# Abstracts of the 2nd International Conference on Translational and Clinical Medicine – Digitalization and Artificial Intelligence in Medical Education and Research

May 23–25, 2024, Tbilisi, Georgia.

The conference was supported by Shota Rustaveli National Science Foundation of Georgia (SRNSFG) [MG-ISE-23-1313].

**See the link on the journal: http://tcm.tsu.ge/index.php/TCM-GMJ/issue/view/23**

**How artificial intelligence could eradicate mortality from colorectal cancer**

*Andrew A. Gumbs*[1,2]

[1]Department of Surgery, Otto von Guericke University Magdeburg, Magdeburg, Germany

[2]Advanced & Minimally Invasive Surgery Excellence Center, American Hospital of Tbilisi, Tbilisi, Georgia

High-risk surgeries carry a substantial burden of complications and adverse outcomes. However, the integration of Surgiomics, a surgical data analytics approach, with autonomous actions, such as available with robotic-assisted surgery, presents a promising avenue for decreasing risks in these complex procedures. Autonomous actions offer real-time decision support, enhancing precision, adaptability, and early detection of potential complications. Surgiomics leverages comprehensive patient data and advanced analytics to provide personalized risk assessment, enabling surgeons to tailor surgical plans to individual patients. By combining Surgiomic insights with autonomous systems, surgeons may be able to proactively address risks and optimize patient outcomes. Furthermore, autonomous actions and Surgiomics facilitate a learning environment, enabling continuous improvement by analyzing surgical data and integrating findings into autonomous systems. This synergistic approach holds significant potential for transforming high-risk surgeries, reducing complications, and improving patient safety, ultimately having the potential to transform the landscape of surgical care.

**Models in kidney transplantation: from AI models to organ models**

*Tim Hamelink*

Department of Surgery – Organ Donation and Transplantation, University Medical Center Groningen Groningen, the Netherlands

Kidney transplantation stands as the most effective treatment for end-stage renal disease. However, its success has led to an increased demand for donor organs, resulting in a growing reliance on kidneys from older donors. These kidneys often exhibit lower quality, reflected in high discard rates. Consequently, enhancing the pre-transplant assessment of donor kidneys is pivotal. This can be achieved through the use of various predictive models to evaluate organ quality and predict transplantation outcomes.

Advanced machine learning algorithms, such as random forest, or extreme gradient boosting, hold significant promise in predicting both short-term and long-term graft survival. Despite their potential, these models necessitate rigorous external validation to ensure their accuracy and generalizability.

Additionally, ex vivo normothermic machine perfusion emerges as a valuable technique for assessing organ quality. When combined with advanced imaging modalities and multi-omics analyses, these methods represent innovative strategies for improving pre-transplant viability assessment.

Ultimately, adopting a comprehensive approach that integrates pre-transplant donor and recipient data, ex vivo perfusion-derived data, and post-transplant information can provide a holistic framework for predicting transplant outcomes. This integrative strategy has the potential to significantly enhance long-term graft survival rates, advancing the field of kidney transplantation.

**For Triger Identification of Liver Regeneration After Partial Hepatectomy**

*Bakar Korchilava[1], Dimitri Kordzaia[1,2]*

[1]Ivane Javakhishvili Tbilisi State University (TSU), Tbilisi, Georgia
[2] Alexandre Natishvili Institute of Morphology, TSU, Tbilisi, Georgia

Liver regeneration after procedures like hemi-hepatectomy is a fascinating and complex process that relies on a delicate interplay of various cytokines, growth factors, and signaling pathways. The liver's response largely depends on the extent of tissue removal: when less than 25% is resected, the liver typically undergoes hypertrophic regeneration, where existing liver cells increase in size. In contrast, removing 50% or more of the liver triggers hyperplastic regeneration, which involves the production of new liver cells to restore mass.

Several key pathways, such as Wnt/β-catenin, Hippo-YAP, JAK/STAT, and PI3K/Akt/mTOR, play crucial roles in coordinating these regenerative processes. They regulate essential functions like cell growth, tissue remodeling, and overall organ size. Additionally, numerous other cytokines and growth factors, including hepatocyte growth factor (HGF) and epidermal growth factor (EGF), also participate in this intricate process, working alongside the major pathways to facilitate effective regeneration.

Changes in portal pressure and shear stress are significant factors in this regenerative response. Shear stress, caused by changes in blood flow dynamics, can act as one of the triggers for activating regeneration pathways. The alteration in mechanical forces on liver cells influences how they communicate and respond, thus playing a pivotal role in the overall regenerative process.

**Liver Regeneration and Structural Remodeling Following 2/3 Partial Hepatectomy: An Experimental investigation**

*Dimitri Kordzaia, Keti Tsomaia, Lika Svanadze, Zurab Chkhaidze*

Aleksandre Natishvili Institute of Morphology, Ivane Javakhishvili Tbilisi State University, Tbilisi, Georgia

In liver structural units such as the classical lobule, portal lobule, acinus, Ekataksin's cholehepaton, Matsumoto lobule/module, and Teutsch's lobule/module, the number of portal triads typically exceeds that of hepatic vein tributaries. However, identifying these units in human and rodent livers is challenging because some regions do not clearly fit within any specific unit. This uncertainty complicates the evaluation of liver architecture after regeneration, particularly following hemihepatectomy, which is essential for both the remaining and transplanted livers as they regenerate

**Methods**: In this study, 24 adult male Wistar rats underwent two-thirds hepatectomy. Liver tissues were examined at 24, 48, and 96 hours, as well as at 1 and 2 weeks post-surgery, using histology, immunohistochemistry, and scanning electron microscopy of vascular corrosion casts. The resected liver sections served as controls, and morphometric analysis was used to compare the findings

**Results**: The study revealed:

- Enlargement and changes in the shape of hepatocytes across all zones of the hepatic lobule/acinus within two weeks post-surgery.
- Formation of atypical membrane protrusions and new intercellular connections between hepatocytes.
- Transformation of the vascular network, including altered shapes and sizes of existing structures, along with the development of new sinusoidal capillaries and venules.
- Hepatic vein tributaries outnumbering nearby portal veins.
- Early-stage hypertrophy and proliferation, followed by spatial transformations affecting cellular, vascular, and connective tissue components, resulting in structural remodeling of liver tissue.
- A tendency for classical lobules and acini to transition into Teutsch's lobules/modules, characterized by the organic merging of sinusoidal compartments within these modules.

**Conclusion:** Liver tissue undergoes significant spatial reorganization following two-thirds hepatectomy. Although some of these observations are novel and not yet fully supported by current literature, further research is required for validation.

**“Chemo-brain”- Doxorubicin-Induced Neurotoxicity in Acute Experiment (Histopathology, Immunohistochemistry)**

*Liana Gogiashvili, Elene Nikobadze, Tamuna Gvianishvili*

Department of Experimental and Clinical Pathology, A.Natishvili Institute of Morphology Ivane Javakhishvili Tbilisi State University (TSU), Tbilisi, Georgia

Chemotherapy is an effective conventional and widely used treatment for cancer patients, that can significantly prolong the survival of patients with different types of cancer, but, unfortunately, it is associated with serious short- and long-term neurological side effects. Neurotoxicity manifests with a wide range of symptoms including fatigue, emotional instability, anxiety, difficulty concentrating, and issues with learning, reasoning, attention, and memory and syndromes such as acute, subacute and chronic encephalopathies, acute brain dysfunction, numerous cognitive disorders, myelopathy, meningitis, peripheral neuropathies. The phenomenon of chemotherapy-induced cognitive decline is termed as post-chemotherapy cognitive impairment (PCCI), chemotherapy-related cognitive impairment (CRCI), chemotherapy-induced cognitive impairment (CICI) or chemo-brain.

PCCI is a common complaint that dramatically impairs the quality of life of survivors and prevents them from returning to their pre-cancer lives among patients with various types of cancer, such as breast or lung cancer. The exact nature of chemotherapy appears complex, but a clear understanding of the mechanisms involved in PCCI, which could provide important information for potential treatments or therapies, is still unclear.

Doxorubicin (DOX) is commonly used in adjuvant chemotherapy for a variety of tumors, but its efficacy against brain tumors is limited due to its poor penetration across the blood–brain barrier (BBB). Despite this barrier, DOX has been shown to be involved in intense central neurotoxicity despite being almost entirely restricted to the periphery. DOX has been detected in the brain following peripheral administration and has caused severe neurotoxicity. However, the exact morphological mechanisms underlying brain chemotherapy remain unclear.

We study the effects of doxorubicin (DOX) in an acute experiment on the cerebral cortex and cerebellum, which would enable us to contribute to the definition of the functional and morphological basis of DOX-induced neurotoxicity.

The experiment involved adult male Wistar rats (m=170-200 g). A control group of intact animals followed standard vivarium protocols (GALS regulation 2023), and four experimental groups received different doses of DOX (5-15 mg/kg) with varying numbers of injections. Histological and immunohistochemical studies were conducted.

We focused on structural changes in the cortex and cerebellum, observing a significantly reduced number of intact neurons, along with phenomena such as swelling, shrinkage, eosinophilia, and "red neurons." Other findings included chromatolysis, neuronophagia, "crystal-like" cells, massive coagulative necrosis, and expanded Virchow-Robin spaces. Marked reactive gliosis, formation of neuritic plaques (β-amyloid protein), and "neurofibrillary tangles" (microtubule-associated tau-protein) showed progressive tendencies over a 15-day period. Additionally, we noted degeneration of astrocytic glial cytoskeletal elements, hypertrophy-hyperplasia of astrocytes with high expression of anti-GFAP, and in the cerebellum, swelling and disorganization of the Purkinje cell layer with strong positive anti-GFAP reactions. In the choroid plexus, findings included hyperemia, hemolysis, hemo- and plasmorrhagia, and marked swelling of the ependyma with a high positive anti-GFAP reaction.

Thus, a study of doxorubicin (DOX) effect showed significant changes in all neural elements of cytoarchitecture causing reactive astrogliosis and the formation of glial scars in the area of inflammation.

These changes can be considered as a significant basis of chemo-brain and subsequent cognitive impairment.

**Structural and Molecular Differentiation of Neuroblastoma-Derived Human Neurons is Associated with Alterations in Spontaneous and Evoked Calcium Dynamics**

*Deepika Negi[1], Susan Shorter[1], Bini Claringbold[1], Iain Goodhall[1], Sukhwinder S. Shergil[2,3] and Saak V. Ovsepian[1,4]*

[1]Faculty of Engineering and Science, University of Greenwich London, Chatham Maritime, ME4 4TB, United Kingdom;
[2]Department of Psychosis Studies, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London SE5 8AF, UK.
[3]Kent and Medway Medical School, Canterbury CT2 7NZ, UK
[4]Faculty of Medicine, Ivane Javakhishvili Tbilisi State University, 0159, Tbilisi, Georgia

**Corresponding author:** Deepika Negi & Saak V. Ovsepian, Faculty of Engineering and Science, University of Greenwich London, Chatham Maritime, ME4 4TB, United Kingdom. Email: d.negi@greenwich.ac.uk and s.v.ovsepian@gre.ac.uk

**Keywords:** Neuroblastoma-derived neurons; BDNF; Calcium imaging; Spontaneous activity; Molecular polarization; SH-SY5Y cells.

**Abstract**

During development, neuronal precursors transform from non-differentiated pluripotent state into specialized neurons. Much research has been conducted into morphological and molecular alterations during this transition, with underlying functional dynamics and mechanisms waiting to be elucidated. We combined structural and molecular imaging studies of neuroblastoma-derived developing neurons with functional characterization of evoked and spontaneous $Ca^{2+}$ dynamics. In a non-differentiated state, we detected trace amounts of neuronal markers, with live imaging showing high-amplitude slow spontaneous $Ca^{2+}$ oscillations. Application of carbochol induced monophasic low-amplitude $Ca^{2+}$ transients. Differentiation of cells into the next 2CL stage, using retinoic acid, has promoted the enrichment of cells with neuron-specific proteins and mild morphological polarization with neurite outgrowth. These changes were associated with strong suppression of $Ca^{2+}$ oscillations, while evoked $Ca^{2+}$ transients remained unchanged. Converting cells further into morphologically differentiated neurons by combining BDNF and retinoic acid treatment promoted extensive polarization of cells with a strong enrichment with neuron-specific markers. These changes were accompanied by a rebound of spontaneous oscillation of $Ca^{2+}$ but of lower amplitude and higher frequency variance. The evoked by carbachol $Ca^{2+}$ transients at this stage were enhanced and showed a bi-phasis decay. At all differentiation stages, ionomycin-induced $Ca^{2+}$ transients were indistinguishable. These findings led us to conclude that the structural and molecular transmutation

of neuroblastoma-derived human neurons is associated with extensive adjustments in $Ca^{2+}$ dynamics, likely contributing to their differentiation.

**Digital Transformation – Challenges and Chances**

*Otto Rienhoff*

Institute of Medical Informatics, Faculty of Medicine, University Medical Center Göttingen, Göttingen, Germany

The digital word in medicine started in the years of the Second World War by documenting cases on punch cards for statistical analyses on early computers. Until the 1990ies, the speed of development grew substantial: Mainframe computers were the infrastructure for many hospital systems worldwide and the first generation of smaller computers managed massively growing medical lab facilities. After the collapse of the Soviet Union several small countries has the chance to legally set up their health care systems in a more flexible way and thus became leading nations in the digital competition worldwide. Many bigger countries were not so adaptive and remained in health system structures from decades before. All of them struggled to utilize possible innovations by changing processes into more efficient digital workflows. In the last decade, this effect led to the situation that the digital transformation of our societies, which we are facing now, has been positively utilized in several smaller countries like e.g. Netherlands or Baltic States and has caused a controversial historical change of national health care systems in some bigger countries like e.g. Germany or France. The perspectives for patient oriented health infrastructures are another highly dynamic development in this digital transformation process. As the digital transformation is more and more transforming our societies, health care systems that do not move to new processes and structures will fall back in international comparisons. That will cause challenging effects: non-attractiveness to health professionals and patients leading to inefficiency in international comparison. Therefore, every institution and every country have to address the digital transformation of our societies to keep health care positive and more efficient for patients as well as professionals.

**Effects of biocidal action of water treated with a liquid activation multicomponent module**

*Giorgi Phichkhaia, Tsiuri Sumbadze, Sarkis Markariani*

Alexander Natishvili Morphology Institute of Ivane Javakhishvili Tbilisi State University, Tbilisi, Georgia

As a result of the significant increase in the mass of technologically polluted water in the environment, one of the urgent problems in the world is the supply of clean water to the population. The problem is exacerbated by the failure of existing water supply systems, which leads to secondary contamination of purified water.

We have created and tested a laboratory model of liquid activation multicomponent module (LAMM), the operation of which, unlike other analogs, is based on such physical methods as treatment with a magnetic field, ultrasound, ultraviolet radiation, and silver ions.

According to the studies conducted at the Institute of Morphology of TSU Alexander Natishvili and Medical Biotechnology named after Vl. Bakhutashvili of TSU, it was established that drinking water treated with LAMM from the city network shows a stable antibacterial effect - that is, the water is sterilized, and at the same time, staphylococcal bacterial cultures do not grow on the soil created on the basis of such water. Water treated with SDM retains its antibacterial properties for a certain period of time, the duration of which depends on the exposure time in the module and the degree of contamination of the water with microbes. Subsequently, these data were confirmed by L. Sakvarelidze's National Center for Disease Control and Public Health, Lugar Public Health Research Center S.aureus -25923, E.coli -25922, Ps. aeruginiosa #-7853, E.hirae #10541 and B.cereus-4342 in an experiment conducted on ATCC strains. In the same laboratory, we separately studied the effect of the biocidal action of the fluids treated with LAMM against the B. anthracis STI vaccine strain using the same method. After 24 hours of incubation, the typical growth characteristic of B. anthracis was observed in the control sums, while no growth was observed in the test culture.

**Distinct Levels of PSMD10 Gene mRNA Expression in Liver Tissue and Blood Plasma of Patients with Cirrhosis and Hepatocellular Carcinoma**

*Mikheil Jangavadze, Gia Lobzhanidze, Levan Gogichaishvili*

Faculty of Medicine, Ivane Javakhishvili Tbilisi State University, Tbilisi, Georgia

**Introduction:** Early diagnosis of hepatocellular carcinoma (HCC) is crucial for improving patient survival rates. Gankyrin/PSMD10 is significantly involved in the carcinogenesis of hepatocellular tumors. This study aims to explore the potential of plasma circulating gankyrin mRNA expression as a biomarker for HCC.

**Methods:** Blood samples were collected from patients with HCC (n = 32), metastatic HCC (n = 5), cirrhosis (n = 7), hepatitis C virus positive (HCV+; n = 5), and healthy controls (n = 5). Gankyrin/PSMD10 RNA expression was assessed in tumor tissue samples from HCC patients (tumor and adjacent tissues; n = 32), cirrhotic patients (n = 5), and normal tissues (n = 5). Plasma samples were isolated from 4 ml of peripheral blood. Total DNA/RNA/miRNA was extracted from the plasma using the RecoverAll Total Nucleic Acid Isolation kit. Sections of formalin-fixed, paraffin-embedded (FFPE) tissue, each up to 20 µm thick, were combined into a 1.5 ml microcentrifuge tube. Total DNA/RNA was extracted from the FFPE tissues of tumor, adjacent liver, and control samples using the same kit. RT-qPCR was conducted with TaqPath 1-Step Multiplex Master Mix, amplifying cDNA using the following TaqMan assays: p28/Gankyrin (Assay ID Hs01100439_g1) and human 18S ribosomal RNA (Assay ID Hs99999901_s1).

**Results:** Gankyrin/PSMD10 RNA was not detected in serum samples from patients with cirrhosis, HCV+, or healthy individuals. The mean ΔCq in the HCC group was 11.69 ± 1.6, while in patients with metastatic HCC, it was 10.16 ± 0.4. A statistically significant difference in ΔCq was observed between groups ($P < 0.0002$). Notable differences in gankyrin expression levels were found in tissue samples. The 2-ΔΔCq mean for gankyrin/PSMD10 in HCC, adjacent tumor tissue (HCC ADJ T), cirrhosis, and control groups were 418.5

± 220.6, 78.68 ± 49.40, 20.62 ± 11.32, and 1.02 ± 0.23, respectively, with statistically significant differences between groups ($P < 0.001$).

**Conclusions:** This study provides compelling evidence that gankyrin RNA expression is significantly elevated in HCC compared to normal and cirrhotic tissues. Additionally, gankyrin RNA levels in tumor-adjacent liver tissue were higher than those in cirrhotic liver tissues of patients without HCC. Gankyrin RNA was undetectable in the blood plasma of healthy individuals and patients without cancer; however, its expression was significantly increased in patients with HCC. Detecting gankyrin RNA in liquid biopsies may be effectively utilized for screening at-risk patients for HCC development. While gankyrin is not specific to HCC, it should be used alongside other molecular markers for HCC diagnosis but can serve as a standalone marker for monitoring and early detection of tumor recurrence.

**Liver Structural Remodeling After Initial and Repeat Resection**

*Keti Tsomaia, Lika Svanadze, Zurab Chkhaidze, Dimitri Kordzaia*

Aleksandre Natishvili Institute of Morphology, Ivane Javakhishvili Tbilisi State University, Tbilisi, Georgia

**Introduction**: While mechanisms of liver regeneration after partial hepatectomy are extensively studied, the specific structural transformations following resection and re-resection are less explored. Study aims to compare architectural differences between normal liver tissue and tissue after primary and repeated partial hepatectomy, exploring the long-term effects on the vascular bed and overall liver structure.
**Methods:** We analyzed liver tissue from 24 Wistar albino male rats, using histology, histochemistry, immunohistochemistry, and scanning electron microscopy of vascular corrosion casts. Comparative study was conducted through morphometric analysis, comparing the data of control and study (liver resection and re-resection) groups.
**Results:**

- After 9 months of partial hepatectomy, liver undergoes significant changes, featuring remodeled lobules of varying sizes. The presence of "mega-lobules" is observed, housing hypertrophic hepatocytes with diverse shapes, primarily in the first and third zones of the acinus. These altered lobules exhibit an increased abundance of connective tissue. Additionally, sinusoidal capillaries exhibit multiplication through the both mechanisms - "sprouting" and "splitting", confirmed by appearance of the typical blind-ended ramifications and “septs” on the vascular corrosion casts;
- After 6 months of repeated partial hepatectomy following a 9-month regeneration, hepatocyte hypertrophy is more pronounced in the 3$^{rd}$ zone of liver acinus. The sinusoidal network is also remodeled, in particular, the diameters of the casts are increased, as well as the number and sizes of the "protrusions" and "vills" developed on them. The local dilations resulted from the merging of 3-4 sinusoids (sinusoidal lakes) were observed. Quite often the areas containing such patterns are difficult to distinguish from small tributaries of the hepatic veins (central and sublobular veins) on histological slices. In comparison with the changes developed in 9 months after PH, the number and size of mega-lobules as well as the content of connective tissue fibers are increased.

**Conclusion**: Liver regeneration following 2/3 resection and re-resection is a complex, months-long dynamic process involving the spatial transformation, altering the shape and number of cellular, vascular, and connective tissue components, resulting in complete lobular structural remodeling.

**Risk of HCC in patients with advanced fibrosis/cirrhosis successfully treated with DAA within the Georgian national hepatitis C elimination program**

*L. Sharvadze*[1,2], *A. Abutidze*[1,2], *M. Zhamutashvili*[4], *M. Todua*[2], *N. Kipiani* [3], *M. Karchava*[1,4]

[1]Infectious Diseases, AIDS and Clinical Immunology Research Center, Tbilisi, Georgia
[2]Ivane Javakhishvili Tbilisi State University, Tbilisi, Georgia
[3]Tbilisi State Medical University, Tbilisi, Georgia
[4]European University, Tbilisi, Georgia
[5]Tbilisi, Medical Academy,Tbilisi, Georgia

**Background and Aims:**

Direct-acting antiviral (DAA) therapy has revolutionized the treatment of hepatitis C virus (HCV) infection, with very high rates of sustained virologic response (SVR) and an excellent safety profile. As a result, the morbidity and mortality associated with HCV has dramatically decreased. However, data on the impact of DAA therapy on the natural history and development of HCC are limited especially in patients with advanced fibrosis/cirrhosis. The aim of the study was to explore the occurrence of HCC in chronic hepatitis C patients with advanced fibrosis/cirrhosis who were successfully treated with DAA within Georgian national hepatitis C elimination program.

**Methods**: This longitudinal study included 469 patients with advanced liver fibrosis/cirrhosis (defined by FIB-4 score and transient elsatography), who achieved SVR in 2015-2022 and who were followed through June 2024. We estimated cumulative and annual risks of incident HCC by period of follow-up. All patients included in the study underwent the following investigations: abdominal ultrasound, AFP, liver function tests and transient elastography every 6 months. The diagnosis of HCC was confirmed by MRI and/or liver biopsy (in case of necessity). These patients had neither HCC nor decompensated cirrhosis prior to study

**Results**: Among the 469 patients with SVR, 36 incident cases of HCC were diagnosed during the mean 5.5 years of follow-up. Among 36 patients with incident HCC 21 were men and 6 women. Mean age at the time of HCC diagnosis was 49 years. The cumulative 1, 2, 3, 4 and 5- year risks of HCC were 0.4%, 1.5% 3.0%, 4..9% and 7.7% respectively. While annual risk estimates were 0.4%, 1.1%, 1.7%, 2.4% and 4.1% for years 1, 2, 3, 4 and 5 respectively. All patients with incident HCC had liver cirrhosis. Among 36 patients with HCC: 8 patients abused alcohol. 11 patients had HCV genotype 3, 7 patients had Non-alcoholic fatty liver disease (NAFLD), 13 patients had type 2 diabetes, 1 patient had Hodgkin's lymphoma and no significant comorbidity was documented in 4 patients.

**Conclusion**: The patients with advanced liver fibrosis/cirrhosis remain at increased risk of developing HCC even after SVR. Therefore all patients with advanced fibrosis/cirrhosis require close surveillance for HCC regardless of SVR. Whether age, NAFLD, diabetes, alcohol abuse or other comorbidities increase the risk of HCC need to be further explored.

**Information about the first steps of implementation of digitalization and AI at the Faculty of Medicine, TSU**

*Lika Svanadze[1,2], Maia Bitskinashvili[2], Mikheil Jangavadze[1,2], Keti Tsomaia[1,2], Roman Shakarishvili[2], Dimitri Kordzaia[1,2]*

[1]Aleksandre Natishvili Institute of Morphology, Ivane Javakhishvili Tbilisi State University, Tbilisi, Georgia
[2]Faculty of Medicine, Ivane Javakhishvili Tbilisi State University, Tbilisi, Georgia

The Faculty of Medicine at Ivane Javakhishvili Tbilisi State University (TSU) has made significant strides in digitalization and the integration of artificial intelligence (AI) within medical education, diagnostics, and research. Key initiatives include the establishment of a Digital Pathology System at the Alexandre Natishvili Institute of Morphology (TSU-IM), the launch of research and development projects in digital pathology, as well as the enhancement of educational programs through Competitive Innovation Fund (CIF) projects.

Digital Pathology Infrastructure: TSU-IM has developed a state-of-the-art Digital Pathology Laboratory, equipped with a MoticEasyScan Pro 6 scanner and advanced IT infrastructure. This system enables remote consultation, research, and education, supporting collaboration with international pathologists. With over 850 slides and 65 patient cases digitized, the platform facilitates remote access, digital analysis, and includes tools for annotation and measurement.

Research Initiatives: A current project, "Development of a Complex Model for Breast Cancer Classification using Digital Pathology," aims to create an advanced breast cancer classification model based on histological images and machine learning. The model leverages techniques such as Fully Convolutional Networks and Convolutional Neural Networks to classify malignancies and hormone receptor statuses, enhancing diagnostic accuracy and efficiency in case analysis.

Educational Program Development (CIF Projects): Supported by CIF, TSU is advancing medical education through the development of modern programs in Translational Neuroscience and Molecular Pathology. The Translational Neuroscience program, a consortium with three Georgian universities, addresses gaps in neuroscience education by introducing an integrated course, a translational research hub, and innovative tools such as virtual patient programs. The Molecular Pathology curriculum bridges basic science and clinical practice, with plans for a molecular pathology lab, bioinformatics center, and comprehensive training for educators across Georgia.

These initiatives reflect TSU's commitment to modernizing medical education, aligning Georgia's standards with international benchmarks, and enhancing the nation's capacity in medical research, education, and healthcare delivery.

**The treatment of tongue squamous cell carcinoma in rats**

*Mariam Kakabadze, Teona Paresishvili, David Chakhunashvili, Zurab Kakabadze*

Department of Clinical Anatomy, Tbilisi State Medical University, Tbilisi, Georgia

**Background**. This paper concerns the development of a local drug delivery system for destroying the residual tumor cells following the excision of squamous cell carcinoma of the tongue.
**Methods**. The local drug delivery system is presented as a two-layer multicomponent gel (MCG) based on fibrin. The internal layer of MCG that directly contacted the surface of the wound contained Cisplatin, which were placed on collagen microcarrier CultiSpher-S. The external layer of MCG was composed with microcarrier CultiSpher-S containing Cisplatin and freeze-dried bone marrow stem cells. The efficacy of MCG was tested in a rat model of squamous cell carcinoma of the tongue created with 4-Nitroquinoline 1-oxide (4NQO).
**Results**. The targeted drug delivery system based on MCG that we developed has shown high efficacy for the treatment of squamous cell carcinoma of the tongue in rats. In 75% of animals with the model of squamous cell carcinoma of the tongue that were treated with MCG, a noticeable suppression of tumor growth was evident throughout 90 days without the phenomenon of tumor recurrence. **Conclusion**. Local drug delivery system based on the MCG has demonstrated efficiency in preventing residual tumor cells caused by local recurrence.

**Spontaneous HBsAg Loss and Seroconversion in Chronic HBV Patients Following Severe COVID-19: A Five-Year Follow-Up of Three Patients**

*Marine Karchava[1,2,3], Natia Dvali[2], Lana Gatserelia[2,3], Lela Dzigua[2], Revaz Mechurchlishvili[2], Manana Todua[4], Maia Zhamutashvili[2,5], Nino Kipiani[6], Akaki Abutidze[2,3,4], Lali Sharvadze[2,3,4,7]*

[1]Tbilisi, Medical Academy, Tbilisi, Georgia
[2]Infectious Diseases, AIDS and Clinical Immunology Research Center, Tbilisi, Georgia
[3]Hepatology Clinic- Hepa, Tbilisi, Georgia
[4]Ivane Javakhishvili Tbilisi State University, Tbilisi, Georgia
[5]European University, Tbilisi, Georgia
[6]Tbilisi State Medical University, Tbilisi, Georgia
[7]The University of Georgia, Tbilisi, Georgia

Spontaneous HBsAg loss is rare in untreated chronic hepatitis B (HBV) patients, with its triggers still largely unknown. This case study reports a five-year follow-up male, treatment-naïve, chronic mono infected HBV patients who experienced spontaneous HBsAg loss and seroconversion following severe COVID-19 infection.

Three HBV mono-infected patients, had been monitored since 2016, they were initially categorized to be in an inactive carriers state, exhibiting low serum HBsAg levels (<55 IU/ml) and HBV DNA (<100 IU/ml). All of them had normal aminotransferases and no liver cirrhosis by transient elastography. During 2020-2021, they showed significant increases in HBsAg (15,000-26,000 IU/ml) and HBV DNA (980-2,500 IU/ml) levels, alongside mild to moderate elevations (80-115 IU/L) in aminotransferases (ALT, AST) GGT and bilirubin levels. In the follow up visits, all three patients' demonstrated HBsAg loss followed by HBV seroconversion (Anti-HBs: 12-55 IU/ml).

The observed increases in aminotransferases, HBsAg and HBV DNA levels might suggest an immune-mediated flare, possibly linked to a cytotoxic T lymphocyte response against HBV. The coinciding severe COVID-19 infection may have played a critical role in triggering such immune responses. Further studies are needed to confirm the possible link between severe COVID-19 and spontaneous HBsAg loss among chronic treatment naïve HBV infected patients.

**Polyembryony, variation and introgression - for expanding the citrus area**

*Zurab Bukia*

Aleksandre Natishvili Institute of Morphology, Ivane Javakhishvili Tbilisi State University, Tbilisi, Georgia
TSMU Bakhutashvili Institute of Medical Biotechnology, Tbilisi,Georgia.

**Key words:** polyembryony, citrus, variability, introgression, area;

The review presents citrus as a special group of flora. It is also indicated that there are many varieties and forms of citrus crops (lemon-Citrus Limon Burm, tangerine Citrus Reticulata Bl., orange-Citrus Sinensis(L.) Osb., grapefruit-Citrus Paradisi Macf.) which is derived from the process of evolution (variation, heredity, selection), from adaptation to natural conditions and conscious selection.

These very interesting plants, after being freed from the phytocenosis of the tropical forest, in the process of cultivation in the open ground, in completely different climatic conditions - in different regimes of moisture, soil and atmosphere, did not lose the properties characteristic of tropical plants, but as a result of natural interbreeding (which they have a noticeable tendency to) they received great biological plasticity, adaptation High resistance to low temperature, dry soil and air.

The fact that citrus trees have gone far in terms of adapting to different thermal regimes is indicated by the data and the scale of their distribution.

The practice of introduction to citrus crops has convinced everyone that the degree of adaptability of lemon, orange and mandarin is very high, and their promising varieties and forms can be seen in areas far from the place of origin (USA, Mediterranean coast, China, Japan, Indonesia, Europe);

In the historical process of the establishment of new forms of citrus fruits, it is striking that the way to further expansion of the area is explored not by the best forms in terms of culture, yield and productivity, but also less adapted ones too to any soil conditions, with relatively average data.

By making methodical selection, it is possible to highlight the role of citrus crops and expand the area;

**Safety of water treated with liquid activation multicomponent module**

*Giorgi Phichkhaia, Tsiuri Sumbadze, Sarkis Markariani*

Alexander Natishvili Institute of Morphology of Ivane Javakhishvili Tbilisi State University, Tbilisi, Georgia

The variety of water pollution caused by various factors led to the variety of drinking water purification-dewatering methods. Water purification and desalination can be based on physical, chemical and biological methods, or various combinations of these methods. In addition, in conditions of equal results, preference should be given to physical methods, since no other substances or organisms are mixed with water.

We tested the safety of water treated with a liquid activation multicomponent module (LAMM) on Wistar rats. Male rats of one litter, up to 3 months of age, were divided into three groups (6 animals in each group):

Group 1 was supplied with drinking water from the city network;

The 2nd group was supplied with LAMM-treated drinking water from the city network;

Group 3 was given distilled water.

Animals were fed standard laboratory rat chow and had free access to water for 4 months. Animals were observed: every 20-25 days: their weight was recorded, feces analysis was carried out. After 4 months, we removed all animals from the experiment and studied the morphology of their internal organs and bacteriological analysis of feces. It was established that: a) the behavior of different groups of animals did not differ from each other; b) The microscopic structure of internal organs of animals does not undergo any changes. c) the analysis of animal excrement did not confirm the difference between the data of different groups of animals, which is particularly noteworthy considering the bactericidal nature of water treated with Sam; d) the weight of animals that were given water treated with LAMM was significantly higher (within 100 grams) than the weight of animals of other groups.

**Malignant tumors of the outer ear**

*Teona Paresishvili, Konstantine Mardaleishvili, David Chakhunashvili, and Zurab Kakabadze*

Department of Clinical Anatomy, Tbilisi State Medical University, Tbilisi, Georgia

According to the literature, the head and neck are the most common site for tumors with a ratio of almost 90%. Almost 6-10% of malignant neoplasms of the skin of the head and neck are located in the auricular or periauricular region. Carcinomas located in the external auditory canal (EAC) are extremely rare and account for 0.2% of all tumors in the head and neck region. Compared with other anatomical regions of the body, all types of ear tumors have a more aggressive course of the disease. Lesions of the skin of the

external ear may require rapid and accurate evaluation by otolaryngologists, dermatologists, oncologists, and surgeons. Both melanotic and non-melanotic malignancies of the ear have a high probability of recurrence and metastasis, so early diagnosis and therapeutic interventions are vital. Diagnosis of malignant neoplasms of the skin of the outer ear may be missed or detected at an invasive stage, as they may not be visible to the naked eye, may be covered by skin or located in the external auditory canal. The treatment approach is still a subject of debate among physicians, as a satisfactory outcome, aesthetics and preserved ear function must be considered simultaneously. Poor prognosis despite the variety of treatment methods, structural and anatomical features of the outer ear, certain surgical risks and recurrence rates also pose a great challenge for reconstructive and oncological treatments.

**Dental Pulp Tissue Engineering**

*Mariam Kakabadze, Inga Sikharulidze, Mtvarisa Kordzaia, Manana Kakabadze*

Faculty of Medicine, Tbilisi State University, Tbilisi, Georgia

The presented work discusses methods for creating dental pulp based on the principles of tissue engineering using decellularized scaffolds and bone marrow stem cells.

**Materials and methods:** Decellularized human dental pulp tissue, which was loaded with rat bone marrow stem cells, was used as a scaffold. The resulting bioengineered pulp was placed into a tooth section/framework, followed by implantation into the subcutaneous space of the rat's back.

**Results:** Research has shown that decellularized human pulp tissue loaded with bone marrow stem cells can be used as a scaffold for dental pulp bioengineering. Studies have shown that our bioengineered pulp, after heterotopic implantation, forms vascularized tissue similar to dental pulp and can express markers involved in dentinogenesis and angiogenesis.

**Conclusions:** Decellularized human dental pulp tissue has great potential for use as a cell carrier in tissue engineering.

**Some hemodynamic parameters of the liver during 24-hour perfusion conditioning using a proprietary device**

*Zurab Chkhaidze, Nodar Khodeli, Dimitri Kordzaia, Otar Pilishvili*

Aleksandre Natishvili Institute of Morphology, Ivane Javakhishvili Tbilisi State University, Tbilisi, Georgia

**Introduction.** The transplantology is one of the most promising and perspective fields of the modern medicine as the replacement of the organs with unrecoverable disease (irreversible changes) with the donor organs has no alternative so far. Boosting the number of liver pathologies in the world and, on the other hand, successful liver transplantations result in an annual increase in the number of people waiting for transplantation. Therefore, attention was drawn to so-called methods of morpho-functional improvement of organs obtained from "marginal" donors. It was revealed that machine perfusion can improve the condition of the donor organ. Numerous experimental studies show that perfusion of the organ with controlled, normothermic, oxygenated blood is a key factor in liver conditioning and perfusion should be prolonged in order to achieve the desired effect.

**Methods.** The study was conducted on 5 pigs weighing 20-25 kg. Perfusion of the cannulated liver began one hour after explantation (warm ischemia) with normothermic oxygenated blood. For perfusion, a two-chamber pump of our own design with a hydraulic drive was used, providing pulsating blood flow in the hepatic artery and non-pulsating - in the portal vein. To condition the liver, heparin, insulin, bile preparations, prostacyclin and nutrients in standard doses were introduced into the perfusate. The condition of the liver was assessed by morphological studies, monitoring of hemodynamic parameters in the portal vein and hepatic artery, as well as the amount of bile secreted. Bile acids, cholesterol, bilirubin, glucose, and transaminases were determined in the blood.

**Results.** In all experiments, perfusion was carried out within physiological hemodynamic parameters (blood pressure in the hepatic artery 82±4.3/58±3.1 mmHg; blood flow in the portal vein 765±36 ml/min. Over 24 hours, the amount of bile released was 114±28 ml). Also, biochemical parameters in the blood iffered slightly from the initial data. Morphological studies showed that less than 3% of cells were suffered by small droplet micro steatosis; mononuclear portal infiltrates were found only in several areas. Mild mixed large droplet micro steatosis and small droplet micro steatosis was found in less than 5 % and 10% of the hepatocytes accordingly on the 16th and 24th hours of perfusion. Similarly the mild venous congestion was present in 1 out of 5 livers after 16-hours perfusion and in 2 out of 5 livers after 24-hours perfusion. The number of necrotic hepatocytes and portal triads infiltrated with mononuclear cells did not exceed 10% and 15% accordingly. However, there were no differences in the degree of biliary damage – cholestasis or ductular proliferation - correlating with the terms of the experiment.

**Conclusion.** 24-hour liver perfusion conditioning by using of the machine of own design providing the pulsatile blood flow guarantees the satisfactory preservation of liver making it useful for successful transplantation.

**Nucellar selection and citrus biodiversity**

*Zurab Bukia*

Aleksandre Natishvili Institute of Morphology, Ivane Javakhishvili Tbilisi State University, Tbilisi, Georgia
TSMU Bakhutashvili Institute of Medical Biotechnology, Tbilisi,Georgia

**Key words:** citrus, nucellar selection, biodiversity;

One of the well-known methods of selection - nucellar selection is characterized in the paper. This measure used to increase biodiversity is discussed in the analysis of practical results. Is explained the essence typical for citrus one of the forms of apomixis - nucellar polyembryony, when one or several additional germs develop from the somatic cells of the nucellus.

The opinion of the authoritative representatives of science is brought to the effect that nucellar selection creates the basis for the emergence of diversity of forms in the citrus nucellar generation, with the aim of creating new varieties with economic properties. Along with the variety of forms, they are characterized by better economic values compared to the original.

Literary materials and practice confirm the fact that the nucellar generation is represented by a great variety of forms that differ from the mother plant and carry valuable economic characteristics.

Almost all citrologists, regardless of their different opinions and views, believe that from nucellar seedlings (which were used as starting material for selection) we can get new citrus varieties with good fruit quality.

In his own observations, while studying the diversity of forms, it was determined that nucellar seedlings are of one origin, characterized by a great variety of biomorphological signs. Among them, we could not determine the presence of forms similar to the mother plant.

Practical results prove that the nucellar generation is represented by a great diversity of forms and differs from the mother plant. They carry valuable economic signs, which must be taken into account when selecting these crops.