDA ≈ 4.5 , ↓ IBD) and *Romboutsia* (LDA ≈ 3.4 , ↓ SAD) emerged as the top discriminatory genera in IBD and SAD patients, respectively. *Streptococcus* showed a bloom in the IBD+SAD, suggesting its potential as a comorbidity biomarker (LDA ≈ 4.0 , ↑ IBD+SAD). *Agathobacter* (LDA ≈ 3.8) and the



**ANNUAL CONFERENCE OF THE VICTOR BABES NATIONAL INSTITUTE OF PATHOLOGY
BUCHAREST, ROMANIA
12-14 NOVEMBER, 2025**

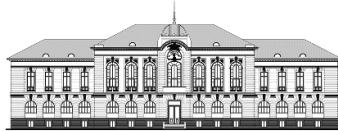
uncultured Ruminococcaceae genus UCG-002 also showed their consistent depletion in the IBD+SAD cohort.

Conclusions

α -diversity declines stepwise from CTRL→SAD→IBD→IBD+SAD, with the lowest Shannon index in the comorbid group. Some putative biomarkers across our four clinical groups were identified. Studies in large cohorts are needed to evaluate the robustness and reproducibility of our findings.

Acknowledgement

This research was funded by ICGEB (Contract No. CRP/22/019, ICGEB Ref. No. CRP/ROU21-01).



O13: FDA approved drug repositioning as modulator of IL-1 β -driven inflammation

Marioara Chiritoiu-Butnaru^{1*}, Gabriela Chiritoiu¹, Simona Ghenea¹, Cristian V.A. Munteanu², Stefana M. Petrescu¹, Gheorghita Isvoranu³

1. Department of Molecular and Cellular Biology, Institute of Biochemistry of the Romanian Academy, Bucharest, Romania

2. Department of Bioinformatics and Structural Biochemistry, Institute of Biochemistry of the Romanian Academy, Bucharest, Romania

3. „Victor Babeş” National Institute of Pathology, Bucharest, Romania

*Presenting author: mari.chiritoiu@biochim.ro

Keywords: interleukin-1 β , CRISPR/Cas-9, high-throughput screening, drug repurposing,

Background

Interleukin-1 β (IL-1 β) is one of the most potent pro-inflammatory cytokines and has been related to a variety of pathological processes. Physiologically relevant studies of IL-1 β secretion primarily rely on primary cells and animal models, as engineered systems fail to accurately recapitulate innate immune physiology. While these models are well suited for mechanistic investigations, drug discovery and large-scale studies require high-throughput systems that still approximate physiological relevance.

Materials and methods

A reporter cell line was generated by CRISPR/Cas9-mediated editing of the IL-1 β locus in J774A.1 macrophages and subsequently employed for high-throughput screening for 1403 compounds from the FDA approved drug library. Tested compounds were validated by ELISA, Western blotting, immunofluorescence microscopy in primary macrophages and animal model for sepsis.

Results

We aimed generated a reporter cell line to quantitatively detect of IL-1 β secretion after exposure to exogenous stimuli mimicking an immune challenge. To achieve this, macrophages were edited to add HiBiT peptide at the C-terminus of endogenous IL-1 β , enabling detection of secreted IL-1 β -HiBiT in the extracellular medium through luciferase reconstitution via complementation with LgBiT. By high throughput screening we identified several of the tested compounds showed anti-inflammatory activity. The most potent drugs were confirmed in primary macrophages, and one was validated in an animal model for sepsis.

Conclusions

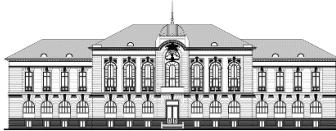
We successfully generated reporter cell line for IL-1 β which we used for high-throughput screening and identified an FDA-approved drug which was efficient at reducing IL-1 β secretion both in primary macrophages and animal model for sepsis.

Acknowledgement



**ANNUAL CONFERENCE OF THE VICTOR BABES NATIONAL INSTITUTE OF PATHOLOGY
BUCHAREST, ROMANIA
12-14 NOVEMBER, 2025**

MC acknowledges support from the Romanian Ministry of Research and Innovation, UEFISCDI grant PED337/2020 (PN-III-P2-2.1-PED-2019-3297), TE156/2020 (PN-III-P1-1.1-TE-2019-1705) and from the Romanian Academy grant GAR155/2023.



ANNUAL CONFERENCE OF THE VICTOR BABES NATIONAL INSTITUTE OF PATHOLOGY
BUCHAREST, ROMANIA
12-14 NOVEMBER, 2025

O14: DEVELOPMENT OF BIOLOGICAL PRODUCTS FROM LABORATORY LEVEL TO PILOT AREA

Crina Stavaru^{1*}, *E.Diana Giol*¹, *Luciana Morogan*², *Ioana Berindan-Neagoe*³, *Bogdan Tamba*⁴, *Norica Nichita*⁵, *Mihaela Gherghiceanu*⁶, *Adrian Bobica*⁷, *Ovidiu Pop*⁸, *Rodica Boca*⁹, *Szilard Fejer*¹⁰

¹ Cantacuzino National Military Medical Institute for Research and Development, Bucharest, Romania

² Military Technical Academy Ferdinand I, Bucharest, Romania

³ Iuliu Hațieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania

⁴ University of Medicine and Pharmacy " Grigore T. Popa", Iasi, Romania

⁵ Institute of Biochemistry of the Romanian Academy, Bucharest, Romania

⁶ National Institute of Pathology Victor Babeș, Bucharest, Romania

⁷ CROMATEC PLUS Ltd, Bucharest, Romania

⁸ Qualipat Ltd, Oradea, Romania

⁹ Dorna Medical Ltd, Vatra Dornei, Romania

¹⁰ Pro-Vitam Ltd, Sfantul Gheorghe, Romania

*e-mail: stavaru.crina@cantacuzino.ro

Keywords: vaccine, monoclonal antibodies, pilot scale

Background:

To develop a biological product, scaling-up studies are essential steps for assessing the practicality of any biotechnological project. The research project "Development of translational research of vaccines and other biological products-Cantavac 2.0" aims to increase, through R&D activities, the technological readiness level (TRL) of innovative prophylactic and therapeutic biological product candidates, based on traditional products with updated technology and on new products, up to TRL 7. The pilot scale can determine whether research lab bench studies are likely to succeed and can identify potential issues that could arise before scaling production to larger industrial scales.

The establishment by this project of an R&D infrastructure and a pilot unit for investigational products will facilitate the fruition of the numerous biological product candidates developed at the laboratory level in recent years, both by the "Cantacuzino" Institute and by other groups, funded through national and international public funding.

The project is in its early phase, but the expected final results are: obtaining at least one influenza virus reassortant on cell culture and a therapeutic monoclonal antibody on a pilot scale, using AI to accelerate development/technological steps, and respecting good laboratory/manufacturing practice standards.

Acknowledgement: The Cantavac 2.0 project no 98856/2024, SMIS 326920, is European co-funded through the Health Programme call no. PS/272/PS_P5/OP1/RSO1.1/PS_P5_RSO1.1_A9.



O15: What to expect on colonic biopsies from patients with chronic diarrhea

Florina Almarii^{1,2,3*}, Gabriel Becheanu^{1,2,3}

1 Victor Babes National Institute of Pathology, Splaiul Independenței, nr. 99-101, Bucharest, Romania

2 Carol Davila University of Medicine and Pharmacy, Bulevardul Eroii Sanitari, nr. 8, Bucharest, Romania

3 Fundeni Clinical Institute, Sos. Fundeni, nr. 163, Bucharest, Romania

*presenting author – correspondence: florina.almarii@umfcd.ro

Keywords: IBD, microscopic colitis, infectious colitis

Background

Chronic diarrhea is a common clinical problem with a wide differential diagnosis, ranging from infectious and inflammatory processes to functional and neoplastic disorders. Histopathologic examination of gastrointestinal biopsies plays a crucial role in identifying underlying causes and guiding management. However, the spectrum of microscopic findings can be broad and often overlapping, posing diagnostic challenges. This case series aims to describe the most frequent histopathological patterns encountered in patients presenting with chronic diarrhea and to highlight key features that aid in differential diagnosis.

Materials and methods

We gathered relevant biopsy cases representing different categories of causes of chronic diarrhea, including inflammatory, infectious, and microscopic colitides. Clinical data, endoscopic impressions, and histologic features were reviewed. Hematoxylin and eosin–stained sections were examined for architectural alterations, inflammatory patterns, epithelial injury, and other diagnostic clues. Special stains and immunohistochemistry were performed when necessary to confirm specific etiologies.

Results

We found representative cases of inflammatory bowel disease, infectious colitis with spirochetosis, and microscopic colitis. The inflammatory bowel disease cases demonstrated chronic architectural distortion, crypt abscesses, and basal plasmacytosis. Infectious colitis with spirochetosis showed a characteristic basophilic fringe along the colonic epithelium.

Microscopic colitis cases included both collagenous and lymphocytic types, with thickened subepithelial collagen bands or increased intraepithelial lymphocytes, respectively. These findings emphasized the value of correlating histologic patterns with clinical and endoscopic data to achieve accurate diagnoses.

Conclusions

Chronic diarrhea encompasses a diverse group of pathologic entities that can be distinguished through careful histopathologic evaluation. Awareness of the spectrum of biopsy findings and their clinical implications enhances diagnostic accuracy and patient care. Pathologists should approach these cases systematically, integrating histologic features with clinical and endoscopic data to reach a meaningful diagnosis.



ANNUAL CONFERENCE OF THE VICTOR BABES NATIONAL INSTITUTE OF PATHOLOGY
BUCHAREST, ROMANIA
12-14 NOVEMBER, 2025

O16: PD-L1 expression testing in non-small cell lung cancer (NSCLC)

Andrei-Marian Niculae^{1,2,3*}, Alexandra Florea^{1,2,3}, Florina Vasilescu²

¹ *Histopathology and Immunohistochemistry Department, Victor Babeș Institute, Splaiul Independenței 99-101, Sector 5, Bucharest, Romania*

² *Pathology Department, Central University Emergency Military Hospital, Calea Plevnei Street, no. 134, sector 1, Bucharest, Romania*

³ *Faculty of Medicine, Carol Davila University of Medicine and Pharmacy, Dionisie Lupu Street, no. 37, Sector 2, Bucharest, Romania*

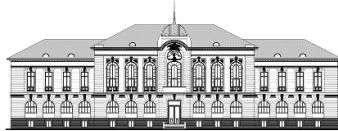
*presenting author – correspondence: niculae.andrei@ivb.ro

Keywords: non-small cell lung cancer, PD-L1, immunotherapy

Non-small cell lung cancer (NSCLC) is a major health problem in Romania, ranking as a leading cause of cancer-related deaths [1]. PD-L1 expression testing plays a critical role as the primary biomarker for guiding immunotherapy decisions in non-small cell lung cancer (NSCLC) [2]. The IVB pathology lab employs multiple antibodies, such as 22C3, SP263, and SP142, and multiple scoring systems, such as TPS (tumor proportion score), CPS (combined positive score), and ICS (immune cell score), for the immunohistochemical evaluation of PD-L1 expression. Although standardized in terms of IHC protocol, from automation of the workflow to IVD antibodies, the experience of IVB lab related to PD-L1 diagnosis showed that one major aspect to take into consideration when assessing its expression is tumor heterogeneity. Also, adnotation of peritumoral stroma may induce a bias in calculation of the final score, when pertaining to SP142 clone. Although PD-L1 testing is essential for directing immunotherapy for non-small cell lung cancer (NSCLC), standardization of testing procedures and incorporation of new biomarkers are required to optimize patient selection and improve clinical outcomes.

References

1. Gaal OI, Ungureanu A, Pop B, Tomescu A, Cătană A, Man M, Râjnoveanu RM, Palade E, Simon M, Luchian SD, Kubelac MP, Fulop A, Fekete Z, Ciuleanu TE, Jentimir I, Popovici B, Cainap C, Preda AC, Magdau C, Lesan A, Fetica B. The Genomic Landscape of Romanian Non-Small Cell Lung Cancer Patients: The Insights from Routine NGS Testing with the Oncomine Dx Target Panel at the PATHOS Molecular Pathology Laboratory. *Cancers (Basel)*. 2025 Jun 11;17(12):1947. doi: 10.3390/cancers17121947. PMID: 40563596; PMCID: PMC12190249.
2. Mao Y, Wang A, Ge X, Zhai J, Hu Y, Wang J. PD-1/PD-L1 inhibitors monotherapy vs. combination therapy in elderly advanced NSCLC: a real-world study and nomogram for survival prognosis. *BMC Pulm Med*. 2025 Jul 23;25(1):350. doi: 10.1186/s12890-025-03791-x. PMID: 40702519; PMCID: PMC12288261.



ANNUAL CONFERENCE OF THE VICTOR BABES NATIONAL INSTITUTE OF PATHOLOGY
BUCHAREST, ROMANIA
12-14 NOVEMBER, 2025

O17: Recent advances in the diagnosis and prognostic assessment of oral cancer

Constantin Caruntu^{1,2*}, Lacramioara Taubner³, Diana Alina Peicu^{1,4}, Nicoleta Roxana Urzica^{1,4}, Ana Caruntu^{4,5}

¹ Department of Physiology, Carol Davila University of Medicine and Pharmacy, 020021 Bucharest, Romania

² Department of Dermatology, Prof. N.C. Paulescu National Institute of Diabetes, Nutrition and Metabolic Diseases, 011233 Bucharest, Romania

³ Clinical Laboratory, Carol Davila Central Military Emergency Hospital, 010825 Bucharest, Romania;

⁴ Department of Oral and Maxillofacial Surgery, Carol Davila Central Military Emergency Hospital, 010825 Bucharest, Romania;

⁵ Department of Oral and Maxillofacial Surgery, Faculty of Dental Medicine, Titu Maiorescu University, 031593 Bucharest, Romania

*presenting author – correspondence: costin.caruntu@gmail.com

Keywords: oral squamous cell carcinoma; head and neck cancer; reflectance confocal microscopy; diagnosis; prognostic biomarkers

Oral cancer remains a major global health issue, accounting for about 2% of all malignancies and nearly 1.9% of cancer-related deaths. Despite medical advances, survival rates have shown little improvement in the last years, as over half of cases are diagnosed at advanced stages.

Key risk factors include tobacco, alcohol, HPV infection, chronic inflammation, and UV exposure. Early detection and reliable diagnostic and prognostic biomarkers are crucial for improving outcomes. This presentation highlights recent updates in diagnostic techniques and prognostic assessment, emphasizing new molecular and imaging biomarkers that enable earlier detection, and improved survival in oral cancer patients.



P1: Mixed Epithelial and Stromal Tumor of the Kidney: A Rare Biphasic Renal Lesion

S S Sivasubramanian^{1*}, Sumiti Vanjani², Limi Mohandas³

¹*Musgrove Park Hospital, Parkfield road, Taunton TA1 5DA, United Kingdom*

²*Musgrove Park Hospital, Parkfield road, Taunton TA1 5DA, United Kingdom*

³*Musgrove Park Hospital, Parkfield road, Taunton TA1 5DA, United Kingdom*

Email: Subhalakshmi.sivasubramanian@somersetft.nhs.uk

Background:

Mixed epithelial and stromal tumor (MEST) of the kidney is a rare, typically benign neoplasm occurring predominantly in middle-aged or perimenopausal women, often associated with hormonal exposure. Although usually benign with minimal risk of recurrence or metastasis, rare malignant transformations have been reported.

Materials and methods:

A 59-year-old female presented with abdominal pain and hematuria. CT imaging showed left hydronephrosis with an obstructed, poorly functioning kidney. Biopsy suggested leiomyoma, in view of risk of obstruction and renal failure pragmatic decision was taken in the MDT for further management by nephrectomy.

Results:

Patient underwent nephrectomy, following which sample showed spongy tumor in the renal medulla which is seen extending into the renal pelvis with renal pelvic dilatation. Histology showed well circumscribed tumor composed of occasional glands and cysts embedded in a variably cellular stroma. Immunohistochemical stains for ER and PR are positive in the stromal component of the tumor. SMA, Inhibin and Calretinin were also done. CD10 shows Peri Epithelial Condensation. Tumor is extending in the renal pelvis. These tumors are commonly located in the renal medulla, sometimes extending into the renal pelvis or involving both cortex and medulla. Angioleiomyoma and MEST were considered as differentials.

Conclusions:

MEST is a rare renal tumor with usually benign behavior. Surgical excision is curative, and prognosis is excellent, though rare malignant transformations have been reported. Awareness of this entity is important for diagnosis and management.

Acknowledgement

References

1. Bakavičius A, Barisiénė M, Snicorius M, et al. Malignant mixed epithelial and stromal tumour of the kidney: a case report and a literature review. *Acta Med Litu.* 2018;25(1):31–7. doi: 10.6001/actamedica.v25i1.3701.



P2: Experimental pharmacological research of new combined medicinal product for treatment of sensorineural hearing loss

Sergiu Parii^{1,4*}, Livia Uncu^{1,2}, Adrian Sochirca¹, Alina Ungureanu¹, Vasile Cabac^{1,3}, Vladimir Valica^{1,2}

¹ Scientific Center of Medicines,

² Department of Pharmaceutical and Toxicological Chemistry,

³ Department of Otorhinolaryngology of the „Nicolae Testemitanu” State University of Medicine and Pharmacy, bd. Stefan cel Mare si Sfant 165,

⁴ Center Neuroscan, str. Eugen Doga 2A, Chisinau, Republic of Moldova

*presenting author – correspondence: sergiu.parii@usmf.md

Background. Sensorineural hearing loss (SHL) affects the perception of sounds from the inner ear, auditory nerve, subcortical, and cortical auditory centers. The drug treatment of SHL is usually symptomatic and includes vasodilators, steroids, nootropics, and antioxidants [1]. Given the complex etiology and multifactorial pathophysiology of SHL, the development of combination therapies is gaining increased attention.

Materials and methods. This study aimed to develop and evaluate a novel oral fixed-dose combination capsule containing nicergoline, piracetam, and hawthorn extract (test product) for SHL management [2]. The preclinical research included: induction of SHL and peripheral vestibulopathy in animal models using gentamicin; experimental audiometric methods (otoacoustic emissions, Preyer reflex) for monitoring SHL; preclinical testing of static and dynamic locomotor coordination in *Wistar rats*.

Results. The test product demonstrated low acute toxicity across administration routes. In gentamicin-induced SHL models, animals treated with the test product showed a clear otoprotective effect, as evidenced by improved otoacoustic emission results (TEOAE, DPOAE > 0 dB SPL; signal-to-noise ratio > 3 dB SPL in the 1000–4000 Hz range), in contrast to the untreated ototoxicity group ($p < 0.05$). Audiological and vestibular testing (horizontal walking, and forced motor activity test to maintain balance) confirmed the efficacy of the test product, with the greatest therapeutic benefits observed in the treated group and no significant side effects noted.

Conclusions. This study pharmacologic characterized a novel combined drug in capsules containing nicergoline, piracetam, and hawthorn extract, for potential use in SHL therapy. The data of experimental audiological and vestibular tests in rats encouraging further preclinical and clinical research. In medical practice, the elaboration and use of the multicomponent preparations, containing synthesis and naturist substances is a perspective direction for the treatment of sensorineural disorders.

Keywords: preclinical research, sensorineural hearing loss, otoacoustic emissions, treatment, fixed-dose combined medicinal product

Acknowledgement This work was supported by the national scientific project of National Agency of Research and Development (no. 20.80012.8007.02SE, 2024-25)

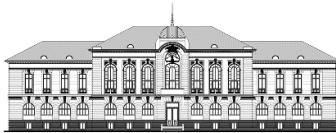
References

1. Hongzhuo L., Jinsong H., Kevin S.Li. Current strategies for drug delivery to the inner ear. *Acta Pharmaceutica Sinica B*. 2013; 3(2):86–96. <https://doi.org/10.1016/j.apsb.2013.02.003>



**ANNUAL CONFERENCE OF THE VICTOR BABES NATIONAL INSTITUTE OF PATHOLOGY
BUCHAREST, ROMANIA
12-14 NOVEMBER, 2025**

2. Rus L.M., Uncu A., Parii S. et al. Development and Preclinical Evaluation of Fixed-Dose Capsules Containing Nicergoline, Piracetam, and Hawthorn Extract for Sensorineural Hearing Loss. *Pharmaceutics*. 2025; 17(8):1-25. <https://doi.org/10.3390/pharmaceutics17081017>



P3: Comparative Proteomic Profiling Reveals Distinct Molecular Signatures of Lesions from an NLRP1-Driven Autoinflammatory Disorder

Catalin George Marinescu^{1,2}, Alexandra Dobre^{3,4*}, Roua Gabriela Popescu^{1,2}, Victor Eduard Peteu^{5,6}, Daciana Silvia Marta⁵, Mihaela Gherghiceanu^{3,5}, Daniela Adriana Ion³, Roxana Ioana Nedelcu^{3,7}, Tudor Emanuel Fertig^{3,5}

¹ Asociația Independent Research, 012416 Bucharest, Romania

² Blue Screen SRL, 012416 Bucharest, Romania

³ Carol Davila University of Medicine and Pharmacy, 050474 Bucharest, Romania

⁴ Elias University Emergency Hospital, Dermatology, Bucharest

⁵ Victor Babeș National Institute of Pathology, 050096 Bucharest, Romania

⁶ Chemical Engineering and Biotechnologies, Faculty of Chemical Engineering and Biotechnologies, National University of Science and Technology Politehnica Bucharest, 011061 Bucharest, Romania

⁷ Derma 360 Clinic, 011274 Bucharest, Romania

*presenting author – correspondence: alexandra.dobre@drd.umfcd.ro

Keywords: inflammasome; NLRP1; autoinflammation; mass spectrometry; keratoacanthoma; Multiple self-healing palmoplantar carcinoma

Background

Multiple self-healing palmoplantar carcinoma (MSPC) is a very rare disorder, characterized by germline mutations of the NLRP1 inflammasome sensor protein. These mutations lead to aberrant inflammasome activation and development of recurrent keratoacanthomas (KA), mainly on acral surfaces¹. The complex imbalance in skin immunity resulting from abnormal NLRP1 inflammasome activity can lead to other inflammatory disorders in these patients. Here we use mass spectrometry (MS) to investigate the proteomic profile of lesions from a patient with MSPC that additionally developed a psoriasis-like lesion (PLL), attempting to understand the pathways leading to KA formation specifically on hairless skin.

Materials and methods

After written informed consent, biopsies were collected from plantar KAs and from an abdominal PLL of a MSPC patient with the A66V NLRP1 mutation. Non-lesional skin was collected from the elbow region of volunteers. After proteolysis, peptides were analyzed using a Triple TOF 5600+ mass spectrometer (AB Sciex) and separated on an Eksigent 5C18-CL-120 column. MS analysis was performed using electrospray ionization in positive mode, in data-independent acquisition SWATH-MS mode. Each sample was analysed in triplicate. Peptide and protein identification was performed using PeakView 2.2, Skyline 22.2.0.255, and DIA-NN 1.9.

Results

We included 2058 proteins in the final comparative analysis of the three skin sample types. We showed upregulation of the IL1 superfamily (IL18, IL1RA, IL36, IL37) and of PYCARD/ASC in the plantar KAs but also, to a lesser extent, in PLL. Additionally, NLRP3 but not NLRP1-associated inflammasome inhibitors (e.g. from the HSP90 family) were more highly expressed in PLL than KA samples.

Conclusions

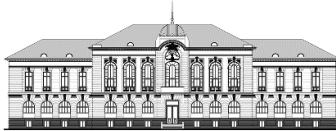


**ANNUAL CONFERENCE OF THE VICTOR BABES NATIONAL INSTITUTE OF PATHOLOGY
BUCHAREST, ROMANIA
12-14 NOVEMBER, 2025**

These results indicate the pathological activation of the NLRP1 inflammasome can occur regardless of anatomical site or lesion type in this MSPC patient, however proteomic analyses alone could not reveal the molecular pathway causing KAs to form specifically on epithelia without hair follicles.

References

1. Dobre A, Nedelcu RI, Turcu G, Brinzea A, Struna I, Tudorache G, Ali A, Hulea I, Balasescu E, Fertig TE, Gherghiceanu M, Harwood C, Ion DA, Forsea AM. Multiple Keratoacanthomas Associated with Genetic Syndromes: Narrative Review and Proposal of a Diagnostic Algorithm. *Am J Clin Dermatol.* 2025 Jan;26(1):45-59. doi: 10.1007/s40257-024-00900-0. Epub 2024 Nov 21. Erratum in: *Am J Clin Dermatol.* 2025 Mar;26(2):305. doi: 10.1007/s40257-025-00921-3. PMID: 39572470; PMCID: PMC11742465.



ANNUAL CONFERENCE OF THE VICTOR BABES NATIONAL INSTITUTE OF PATHOLOGY
BUCHAREST, ROMANIA
12-14 NOVEMBER, 2025

P4: Phenotypic changes in caveolin-1 deficient murine models

F.C. Mureşan^{*1,2}, T.E. Fertig^{1,2}, D.S. Marta¹, V.E. Peteu^{1,3}, G. Isvoraru¹, M. Gherghiceanu^{1,2}

¹ Victor Babeş Institute of Pathology, Bucharest, Romania

² Carol Davila University of Medicine and Pharmacy, Bucharest, Romania

³ National University of Science and Technology Politehnica, Bucharest, Romania

*presenting author – correspondence: filip.muresan@rez.umfcd.ro

Keywords: caveolae, caveolin-1, amyloidosis, pulmonary adenocarcinoma

Background

Caveolae (latin, meaning “little caves”) are 50-100 nm diameter, flask-like, “uncoated” plasma membrane invaginations. Caveolin-1 (CAV1) is the main proteic constituent of non-striated muscle caveolae. Significant progress has been made in elucidating caveolae structure and assembly mechanisms. Paradoxically, the advances in structural knowledge have not been doubled by equivalent progress in clarifying the mechanisms governing caveolae and caveolin functions. We show data on the pathological effects induced by the absence of CAV1 in tissues from a knockout mouse model (CAV1^{-/-}) and we compare these findings to wild-type (WT) controls.

Materials and methods

Six pairs of CAV-1 ^{-/-} mice (male and female) aged 14–22 months (The Jackson Laboratory, USA) and age- and sex-matched wild-type (WT) pairs were included in the study. Mice were sacrificed in accordance with European regulations. Spleen, liver, kidney, brain, heart, and intestine were collected and examined by optical and electron microscopy.

Results

The two groups presented several differences regarding disease development. First, a single CAV1 ^{-/-} mouse developed systemic amyloidosis (affecting the intestine, liver, spleen, kidney), versus 12 in the WT group. Second, 10 CAV1 ^{-/-} mice showed chronic, nonspecific perivascular inflammatory infiltrates in multiple organs, versus one WT individual. Third, 3 CAV1 ^{-/-} mice developed pulmonary adenocarcinoma with a predominant papillary growth pattern, versus none in the WT group. Another 3 CAV-1 ^{-/-} mice developed idiopathic crystalline pneumonia, versus none in the WT group. Finally, one case of mastocytosis was present in the CAV-1 ^{-/-} group.

Conclusions

Surprisingly, CAV1 deficiency seems to confer protection against amyloidosis, which is frequently described in ageing C57BL/6 mice, while predisposing to pulmonary adenocarcinoma and chronic inflammation. These findings suggest that CAV1 may contribute in maintaining respiratory epithelial integrity, homeostasis and turnover, as well as to the regulation of inflammatory responses.

Acknowledgement: This work was supported by MEC grant PN no. 23.16.01.01



P5: Combined EGFR and STAT3 inhibition in ETV1/ETV4-overexpressing prostate cancer: insights from 2D and 3D co-culture models

Elsa Gomes Paiva 1,2*, Beatriz Namorado3, Manuel R. Teixeira1,4,5 and Paula Paulo1,5

1 *Cancer Genetics Group, IPO Porto Research Center (CI-IPOP)/RISE@CI-IPOP (Health Research Network), Portuguese Oncology Institute of Porto (IPO Porto)/Porto Comprehensive Cancer Center, Raquel Seruca (Porto.CCC Raquel Seruca), 4200-072 Porto, Portugal;*

2 *PhD Program in Biomedical Sciences, School of Medicine and Biomedical Sciences (ICBAS), University of Porto, 4050-313 Porto, Portugal;*

3 *Master Program in Oncobiology, School of Medicine and Biomedical Sciences (FMCB), University of Algarve, 8005-139 Faro, Portugal;*

4 *Department of Laboratory Genetics, Portuguese Oncology Institute of Porto (IPO Porto)/Porto Comprehensive Cancer Center Raquel Seruca (Porto.CCC Raquel Seruca), 4200-072 Porto, Portugal;*

5 *School of Medicine and Biomedical Sciences (ICBAS), University of Porto, 4050-313 Porto, Portugal.*

**elsa.paiva@ipoporto.min-saude.pt*

Keywords: Prostate cancer; ETV1; ETV4; TTI-101; Erlotinib; Co-culture models.

Background

Prostate cancer (PCa) remains the second most frequently diagnosed cancer worldwide. Genomic rearrangements leading to overexpression of ETV1 or ETV4 occur in ~10–15% of cases and are linked to poorer prognosis. We recently identified the EGFR–STAT3 signaling axis as a key driver of ETV1-mediated oncogenic activity. Here, we investigated the potential of EGFR and STAT3 inhibition for targeting of this molecular subtype, and how tumor–stroma interactions modulate therapeutic response.

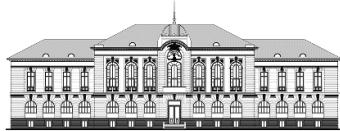
Materials and methods

The therapeutic efficacy of Erlotinib and TTI-101, as EGFR and STAT3 inhibitors, respectively, was evaluated either as single agents or in combination. Stromal modulation of treatment response was investigated using 2D and 3D co-culture models. In 2D, two approaches were used: a “secretome” approach, in which PC3 cells with distinct ETS backgrounds were cultured in conditioned medium from prostate cancer–associated fibroblasts (PCAFs), and a cell–cell interaction approach, where GFP-PC3 cells were co-cultured with PKH26-labeled PCAFs at varying tumor–stroma cell ratios. Cytotoxicity and proliferation were quantified using LDH and XTT assays, respectively. For 3D studies, the same cells were co-cultured at different tumor–stroma ratios in 384-well ULA plates to generate spheroid cultures. High-content imaging quantified growth, evaluated spheroid integrity, and assessed the spatial distribution of tumor and stromal cell populations, in 2D and 3D settings.

Results

In 2D cultures, conditioned medium from PCAFs promoted PC3 cells’ proliferation without inducing cytotoxicity, independently of ETS status. However, in direct 2D co-culture, higher proportions of PCAFs suppressed PC3 cells’ proliferation, suggesting a complex interplay between tumor and stromal cells in tumor cell growth. Nevertheless, co-inhibition of EGFR and STAT3 impaired cells proliferation/growth both in 2D and 3D co-culture models, regardless of the PC3/PCAFs ratio, suggesting that the combination therapy may effectively counteract the positive stromal influence on tumor growth.

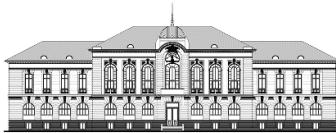
Conclusions



**ANNUAL CONFERENCE OF THE VICTOR BABES NATIONAL INSTITUTE OF PATHOLOGY
BUCHAREST, ROMANIA
12-14 NOVEMBER, 2025**

These findings support the therapeutic potential of combined EGFR and STAT3 inhibition for the treatment of ETV1/ETV4-overexpressing PCa. On going co-culture experiments will clarify how stromal components influence treatment efficacy in different ETS backgrounds, providing insights for future preclinical validation.

Acknowledgments: *This work has been partially supported by IPO-Porto Research Center (CI-IPOP-30-2023) and Fundação para a Ciência e Tecnologia (UI/BD/154819/2023)*



P6: Human Intestinal Organoids as Translational Models for Colorectal Cancer: From Molecular Profiling to Personalized Medicine

Radu Marian Marinescu^{1*}, Maria Dudau², Elena Codrici^{1,2}, Daniela Ionela Popescu², Vlad Herlea^{1,3}, Ana Maria Enciu^{1,2}, Mihaela Gherghiceanu^{1,2}

¹ University of Medicine and Pharmacy „Carol Davila”, Bucharest, Romania

² National Institute of Research & Development in Pathology and Biomedical Sciences „Victor Babeș” Bucharest, Romania

³ Department of Pathology, Fundeni Clinical Institute, Bucharest, Romania

*Correspondence author: radu-marian.marinescu@drd.umfcd.ro

Keywords: intestinal organoids, colorectal adenocarcinoma, molecular pathology, immunohistochemistry, personalized medicine

Background

Human intestinal organoids generated from crypt stem cells reproduce the architecture and function of the native gut epithelium in a three-dimensional system. In the context of colorectal adenocarcinoma, these structures provide a platform for molecular tumor profiling and in vitro therapeutic testing. However, limited evidence exists regarding the molecular concordance between organoids and primary tumors, challenging their validation as predictive models. This systematic review analyzes original and secondary studies published between 2011 and 2025 that evaluated the molecular concordance between human intestinal organoids derived from colorectal adenocarcinoma and their primary tumors, while identifying emerging research trends and current methodological limitations.

Materials and methods

A literature search was conducted according to the PRISMA 2020 guidelines in the PubMed, Scopus, and Web of Science databases, covering the period 2011–2025. The inclusion criteria comprised original or review articles written in English that used human intestinal organoids derived from colorectal adenocarcinoma for molecular, immunohistochemical, or transcriptomic (gene expression) analyses. Studies performed on animal models, normal mucosae, or dysplastic lesions were excluded.

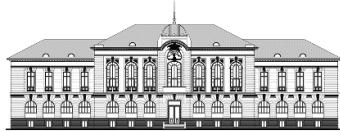
Results

Recent studies increasingly employ patient-derived intestinal organoids for molecular analyses, showing comparable expression of epithelial (CK20, CDX2) and, partially, stemness markers (LGR5) with primary tumors. However, variability in culture protocols and lack of transcriptomic standardization still hinder reproducibility.

Conclusions

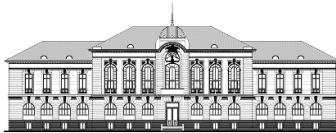
Human intestinal organoids derived from colorectal adenocarcinoma recapitulate key molecular and immunophenotypic features of primary tumors, supporting their role as personalized screening models. Further standardization and multi-omics integration are essential for translational implementation.

References



**ANNUAL CONFERENCE OF THE VICTOR BABES NATIONAL INSTITUTE OF PATHOLOGY
BUCHAREST, ROMANIA
12-14 NOVEMBER, 2025**

1. Sato T, Stange DE, Ferrante M et al., Long-term expansion of epithelial organoids from human colon, adenoma, adenocarcinoma, and Barrett's epithelium. *Gastroenterology*. 2011;141(5):1762–1772.
2. Sato T, van Es JH, Snippert HJ et al., Paneth cells constitute the niche for Lgr5 stem cells in intestinal crypts. *Nature*. 2011; 141(5):1762-72.
3. van de Wetering M, Francies HE, Francis JM et al., Prospective derivation of a living organoid biobank of colorectal cancer patients. *Cell*. 2015;161(4):933–945.



P7: The impact of high-fat diet on Natural Killer cells in tumor-bearing mice

Gheorghita Isvoranu^{1*}, Mihaela Surcel¹, Ana-Maria Enciu¹, Elena Codrici¹, Daniela Popescu¹,
Marioara Chiritoiu-Butnaru²

¹ Victor Babeș National Institute of Pathology, 050096 Bucharest, Romania.

² Institute of Biochemistry of the Romanian Academy, 060031, Bucharest, Romania.

* Gheorghita Isvoranu: gina_isvoranu@yahoo.com

Keywords: high-fat diet, NK cells, melanoma, mice

Background

Obesity is associated with and increased risk of cancer and various infections. Recent findings highlight that a high-fat diet induces altered immune cell functionality, including Natural Killer (NK) cells. Aim of the study was to examine immune cell populations, focusing on the phenotype and function of NK cells from melanoma-bearing mice fed a high-fat diet.

Materials and methods

C57BL/6 mice received a normal-fat diet (NFD, 4% fat) or high-fat diet (HFD, 22.6% fat) for 22 weeks. B16-F10 melanoma cells were injected subcutaneously after 19 weeks of diet. Immune cell populations were investigated by flow cytometry and serum proteins by multiplex immunoassay analyses. NK cell functionality was investigated on splenic NK cells activated overnight with cytokines.

Results

In the spleen, the percentage of CD4 T cells was slightly increased and the percentage of CD8 T cells was reduced in the HFD compared to NFD-melanoma group, while in the blood, the distribution of T cell subsets was reversed. NK cells were reduced in both the spleen and blood, and no differences were observed in lymph nodes between HFD and NFD melanoma groups. Cytokines pre-activated NK cells from healthy mice upregulated CD69 and CD25 receptors and enhanced the production of IFN-γ compared to tumor-bearing mice. Analyses of several serum inflammation-related parameters showed increased levels of S100A9 and ICAM-1, while serum pancreatic polypeptide levels were lower in HFD compared to NFD melanoma group.

Conclusions

These data indicate an association of impaired NK cell functionality and high-fat diet, and this dysfunction could lead to an elevated risk of cancer development and an impaired response to treatment.

Acknowledgement

This research was funded by the Romanian Ministry of Education and Research and CNCS-UEFISCDI, projects PN 19.29.02.03, PN 23.16.02.02 and PN-IV-P2-2.1-TE-2023-1169.