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CONTENTS

MEDICINE

Basic Sciences	\$7-\$16
Medical Specialties	S19-S39
Surgical Specialties	\$43-\$46

PHARMACY

Fundamental Research	. 849-856
Pharmaceutical Specialties	. \$59-\$68

DENTAL MEDICINE

Abstracts	-S82
-----------	------

DOCTORAL SCHOOL

Abstracts	S85-S8	6
-----------	--------	---

RESEARCH CENTERS

Abstracts	S89-S104
-----------	----------



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BASIC SCIENCES

Application of FISH and FICTION for the assessment of the HER2 status in breast invasive carcinomas - a pilot study

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Corresponding Author: Bogdan Pop e-mail: pop.bogdan21@gmail.com **Introduction**. The scope of this study was to evaluate the FICTION technique as a possible candidate for the assessment of the Her2 status in breast invasive carcinomas (IBC). The objective of the current study to apply and validate a modified FICTION protocol on IBC samples for the determination of the HER2 status.

Material and methods. The study group was represented by five cases of IBC, selected from the case files of the Pathology Department of the IOCN. The FICTION technique was assessed by performing a comparative analysis with the gold-standard assays for Her2 status evaluation represented by sequenced IHC and FISH assays.

Results. Three IBC of NST type, one lobular IBC and one pleomorphic lobular IBC were selected. By IHC expression three cases showed a 2+(equivocal) Her2 score one case showed a 1+(negative) score and one case was 3+(positive). Two cases were classified by FISH examination in the ASCO/CAP group 5, one case in group 1, one case in group 3 and one case in group 4. After combined analysis two out of five cases were classified as Her2 positive. FICTION analysis showed absolute agreement for IF expression of the Her2 protein as compared to the IHC expression. For the percentage of tumor cell showing Her2 expression Pearson's correlation coefficient was 0.94 and the p value for the student t test was p=0.12. FICTION analysis showed absolute agreement for ISH assays expression of the Her2 protein as compared to the Her2 protein as compared to the FISH results. The correlation coefficients for the centromeric average copy number, the Her2 average copy number and the HER2/CEP17 ratio were: 0.98, 0.99, respectively 0.99 and all p values of the t tests were above 0.05.

Conclusion. The current study showed an excellent correlation between the two techniques and warrants the extension of the study groups.

Acknowledgement. This work was supported by a grant of the Romanian Ministry of Education and Research, CCCDI - UEFISCDI, project number PN-III-P2-2.1-PED-2019-2308, within PNCDI III.

Gut microbiota: a potential new target in dyslipidemia treatment

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1) Department of Pharmacology, Toxicology and Clinical Pharmacology, Faculty of Medicine, Iuliu Hațieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania **Introduction.** Dyslipidemia is an important factor in assessing cardiovascular risk, especially by correlating it with the atherosclerotic process evolution, which is a significant cause of cardiovascular morbidity and mortality. There is a continuous need

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Corresponding Author: Maria Adriana Neag e-mail: maria.neag@umfcluj.ro for new and better therapies aimed at lowering lipid parameters.

The aim of this study was to investigate the possible protective effect of Bacillus (B) sp. spores (B. Licheniformis, B. Indicus, B. Subtilis, B. Clausii, B. Coagulans) against experimentally induced dyslipidemia in rats.

Material and methods. A total of 30 rats were randomly divided into five groups: group I served as a negative control; group II received only a hyperlipidemic diet (positive control); group III received hyperlipidemic diet and MegaSporeBiotic (MSB); group IV received a hyperlipidemic diet and atorvastatin (ATV); group V hyperlipidemic diet and MSB and ATV. The specific diet was administered for 6 weeks and the treatment for 2 weeks.

Liver for histopathological examination and blood samples were collected on the last day of the experiment. Triglycerides, blood glucose, AST and ALT, tumor necrosis factor (TNF) α , interleukin (IL) 6 and plasma concentrations of atorvastatin were determined.

Results. The hyperlipidemic diet induced metabolic changes with a negative impact on triglycerides, blood sugar, liver function and systemic inflammation. MSB treatment resulted in a significant reduction in serum TC, ALT, TNF α , IL-6 and also improved histopathological changes. Co-administration of MSB with ATV increased its effect, most likely due to increased plasma concentrations of ATV.

Conclusion. Bacillus sp spores have a protective effect on metabolic and liver damage induced by dyslipidemia. MSB decreased hyperlipidemia-induced serological changes and improved histopathological liver damage. Moreover, MSB significantly increased the plasma concentration of ATV, posing as a possible future adjuvant therapy.

Probiotic bacillus spores together with amino acids and immunoglobulins exert protective effects against diclofenacinduced enteropathy in rats

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2) Department of Pharmacology, Toxicology and Clinical Pharmacology, Faculty of Medicine, Iuliu Hațieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania **Introduction.** Non-steroidal anti-inflammatory drugs (NSAIDs) are among the most widely used drugs worldwide, even though they have significant side effects, especially in the gastrointestinal tract. These side effects often limit the use of these drugs.

The aim of the present study was to investigate the possible protective effect of Bacillus (B) sp. spores (B. Licheniformis, B. Indicus, B. Subtilis, B. Clausii, B. Coagulans) with or without combination of serum-derived Ig concentrate, amino acids (L-proline, L-serine, L-cysteine, L-threonine), and bioflavonoids on NSAID (diclofenac)-induced enteropathy in a rat model.

Material and methods. A total of 25 rats were randomly divided into five groups: group I served as a negative control; group II received only diclofenac (positive control); group III received diclofenac and MegaSporeBiotic (MSB); group IV received diclofenac and combination of amino-acids and immunoglobulins (MM); group V received diclofenac, MSB and MM. The treatment was administered for 10 days. 3) Department of Pharmaceutical Technology and Biopharmacy, Faculty of Pharmacy, Iuliu Hațieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania

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Corresponding Author: Maria Adriana Neag e-mail: maria.neag@umfcluj.ro Fragments of small intestine were taken for histopathological examination and blood samples were collected on the 11th day of the experiment. Transaminases (AST, ALT), creatinine, total antioxidant capacity, catalase, tumor necrosis factor (TNF) α , interleukin (IL) 6, prostaglandin 2 (PGE2) and iNOS were determined.

Results. Administration of diclofenac caused enteropathy in the small intestine, while also causing hepatotoxicity and a decrease in PGE2. The combination of probiotic or amino acids with immunoglobulins or both with diclofenac decreased the inflammation and oxidative stress, leading to the amelioration of diclofenac-induced enteropathy injuries.

Conclusion. Probiotic spore-forming Bacillus strains and a supplement of amino acids in combination with immunoglobulins exhibited anti-inflammatory and antioxidant effects in a diclofenac-induced rat model of enteropathy.

Covid-19 vaccine efficacy among Romanian health workers: a prospective cohort study (primary results)

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Corresponding Author: Irina Brumboiu e-mail: ibrumboiu@umfcluj.ro **Introduction.** Since December 2019, Coronavirus disease 2019 (COVID-19) has spread to become a global pandemic. Romania officially declared its first case of COVID-19 on February 26, 2020. The emergency use authorization for COVID-19 vaccines brought both hopes and concerns to health workers who were at the frontline against COVID-19 pandemic for saving human lives, with great effort and sacrifices.

Objective. We aimed to assess the effectiveness of COVID-19 vaccines in preventing laboratory-confirmed SARS-CoV-2 infection among a group of health workers in Cluj-Napoca, Romania.

Methods. A prospective cohort study focused to observe two groups of health personnel (vaccinated/unvaccinated) from December 27, 2020 to December 27, 2021. If a confirmed case of Sars-CoV2 is recorded by a positive RT-PCR test, the investigator collects additional epidemiological data by telephone interviews.

Results. In a total of 748 health personnel, 36.7% were confirmed positive of COVID-19 since the start of the pandemic. 71.3% were infected with COVID-19 in 2020 and 28.7% were infected in 2021. A female predominance was observed with 80.0% among all infected. Overall, the medical staff was the most infected group with 78.9%. The origin of exposure was unknown for 56.4% of cases but 28.7% supposed that it was through the community. 79.6% of cases developed symptoms typical of COVID-19. The relative risk (RR) was determined at 0.18 (95% CI (0.124-0.260), knowing that vaccination was the exposure factor. Therefore, the vaccine efficacy was estimated at 82.0% in our study population.

Conclusion. Vaccine efficacy is still the current debate in several studies. This result can provide some answers to questions about the effectiveness of COVID-19 vaccines in real conditions.

Development and validation of an experimental model of atherosclerosis - a study protocol

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Corresponding Author: Paul-Mihai Boarescu e-mail: boarescu.paul@umfcluj.ro **Introduction.** Cardiovascular diseases, secondary to atherosclerosis, is a global public health problem and the leading cause of death. Atherosclerosis is a progressive disease characterized by the accumulation of lipids and fibrous elements leading to plaque formation at specific sites of the arterial tree. The aim of this study is to identify an easily reproducible experimental model of atherosclerosis in rats.

Material and methods. Twenty-eight Wistar-Bratislava white male rats, weighing between 400 and 500 grams will be evaluated. The rats will be randomly divided into four groups as follows: Group 1 will be the control group (C), Group 2 the Hypertension (H) group, Group 3 the Dyslipidemia (D) group, and Group 4 will be the Diabetes Mellitus (DM) group. Hypertension will be induced with 40 mg/kg N-omega-Nitro-L-argininemethyl (L-NAME) for 28 days. Group 3 will receive only pellets with a high cholesterol (11,65%) content. Diabetes Mellitus will be induced by intraperitoneal administration of a single dose of streptozocin (65 mg/kg). After 28 days, blood samples and aorta fragments will be collected. The serum and tissue levels of high-sensitivity C-reactive protein (hs-CRP), cytokines such as tumor necrosis factor (TNF)- α , interleukin (IL)-6, IL-1 α , IL-1 β , matrix metalloproteinases MMP-2 and MMP-9, and parameters of oxidative stress: malondialdehyde, thiol, nitric oxide, total oxidative status and total antioxidant capacity will be evaluated. At the end of the experiment, fragments from the aorta will be collected for histopathological evaluation of the degree of atherosclerosis.

Expected results. The results of this study are expected to allow the identification of an easily reproducible experimental model of atherosclerosis. This experimental model of atherosclerosis can later be used in studies to validate compounds with antioxidant and anti-inflammatory effects in the atherosclerotic process.

Students' perception of the first semester of online education in the medical school during the COVID-19 pandemic

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Corresponding Author: Valeriu-Mihai But e-mail: butvaleriu@yahoo.com **Introduction.** The rapid spread of the severe acute respiratory syndrome coronavirus 2 (COVID-19) determined the implementation of e-learning methods at Iuliu Hațieganu University of Medicine and Pharmacy Cluj-Napoca. This research aimed to evaluate the impact of e-learning methods on students' learning process at the Faculty of Medicine and the learners' perceptions of e-learning in medical education.

Material and methods. A cross-sectional designed study was conducted from May to August, 2020. The data was collected by a questionnaire distributed in electronic format to undergraduate students using the Facebook groups of specializations of the Faculty of Medicine, Romanian section. We compared the differences between the answers of Medicine students (Medicine) and other specializations (Others). We also divided the participants according to the year of study into 3 groups: freshman (Fr) first year, sophomore (So) intermediate years and senior (Se) last year.

Results. The developed instrument proved internal consistency (Cronbach's Alpha = 0.840 (95% CI = [0.819 to 0.856], P-value < 0.0001). The number of study respondents was 635 out of 2926 eligible. When comparing the groups, significant differences were observed at 7 of 11 questions. All the specializations agreed that they encountered difficulties in assimilating practical skils (Medicine 85.5%, Others 85.7%). The largest difference of opinion observed over the students' answers was between Fr (56.8%) and Se (22.5%) in regards of difficulties encountered in the process of assimilating theoretical knowledge (p<0.0001).

Conclusion. The practical skills and aptitudes were the most affected aspects of the learning process during the COVID-19 pandemic as identified by our respondents. Our study showed that students' needs as well as their perceptions differ both between specializations as well as years of study.

Grape seed oil protective effects in a rat experimental model of myocardial infarction

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2) Research Station for Viticulture and Enology Blaj (SCDVV Blaj), Blaj, Romania **Introduction.** Cardiovascular diseases (CVD) are considered the major cause of morbidity and mortality worldwide. Even though an important effort is put into the proper management of CVD, globally they are still considered a major public concern that has a high impact on health and economic burdens. Therefore, solutions targeting the prevention and control of CVD are needed. Complementary therapies focused on the use of plant bioactive compounds are intensively studied for their effect in reducing CVD risk factors. Among natural products, grape seed oil of Vitis vinifera (GSO) is a rich source of phenolic compounds mainly known for their protective effect in CVD, due to their properties of modulating oxidative stress processes, endothelial dysfunction inhibition,

Corresponding Author: Raluca Maria Pop e-mail: raluca parlog@yahoo.com and the induction of vascular relaxation through nitric oxide (NO) production and redox regulation. This study aimed to evaluate the grape seed oil effect using a rat in vivo model of induced myocardial infarction (MI) with isoproterenol.

Material and methods. The phytochemicals in grape seed oil were characterized using Fourier-transform infrared spectroscopy (FTIR) and Liquid chromatography-mass spectrometry (HPLC-MS) analysis. Thirty rats were split into three groups: the control group which received saline solution (gavage), the isoproterenol group which received 45 mg/kg isoproterenol (subcutaneously), and the GSO group which received both isoproterenol (45 mg/kg, subcutaneously) and 0.4 mL/100g grape seed oil (gavage). MI was induced within the 14th day of the experiment. To evaluate the MI, electrocardiography was taken before MI induction and after one day. Serum biochemical evaluation was performed quantifying alanine aminotransferase (ALT), aspartate aminotransferase (AST), and the myocardial fraction of creatine kinase (CK-Mb). The inflammatory process was evaluated by measuring interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF- α), and interleukin-1 β (IL-1 β).

Results. Grape seed oil was rich in catechin derivatives, tannins, and phenolic acids. The administration of ISO produced specific changes characteristics for acute MI as seen in the ECG records after 24 hours since MI, with increased RR interval, ST-segment depression, QT interval prolongation, and QRS complex enlargement. GSO pre-administration prevented heart rate increase as induced by isoproterenol ($p \le 0.036$) but did not prevent QRS complex enlargement. The increase of QT and QTc intervals was significantly reduced as compared to the isoproterenol group (p<0.001). RR interval was significantly increased (p = 0.036), while the reduction of R wave amplitude was significantly prevented (p<0.001). Also, GSO administration significantly reduced IL-6 (p=0.005), IL-1 (p=0.0047), and TNF- α (p<0.001) inflammatory markers after MI.

Conclusion. Grape seed oil anti-inflammatory and cardioprotective effects obtained in the isoproterenol-induced experimental MI suggests its beneficial use in human diets and also suggests its potential use as food supplements in the control of CVD.

A global predictive model after the first twenty months of Covid-19 pandemic evolution in Romania

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Corresponding Author: Irina Brumboiu e-mail: ibrumboiu@umfcluj.ro **Introduction.** The recommendation of the most appropriate control measures to reduce the impact on the community and the possibility of resumption to normal activities, can be done only by having the most accurate prediction of the disease's evolution at population level. The aim of this paper is to analyze a global predictive model for the subsequent evolution, after twenty months of pandemic evolution in Romania.

Material and methods. Predictive models of the dynamics of an epidemic based on the rate of transmission, the people categories as susceptible, infectious and resistant were used. The main data sources were the daily reports of number of cases and deaths, the cumulative data and the daily vaccination reports and the proportion of fully vaccinated population. Also, the non-medical measures (quarantine, mask, mechanical barriers etc.) imposed because of the high number of cases. **Results.** The starting dates for models were the data recorded until 1 November 2021, these being 1,655,024 Covid-19 cases, 4,473 deaths and 6,334,232 anti-Covid-19 people fully vaccinated. In the models in which the main control measures are non-medical, with vaccine rejection high rate, it is possible to register more 1,919,196 of moderate, 349,028 severe and 172,056 of critical cases and 70,710 deaths. In a model with 79% vaccinated population, until the pandemic control, it may occur up to 380,981 moderate cases, 73,738 severe 36,869 critical and 3,406 deaths. A model with an improved vaccination program, the number of cases is reduced to 101,390 moderate, 18,434 severe and 9,217 critical cases and 851 deaths. Others models with the different levels of vaccination acceptance and the change of SARS-CoV-2 variant are very heterogenic.

Conclusion. Predictive models may include different numbers of variables and give very different results. The immediate usefulness of the provisional models is in the management of the medical resources and in providing medical services that patients need.

The impact of *Sambucus nigra* L. extract on inflammation, oxidative stress and tissue remodeling in a rat model of lipopolysaccharide-induced subacute rhinosinusitis

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Corresponding Author: Cristina Nicoleta Schnell e-mail: cristina_tiboc@yahoo.com **Objective.** The study aims to investigate the effect of intranasal Sambucus nigra L. subsp. nigra (SN) extract against inflammation, oxidative stress, and tissue remodeling in nasal and sinus mucosa, but also in serum, lungs, and brain, in Wistar rat model of subacute sinonasal inflammation induced by local administration of lipopolysaccharides (LPS), from Escherichia Coli.

Material and methods. Wistar rats were divided into five groups of 10 animals each. The medication used for the study was dropped into the nasal cavities using a micro-pipette, three times a week, for three consecutive weeks. The control group received intranasal saline solution. Rats in groups 2 and 3, received low-dose (5 μ g) and high-dose (10 μ g) of LPS, and rats in groups 4 and 5, received low-dose (5 μ g) and high-dose (10 μ g) of LPS and after 2 h, 40 mg/kg of SN extract. The cytokines (TNF- α , IL-1 β , IL-6) and oxidative stress (malondialdehyde) in nasal mucosa, blood, lungs, and brain were analyzed. In addition, a histopathological examination was performed, and NF-kB, MMP2, MMP9, TIMP1 expressions were also evaluated in nasal mucosa.

Results. Both doses of LPS increased the production of cytokines in all the investigated tissues, especially in the nasal mucosa and blood (p<0.01 and p<0.05), and stimulated their secretion in the lungs, and partially in the brain. Malondialdehyde increased in all the investigated tissues (p<0.01 and p<0.05). In parallel, upregulation of NF-kB and MMP2 expressions with downregulation of TIMP1, particularly at high dose of LPS, was observed. SN extract reduced the local inflammatory response, maintained low levels of IL-6, TNF- α , and IL-1 β . In lungs, SN reduced all cytokines levels while in the brain, the protective effect was noticed only on IL-6. Additionally, SN diminished lipid peroxidation and downregulated NF-kB in animals exposed to a low dose of LPS, with increased TIMP1 expression, while in animals treated with a high dose of LPS, SN increased NF-kB, MMP2, and MMP9 levels.

Conclusion. SN extract diminished the inflammatory response, reduced generation of reactive oxygen species and, influenced MMPs expressions, suggesting the benficial effect of SN extract on tissue remodeling in subacute rhinosinusitis and on systemic inflammatory response.

Acknowledgments. This work was supported by the financing project within the PhD School of Iuliu Hațieganu University of Medicine and Pharmacy, Cluj-Napoca.

Anti-edematogenic effects of curcumin and curcumin nanoparticles in addition to diclofenac sodium in carrageenan-induced paw edema

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Corresponding Author: Ioana Boarescu e-mail: ioana.boarescu@gmail.com **Introduction.** Acute inflammation (AI) is a process that involves the release of several pro-inflammatory mediators, overproduction of free radicals, and activation of complex enzymes. The carrageenan-induced paw edema is a well-known experimental model of acute inflammation.

Material and methods. Seven groups of 8 Wister Bratislava male rats were involved in the study. Group 1 was the normal control; group 2 was with AI; group 3 was with AI and treated with diclofenac sodium (D); group 4 was with AI and treated with conventional curcumin (cC); group 5 was the group with AI and treated with D and cC; group 6 was with AI and treated with curcumin nanoparticles (nC) and group 7 was with AI and treated with D and nC. Groups 1 and 2 were treated with saline. Diclofenac sodium was administered in a dose of 5 mg/bw, while cC and nC were both administered in an amount of 200 mg/bw.

Results. One hour after carrageenan administration, all rats that received carrageenan presented a marked unilateral peripheral paw edema. The maximum values of paw edema were observed at 5 hours' time point for all groups with AI, with the highest values in the rats from group 2. The antiedematogenic effect of nC was observed starting from the first hour, while for cC this effect was observed at 3 hours. The cC and D showed better effects than diclofenac alone at 7 and 24 hours (p \leq 0.024). Combination of nC to D better reduced paw edema after 5, 7 and 24 hours than D alone (p \leq 0.01). The maximum level of inhibition (30.08%) was observed after 7 hours in group 7 (nC+D).

Conclusion. Curcumin nanoparticles present anti-edematogenic effect from the first hour after acute inflammation induction, while conventional curcumin presents this effect after 3 hours. Association of curcumin or curcumin nanoparticles to diclofenac can improve edema reduction, with better effects for curcumin nanoparticles.

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Celecoxib in cutaneous melanoma: the dark side of the coin

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Corresponding Author: Diana-Valentina Tudor e-mail: dianatudor91@gmail.com **Introduction.** Cutaneous melanoma is a versatile type of skin tumor, holding a rapidly switching molecular and cellular phenotype. MITFlow/AXLhigh status expressed by melanoma cells prefigures early resistance to multiple targeted drugs. Celecoxib seemed a promising adjuvant in melanoma preclinical studies. A clear validation of these properties in clinical trials is still missing. This current study evaluated for the first time how celecoxib impacts on phenotype switching in human melanoma cells treated with dabrafenib.

Methods. The *in vitro* experimental design used BRAF (+) SK-MEL-28 human melanoma cell lines, subjected to dabrafenib and celecoxib novel drug combination, for 72 h. Of major interest was the Western Blot assessment of key molecules expressed during phenotype switching from a proliferative to an invasive phenotype in melanoma cells (TGF – β , MITF, YAP, TAZ, AXL), correlated with cell death and oxidative stress-related mechanisms.

Results. Even though celecoxib enhanced the apoptotic effect of dabrafenib in SK-MEL-28 melanoma cell line compared to dabrafenib group (p<0.0001), it also facilitated low MITF expression correlated with high AXL levels (p<0.0001). Results suggested that low doses celecoxib might promote MITFlow/AXLhigh expression, a positive hallmark for the phenotype switch to an invasive state.

Conclusion. Celecoxib showed interesting capabilities as an adjuvant in melanoma. Our results suggest that we might have missed the bigger picture, as low doses celecoxib promoted phenotype switching in vitro in cutaneous melanoma treated with dabrafenib. This finding could partially explain a limitation of its use in future clinical trials.

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Neurobehavioral and ultrastructural changes induced by phytosynthesized silver nanoparticles toxicity in an *in vivo* rat model

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Introduction. Nanotechnology is a field of study that keeps growing by the day. Silver Nanoparticles are increasingly used in consumer products worldwide mainly for their antimicrobial properties and human exposure has been documented. It is of paramount importance to know the potential toxic effects that occur after prolonged exposure to these compounds. The aim of our study was to assess neurobehavioral changes and ultrastructural, histopathological, inflammatory and oxidative stress modifications induced by silver nanoparticles synthesized with Cornus mas L. extract (AgNPs-CM) in the rat brain.

Annual Meeting Iuliu Hațieganu University of Medicine and Pharmacy 2021

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Corresponding Author: Răzvan-Vlad Opriș e-mail: opris.razvan93@yahoo.com **Material and methods.** For 45 days, two groups of animals received different doses of AgNPs-CM (0.8 and 1.5 mg/kg b.w.), while control group was given the buffer used as vehicle for the AgNPs-CM. Prior to sacrificing, the OFT and EPM tests were conducted in order to record neurobehavioral changes in the animals. Animals were sacrificed immediately after and 15 days post-treatment, after which transmission electron microscopy, GFAP immunohistochemistry, evaluation of TNF α , IL-6, MDA levels, and CAT activity were performed on the recovered rat frontal cortex and hippocampus.

Results. Treated animals displayed dose and time-dependent increase in anxietylike behavior. Transmission electron microscopy revealed severe ultrastructural changes of neurons, astrocytes and capillaries in both brain regions. Immunohistochemistry revealed astrogliosis with altered cell morphology. $TNF\alpha$, IL-6, MDA levels, and CAT activity were significantly altered depending on brain region and time post exposure.

Conclusion. AgNPs-CM induced severe cell lesions identified a long time after cessation of exposure that was correlated with neurobehavioral changes in rats.

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Importance of olive leaves in stress and brain activity, a short review

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Corresponding Author: Ramona-Niculina Jurcău e-mail: ramona_mj@yahoo.com **Introduction.** The olive tree, considered the tree of life, is known for the usefulness of its fruit and leaves in food as well as in various forms of treatment.

Objective. The aim of the study was to highlight the importance of olive leaves in stress and brain activity.

Material and methods. In a short review, studies on olive leaves, their composition, and their importance in mental stress and oxidation, as well as on nervous activity, were analyzed.

Results. Olive leaves. The benefits of olive leaves are scientifically proven, as is their composition, rich in active ingredients. It is a rich source of bioactive ingredients. There are five groups of phenolic compounds present in olive leaves, the major ones identified in the extracts of olive leaves are oleuropein, verbascoside and luteolin-7-O-glucoside. Oleuropein (OLE). It is responsible for the pharmacological and potentially beneficial effects of olive leaves in various diseases, such as neurodegenerative ones. OLE and oxidative stress. Olive leaf extract, as the main source of oleuropein, reduces the oxidative stress induced by aging. OLE has a high antioxidant activity, lowers the level of malondialdehyde, an action that could be due to the presence of phenolic compounds and hydroxyl groups in its structure. OLE, cognition, memory and learning. The administration of olive polyphenols is associated with improved cognitive functions. OLE reduces lipid peroxidation and induces the activation of antioxidant enzymes, has neuroprotective effects against cognitive dysfunction and neurodegeneration

Conclusion. Olive leaves and especially oleuropein are an important natural source for stress modulation, antioxidant and neuropsychic protective effects.

MEDICAL SPECIALTIES

Effect of Dulaglutide on glycemic and weight control in patients with type 2 diabetes

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Corresponding Author: Dana Ciobanu e-mail: dana.ciobanu@umfcluj.ro **Introduction.** Rapid economic development and increasing life expectancy worldwide accompanied by accelerating urbanization and expanding prevalence of sedentary lifestyle have resulted in a marked increase in type 2 diabetes mellitus incidence. Approved for the treatment of type 2 diabetes in 2014, Dulaglutide has shown benefits related to cardiovascular risk associated with diabetes in addition to improved glycemic control and body weight reduction in previous clinical trials (e.g., REWIND). We aimed to investigate the effect of Dulaglutide on glycemic and weight control in type 2 diabetes patients.

Material and methods. In our prospective observational study we evaluated type 2 diabetes patients newly initiated on Dulaglutide after 6 months (n=52) and 12 months (n=32) of treatment. Patients were recruited from the Center of Diabetes, Nutrition and Metabolic Diseases, Cluj-Napoca.

Results. Dulaglutide treatment resulted in significant decrease in glycated hemoglobin after 6 months (9.6 \pm 2.0% vs. 7.9 \pm 1.4%; p<0.001) and 12 months (9.7 \pm 2.0% vs. 7.7 \pm 1.4%; p<0.001); and in fasting glycemia after 6 months (191 \pm 54 mg/dl vs. 143 \pm 31 mg/dl; p<0.001) and 12 months (185 \pm 56 mg/dl vs. 136 \pm 25 mg/dl; p<0.001) of Dulaglutide treatment. In addition, significant body weight reduction was found after 6 months (95.5 \pm 16.9 kg vs 92.9 \pm 16.2 kg; p=0.003) and 12 months (97.8 \pm 18.0 kg vs. 94.5 \pm 17.0 kg; p=0.002); and significant body mass index reduction of 1.0 kg/m2 (-3.0%; p=0.001) after 6 months and 1.4 kg/m2 (-4.1%; p=0.002) after 12 months of Dulaglutide treatment. There were no serious drug-related adverse events.

Conclusion. Dulaglutide demonstrated significant improvement in glycemic and body weight control over the 6 and 12 months periods. The results found in our study are similar to those reported in the literature and motivate research into possible use of this glucagon-like peptide-1 agonist to treat conditions such as obesity and metabolic syndrome.

E-selectin is associated with 24-hour ambulatory blood pressure variability in patients with type 2 diabetes

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2) Center of Diabetes, Nutrition and Metabolic Diseases, Emergency Clinical County Hospital Cluj-Napoca, Romania **Introduction.** E-selectin is an endothelial cell adhesion molecule involved in the inflammation and activation of vascular endothelial cells. Hypertension and diabetes are associated with endothelial dysfunction. In this study, we hypothesized that elevated serum E-selectin might be associated with increased 24-hour ambulatory mean blood pressure and blood pressure variability.

Material and methods. Serum E-selectin was measured using ELISA technique. Systolic and diastolic blood pressure variability were assessed as the standard deviation of 24-hour ambulatory blood pressure recordings in a cohort of patients with type 2 diabetes

Annual Meeting Iuliu Hațieganu University of Medicine and Pharmacy 2021

Corresponding Author: Dana Ciobanu e-mail: dana.ciobanu@umfcluj.ro (n=132) selected from Center of Diabetes, Nutrition and Metabolic Diseases, Cluj-Napoca.

Results. Of the whole group, 60 (45.5 %) were men and 16 (12.1 %). Mean age was 60.1±8.0 years, had body mass index 32.6±5.3 kg/m2, glycated hemoglobin 9.6±2.2 % and diabetes duration 8.0 (3.0-13.5) years. Hypertension was diagnosed and treated with medication in 118 (89.4 %) patients and had a duration of 8.0 (4.0-14.0) years. Median E-selectin levels were 2.5 (1.4-4.8) ng/mL. We found that lgE-selectin was significantly associated with daytime and 24-hour diastolic BP variability in patients with type 2 diabetes (β =0.258; p=0.012 and β =0.238; p=0.019, respectively) in linear regression analysis, adjusted for age, sex, smoking status, fasting glycemia and HbA1c, diabetes and hypertension duration, body mass index. No associations were found between E-selectin and mean systolic and diastolic blood pressure.

Conclusion. The association of serum E-selectin with daytime and 24-hour diastolic blood pressure variability in patients with type 2 diabetes indicates that endothelial activation might be associated with increased blood pressure variability.

Adherence to Mediterranean diet in patients with acromegaly

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Corresponding Author: Dana Ciobanu e-mail: dana.ciobanu@umfcluj.ro **Introduction.** Acromegaly is characterized by persistent hypersecretion of growth hormone during adulthood. In the absence of proper treatment, acromegaly is associated with cardiovascular, respiratory and metabolic complications. The Mediterranean diet has been proven to have numerous beneficial health effects. Currently, there are not enough studies to show how Mediterranean diet influences the lives of patients with acromegaly. The aim of this study is to asses the adherence to Mediterranean diet in patients with acromegaly and to perform correlation with clinical and laboratory data.

Material and methods. A number of 31 patients with acromegaly, aged 30-80 years, 52% females were included in the study. Data were obtained from a food frequency questionnaire and from medical evaluation of patients with acromegaly. Adherence to the Mediterranean diet was assessed by a validated questionnaire. Low adherence was defined as less than 5 points, moderate adherence between 6-9 points and over 10 - high adherence.

Results. We found a significant negative correlation between adherence to the Mediterranean diet and glycated hemoglobin (HbA1c) (R= -0.42; p=0.018). The lower the adherence, the higher the HbA1c, and as the adherence increases, HbA1c decreases and falls within normal limits. Also, we found a significant negative correlation between adherence to the Mediterranean diet and body mass index (R= -0.41; p=0.002). However, no correlation was observed between adherence to Mediterranean diet and lipid profile or acromegaly control and treatment.

Conclusion. The introduction of the Mediterranean diet into the daily lives of patients with acromegaly could have beneficial metabolic effects. Patients need to be informed and helped to follow a healthy and balanced diet to improve their quality of life. To see if Mediterranean diet could be beneficial in controlling the disease and in preventing complications, additional clinical trials are needed.

Pulmonary hemosiderosis - pediatric case report

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Corresponding Author: Florina Steliana Rusu e-mail: florina.steliana92@gmail.com Pulmonary hemosiderosis is a rare disorder in pediatric patients. This condition is characterized by alveolar hemorrhage and abnormal hemosiderin accumulation in pulmonary macrophages, which leads to a thickening of the alveolar basement membrane and, finally, to interstitial fibrosis. The pathogenesis is unwell known, but it's considered to be an immune mediated mechanism. The main clinical signs are hemoptysis, irondeficiency anemia, and diffuse parenchymal consolidation on chest radiology.

We present a case of a 10-year-old girl who was admitted to our department for dyspnea, fatigue, wheezing, inferior limb pain, in the absence of fever and hemoglobin level of 3 g/dl. Her past medical history includes commune atrioventricular canal, surgically treated, pulmonary hypertension, NYHA III heart failure, and one recent episode of severe anemia associated with respiratory distress. She was tested for different causes of anemia, which were gradually ruled out, the bone marrow aspiration was normal. Because of the respiratory symptoms and radiological aspect of the lungs, a bronchoscopy was performed and the bronchoalveolar lavage showed macrophages filled with hemosiderin which confirmed the diagnosis of pulmonary hemosiderosis. This was interpreted as idiopathic pulmonary hemosiderosis as the tests for secondary causes as Heiner syndrome and Goodpasture syndrome were negative although we could not exclude the link between the pulmonary hemosiderosis and congenital heart malformation.

Acute surgical abdomen or multisystemic inflammatory syndrome in children (MIS-C)?

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Corresponding Author: Alexandra Mititelu e-mail: perta_alexandra@yahoo.com **Introduction.** In the pediatric population, infection with Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) is often asymptomatic, and if respiratory symptoms appear, they are usually mild. However, in April 2020, severe evolution after Coronavirus disease 2019 (COVID 19) in children was reported, resembling Kawasaki disease or toxic shock syndrome. After the reports of other cases, the concept of pediatric inflammatory multisystem syndrome temporarily associated with SARS-CoV-2 infection was presented (MIS-C or PIMS). The World Health Organization and Center for Disease Control and Prevention developed diagnosis criteria.

Case presentation. We present the case of a 10-year-old boy who was admitted to our department for refractory fever and altered general status after appendectomy. The symptoms started four days before the admission, with fever, abdominal pain and vomiting. After a surgical consult and abdominal imaging, acute appendicitis was suspected, and classic appendectomy was performed. The fever persisted and did not respond to acetaminophen and ibuprofen. He associated diarrhea, asthenia, and the inflammatory parameters were increasing. He was then transferred to our Pediatric Clinic with MIS-C suspicion. The patient was admitted with an altered general status, bilateral conjunctivitis, erythematous lips, tachycardia (HR 120 b/min), low blood pressure (89/39 mmHg); the abdominal wound was healing properly. Laboratory investigations revealed bi-cytopenia

(anemia and thrombocytopenia), marked inflammatory syndrome, hypoalbuminemia, hyponatremia, hypertriglyceridemia, increased D-dimers, fibrinogen and NTproBNP. The serology for viral infections (EBV, CMV) and cultures for bacterial infections were negative. The RT-PCR for SARS-CoV-2 infection was also negative, with positive IgG antibodies to SARS-CoV-2. According to current recommendations, we administered 2g/kg of intravenous immunoglobulin, methylprednisolone, anticoagulant (Clexane), antibiotic therapy (meropenem, gentamicin) and albumin. The evolution was rapidly favorable clinically and regarding biological markers.

Conclusion. This case emphasizes the need to include MIS-C in the differential diagnosis of acute abdomen, given the increased frequency of such cases with gastrointestinal manifestations. Prompt recognition of MIS-C and treatment according to the guidelines may avoid surgical intervention.

Impact of SGLT2i-empagliflozin treatment on the cardiovascularrenal risk in Diabetes Mellitus type II patients

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Corresponding Author: Florin Casoinic e-mail: fcassoinic@yahoo.com **Introduction.** The objective of this study was to assess the effects of Sodium glucose co-transporter 2 (SGLT2) inhibitors – empagliflozin, on renal and cardiovascular risk in patients with DMT2 and CKD (albuminuria, urine albumin-to-creatinine ratio, eGFR).

Material and methods. 52 patients were assigned to two groups: Group I (25 patients) with empagliflozin 10mg/day with standard antidiabetic therapy vs Group II (27 patients) without empagliflozin were followed for 12 months. We evaluated several clinical parameters, changes of metabolic markers (glycemia, HbA1C), hs-CRP, seric 8-isoprostane, uric acid, NT proBNP and renal function (albuminuria, urine albumin-to-creatinine ratio, eGFR).

Results. After one year in Group I, treated with empagliflozin patients presented a significant reduction in microalbuminuria (p = 0.03) and urine albumin-to creatinine ratio (p = 0.02) compared with Group II; eGFR was not different between these two groups (p = 0.22). The levels of NT-proBNP (from 273 ± 45.2 ng/l were decreased to 135 ± 33.6 ng/l in Group I (p = 0.01) and no significant changes in Group II. SBP was reduced with a mean of 6.5 mmHg in Group I vs 2.3 mmHg Group II (p = 0.02), and DBP 3.1 vs 1.1 in Group I versus Group II (p=0.03). Serum levels of hs-CRP was decrease from 7.6 ± 3 mg /l to 3.11± 4 mg /l in Group I (p = 0.02) and 7.7 ± 4 mg /l to 6.3 mg ± 1.2 /l in Group II (p = 0.65). 8-isoprostane after empagliflozin treatment Group I: 214.2 ± 22.2 from 285.3 ± 53.5 pg/ml initial level, p = 0.014, vs in Group II: 290.92 ± 61.7 from 299.11 ± 48.5 pg/ml, p = 0.23. Seric uric acid was improved in Group I (6.5 ± 1.65 to 5.7 ± 1.33 mg/dl, p = 0.012) vs Group II (6.3 ± 0.98 to 6.2 ± 1.2 mg/dl, p = 0.21). HbA1C decreased from 8.4% to 7.1% in Group I and from 8.5% to 7.74% in Group II, p=0.05.

Conclusion. Treatment with empagliflozin had beneficial effects not only on glycemic control but also in reducing the renal and cardiovascular risk in patients with DMT2.

CPAP therapy improves quality of life and cardiovascular outcomes in OSA patients

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Corresponding Author: Doina Adina Todea e-mail: doina_adina@yahoo.com; dtodea@umfcluj.ro **Introduction.** Obstructive sleep apnea (OSA) is a major health problem, with growing evidence showing an association with cardiovascular morbidity and mortality. The typical sleep laboratory measurements are unable to assess the total impact of OSA on human life. As a result, it is also important to assess OSA patients' Quality of Life (QoL). The gold treatment for patients with OSAS is continuous positive airway pressure (CPAP). Despite the fact that the CPAP effect has previously been studied in relation to cardiovascular outcomes, a one-year follow-up of the treatment effects on cardiovascular risk factors and quality of life in a Romanian population is lacking. Thus, we aim to evaluate the impact of CPAP therapy on blood pressure, lipid profile and heart function, alongside with its effects on QoL on a cohort of Romanian OSA patients.

Material and methods. We enrolled 163 subjects and recorded their baseline demographic and clinical characteristics with a follow-up for 12 months. In order to quantify the quality of life, we used the Quebec Sleep Questionnaire (QSQ), which was locally validated. Cardiovascular risk factors and QoL questionnaires were assessed at baseline and follow up.

Results. Our results show that CPAP therapy leads to attenuation of cardiovascular risk factors including echocardiographic parameters and significantly improves quality of life, in all the five domains of the QSQ.

Conclusion. CPAP therapy after one year of usage, managed to improve cardiovascular outcome, as well as the quality of life according to Quebec Sleep Questionnaire. The QSQ is a useful tool to evaluate quality of life in sleep apnea, especially to highlight the benefits of CPAP therapy.

Can inflammation and oxidative stress become a cornerstone in obstructive sleep apnea patients?

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Corresponding Author: Doina Adina Todea e-mail: doina_adina@yahoo.com; dtodea@umfcluj.ro **Introduction.** Obstructive sleep apnea (OSA) is characterized by chronic intermittent hypoxia, which enhances oxidative stress and systemic inflammation. We assessed the impact of respiratory parameters on inflammatory and oxidative stress profile in patients with moderate/severe OSA.

Material and methods. The study included 42 consecutive patients diagnosed with moderate/severe OSA. We assessed body mass index (BMI), smoking status, nocturnal respiratory parameters (Apnea-hypopnea index – AHI, Oxygen desaturation index – ODI, minimum and medium SpO2), complete blood count, inflammatory parameters (C-reactive protein/CRP, neutrophile/lymfocite ratio NLR) and markers of oxidative stress as exhaled carbon monoxide level (eCO) and blood carbon monoxide (COHb) in the morning following the nocturnal cardiorespiratory poligraphy.

Results. In our study group, the majority of the patients were male (66.7%), with a mean age of 58.04 years, which associate obesity with a mean BMI of 41.12 ± 8.33 kg/m2. Taking into account the smoking habit, 33.3% were active smokers, 21.4% exsmokers and 45.2% non-smokers (NS). The mean AHI was 69.56 ± 40.41 events/hour of sleep, the mean oxygen desaturation index (ODI) was 70.89 ± 41.35 evets/hour of sleep, with a mean nocturnal SpO2 of $82.9\pm 11.42\%$ and a minimum SpO2 of $67.76\pm 13.11\%$. There were statistically significant correlations between oxidative stress parameters (eCO) and CRP (p=0.008), NLR (P=0.001), AHI and ODI (p<0.001) and also mean and minimum SpO2 (p<0.001). Patients with severe OSA have higher values of eCO (4.31 ± 2.83) compared to those with moderate OSA (2/p=0.003). Considering the smoking habit, in patients with severe OSA, the eCO value was 5.8 ± 2.52 ppm in the smokers' group versus 1.83 ± 0.93 ppm in NS (p<0.001) and the COHb was $3.08\pm 1\%$ in the smokers group versus $2.12\pm 1.03\%$ in the NS (p=0.011).

Conclusion. In patients with severe OSA, we found higher levels of inflammatory/ oxidative stress markers compared with those with moderate OSA.

Pulmonary thromboembolism with hemodynamic stability: case report

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Corresponding Author: Doina Adina Todea e-mail: doina_adina@yahoo.com; dtodea@umfcluj.ro **Introduction.** The high incidence of thromboembolic events among the patients diagnosed with COVID-19 was revealed in many studies until nowadays. Arterial thrombosis occurs in 4% of severe/critical cases of COVID-19. In 3-6% patients, the location of thrombosis is at the pulmonary trunk. Even though the thrombosis located at the pulmonary trunk level is associated with hemodynamic instability and exitus, this paper would emphasise the case of a patient with a favorable evolution, despite this localization of thrombosis.

Material and methods. We report the case of a 40-year-old male Caucasian patient, normal bodyweight (BMI=22.14 kg/m2), with no personal history of illness, who was admitted to our hospital after being confirmed with SARS-CoV-2 infection. We should mention that the patient had for 10 days mild symptoms, for which he followed treatment at home (only symptomatic drugs). At the admission, he presented with a productive cough, dyspnea and extreme fatigue. Blood tests results revealed increased inflammatory biomarkers: C reactive protein 209 mg/L, ferritin 2470 ug/l and D-dimer 54939 ng/mL. Computed tomography (CT) with contrast infusion detected massive acute pulmonary thromboembolism at the bifurcation of pulmonary trunk, with bilateral extension to the segmental pulmonary arteries and a 30% lung involvement regarding the SARS-COV2 infection. The diagnosis of severe COVID-19 and massive acute pulmonary thromboembolism was raised

Results. The evolution was favorable under the specific treatment for SARS-CoV-2 infection and conservative treatment with curative dose of anticoagulant therapy.

Conclusion. This case enhances the importance of corroborating the clinical findings with the paraclinical findings in order to raise an accurate diagnosis and, also, the necessity of the anticoagulant treatment among COVID-19 patients.

The challenges of the autoimmune manifestations after SARS-CoV-2 infection: case report

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Corresponding Author: Doina Adina Todea e-mail: doina_adina@yahoo.com; dtodea@umfcluj.ro **Introduction.** The actual health problem all over the world, the COVID-19 pandemic, has brought many challenges in the development and diagnosis of autoimmune diseases during the acute phase of infection and after recovery. Lasting effects including dyspneea, persistent fatigue, headache, loss of taste and smell and loss of memory are known and reported. Current data about long term effects of the infection upon rheumatic disorders and in particular myositis and dermatomyositis are limited.

Material and methods (Case presentation). A 58-year-old female patient was admitted in our hospital complaining of dyspnea, fatigue, myalgia and muscle weakness. The patient was known with mediastino-pulmonary sarcoidosis and with a severe form of COVID-19 pneumonia 6 months before this actual hospitalization treated with Azathioprine, Colchicine and 2 months before admission Prednisone was prescribed. Clinically, she presented Gottron's papules, dermatomyositis glasses, general skin exfoliation, hypotrichosis in the outer third of the eyebrows. She was in respiratory acute failure with oxygen requirement. Paraclinical, she had an inflammatory reaction with elevated levels of C-reactive protein, ferritin, lactate-dehydrogenase, glycemia, elevated levels of transaminases and an isolated increased level of gama glutamil transferase. The thoracic CT scan performed revealed multiple areas of "ground glass" and fibrotic bands. The autoimmune profile of the patient revealed anti Mi-2 alpha, anti-MI-2 beta, anti PL-7, anti SRP, anti centromer and anti RO 52 antibodies positive. The big question is if these autoimmune diseases are secondary to a post-viral myopathy after SARS-CoV-2 infection, in a paraneoplastic context or secondary to sarcoidosis.

Result and Conclusion. The infection with SARS-CoV-2 can lead to the development of dermatomyositis and antisynthetase syndrome not only in the viral phase but also 6 months after.

Genes and circulating microRNAs as potential diagnostic and prognostic biomarkers in celiac disease

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2) Research Center for Functional Genomics, Biomedicine and Translational Medicine, Iuliu Hațieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania **Introduction.** Celiac disease (CD) is an enteropathy caused by the intolerance to gluten/gliadin peptides, with genetic and environmental determinisms and characteristic intestinal alterations. Studies in the literature have shown the involvement of different genes and microRNAs (miRNAs) in pathogenesis. The present study aimed to evaluate expression of certain genes (WNT3, WNT11, TNF α , MAPK1, AKT3, PIK3CA, CCND1) and miRNAs (miR-192-5p, miR-194-5p, miR-449a, miR-638) in adult patients with CD.

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Corresponding Author: Elena-Maria Domşa e-mail: elennmary@yahoo.com **Material and methods.** We prospectively included 15 patients with CD at diagnosis (newly diagnosed), 33 patients on gluten-free diet (GFD) for at least 1 year and 10 healthy volunteers (control). The subjects were recruited from the Regional Institute of Gastroenterology and Hepatology "Prof. Dr. Octavian Fodor" and from the 4th Medical Clinic, Cluj-Napoca, between 2015-2018. Duodenal biopsies, IgA anti-transglutaminase and / or IgA anti-endomysium antibodies were performed either for diagnostic purposes (new CD cases) or for follow-up (GFD cases), either for validation of the control group (normal duodenal histology and negative antibodies). Blood samples were evaluated by quantitative real-time PCR.

Results. TNF α , MAPK1 and CCND1 had elevated and statistically significant values (p=0.0249, p=0.0019, respectively p=0.0275) when were compared the newly diagnosed group to the controls. The other genes studied, although they had an increased expression compared to the controls, they did not reach the statistical significance. Among the miRNAs studied, miR-194-5p had a level close to the statistically significant one, respectively p=0.0510 comparing the newly diagnosed group versus controls and p=0.0671 comparing the GFD group versus control group. miR-449a and miR-192-5p showed significant functional activity according to the Diana and miRNet databases. These databases also revealed connections of miR-194-5p and miR-449a with CCND1.

Conclusion. Genes and circulating miRNAs could represent important biomarkers in CD, but further studies are needed to confirm their importance in clinical practice.

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Left atrial 3D volumes and differences between genders in patients with STEMI after percutaneous revascularization

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Corresponding Author: Raluca Tomoaia e-mail: raluca.tomoaia@gmail.com **Introduction.** Increased left atrium (LA) volume is associated with wall stress after ST-elevation acute myocardial infarction (STEMI). The aim of this study was to evaluate the values of LA 3D volumes in patients with STEMI after PCI and to test the differences between genders.

Material and methods. We included 53 patients with STEMI and preserved or mildly reduced left ventricular ejection fraction (LVEF). Echocardiography was performed using a Vivid E95 scanner with a 3D phased-array transducer. LVEF and diastolic dysfunction parameters were calculated and plasma concentrations of NTproBNP were measured. LA Vmin (minimum volume), Vmax (maximum volume), VpreA (at pre A phase), EV (ejection volume) and EF (ejection fraction) were assessed using the 4D Auto LAQ software analysis.



Results. Patients had a mean age of 64 ± 13 years and 43% were women. Female patients were significantly older than males (71±12 vs. 59±12 years, p=0.002) and presented more frequently with diabetes, while male patients were more frequently smokers. NT-proBNP values were significantly higher in females, 664 (320, 1405) vs. 292 (105, 642) ug/mL, p=0.01). Standard diastolic dysfunction parameters were not significantly different between groups. Regarding 3D measurements, mean LA EF was of $46\pm13\%$, EV of 46 ± 13 mL, Vmax of 60 ± 26 mL, Vmin of 32 ± 16 mL and V preA of 46 ± 19 mL. LA VpreA, Vmax and Vmin showed strong correlations to LA 2D volume (r=0.70, 0.62 and 0.60). NT-proBNP showed moderate correlations with LA VpreA (r=0.41) and Vmin (r=-0.49), while the correlation with LA 2D volume was significantly weaker. Only LA EF (41.6 ± 12.8 vs. $51\pm12\%$, p=0.009) and EV (19.6 ± 12 vs. 29.6 ± 17 mL, p=0.018) were significantly different between genders.

Conclusion. LA 3D parameters reflect increased myocardial wall stress in patients with preserved or mildly reduced LVEF after STEMI. LA EF and EV show significant differences among genders, even in the presence of a normal LA 2D volume.

Benign recurrent intrahepatic cholestasis in an adolescent

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Corresponding Author: Patricia-Lorena Lorințiu e-mail: lrntpatricia@yahoo.com **Introduction.** Benign recurrent intrahepatic cholestasis (BRIC) is an autosomal recessive disorder characterized by acute episodes of severe jaundice and pruritus, with symptom-free intervals and no progression to end-stage liver disease, caused by variants of genes encoding proteins involved in biliary secretion.

Case presentation. We report a case of a 16-year-old girl, who was admitted to our hospital for intense jaundice, severe pruritus with scratching lesions, dark urine and fatigue, with a sudden onset triggered by an acute upper respiratory tract infection. The patient reported two similar episodes, the first one at the age of 7 and the second at 15, both associated with infectious triggers, with symptom-free periods between episodes. On clinical exam, the patient presented jaundice, multiple excoriation marks on her body, with no sign of chronic liver disease. The laboratory tests revealed mildly increased transaminases, moderate cholestasis with a normal gamma-glutamyl transferase. On further questioning, we excluded the consumption of potentially hepatotoxic drugs. The laboratory results excluded infectious causes, metabolic disorders, autoimmunity, hematological diseases and Gilbert syndrome. The abdominal ultrasound revealed normal liver and biliary ducts, and the transient elastography was normal (no fibrosis). Molecular genetic testing is in progress. We initiated the treatment of the cholestasis and pruritus with ursodeoxycholic acid, rifampicin, cholestyramine, H1-antihistamines and phenobarbital in exacerbations, with a good outcome.

Conclusion. Although the long-term prognosis of BRIC is generally good, with no significant liver damage, the acute episodes can alter the quality of life of the patients and, for this reason, it is essential to establish the correct diagnosis and treatment.

Media exposure, risk perception, and preventive behaviors among university students before the fourth COVID-19 pandemic wave

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Corresponding Author: Adela-Viviana Sitar-Tăut e-mail: adelasitar@yahoo.com **Introduction.** SARS-CoV-2 infection is responsible for the major pandemic facing the world today. Although, SARS-CoV-2 primarily causes lung infection and acute respiratory distress syndrome, other complications such as shock, acute cardiac injury, coagulopathy, and acute kidney injury have been reported. At the same time, a large percentage of COVID-19 patients, are developing psychiatric symptoms, changes in mental health. Social media has an important role in the diffusion of information, in coping distressing symptoms, in promoting preventive behaviors. However, its contribution and the pathway in short and long-term preventative attitudes in global health are still unclear. Previous research has failed to define the role of media exposure in recognizing risk perception and triggering COVID-19 and general vaccine preventative attitudes and actions. The purpose of the present study was to evaluate the relationship between media exposure - fear - risk perception - vaccination attitude.

Material and methods. We have conducted an explanatory-predictive study on 368 Romanian students, using partial least squares structural equation (PLS-SEM, software: SmartPLS v.3.3.3) modeling.

Results. Important relationships were discovered between fear - risk perception - vaccination degree and also between media exposure and fear, respectively risk perception.

In **conclusion**, in the media, organizations and authorities must have a positive and convergent presence, taking into consideration the influence of media exposure over the vaccination degree and attitudes.

Acute acalculous cholecystitis associated with SARS-CoV-2 infection in children: a case report

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3) Radiology and Imaging Department, Emergency Clinical Hospital for Children Cluj-Napoca, Romania **Introduction.** The novel Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) has rapidly spread, affecting people of all ages worldwide. Although the clinical manifestations of the coronavirus disease 2019 (COVID -19) seem to be less severe in children, they may also develop serious complications, including the Multisystem Inflammatory Syndrome in Children (MIS-C). In the pediatric population, gastrointestinal involvement is frequently associated with SARS-CoV-2 infection and MIS-C and may appear in the absence of respiratory symptoms, making the diagnosis difficult.

Case report. We report the case of a 6-year-old boy who presented 24 hours of fever, vomiting, abdominal pain and generalized rash. On admission, there was no

Corresponding Author: Georgiana-Laura Cioancă e-mail: georgianacioanca@gmail.com evidence of COVID-19 infection (negative rapid antigen test, RT-PCR test and serology). Laboratory findings showed lymphopenia (870/ μ L), increased inflammatory markers (CRP 5.80 mg/dL, ESR 56 mm/h), increased transaminases (AST 257 U/L, ALT 333 U/L), hyperbilirubinemia (total bilirubin 2.98 mg/dL, direct bilirubin 2.16 mg/dL). Abdominal ultrasound showed gallbladder distention (46.3 mm) in the absence of gallstones and without pericholecystic fluid or mural thickening. The patient was managed conservatively with intravenous fluids, antibiotics (cefuroxime) and symptomatic medication, but he presented persistent fever associated with bilateral conjunctivitis and periungual desquamation. Positive IgM SARS-CoV-2 antibodies confirmed the diagnosis on day 13 after admission. The further evolution was favorable, with the resolution of clinical, laboratory, imaging findings over the next couple of weeks.

Conclusion. Our patient developed this complication most probably due to the recent SARS-CoV-2 infection and the associated systemic inflammatory response. While the underlying pathophysiology of gallbladder dysfunction in COVID-19 patients is not fully understood, early diagnosis and treatment may improve the outcome of these patients.

The profile of the patients admitted to the Psychiatric Emergency room during the COVID-19 pandemic - a retrospective study

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Corresponding Author: Maria Bonea e-mail: maria.bonea@yahoo.com **Introduction.** The COVID-19 pandemic brought major changes in the dynamics of the medical system, including a major influence on the mental health of the population. The aim of the study was to assess the profile of the psychiatric patient hospitalised in the emergency room.

Material and methods. All hospitalizations on the three Psychiatric wards of the Cluj-Napoca County Emergency Clinical Hospital were analyzed, between 01.01.2019-31.10.2021. The data was analyzed using the Atlasmed hospital data base.

Results. After the onset of the COVID-19 pandemic in Romania, the total number of hospitalizations decreased by 9.53%. Significantly more men were hospitalized, both before and during the pandemic (62.3% and 63.4%, respectively). After the onset of the pandemic, there was a significant increase in cases of acute psychotic disorder (9.1% versus 7.7%, p = 0.029), manic episodes (2.6% versus 1.6%, p = 0.01), substance use disorder, other than alcohol (13.5% versus 11.6%, p = 0.08). There were no significant differences in the number of hospitalizations with diagnoses of schizophrenia, alcohol dependence, dementia, mental disability with behavioral disturbances or suicide attempts. During the pandemic, the frequency of hospitalizations for depressive episodes decreased significantly (18.7% versus 24.4%, p < 0.001) as well as cases with personality disorders (32.8% versus 35.9%, p = 0.003). 4% of patients were infected with COVID-19 virus, with no differences between the main psychiatric disorders, except for patients consuming psychoactive substances other than alcohol, among whom significantly fewer cases of infection were identified.

Conclusion. The period of the COVID-19 pandemic brought changes in the profile of emergency hospitalized patients with psychiatric pathology, namely: male, middle-aged, addicted to psychoactive substances, with diagnoses of acute psychotic disorder or manic episode.

Autoimmune features associated with drug-induced liver injury: case report

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Corresponding Author: Bianca Raluca Mateescu e-mail: bianca.mateescu18@yahoo. com **Background.** Drug-induced liver injury (DILI) is a common cause of hepatitis, the disease spectrum varying from asymptomatic forms to a severe, life-threatening presentation of acute liver failure. The mechanism of DILI is unrelated to the pharmacodynamics of the drug itself, being immune-mediated. The immune system's involvement results in antibody production, directed against the incriminated drug or, frequently, against self-antigens. The presence of autoantibodies, especially antinuclear antibodies (ANA), can interfere with the diagnostic process, making the differentiation from autoimmune hepatitis (AIH) difficult.

Case presentation. We report the case of a 15-year-old boy who presented in a regional hospital with jaundice, asthenia, anorexia and pruritus, for 1 month. The symptoms had developed 8 days after the first dose of albendazole and had been progressive since then. The clinical exam revealed moderate hepatomegaly and acholic stools. Laboratory studies showed elevated transaminases (ALT 767 U/L, AST 189 U/L), direct hyperbilirubinemia (total bilirubin 21 mg/dl, conjugate bilirubin 14 mg/dl), mild cholestasis and normal values of albumin and INR. The patient was discharged after 2 weeks and was transferred for further investigations in our clinic. We excluded other causes of hepatitis (infectious, Wilson's disease, alpha-1 antitrypsin deficiency and obstructive jaundice). However, immunological studies revealed a high level of IgG and positive ANA, suggestive of AIH. We administered prednisone (0.5 mg/kg/d) with rapid normalization of transaminase and bilirubin levels. Therefore, we reduced glucocorticoid doses and plan to discontinue immunosuppression if the course of disease permits.

Conclusion. In the presence of autoimmune features, the differential diagnosis between DILI and AIH can be difficult, as the two entities have many similarities. The long-term evolution of the case will be the one to prove the final diagnosis.

The etiology of cognitive deficits associated with COVID-19

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Corresponding Author: Octavia Căpățînă e-mail: o.capatina@yahoo.com **Introduction.** The aim of this study was to present a narrative review on the etiology of the literature on cognitive impairment associated with COVID-19.

Material and methods. We searched the PubMed database for studies performed between January 2019 and July 2021 on human subjects discussing the etiology of the cognitive consequences in patients who recovered from COVID-19.

Results. The etiology of the cognitive impairment associated with COVID-19 is still not clear. Several mechanisms have been proposed and these include: 1. General ischemia secondary to respiratory insufficiency. 2. Neuroinvasion. 3. Coagulopathies. 4. Systemic inflammatory response.

Conclusion. All of the mechanisms reported above could play a role in the etiology of the cognitive impairments associated with COVID-19. At the present moment there is an ongoing discussion if these cognitive deficits are transitory or progressive. However, it is necessary to conduct further research to assess the cognitive function on long term in this category of patients.

Treponema Pallidum as the etiologic agent of acute liver failure in infancy: case report

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Corresponding Author: Emilia Augusta Pop e-mail: dr.emiliapop@gmail.com **Introduction.** The etiology of pediatric acute liver failure is different from that of adults. In infancy, the most common causes are inborn errors of metabolism and infections. Hepatitis is found in 20% of children with congenital syphilis, but a small number of patients develop acute liver failure.

Case presentation. We are presenting the case of a 2-month-old male infant who presented to our hospital with jaundice, hepato-splenomegaly and generalized edema. He had elevated transaminases, coagulopathy (increased International Normalized Ratio, INR), elevated inflammatory markers (C reactive protein and procalcitonin) and acute kidney injury. We performed metabolic profile testing (serum amino acids, urinary organic acids, carnitine profile), which were negative and serologic testing for infectious causes, which excluded viral causes. The Venereal Disease Research Laboratory (VDRL) test was positive, demonstrating congenital syphilis. The patient needed supportive treatment in the Intensive Care Unit (ICU), including erythrocyte and plasma transfusions, and we initiated Penicillin G treatment. The evolution was slowly favorable with the resolution of the liver failure in five days on the etiologic treatment.

Conclusion. Syphilitic hepatitis is diagnosed in patients with hepatitis with serological evidence of Treponema Pallidum infection without an alternative cause of hepatic dysfunction. Usually, syphilitic hepatitis is mild with complete resolution after the treatment of the infection, but in rare cases may present with acute liver failure with an unfavorable prognosis and need of ICU treatment or even liver transplantation.

Insomnia in patients with dementia: a therapeutic challenge

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Corresponding Author: Mihaela Fadgyas Stănculete e-mail: mihaelastanculete@yahoo. com **Background.** Dementia is associated with sleep disorders (especially insomnia), which negatively impact the patients' quality of life and increase the caregiver burden, insomnia being associated with earlier admission to institutional care. This presentation will review the bidirectional relationship between insomnia and dementia, discussing the benefits and common adverse events of molecules used to treat sleep problems in people with dementia.

Methods. Articles were chosen from PubMed and Medscape to evaluate the current knowledge regarding interventions for insomnia in people with dementia living in the community.

Results. No treatment showed superior effectiveness, although preliminary work about non-pharmacological interventions can be built on.

Conclusion. Given the importance of sleep and the many consequences of its disruption, well-designed controlled trials are needed to determine acceptable, safe, and cost-effective treatment strategies that work for insomnia in patients with dementia.

The emotional impact of information sources in the context of the COVID-19 pandemic

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Corresponding Author: Bianca Crecan-Suciu e-mail: suciu.bianca@umfcluj.ro **Introduction.** The COVID-19 pandemic is considered to have important consequences due to social and economic disruption but also with an impact over the emotional state of individuals. This study aimed to understand the relationship between media exposure of different source information of coronavirus data and coping mechanism. The objectives of the present study were to identify different clinical variables that characterize the study group, describe the frequency of use of information sources, their number and the level of clarity of the information accessed, and also the coping strategies.

Material and methods. The study included 85 participants, with ages between 12 and 52, who answered an online questionnaire, containing questions regarding media sources and the Bref- Cope questionnaire.

Results. Participants used frequently the social networks and the Ministry of Health website with a decrease in the use of classical information methods or obtaining information from family members, friends or colleagues. They reported elevated levels of anxiety, depression, confusion, anxiety, and frustration after accessing pandemic information. We identified statistically significant correlations between information sources and problemoriented coping mechanism.

Conclusion. Different aspects of community health must be taken into consideration, such as media consumption, which can impact the mental health of individuals, suggesting this domain to be relevant for interventions to address the consequences.

A case report of biliary atresia diagnosed early after birth

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4) 1st Pediatric Surgery Department, "Maria Skłodowska Curie" Emergency Clinical Hospital for Children, Bucharest, Romania **Introduction.** Biliary atresia is a congenital disorder characterized by obliteration or discontinuity of the bile ducts, resulting in obstruction to bile flow. Although a rare disease with an incidence in Europe of 1 in 12.000 births, it is one of the most common causes of neonatal cholestasis and the leading cause of pediatric liver transplantation.

Case report. We report the case of a 7-days old male neonate presenting with generalized jaundice, acholic stools and dark urine. Laboratory tests revealed direct hyperbilirubinemia (total bilirubin 13.2 mg/dl, direct bilirubin 9.7 mg/dl), increased gamma-glutamyltransferase (1244 U/L), normal transaminases. He was first diagnosed with neonatal sepsis, but despite receiving broad-spectrum antibiotic treatment, the symptomatology persisted. The abdominal ultrasound revealed the absence of the gallbladder, highly suggestive of biliary atresia. Therefore, the patient war referred to Surgery Clinic, and the Kasai procedure was performed at the age of one month and twenty days. This procedure involves removing the obliterated bile ducts and the anastomosis of a Roux-en-Y jejunal loop to the portal plate to enable bile to enter the bowel. Cholestasis started to improve with decreasing bilirubin level, indicating

Corresponding Author: Adina Andreea Pop e-mail: adinna.pop@gmail.com a successful Kasai procedure. Unfortunately, transaminases started to increase at the last check-up as the patient was diagnosed with acute cytomegalovirus infection.

Conclusion. Biliary atresia is an idiopathic, fibro-inflammatory process that affects both intra and extra-hepatic bile ducts. It typically presents during the first weeks of life, and early diagnosis and treatment may improve the prognosis; otherwise, it rapidly progresses to biliary cirrhosis. The Kasai procedure is considered a palliative operation since most of the patients will further require liver transplantation, given the progressive nature of this disease.

Impact of left ventricular longitudinal contraction on the left atrial appendage function and the occurrence of thromboembolic events in patients with atrial fibrillation

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Corresponding Author: Adriana Daniela Porca e-mail: adriana_porca@yahoo.com **Introduction.** Previous research has revealed a relationship between left ventricular (LV) function and incidence of stroke in atrial fibrillation (AF) but the mechanism remains unknown. Given the anatomical vicinity between the left atrial appendage (LAA) and LV base, the purpose of this study was to investigate using transesophageal echocardiography (TEE) whether LV longitudinal contraction impacts LAA function parameters, LAA thrombus (LAAT) formation, and occurrence of ischemic stroke.

Material and methods. We included in our study 102 consecutive patients (age 59 ± 11 ; 55 men) undergoing TEE-guided cardioversion for AF. LV longitudinal function was assessed using the mitral annulus plane systolic excursion (MAPSE). LAA function was evaluated using the LAA emptying velocity (LAAEV) and LAA ejection fraction (LAAEF). The presence LAAT and spontaneous echo contrast (SEC) were evaluated as well.

Results. Our patients had a median CHADS2vasc score = 3 (IQR 2-4), FEVS= $50\pm11\%$, and MAPSE= 7.3 ± 1.7 mm. MAPSE showed a positive significant correlation with both LAAEV (r=0.34; p<0.01) and LAAEF (r=0.23; p<0.05). LVEF correlated significantly with LAAEV (r=0.42, p<0.01), and LAA area (r=-0.34; p<0.05), respectively. Additionally, patients who exhibited SEC had significantly lower LAAEF as well as LAAEV when compared with patients without SEC: $31\pm12\%$ vs $38\pm12\%$ P=0.022 and 35 ± 18 cm/s vs 49 ± 21 cm/s P=0.005. Patients who displayed both SEC and LAAT had wider LAA neck when compared to the rest of the group (21.46 ± 3.96 mm vs. 18.23 ± 3.78 mm; P=0.021).

Logistic regression analysis revealed that MAPSE independently predicted the occurrence of ischemic stroke both in univariate and multivariate models that also included the CHADSvasc2 score.

Conclusion. LV longitudinal contraction appears to influence LAA function. This relationship could potentially have an impact on occurrence of thromboembolic events in patients with atrial fibrillation.

Evaluation of a correction method for the measurement of plasma human chitotriosidase activity in pediatric obesity depending on two CHIT1 gene variants

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Corresponding Author: Ioana Țaranu e-mail: taranu.ioana@umfcluj.ro **Introduction.** Elevated plasma activity of the human chitotriosidase secreted by activated macrophages was found in chronic inflammatory conditions associated with obesity. The 24 base-pair-duplication in exon 10 (dup24) and the 304 G-A-transition in exon 4 (G102S) of the CHIT1 gene constitute potential sources of variation of plasma CHIT1 activity. Bussink et al. proposed a correction method for CHIT1 plasma activity according to the two alleles.

We aimed to evaluate the utility of correction of CHIT1 plasma activity according to heterozygous and homozygous G102S and dup24 alleles in children with different obesity classes.

Material and methods. A longitudinal study with prospective data collection was conducted between October 2019 and March 2021 in the outpatient Endocrinology Department of the Infectious Disease Hospital in Cluj-Napoca. Overweight or obese patients from five to 18 years old were evaluated twice at 2 to 14 months interval.

In patients without 24dup allele, we multiplied CHIT1 plasma activity by a factor of 1.3 in the case of carriers for the G102s allele and by a factor of 1.6 in the case of homozygotes for G102S allele.

Results. We included twenty-nine children (16 (55.2 %) girls and 13 (44.8%) boys): four overweight, 15 obese and ten extremely obese patients.

We found no significant change in BMI-for-age z score at the follow-up (Wilcoxon test, p = 0.121), while a significant decrease in both uncorrected and corrected CHIT1 plasma activity was observed (Wilcoxon test, p=0.014, respectively, p=0.017).

No significant correlation between CHIT1 plasma activity and BMI-for-age z score was found in the baseline or at follow-up (Spearman rank correlation, p>0.05).

Conclusion. Correction factors based on the presence of the dup24 and the G102S allele in CHIT1 gene might have no effect on the CHIT1 plasma activity in paediatric patients.

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Coping mechanisms in students during COVID19 pandemic

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The COVID-19 pandemic has a profound impact on all domains of day-today life, causing an important psychological distress and forcing individuals to make substantial change in the way of living. Good coping mechanisms can be the key to overpass this difficult period.



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Corresponding Author: Cătălina Crișan e-mail: ccrisan2004@yahoo.com ioanamiclu@elearn.umfcluj.ro **Objectives.** The aim of this study was to evaluate how the Romanian students succeed to adapt during COVID-19 pandemic (March 2020 until October 2021).

Material and Methods. 285 students (different lines of study) (20.4% males and 79.6% females) completed an online questionnaire which included questions about different socio-demographical variables and coping mechanisms (we used BrefCope scale with 28 items).

Results. 1/3 of students used frequently work or other activities as a coping mechanism and concentrated their efforts in order to find a solution. Over 70% of students did not use alcohol or other substances as coping mechanism. 1/3 had emotional support from other persons. 50% of students did not give up to face the situation and 1/3 used communication to get rid of unpleasant problems.

Conclusion. A good coping mechanism represents a key element to adapt during a stressful period of life, including COVID-19 pandemic.

The veins of the left ventricular summit

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Corresponding Author: Iulia-Georgiana Zehan e-mail: iuliazehan@gmail.com **Introduction.** While the coronary sinus and its left ventricular branches have been extensively described, the veins of the left ventricle summit (LVS) have been much less studied. The emergence of new ablation techniques for ventricular tachycardias, which make use of the LVS veins, has generated a renewed interest in the anatomy of these venous conduits. The aim of the study was to describe in detail the anatomy of the LVS veins using rotational venous angiography.

Material and methods. All patients (N=80, age 66±13 years, 57 men) underwent rotational venography during the cardiac resynchronization implant procedures. This technique allowed a multiangle visualization of the LVS veins.

Results. The LVS veins identified were the great cardiac vein (GCV), the anterior interventricular vein (AIV) and the mitro-aortic LVS vein (MALVSV). The MALSV emerged from the GCV between 12 and 2 o'clock on the mitral ring, coursed inside the left atrioventricular groove, towards the aorto-mitral continuity (AMC), where it turned towards the ventricular septum and coursed parallel to the AIV, tapered down and ended at midventricular level. Most of the course of this vein was in the region of the LVS. The diameter of the venous conduit at the GCV-AIV junction was 4.9 ± 1.0 mm. The MALVSV was present in 59 patients (72.5%). The takeoff position from GCV was between 12:00 and 2 o'clock on the mitral ring in all cases. The MALVSV diameter was 2.3 ± 0.6 mm at the ostium and 1.7 ± 2.0 mm at the AMC. The takeoff angle was $134\pm27^{\circ}$. The total length of the vein was 31 ± 15 mm, of which 22 ± 13 mm were inside the AV groove and 8 ± 9 mm, were along the ventricular septum. The length of the MALSV segment embedded in the left AV groove as well as the total length of MALSV correlated significantly with the left atrial diameter (r=0.44; P=0.040 and r=0.45; p=0.016 respectively) as well as with the right ventricular systolic pressure (r=0.50; p=0.028 and r=0.57; P=0.030 respectively).

Conclusion. This study brings new insights into the geometry and distribution of the LVS veins. This could help with optimization of the current techniques as well as with development of new strategies for ablation of LVS tachycardias.

Types of communication during Covid-19 pandemic and their impact on public health

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Corresponding Author: Ioana Micluția e-mail: ioanamiclu@yahoo.com Data regarding the SARS-Cov2 infection, Covid-19 illness, recommendations regarding the preventive measures against the spread of the infection were transmitted via different official media in a clear, simple, easy way to be applied. Shortly, another type of messages invaded especially via social media and overshadowed the official messages due to the emotional load and less scientifically documented, called infodemia. The two types of communication were analyzed, and their consequences in reaching some vulnerable populations, with important consequences regarding the mistrust in medical personnel, disobedience regarding restrictions, and devastating consequences on incidence, morbidity and death rates.

Pityriasis Rubra Pilaris and autoimmune hepatitis in an 8-yearold boy

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Corresponding Author: Claudia Sîrbe e-mail: claudia.sirbe@yahoo.com **Introduction.** Pityriasis rubra pilaris (PRP) is a rare skin disease that presents with a reddish-orange scaly rash with well-defined borders. Autoimmune hepatitis (AIH) is a chronic liver disease that has an increasing global prevalence. The specific underlying causes of PRP and AIH are incompletely described.

Case presentation. We present the case of an 8-year-old boy who was admitted to our hospital for generalized scaly rash and hepatomegaly. Clinical manifestations started 10 days earlier with erythematous patches with perioral and groin localization and progressive extension, becoming intensely scaly. In addition, the patient had marked fatigue and decreased appetite. Clinical examination revealed mild growth failure, pallor, maculopapular erythematous rash on extensor surfaces, the liver palpable at 2 cm below the costal margin. These skin patches tended to join together to form groups of thickened, rough plaques covered with scales and crusts. The rash was slightly itchy, painless and did not involve the mucous membranes. Laboratory analyses revealed elevated liver enzymes (ALT 8x times normal, AST 6x times normal), increased IgG level, and presence of antinuclear antibodies, antismooth muscle antibodies and anti-myeloperoxidase antibodies (p ANCA). Acute infections and Wilson's disease were excluded, and there was no exposure to a toxic medication. Abdominal ultrasound described increased diffuse liver echogenicity. Based on these data, we defined the case as type I AIH. A skin biopsy was performed from the maculopapular lesions. Considering its time course, clinical appearance and morphopathological result, we established the diagnosis of PRP. Treatment was started with prednisone and isotretinoin, in addition to topical emollients. At 6 months
follow-up, the skin lesions were in remission alongside the improvement of liver analyses and negative autoantibodies.

Conclusion. Although overlapping autoimmune diseases are common, the association between PRP and AIH is rarely encountered. As a rare disease, difficulties in timely diagnosis can be found as PRP is often initially mistaken for another skin condition, usually psoriasis. Even if the diagnosis is established early, specific treatment in these disorders is complex and requires long-term immunosuppression.

Depression and anxiety among peripartum women during COVID-19 pandemic

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Corresponding Author: Patricea Hulubă e-mail: patricea.huluba@yahoo.com **Introduction.** The infection with the novel coronavirus correlates with high mortality and morbidity and has a negative impact on mental health. Peripartum women are more vulnerable to psychiatric conditions such as depression and anxiety. The risk factors for these conditions include personal history of psychiatric diseases, environmental factors, and hormonal fluctuations which occur during pregnancy and during postpartum period. There is a negative impact on newborns also, because of the somatic and psychiatric comorbidities which cand lead to premature births. Pregnant and postpartum women are more vulnerable to infection with the novel coronavirus. Therefor the psychiatric evaluation is very important.

Methods. The papers were searched in PubMed using the key words "depression", "anxiety" "Covid-19" "pregnant". There were 160 papers in total, of which 12 fulfilled all 4 criteria.

Results. There are few studies which evaluated the mental health of peripartum women among COVID-19 pandemic. Researches showed that pregnant women have a higher risk of infection than general population. In time of COVID-19 pandemic low access to medical facilities lead to the growth of anxiety and depression, showed by a positive correlation between them. One of the papers shows that anxiety during pregnancy leads to a higher risk of premature birth and low weight at birth. There were two major factors implicated in pregnancy related anxiety: "real or anticipated threat to pregnancy or its outcomes" and "low perceived control". These two factors are amplified by COVID-19 pandemic.

Conclusion. Pregnant women have high symptoms of anxiety and depression, correlated with the effect of COVID-19 infection on them and on the newborns, and with a more difficult access to medical services. In conclusion there is an urgent need to offer support to these persons, in order to reduce the negative effects of psychiatric diseases on pregnant women and newborn children.

Correlations between voltage map and p wave duration in patients with Bayes syndrome undergoing catheter ablation for paroxysmal atrial fibrillation

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Corresponding Author: Ioan-Alexandru Minciună e-mail: iaminciuna@gmail.com **Introduction.** Bayes syndrome is defined as interatrial conduction block and is objectivized on surface ECG by a P wave duration (PWD) greater than 120ms. This causes delayed and asynchronous left atrial (LA) activation which leads to electrophysiological and structural remodeling (dilatation, fibrosis), thus predisposing to atrial fibrillation (AF) development. Electroanatomical voltage mapping (EAM) is a reliable marker of LA fibrosis by identifying low-voltage areas in the myocardium. The aim of this study is to see whether there is a correlation between PWD in Bayes syndrome patients and LA fibrosis assessed by low-voltage area at EAM prior to paroxysmal AF catheter ablation.

Material and methods. 12 patients undergoing catheter ablation for paroxysmal AF were subjected to bipolar voltage EAM. We compared maximum and minimum PWD (Pmax, Pmin), P wave dispersion (Pd =Pmax-Pmin) and LA PWD (measured from -dV/dt in leads V1 and V2 until the end of the P-wave) on surface amplified 12-lead ECG with LA low-voltage area before starting ablation shots. The presence of LA low-voltage area was defined as total area >2 cm² at voltages <0.5 mV.

Results. 6 patients had LA low-voltage area > 2 cm² (50%) in which the mean value was 10.42 ± 6.4 cm². We found that higher LA low-voltage area was correlated with higher Pd (R = 0.68, p = 0.015), LA PWD (R = 0.73, p = 0.007) and Pmax values (R = 0.68, p = 0.015), whereas there was no correlation with Pmin. Patients that had LA low-voltage area >2 cm² had also higher interatrial conduction times - Pmax (139.83 ± 15.3 vs. 122.33 ± 4.5, p = 0.0231), Pd (49.8 ± 9.9 vs. 34.3 ± 6.9, p = 0.011) and LA PWD (54.5 ± 10.6 vs. 41.5 ± 3.73, p = 0.018) compared to patients with LA low-voltage area < 2 cm².

Conclusion. The presence of LA fibrosis assessed by EAM is associated with higher interatrial conduction times in Bayes syndrome patients and could be a predictor of arrhythmia recurrence after paroxysmal AF catheter ablation.

The relationship between left ventricular geometry and respiratory sinus arrhythmia in patients with vasovagal syncope

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Corresponding Author: Giorgia Coșeriu e-mail: giorgia23pastiu@yahoo.com **Introduction.** The study was prompted by our observation that a significant number of patients with vasovagal syncope (VVS) have marked respiratory sinus arrhythmia as well as thin left ventricular (LV) walls. We hypothesized that the geometry of the LV walls may play a role in the pathogenesis of VVS. The aim of this study was to assess LV geometry in relationship to respiratory sinus arrhythmia in patients with VVS.

Material and methods. We included 191 patients (age 52 ± 20 years, 101 women) with VVS who had either a positive or negative response to tilt table testing TTT (n=64 TTT+, and n=127 TTT-). The VVS group was compared to a group of 75 patients with no syncope (NL) and similar age, sex and BMI distributions. Standard 12-lead electrocardiograms (ECG), vectorcardiograms, and transthoracic echocardiograms were performed to assess electrical activation as well as ventricular geometry and function. The magnitude of respiratory sinus rhythm arrhythmia was measured as the maximum percent change in RR interval on a 10 second 12-lead ECG (dRR) performed before the TTT.

Results. When compared to NL group patients with VVS had significantly higher dRR and LV end diastolic diameter $(12\pm8\% \text{ vs } 10\pm8\%, \text{ p}=0.047 \text{ and } 44\pm5 \text{ vs } 46\pm6 \text{ mm p}=0.006$ respectively) The end-diastolic thickness of the interventricular septum (IVS) and that of the LV posterior wall (PWT) in the VVS group were significantly smaller than in the NL group ($8.9\pm1.7 \text{ mm vs } 9.6\pm1.8 \text{ mm p value}=0.003$ and $8.4\pm1.5 \text{ mm vs } 9.2\pm1.6 \text{ mm p value}=0.0002$). The magnitude of respiratory sinus arrhythmia expressed as dRR correlated inversely and significantly with IVS (r=-0.32; p value=0.042). The was however no significant correlation between dRR and PWT. These results suggest that a more pronounced respiratory sinus arrhythmia could be related to more ample variations in right and left ventricular filling due to increased ventricular interdependence via a thinner and more compliant ventricular septum.

Conclusion. The geometry of the LV, as well as the cardiovascular impact of respiratory movements, may play a role in the pathogenesis of VVS.

SURGICAL SPECIALTIES

Miniseries of rare appendicular pathologies

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Corresponding Author: Raluca-Cristina Apostu e-mail: ralucaapostu@ymail.com **Introduction.** Appendicular pathology is mostly represented by acute appendicitis, solved by an emergecy appendectomy. There are however other pathologies that are difficult to diagnose preoperatively and require an extensive management. Appendiceal mucocele, diverticulum and appendicitis of appendicular stump are among the rarest diseases of the appendix, with an incidence that varies between 0.014-3.7%. We decided to perform an analysis of the appendicectomized patients and evaluate a miniseries of representative patients for these rare diseases.

Material and methods. We performed a retrospective analysis of the patients operated with appendectomy in the last 3 years in the First Surgical Clinic Cluj-Napoca, searching for rare pathologies. We excluded patients with a histopathological result of colon cancer and cases were a tactical appendectomy was performed. A miniseries of patients was identified as representative for each pathology. The diagnostic methods, investigations, surgical treatment and evolution were analyzed.

Results. We identified 330 patients with appendectomy, performed chronically in ten cases. The histopathological reports analysis revealed five cases with neoplastic appendiceal mucinous lesions, including two with mucinous cyst adenoma. Other pathologies were appendicular diverticula in one case and one appendicitis of the appendicular stump. All patients were diagnosed based on computer tomography/magnetic resonance imaging evaluation. As surgical treatment, appendectomy was performed for appendicular diverticula, stump appendicitis and mucinous cyst adenoma, while right hemicolectomy was the indication for the neoplastic mucinous lesions. Patients were discharged without complications. Cases with neoplastic mucinous lesions were included in a follow-up programme.

Conclusion. It is important to raise awareness of these rare appendicular pathologies, as the unspecific presentation can lead to improper management, associated with high mortality.

Perineal hernia mesh repair after abdominoperineal resection: two case reports

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2) Department of Surgery III, Faculty of Medicine, Iuliu Hațieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania **Introduction.** Perineal hernia is a rare complication that can occur following major pelvic resections. The treatment is surgical, usually consisting of mesh repair, but with no well-established ideal approach.

Material and methods. We describe two cases of symptomatic perineal hernias, one being the case of which was a 75-year-old woman, and the other, a 57-year-old woman, both occurring after abdominoperineal resection for rectal cancer.

Corresponding Author: Hunor Levente Horvath e-mail: hunorlevente.horvath@yahoo. ro **Results.** The perineal approach was preferred in both cases. After dissection, reduction of the hernial contents, and excision of the hernial sac, the defect was closed with a polypropylene mesh.

Conclusion. We report two cases of PH after APR. A perineal approach was successfully utilized in both cases, which has been proven to be a simple and effective method for uncomplicated cases. Reconstruction of the perineal floor and, closure of the defect were performed using a synthetic mesh.

Chitotriosidase and neopterin as perioperative biomarkers in gastric cancer and cholelithiasis

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Corresponding Author: Vlad-Ionut Nechita e-mail: nechita.vlad@umfcluj.ro **Introduction.** Gastric cancer is the 5th most frequent type of neoplasia. About 10-20% of the world's population develop gallstones. We aimed to evaluate the differences in chitotriosidase and neopterin levels between malign (gastric cancer) and benign pathology (gallstones) respectively the postoperative changes regarding surgery invasiveness.

Material and methods. A prospective cohort study from August 2019 to January 2021 was conducted. Patients with open surgery for gastric adenocarcinoma or laparoscopic approach for gallstones at the Regional Institute of Gastroenterology and Hepatology, Cluj-Napoca that give informed consent were eligible. Blood samples were collected on EDTA at the presentation and at 24-48 hours after surgery. Only patients with gastric adenocarcinoma, without recurrent neoplasia, biliary pancreatitis or reactive hepatitis were included.

Results. Thirty-nine subjects with gastric adenocarcinoma and fifty-three with cholecystitis were included in the study. A significantly higher level was observed at baseline for chitotriosidase 280 (165-400) nmol/mL/h in gastric cancer than 170 (110-230) nmol/mL/h for gallstone subjects (p<0.01 - Mann Whitney test). No significant differences for neopterin 10.06 (9.26-18.15) nmol/L in gastric cancer vs. 13.03 (7.77-18.34) nmol/L for cholecystitis (p=0.149 - Mann Whitney test) were observed. When comparing the prepostoperative values, no significant changes were observed for laparoscopic intervention. In contrast, a significant increase after the open procedure (p<0.001 - Wilcoxon test) was observed for neopterin 21.96 (12.09-34.69) nmol/L vs. 10.06 (5.3-18.15) nmol/L at baseline. Chitotriosidase reveal no significant changes after laparoscopic or open procedure.

Conclusion. Macrophage activation and chitotriosidase levels are higher for malignant pathology like gastric cancer in comparison with non-malignant pathology (cholecystitis). Neopterin can be considered to evaluate surgical procedure invasiveness.

3D laparoscopic inguinal lymphadenectomy in penile carcinoma

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 Department of Urology, Faculty of Medicine, Iuliu Hațieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania **Introduction.** N+ penile carcinoma requires a multimodal and interdisciplinary approach for optimal treatment. Even if associated with high morbidity, surgical removal of lymph node masses is indicated bettering the prognosis for the patient.

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Corresponding Author: Cristina Eliza Bujoreanu e-mail: bujoreanucristina@yahoo.com **Material and methods.** We exemplify our experience of 3D laparoscopic treatment of inguinal lymph node metastases in patients that prior underwent surgical treatment for penile squamous carcinoma. The steps of the surgical technique are explained with intra operatory images with emphasis on the anatomy, dissection in a small working space and associated peri and post operatory complications.

Results. 7 patients underwent 3D laparoscopic treatment for inguinal lymph node penile carcinoma metastases with 1 case requiring conversion and en block excision of the lymph node mass and the adjacent tegument for oncologic safety. Mean peri/ post operatory data is reported- operatory time, blood loses, lymph node yield and 30 days Clavien-Dindo complication grade.

Conclusion. Minimal invasive treatment is safe and feasible to be offered in treating inguinal lymph node metastases of penile carcinoma offering decreased related morbidity with fast healing. This enables a rapid initiation of adjuvant therapy along with a better cancer specific survival.

3D laparoscopic treatment of renal carcinoma with venous tumoral thrombus involvement

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Corresponding Author: Cristina Bujoreanu e-mail: bujoreanucristina@yahoo.com **Introduction.** Venous tumoral thrombus involvement in renal carcinoma imposes technical challenges for the surgical management, especially when performed minimally invasive.

Material and methods. We report our experience of 3D laparoscopic radical nephrectomy and thrombectomy with highlights on tumoral thrombus management and cavoraphy solutions using intra operatory images.

Results. 39 patients underwent 3D laparoscopic treatment for renal carcinoma with tumoral thrombus at different levels, the highest thrombus presentation being infrahepatic-inferior vena cava. Cavoraphy was performed in 19 cases (13 right sided +6 left sided) out of which 8 needed clamping of the contralateral pedicle. 21 cases required lymph node dissection with 1 case requiring conversion. Mean peri- and postoperative data are also reported - operatory time, blood loss, 30 days Clavien-Dindo complication grade.

Conclusion. Even if it is highly complex, the minimal invasive treatment of renal carcinoma associating venous tumoral thrombus (both at the level of renal vein and inferior vena cava) is safe and feasible. The cavoraphy and lymphadenectomy are key moments when the laparoscopic skills are challenged.

3D laparoscopic totally intracorporeal ileal neobladder

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1) Department of Urology, Faculty of Medicine, Iuliu Hațieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania **Introduction.** A neobladder represents a complex surgical treatment of bladder cancer with the reconstruction of a new urinary reservoir, involving besides the radical cystectomy and pelvic lymphadenectomy step (+/- prostatectomy/hysterectomy),



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Corresponding Author: Cristina Bujoreanu e-mail: bujoreanucristina@yahoo. com the ileal management and the molding of part of the ileum to mimic the urodynamic properties of a physiological urinary bladder.

Material and methods. We report 45 cases of totally intracoporeal 3D laparoscopic ileal neobladder and discuss surgical steps with technical particularities of key operatory steps: ileal loop selection, digestive tract restoration, ileal loop preparation and molding, crafting the neobladder along with urethral-neobladder- ureteral anastomosis. Indocyanine green fluorescence is used to view tissue vascularization.

Results. Mean operatory time- 300 minutes, mean blood loses – 550 ml, mean hospitalization – 21 days, mean Clavien-Dindo complications at 30 days- I. Indocyanine presents a safe usage profile and impacts the surgical steps imposing distal end excision (ureteral/ileal). Mean neobladder capacity (by ultrasound evaluation) – 420 ml.

Conclusion. Totally intracorporeal 3D laparoscopic neobladder reconstruction is safe and feasible to be performed, offering a functional urinary reservoir as a complete treatment for bladder cancer patients, impacting their life quality in a positive way. Technical aspects are crucial for peri and post operatory evolution, along with post operatory management. Indocyanine dye offers promising implications in functional peri and post operatory results.

Da Vinci X robotic totally intracorporeal pure Studer ileal neobladder

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Corresponding Author: Cristina Bujoreanu e-mail: bujoreanucristina@yahoo. com **Introduction.** Patients with bladder cancer and indication of radical cystectomy may be offered different options for urinary derivations. Reconstructive surgery is one of the most challenging surgeries in Urology.

Material and methods. We exemplify our initial experience of 22 cases of Da Vinci X pure Studer ileal neobladder highlighting the operatory technique which includes Indocyanine green dye usage under the Firefly mode of the Da Vinci robot. Optimizing key elements are discussed regarding the operatory technique.

Results. Mean operatory time- radical cystoprostatectomy 150 minutes, robotic reconstructive surgery- 210 minutes, mean blood loses 600 ml, mean hospitalization stay- 21 days. Mean neobladder capacity – 420 ml, mean grade- 30 days Clavien-Dindo complication- I. Indocyanine green presented no adverse reaction.

Conclusion. Robotic surgery brings precise gentle movements with impact on the surgical act. Reconstructive surgery is advantaged by the robot as the dissection is more precise and tissue manipulation with lower trituration. The totally intracorporeal robotic Studer neobladder offers promising functional results, along with ICG usage.

FUNDAMENTAL RESEARCH

Stereoselective synthesis and characterization of new optically active thiazole N-Fmoc-beta-amino acids suitable for peptide synthesis

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Corresponding Author: Denisa Leonte e-mail: leonte.denisa@umfcluj.ro **Introduction.** Optically active N-Fmoc-beta-amino acids are of increasing interest for peptide synthesis, as beta-peptide bonds can enhance metabolic stability and potency of bioactive peptides. In the continuation of our previous research regarding the synthesis of new neurotensin peptide analogues with improved functions, the aim of this study is the stereoselective synthesis of new thiazole N-Fmoc-beta-amino acids in both enantiomeric forms, as valuable building blocks directly usable for solid phase peptide synthesis.

Material and methods. Optically active thiazole beta-amino acids were obtained by lipase catalyzed kinetic resolution of the corresponding racemic ethyl beta-amino esters, based on enantioselective hydrolysis of their ester function. Chiral RP-HPLC analysis was performed for monitoring the enzymatic reactions and for determining the enantiopurity of final products. The absolute configurations were established by 1H NMR analysis of Mosher diastereomeric derivatives. The obtained (R)- and (S)-beta-amino acids were further N-protected by treatment with Fmoc N-hydroxysuccinimide ester in the presence of sodium carbonate, in dioxane.

Results. The enantioselective enzymatic hydrolysis of thiazole beta-amino esters occurred with S selectivity, affording the corresponding (S)-beta-amino acids (ee>95%) and (R)-beta-amino esters (ee>98%). Thiazole (R)-beta-amino acids were obtained with ee>98% by acid hydrolysis of (R)-beta-amino esters. Further N-protection of optically active beta-amino acids afforded the corresponding (R)- and (S)-N-Fmoc-beta-amino acids with 54-100% yields and their structure was confirmed by 1H NMR, 13C NMR and LC-MS analysis.

Conclusion. A stereoselective chemoenzymatic procedure was implemented for the preparative scale production of new (R)- and (S)- thiazole N-Fmoc-beta-amino acids of high enantiopurity, suitable for solid phase peptide synthesis.

Synthesis, physicochemical characterization and cytotoxicity of some new thiazole flavones and hydroxyflavones

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2) Departament of Toxicology, Faculty of Pharmacy, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania **Introduction.** Flavones possess a wide range of biological activities: anticancer, antioxidant, antimicrobial etc. and they have generated interest among medicinal chemists. Continuing our research on the study of synthetic analogues of natural compounds, we have proposed the synthesis, spectral characterization, lipophilicity investigation and evaluation of the cytotoxicity of several new thiazole flavonoids.

Material and methods. Thiazole flavones and hydroxyflavones were synthesized by the oxidative cyclization of some previously synthesized thiazole ortho-hydroxychalcones in different reaction conditions. The structural analysis was performed by spectral methods: 1H NMR, 13C NMR, MS and IR. The lipophilicity of the compunds was investigated by

Corresponding Author: Fana-Maria Coman e-mail: Coman.Fana@umfcluj.ro RP-TLC, RP-HPLC and computational methods. The cytotoxicity was determined on the MDA-kb2 breast cancer cell line.

Results. A new series of thiazole flavones and hydroxyflavones was synthesized by the oxidative cyclization of the corresponding thiazole ortho-hydroxychalcones with good yields. The spectral analysis confirmed the structures of the newly synthesized compounds. A statistically significant correlation has been noticed between the chromatographic and some of the computed lipophilicity parameters. Using the PCA analysis the investigated flavones and hydroxyflavones were classified according to their lipophilicity and structural similarities. Some of the compounds showed moderate cytotoxicity on the MDA-kb2 breast cancer cell line.

Conclusion. New thiazole flavones and hydroxyflavones were synthesized from the corresponding thiazole ortho-hydroxychalcones. The structures of the synthesized compounds were confirmed on the basis of spectral analysis. A good correlation was revealed between the experimental lipophilicity parameters and several computed log P values. Some of the synthesized compounds showed cytotoxic activity on the tested tumor cell line.

Multi-walled carbon nanotubes-based sensor for the electrochemical detection of cocaine

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Corresponding Author: Florina Maria Truță e-mail: Florina.Truta@umfcluj.ro **Introduction.** In the last years, illicit drug consumption has increased tremendously and it seriously affects the public health worldwide. Cocaine is an alkaloid, and is the second most used illicit drug in Europe. This drug is highly addictive because it stimulates the central nervous system and causes euphoria and dependence, and at the same time is very harmful for people's health.

Material and methods. For the detection of cocaine numerous techniques were applied. Among them, the most popular are GC–MS, HPLC, LC-MS, etc. These techniques have some disadvantages like high cost, complicated operations, and lengthy analysis time. However, electrochemical methods offer a fast, portable, low-cost, and accurate alternative.

Nanomaterials have gained much attention over the last decade in the development of sensors for a myriad of applications. The applicability of these nanomaterials, functionalized or not, significantly increases and is therefore highly suitable for use in the detection of drugs of abuse.

Results. In this study the influence of several platforms was investigated such as graphite and graphite modified with nanomaterials (graphene and multi-walled carbon nanotubes), for the detection of cocaine, and the adulterants. Two electrolytic media with different pH values were used, and real samples were successfully analyzed in order to have enough insights for the detection of cocaine in real scenarios. A calibration curve was also performed and the quantitative analysis of cocaine from different type of real samples such as: waste water, tap water, and seized samples were successfully performed.

Conclusion. The electrochemical detection of cocaine using the multi-walled carbon nanotubes-based platform was successfully employed for the analysis of street and water samples, showing the applicability of this method in the field of illicit drug detection.

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Voltametric profiling of MDMA using nanomaterial-based platforms

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Corresponding Author: Ana-Maria Drăgan e-mail: ana.dragan@umfcluj.ro **Introduction.** MDMA (3,4-methylenedioxymethamphetamine, ecstasy) is one of the synthetic psychostimulant illicit drugs, whose increased spread and abuse inflict various consequences on society, from increased violence and criminality to health and environmental implications. Globally, around 20 million people consumed MDMA in 2019, according to the latest World Drug Report. Hence, an analytical tool for the fast and accurate detection of MDMA is of great importance. In this regard, the present study explored the potential of voltametric profiling of MDMA for its fast detection using nanomaterial-based platforms.

Material and methods. Firstly, two pH values (7 and 12) and several platforms (working electrode of graphite and graphite modified with nanomaterials: gold and silver nanoparticles, graphene and multi-walled carbon nanotubes) were tested using square wave voltammetry. Then, the influence of common adulterants/cutting agents on the voltametric profile of MDMA was studied in optimal conditions. Subsequently, the method was evaluated through the analytical figures of merit (linear range, limit of detection and limit of quantification). Finally, the voltametric detection of MDMA was performed in seized samples and spiked water samples.

Results. The graphene platform and pH 12 proved to be better for the voltametric detection of MDMA, with a limit of detection of 15 μ M. In these conditions, MDMA was successfully detected in combination with the tested adulterants/cutting agents and its presence was confirmed in the analyzed street and water samples.

Conclusion. The voltametric profiling of MDMA using the graphene platform was successfully employed for the analysis of street and water samples, showing the applicability of this method in the field of illicit drug detection.

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Aptamer-modified pronanosomes for targeted drug delivery

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Corresponding Author: Alexandra Pusta e-mail: alexandrapusta@gmail.com **Introduction.** Cancer is a major public health issue in today's society, accounting for nearly 10 million deaths in 2020 alone. Various treatment strategies for cancer exist, with chemotherapy being one of the most widely used. Chemotherapy presents certain well-known disadvantages, such as high toxicity to non-malignant tissues. In this context, the specificity of chemotherapeutic drugs to cancer cells needs to be increased by different strategies. This work presents the preliminary results for the development of a specific platform for chemotherapy delivery to tumor cells.

Material and methods. Commercial carboxyl-modified pronanosomes were activated using NHS/EDC chemistry and incubated with the amino-terminated AS1411

aptamer to obtain aptamer-modified pronanosomes. Different parameters were varied in order to choose the optimal conditions. The formation of aptamer-modified pronanosomes was investigated by UV-Vis spectrophotometry.

Results. A change in the absorption spectra of the free aptamer solution and the aptamer solution after incubation with activated pronanosomes was noticed. This change was attributed to the formation of the aptamer-pronanosome complex and the subsequent reduction of the concentration of free aptamer in the solution. The optimized parameters were chosen as follows: NHS concentration 0.13 mM, EDC concentration 0.26 mM, aptamer concentration 2 μ M, pronanosome concentration 0.1 mg/mL activation time: 1 h, aptamer incubation time 1 h, incubation temperature 25°C.

Conclusion. The preliminary results obtained in this work represent a promising solution for the future development of aptamer-modified pronanosomes for targeted drug delivery. Further studies regarding drug loading and release, as well as the implementation of complementary techniques for the confirmation of aptamer-pronanosome complex formation, need to be employed.

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Innovative electrochemical platform for the detection of bacteria

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Corresponding Author: Alexandra Canciu e-mail: ALEXANDRA.CANCIU@ elearn.umfcluj.ro **Introduction.** Pathogenic strains of Escherichia coli (E. coli) are a major threat to human health causing foodborne and waterborne diseases. Standard detection techniques are often inconvenient for testing in various on-field settings when a quick response is needed; hence, the necessity for rapid, reliable and portable detection tools of this contaminant microorganism.

Electrochemical sensors have gained considerable attention lately due to their sensitivity, versatility, low cost and miniaturization capability. One such approach is the detection of bacteria through their specific virulence markers. Enterobactin is the principal siderophore secreted by E. coli, important in bacterial growth, replication and infection process.

The aim of this study was to develop an innovative electrochemical platform for the detection of enterobactin as a marker for the presence of E. coli.

Material and methods. Commercially available graphite screen-printed electrodes were modified with a hybrid layer consisting of agar hydrogel and Au/Ag nanoparticles for the platform elaboration. Standard solutions and lysogeny broth (Miller) containing enterobactin were tested by differential pulse voltammetry.

Results. The electrochemical fingerprint of enterobactin was achieved. The developed platform was successfully employed for the quantification of the bacterial marker.

Conclusion. Given the short assay time, this method can be further developed for fast and accurate detection of E. coli in industrial and environmental applications.

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Gold-chip biosensors for the assessment of food contaminants

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Corresponding Author: Oana Hosu e-mail: hosu.oana@umfcluj.ro **Introduction.** Prolonged exposure to contaminated food often leads to chronic diseases as cancer, kidney or liver failure, immunosuppression, or genotoxicity. Unfortunately, the causal connection is hardly proven, making it difficult to measure the burden of foodborne diseases and their actual influence on lives and economies. Food contaminants represent possible threats for both humans and animals being identified as severe food safety hazards; therefore, their careful management in food industries and food control agencies is essential to ensure controlled food safety management systems and safe health strategies. Thus, the development of easy-to-use, fast, and accurate analytical methods for the determination of food contaminants is of high priority to prevent foodborne illnesses.

Material and methods. The sensing strategy to produce DNA microarrays was performed using a 32-electrode chip comprising $70 \times 70 \ \mu m^2$ gold electrodes at Dotria potentiostat and synthetic DNA strands with sequences specific to Aflatoxin B1 (AFB1).

Results. The affinity reaction between the DNA strands and AFB1 causes conformational and structural changes in the recognition layer, which can be assessed by electrochemical approaches. Each step of electrode modification was characterized by cyclic voltammetry in Ferro-Ferricyanide redox probe. Applications on food samples are foreseen.

Conclusion. The development of electrochemical DNA-miniaturized sensors at array gold-chip to be used as a tool with multiplexing capabilities was demonstrated. The current progress of the electrochemical determination of AFB1 using a biomimetic approach using oligonucleotide-modified microarray gold chips will be presented.

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Highly sensitive electrochemical detection of endosulfan on polybithiophene modified gold electrodes

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 National Institute for Research and Development of Isotopic and Molecular Technologies, Cluj-Napoca, Romania **Introduction.** Great efforts are made to phase out endosulfan (ES), a highly lipophilic hazardous chemical associated with a large panel of common chronic diseases. Sensitive, low-cost and fast detection methods are required. Electrochemical (EC) detection of ES has not been yet reported at environmentally relevant concentrations. An efficient preconcentration and detection of ES at the electrode's interface can be achieved using a thin layer of potentiodynamically-deposited polybithiophene, fine-tuned using response surface modeling.

Material and methods. Multiple variables were considered (electrolyte, bithiophene conc., scanning direction and rate, etc.) for screening and optimization of

Annual Meeting Iuliu Hațieganu University of Medicine and Pharmacy 2021

Corresponding Author: Rebeca (Magda) Moldovan e-mail: rebeca.magda@umfcluj.ro electropolymerization by cyclic voltammetry. The resulted sensor was washed 4 minutes in methanol and PBS buffer. ES was preconcentrated from 0.1-10 nM solutions (50 mM phosphate buffer) under magnetic stirring. Differential pulse voltammetry (DPV) and electrochemical impedance spectroscopy (EIS) were employed in the presence of 2 mM ferrocenedimethanol to assess ES surface enrichment. Tapping mode atomic force microscopy (AFM) was used to investigate the surface morphology.

Results. In optimized conditions, a continuous hydrophobic film resulted, with an average thickness of 10 nm. A good correlation was observed between the electrochemical response (DPV, EIS) and ES concentration over the range of 0.1 - 10 nM with an optimum preconcentration time of 10 minutes. A limit of detection was estimated at 0.08 nM. The analyte could be washed from the polymer after detection and the sensor reused for over 20 times.

Conclusion. Response surface modeling can be successfully employed to finetune experimental parameters. ES could be preconcentrated from aqueous samples in a hydrophobic polymeric film and sensitively detected EC to 0.1 nM concentrations.

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High frequency of low serum vitamin B12 levels in males: a cross sectional study

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Corresponding Author: Elena Cristina Crăciun e-mail: ecgagyi@yahoo.com **Introduction.** This study aimed to explore the vitamin B12 status in a sample of male population from the city of Cluj-Napoca and the surrounding rural localities.

Material and methods. The study group included 77 males, aged between 23 and 93 years, divided into three groups: (group A - 33 individuals with omnivorous diet, group B - 20 individuals with ovo-lacto vegetarian diet and group C - 24 individuals with type 2 diabetes mellitus treated with metformin). A complete blood count was performed, and the vitamin B12 serum concentration was measured. Vitamin B12 deficiency was defined at serum levels under 200 pg/mL, a concentration between 200 and 350 pg/mL was defined as borderline level and anemia was defined as hemoglobin <13 g/dl.

Results. The frequencies of the deficiency and the suboptimal status of vitamin B12 were: 12.12% and 42.42% in group A, 35% and 55% in group B, and 25% and 58% in group C. In group B, 70% of subjects with low serum vitamin B12 levels were under 50 years old. The anemia observed in 6% of group A subjects and in 16.66% of group C subjects, was associated with deficiency or suboptimal vitamin B12 status. Mean corpuscular volume above 100 fL was found in 3% of group A subjects and in 8.33% of group C subjects.

Conclusion. The high frequency of low vitamin B12 levels observed in this study, in all investigated groups, highlights the need to develop a strategy for periodically assessing the status of vitamin B12 in at-risk subjects as well as those over 50 years of age.

Simple and fast direct detection of gemcitabine from pharmaceutical formulations

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Corresponding Author: Iulia Rus e-mail: iiuliarus@gmail.com **Introduction.** Gemcitabine is an antitumor drug which acts as a nucleoside analogue, being incorporated in DNA instead of cytidine by DNA-polymerases and stopping thus DNA synthesis. It is a widely used antitumor drug, very effective in pancreatic, ovarian, breast and non-small cell lung cancer. The purpose of this study was to develop a simple and fast electrochemical strategy for the detection of gemcitabine from new pharmaceutical formulations.

Material and methods. An electrochemical characterization of gemcitabine was performed, regarding the influence of the electrode material, electrolyte solution, pH and scan rate on the detection of the target molecule. Based on the results obtained, a DPV electrochemical procedure was optimized, calibration curves were built and tests on real samples were performed.

Results. Different electrode materials were tested, like graphite, gold and platinum based screen printed electrode, glassy carbon electrode and boron doped diamond electrode (BDDE). An analytical signal was observed for the oxidation of gemcitabine only on BDDE, at a potential around 2 V. The results showed that the intensity of the analytical signal of gemcitabine is the highest at pH 5 and at higher values of scan rate. However, further tests were done at pH 7.4, simulating the media of the real samples. The tests performed on real samples of gemcitabine solution for infusion showed good recovery and a good correlation was observed between the results obtained using UV-Vis, HPLC-UV and the optimized electrochemical techniques.

Conclusion. A new successful electrochemical method for the detection of gemcitabine from pharmaceutical samples was developed using BDDE.

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Molecularly imprinted polymer for the electrochemical detection of Pseudomonas aeruginosa

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Corresponding Author: Denisa-Elena Căpățînă e-mail: DENISA.ELEN.CAPATINA@ elearn.umfcluj.ro **Introduction.** Quorum sensing (QS) is a form of cell-to-cell communication between bacteria, important in determining virulence and in biofilm formation, which poses a great threat to human health due to the films' resistance to antimicrobial agents. Because of its intrinsic resistance to numerous antibiotics, P. aeruginosa is a very dangerous pathogen responsible for many nosocomial infections. A specific molecule responsible for QS in P. aeruginosa is N-3-oxo-Dodecanoyl-Homoserine Lactone (3-O-12-HSL). Analyzing this molecule would facilitate the rapid identification of nosocomial infections and their appropriate antibiotherapy. Due to their advantages, molecularly imprinted polymers (MIPs) have played an increasingly important role in the development of biosensors and have been very useful in the dosage of a wide variety of molecules. In this study, we developed a sensitive and specific electrochemical sensor based on MIP for the



detection of QS molecules in P. aeruginosa.

Material and methods. The MIPs and NIPs were obtained by electropolymerization using cyclic voltammetry (CV). Several monomers and several electrode surfaces were tested. The modified electrodes were characterized by CV in [Fe(CN)6]3-/4- solution. The composition of the polymerization mixture, the electropolymerization method, the template extraction and the rebinding process were also optimized.

Results. Based on initial results, methylene green was selected as the monomer for our study and glassy carbon electrode (GCE) was preferred for modification with MIP. The method showed good results for the detection of 3-O-12-HSL in standard solution.

Conclusion. A polyMG-based MIP for the detection of 3-O-12-HSL was developed on a GCE. Future studies will focus on optimization to increase the reproducibility of the method.

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Optimization of the extraction process, evaluation of the phytochemical profile and biological properties in five Epilobium species

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Corresponding Author: Ana-Maria Vlase e-mail: anamaria.gheldiu@yahoo.com **Objectives.** To determine the optimal extraction conditions of polyphenols from five species of Epilobium and to evaluate the biological properties of optimized extracts.

Material and methods. Five native species of the genus Epilobium were harvested from Romanian flora. For enhanced recovery of polyphenols, a D-optimal experimental plan was developed using Modde software. Subsequently, extracts were made from different parts of the plants and in optimal working conditions, and their biological properties were evaluated. Multivariate data analysis was performed to highlight possible interspecies differences leading to variability in phytochemical composition and biological activity. For optimized extracts, antifungal and antimicrobial activity was evaluated on yeast strain and various Gram-positive and Gram-negative bacteria. The anticancer potential of optimized extracts was investigated using a prostate carcinoma cell line and a normal cell line.

Results. The optimal working conditions were turboextraction for 8 min, in 30% ethanol solvent. High concentration of caftaric acid was determined in E. palustre herba extract, whereas chlorogenic acid and quercitrin were found in high concentrations in E. angustifolium herba extract. The multivariate analysis revealed as a source of variability of the results the plant part used for extraction and the species. The extracts proved moderate efficacy against Gram-positive bacteria, with increased activity against Bacillus cereus. The extracts showed a concentration-dependent cytotoxic effect on both cellular phenotypes. E. parviflorum herba extract had a more selective cytotoxic effect on cancer cells.

Conclusion. The complex phytochemical composition of indigenous species of Epilobium provides the antioxidant, antimicrobial and antifungal action of extracts, as well as a selective cytotoxic potential on prostate cancer cells.

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PHARMACEUTICAL SPECIALTIES

Evaluation of the oxidative stress and DNA lesions reduction by a polyphenolic enriched extract of Thymus marschallianus Willd. in comparison with rosmarinic acid on endothelial vascular cells exposed to hyperglycemia

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Corresponding Author: Irina Ielciu e-mail: irina.ielciu@umfcluj.ro **Introduction.** The present study aims to compare a polyphenolic enriched extract obtained from the Thymus marschallianus Willd. (Lamiaceae) species and one of its major chemical components, rosmarinic acid, by evaluating their biological effects on human umbilical vein endothelial cells (HUVECs) exposed to normoglycemic and hyperglycemic conditions.

Material and methods. The tested extract was obtained by solid phase extraction (SPE) and its chemical composition was analyzed by a HPLC-DAD method. Effects on hyperglycemia were evaluated by the quantification of oxidative stress and the expressions NF- κ B, pNF- κ B, HIF-1 α , γ -H2AX.

Results. HPLC-DAD analysis showed important amounts of rosmarinic acid, luteolin, kaempferol and apigenin in the extract. Exposure to hyperglycemia induced oxidative stress and activation of NF-kB, increased the expression of HIF-1 α and produced DNA lesions. The polyphenolic enriched extract proved significant reduction of oxidative stress and γ -H2AX formation and improved the expression of HIF-1 α suggesting a protective role on endothelial cells exposed to hyperglycemia. Moreover, the extract reduced the total NF-kB expression and increased its activation in hyperglycemic conditions. On the other side, rosmarinic acid had similar effects on oxidative stress and γ -H2AX formation, on the total NF-kB expression and on its activation, but diminished the expression of HIF-1 α , suggesting partial protection on endothelial cells exposed to hyperglycemia.

Conclusion. The experimental findings demonstrated antioxidant, antigenotoxic and angiogenic properties of the tested extract and of rosmarinic acid, bringing evidence for its use as adjuvant in hyperglicemia related conditions.

Acknowledgement. This work was supported by a grant of the Romanian Ministry of Education and Research, CNCS - UEFISCDI, project number PN-III-P1-1.1-PD-2019-0967, within PNCDI III.

Ethics and business in community pharmacies – a framework for ethical dialogue

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Department of Pharmaceutical Legislation and Management, Faculty of Pharmacy, Iuliu Hațieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania **Introduction.** Community pharmacy is, at the same time, a health institution and a business. Often pharmacists find themselves in situations of conflict between professional ethics and business interests. The objective of this paper is to suggest a framework for ethical dialogue to manage those situations.



Annual Meeting Iuliu Hațieganu University of Medicine and Pharmacy 2021

Corresponding Author: Alexandra Toma e-mail: alexandra_pharm@yahoo. com **Material and methods.** The most common situations of this type were decided based on literature analysis and following an iterative process of discussion and reflection on pharmacy practice. Those situations were analyzed using the model for ethical problem solving of Veatch et all and methods of legal interpretation of principles from the Pharmacist's Deontological Code.

Results. The most common situations of conflict between professional ethics and business interests are linked to establishing a sales target by employers, devoting time for patient counselling, dispensing associated products, and collecting expired medicines from population. To solve those situations, the professional organization should intervene by providing an institutional framework for ethical dialogue, including the steps of assessing the conflict situations and their consequences on the quality of pharmacists' activity, identifying and analyzing the ethical problems, searching for morally acceptable solutions for all parties involved, and collaborating for their implementation.

Conclusion. Making the right decisions in situations of conflict between professional ethics and business interests requires the collaboration of all those involved, based on mutual professional respect. The development of ethics training and the collaboration of employers with the professional organization are essential to preserving the professional character of pharmacists' activity in the community pharmacy.

Development of lipobeads loaded with gemcitabine: a screening study

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Corresponding Author: Cristina-Ioana Barbălată e-mail: Barbalata.Cristina@umfcluj.ro **Introduction.** Gemcitabine (GEM) is a chemotherapeutic drug used to treat cancer, particularly pancreatic cancer. Due to its hydrophilic character, GEM represents a challenge as concerns its encapsulation into nanosystems. Through this study, we aimed to investigate the development process of lipobeads (LB) encapsulated with GEM (LB-GEM) using the Quality by Design approach.

Material and methods. Hydrogel nanoparticles (NG) encapsulated with GEM (NG-GEM) were prepared via precipitation/dispersion polymerization technique. LB-GEM were prepared via the film hydration method, where the dispersion of NG-GEM served as hydration medium for the lipid film.

Results. Preliminary results evidenced that the size of the NG varied between 85 and 160 nm, while the polydispersity index (PdI) between 0.04 and 0.28. These variations were caused by the concentration of the crosslinker and the surfactant, by the rotation speed used in the polymerization process and by the duration of the initiation phase of the polymerization process. On the other hand, the use of a lower rotation speed (100 rpm vs. 400 rpm) during the polymerization process was observed to reduce the entrapment of GEM into NG, given that the EE% of LB-GEM decreased from 43% to 30%. Considering these results, four material attributes, i.e. the concentration of the monomer, crosslinker, surfactant and GEM, and two process parameters, i.e. the rotation speed during the polymerization process and the duration of the initiation phase of the polymerization process were investigated in a design of experiments as a means to interlink the independent variables with the critical quality attributes (size, PdI, zeta potential, EE%, entrapped drug concentration) of NG-GEM and of LB-GEM.

Conclusion. GEM can be successfully incorporated into LB with a high EE%, while the size and the PdI value of NG-GEM can be easily controlled during the preparation process by optimizing the concentration of the excipients and the process parameters.

Silanization of ferromagnetic iron oxide magnetic nanoparticles significantly enhances their hyperthermia performances for efficiently inducing cancer cells death *in vitro*

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Corresponding Author: Ionel Fizeşan e-mail: ionel.fizesan@umfcluj.ro **Introduction.** Increasing the biocompatibility, cellular uptake, and magnetic heating performance of ferromagnetic iron-oxide magnetic nanoparticles (F-MNPs) is required to efficiently induce cellular death of cancer cells by magnetic hyperthermia (MH). The aim of this work was to obtain F-MNPs coated with a homogeneous silica shell and to evaluate their properties for MH therapy.

Material and methods. F-MNPs were coated with silica layers of different thicknesses via a reverse microemulsion method, and their morphological, structural, and magnetic properties were evaluated. The biocompatibility of the most promising silica coated F-MNPs was investigated on two cancerous cell types and on normal foreskin fibroblasts using two complementary viability assays. The cellular uptake and the potential of the silanized F-MNPs to induce selective cellular death on cancerous cells after MH treatment was further explored.

Results. Biocompatibility assays, following a 24 h exposure period, revealed a marginal toxicity that decreased the viability by no more than 20% at a concentration of 125 μ g/cm2. A higher cytotoxicity was observed on the cancerous cells. The silica-coated F-MNPs were internalized in a dose-dependent manner in all three types of cells. Starting from the lowest exposure dose of 7.81 μ g/cm2, at a field intensity of 60 kA/m, MH treatment induced cellular death in cancerous cells, while preserving the viability in normal cells. Due to increased cellular internalization of these particles in cancerous cells, MH treatment resulted in a more pronounced cancerous cell death at all concentration and intensity fields tested.

Conclusion. Silica-coated F-MNPs are promising candidates for in vitro destruction of cancer cell through MH therapy.

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Studying the effect of Zn-substitution on the morphological, magnetic, cytotoxic and *in vitro* hyperthermia properties of polyhedral magnetite particles

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1) Department of Toxicology, Faculty of Pharmacy, Iuliu Hațieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania **Introduction.** Modification of the chemical composition of Fe3O4 magnetic nanoparticles (MNPs) by introducing dopants such as zinc, manganese and nickel represents an efficient strategy to improve the magnetic and heat generation properties of

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Corresponding Author: Ionel Fizeşan e-mail: ionel.fizesan@umfcluj.ro MNPs. In the present work, a modified polyol synthesis was used to elaborate Zn ferrite (ZnF) MNPs that were further characterized as candidates for magnetic hyperthermia treatment (MHT).

Material and methods. By modifying the Zn/Fe molar ratio in the synthesis conditions, a series of ZnF nanoparticles of different sizes, shapes, and zinc contents have been obtained. The biocompatibility of the two most promising ZnF candidates was investigated using two complementary viability assays. The cellular uptake of the ZnF MNPs was qualitatively and quantitatively analyzed. The MHT potency in selectively inducing cellular death in cancerous cells was further evaluated.

Results. Among the six samples, ZnF01 and ZnF02, exhibited the best magnetic and heat-inducing performance and were selected for the in vitro studies. No statistical differences were observed between the toxicities elicited by the two types of ZnF MNPs, with cancerous cells being more susceptible to the cytotoxic potential. ZnF01 and ZnF02 were internalized in a dose-dependent manner in both types of cells, a higher internalization being observed for ZnF02 and in the case of cancerous cells. As a result of the higher internalization of ZnF MNPs in cancerous cells, higher temperatures and higher cellular death were recorded in the MHT.

Conclusion. Our results indicate that ZnF MNPs with increased heating capabilities are promising candidates for MHT.

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Design Space based formulation development: in depth understanding of granule compression behavior under variable raw materials and processing conditions

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Corresponding Author: Tibor Casian e-mail: casian.tibor@umfcluj.ro **Introduction.** Tablet manufacturing involves the processing of raw materials through several unit operations, thus the mitigation of input induced variability should also consider the downstream processability of intermediate products. The objective of the present work was to study the effect of variable raw materials and processing conditions on the compression properties of granules containing two APIs and a diluent.

Material and methods. Granule preparation was done using a lab scale fluidized bed granulator (Aeromatic Strea 1, GEA, Switzerland), by processing 200 g sized batches according to the D-optimal design (39 runs). Dynamic compaction analysis was performed using a single punch Gamlen GTP, series D tablet Press (Gamlen Tableting Ltd. Biocity Nottingham, UK). 100 mg sized compacts were prepared from each formulation, by using 6 mm punches at a speed of 10 mm/min at five different loads (100 kg–200 kg–300 kg–400 kg–500 kg).

Results. In case of the first API, differences in tabletability were highlighted between suppliers, thus leading to a variable tablet tensile strength. The effect of changing the supplier of the second API, was efficiently controlled by adapting the pulverization rate and atomizing pressure during binder solution addition. By fitting mathematical models on the available compression data, the influence of diluent sorts on granule compactability and tabletability was identified. These differences resumed to the ease of compaction, tableting capacity and pressure sensitivity index.

Conclusion. Building the design space for different raw material combinations enabled the identification of the most robust formulations that tolerate larger variations in the way the binder solution is pulverized (pulverization rate/ atomizing pressure). Thus, quality variations will be minimized, ensuring a reproducible performance and consistent tableting properties.

Augmenting the antitumor activity of a phytotherapeutic preparation by optimizing its composition through *in vitro* testing

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Corresponding Author: Alina Uifălean e-mail: alina.uifalean@umfcluj.ro **Introduction.** Suitable combination of natural compounds can lead to superior anticancer efficacy. The present research aims to evaluate and optimize the composition of a phytotherapeutic preparation to potentiate its antitumor activity.

Material and methods. The hydroalcoholic extracts of the whole product (Taraxaci radix, Equiseti herba, Millefolii herba, Filipendulae ulmariae herba, Allii ursini folium, Menthae folium, Geranii robertiani herba, Salix cortex, Urticae herba) and the individual components were analyzed. For the phytochemical profile, the I-Class UPLC coupled with Waters Synapt G2-Si mass spectrometer was used. The cytotoxic activity was evaluated on tumor (SK-HEP-1) and normal (LX2) liver cells, as follow: cell viability by MTT, total protein, cell membranes integrity, DNA synthesis capacity, colony formation capacity, resistance to apoptosis-inducing factors.

Results. Based on the identified bioactive compounds, plant components were grouped into: T1 phenolic acids (chlorogenic acid, caffeic acid), T2 flavonoids (rutin, quercetin, luteolin), T3 kaempferol and derivates. GR50, GRmax, GRAOC and hGR parameters confirmed the superior cytotoxicity of the capsule extract and T1-T3 groups on tumor line. Purified extracts of T1 group led to suitable IC50 doses and an inhibitory effect on the colony formation on tumor lines, without affecting normal cells viability. The new optimized formula will contain phenolic acids (chlorogenic acid, caffeic acid) and flavonoids (rutin, quercetin, luteolin). Standardization in total polyphenols and flavonoids will be carried out.

Conclusion. The composition of a phytotherapeutic preparation was tested in vitro and optimized, contributing to the development of a finished product with superior antitumor activity on SK-HEP-1 cell line.

Acknowledgement. Project frame "Knowledge transfer in clinical applications of biogenomics in oncology and related fields (BIOGENONCO, ID P_40_318)", subsidiary contract no.28781/23.09.2020.

Anti-biofilm activity assessment of some 2-(4-pyridine)-thiazolylazoles: preliminary *in vitro* and *in silico* studies

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Corresponding Author: Cătălin Araniciu e-mail: araniciu.catalin@umfcluj.ro **Introduction.** The treatment of infectious diseases remains an important issue because of the rapid rise in microbial resistance to traditional antibiotics. One of the mechanisms by which bacteria and fungi gain resistance to antibiotics is biofilm formation. The development of anti-biofilm strategies is therefore of major interest and currently constitutes an important field of research. Considering our encouraging previously reported results concerning the anti-biofilm activity of some thiazolyl-azoles, we focused on the investigation of antimicrobial and anti-biofilm activity of some previously synthetized compounds incorporating the 2-(4-pyridine)-thiazole moiety, substituted with various heterocycles.

Material and methods. The influence of the obtained compounds on bacterial and fungal cells growth was evaluated by an adapted disk diffusion method and two-fold microdilutions method for establishing the minimal inhibitory concentration (MIC). The anti-biofilm activity, of the synthesized compounds, was assessed by performing the microtiter method to obtain the minimum biofilm eradicating concentration (MBEC). Molecular docking studies were performed to investigate the interaction mode between the compounds and microbial macromolecular targets like MrkD and MrkH (key elements in biofilm formation by K. pneumoniae). Also, cytotoxicity studies were performed for the most active compounds.

Results. The antimicrobial activity was moderate, but some compounds presented a good anti-biofilm activity against K. pneumoniae. The molecular docking study results suggested that inhibition of MrkD and MrkH could be a possible mechanism of action for our compounds. The cytotoxicity data showed lack of toxicity.

Conclusion. The 2-(4-pyridine)-thiazole derivatives constitute a good starting point for the development of new anti-infective agents.

Compatibility studies for the development of film-coated tablets with sitagliptin

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 National Institute for Research and Development of Isotopic and Molecular Technologies, Cluj-Napoca, Romania **Introduction.** Type 2 diabetes is one of the diseases with the greatest impact on people in modern society. Sitagliptin is an oral antihyperglycemic agent that belongs to the class of dipeptidyl peptidase 4 (DPP-4) inhibitors. The present study is part of a complex one that aims to obtain sitagliptin film-coated tablets, for the treatment of this condition. The choice of the active component was made based on its therapeutic indication. A pharmaceutical formulation is considered appropriate when no interactions medicament-excipient appears. The objective of this study was to assess the compatibility between the Active Pharmaceutical Ingredient (API) and excipients in the preformulation stage of film-

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Corresponding Author: Lucia Maria Rus e-mail: lucia.rus@umfcluj.ro coated tablets with sitagliptin, by using Differential Scanning Calorimetry (DSC), X-Ray Powder Diffraction (XRPD) and Fourier Transformed Infrared Spectroscopy (FTIR) methods.

Material and methods. Sitagliptin was used as active pharmaceutical ingredient and sodium croscarmellose, microcrystalline cellulose, calcium dihydrogen phosphate, magnesium stearate and sodium stearyl fumarate as excipients. The individual components as well as their 1:1 (m/m) physical mixtures were analyzed using DSC, XRPD and FTIR methods in order to determine the compatibility of the API with excipients, respectively.

Results. Following DSC, XRPD and FTIR results obtained in the preformulation stage, sitagliptin was found to be compatible with selected excipients.

Conclusion. In conclusion, based on the results obtained in the preformulation stage the active pharmaceutical ingredient, sitagliptin, as well as the chosen excipients can be further used in the film-coated tablets formulation stage.

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Salinomycin and gemcitabine-loaded liposomes: development and *in vitro* characterization

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Corresponding Author: Lucia Ruxandra Tefas e-mail: tefas.lucia@umfcluj.ro **Introduction.** The entrapment of anticancer agents in liposomes for tumor targeting improves drug pharmacokinetics, toxicity and efficacy. Gemcitabine (GEM) is an ideal candidate for entrapment in liposomes because of the short half-life and side effects. However, its increased hydrophilicity poses difficulties in achieving high entrapment. Salinomycin (SAL), a lipophilic polyether ionophore antibiotic, has reduced aqueous solubility and bioavailability which makes it a suitable candidate for liposomal encapsulation. Also, SAL has demonstrated specific anti-cancer stem cell (CSC) effects in different types of cancer. The simultaneous eradication of both CSCs and bulk cancer cells could allow complete recovery from cancer and prevent relapse. Here, we developed liposomes encapsulating SAL and GEM for colorectal cancer (CRC) therapy.

Material and methods. The liposomes (LCL) loaded with GEM and SAL were prepared by the film hydration method. Passive and remote loading methods were evaluated for GEM entrapment in LCL. Design of Experiments (DoE) was used to evaluate the influence of 3 formulation factors (phospholipid and SAL concentrations, phospholipid:cholesterol molar ratio) on LCL attributes.

Results. The passive loading method proved convenient and led to good encapsulation of GEM. LCL-GEM-SAL showed adequate characteristics in terms of size (<200 nm), homogeneity (PDI<0.10), Zeta potential (<-30 mV) and drug encapsulation (2-16% GEM and 6-55% SAL). The DoE showed the relation between the formulation factors and LCL attributes.

Conclusion. We have demonstrated the successful application of DoE in developing liposomes as efficient drug delivery systems for GEM and SAL. Furthermore, the GEM and SAL co-loaded liposomes might have potential application in CRC therapy.

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Liposomes for miRNA delivery: first steps of pharmaceutical development through the QbD approach

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Corresponding Author: Ioana Toma e-mail: ioana.toma@elearn.umfcluj.ro **Introduction.** Gene therapy represents the transfer of genetic material into a specific cell. The main challenge for gene delivery into the target cell is choosing the appropriate vector. MicroRNAs (miRNAs) play an important role in the regulation of gene expression and modulation of malignant cell transformation. Nanoparticles improve miRNA in vivo delivery and their tissue distribution, leading to an enhanced therapeutic outcome and limited adverse effects. Lung cancer (LC) is the second most frequent type of cancer with an increased death rate because of poor prognosis and late diagnosis being often related to abnormalities in miRNAs expression. The aim of this study was the development of liposomes for miRNA-155-inh delivery.

Material and methods. The liposomes were obtained using the thin lipid film hydration method. A screening study was performed using the Design of Experiments (DoE) methodology employed to study the impact of formulation factors, the concentration of phospholipids and cholesterol on the responses.

Results. The results showed a proper polydispersity index (<0.2), size around 100 nm, and positive zeta potential, except for the formulations with a higher concentration of structural lipid. The cellular uptake of the liposomes was evaluated in 3 LC cell lines using an inverted fluorescence microscope. It is noteworthy that 5 out of 9 formulations crossed the cell membrane. To assess cell viability, an MTT assay was performed on the A549 LC cell line for the formulations that entered the cell. After the treatment period with increasing sample volumes, a microscopy evaluation was performed. The MTT assay proved a zeta potential-dependent and phospholipids concentration-dependent cell viability.

Conclusion. Finally, our research suggests that liposomes for miRNA delivery could be a feasible candidate for cancer treatment.

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Investigating the availability of essential pediatric medicines on the Romanian pharmaceutical market

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Introduction. Every two years, the World Health Organization (WHO) publishes The Model List of Essential Medicines for Children (MLEMC). As the regulatory agencies have recently emphasized the need for novel adapted formulations for paediatric use, this study aims to investigate the pediatric products authorized in Romania and their availability in community pharmacies.

Material and methods. The Romanian Index of Medicinal Products (RIMP, downloaded at 31.03.2021) for human use was compared to the MLEMC 2019. To

Corresponding Author: Sonia Iurian e-mail: iuriansonia@yahoo.com investigate the presence of pediatric medicines in community pharmacies, a survey was sent throughout the Romanian College of Pharmacists. Six priority conditions and their representatives were included into the survey and the availability of adult and/or pediatric dosage forms was inquired. One survey was completed per pharmacy.

Results. Out of the total products found in the RIMP, solid pharmaceutical forms account for 74.91%, followed by liquids (21.98%), and semi-solids (3,10%). Most are intended for oral administration (68.57%), 22.47% for parenteral use, and 8.95% for external routes. The dosage forms with an appropriate design for children were identified and out of them, 305 (68.53%) were authorized for paediatrics (< 18 years of age), with a majority of liquids and solids for reconstitution. 29 classes of drugs are listed in MLEMC with a total of 346 active principles. 29.77% were not found in the RIMP. 160 surveys were collected up to date. From the selected classes, cardiovascular and diuretic drugs had the weakest representation of in pediatric dosage forms, which explains the requests for compounded formulations.

Conclusion. From the partial results it appears that the availability of paediatric drugs is low in community pharmacies, even within the authorized products.

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Study of the compliance of patients with lactose and/or gluten intolerance to diet

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Corresponding Author: Dana Stanciu e-mail: dana.stanciu7@yahoo.com **Introduction.** The metabolic disorders associated with gluten and lactose are more and more common, which is why they have attracted the attention of researchers and are intensively studied.

A very important aspect is the diet therapy, being often the only possible treatment. This can be overwhelming, particularly at the beginning, when the diagnosis seems a real burden and the patient need to accumulate a lot of information. Adherence to diet therapy and patient compliance are crucial, as they are the elements that lead to the improvement of the general condition. The aim of this study is to observe how patients relate to these conditions, their compliance with diet therapy and the impact on quality of life.

Material and methods. For this study, a questionnaire with 36 questions (in the form of single or open-ended statements) was used, divided into 5 sections: agreement to be included in the study, general data about the patient, information about the diet the patient follows, compliance and adherence to therapy, and the last part included an open response in the form of a testimonial.

The study took place between April and May 2021, and 516 subjects have been included.

Results. The results showed that 24% of respondents resorted to self-diagnosis without medical support. According to the present study, 55% of those who perceived the medical verdict as extremely difficult had to learn about it on their own.

Almost 70% of the subjects stated that they did not receive guidance in diet therapy, but if at diagnosis 76% of respondents considered difficult to follow a strict diet, the percentage has decreased to 17% in the present, indicating adaptation over time to new changes.

Regarding the compliance to diet therapy, the most adherent are the patients with celiac disease or lactose intolerance + celiac disease, almost 80% of them stating that they do not consume gluten / lactose voluntarily.

Conclusion. Patients with metabolic disorders associated with gluten and lactose face many difficulties after the diagnosis, such as: lack of adequate counseling regarding the new lifestyle to be adopted, low availability of food alternatives or their high cost and discrimination from others, issues that also affect the compliance to diet therapy.

DENTAL MEDICINE

Osteogenesis imperfecta and potential orthodontic treatments

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Corresponding Author: Ana Zastulka e-mail: anazastulka@yahoo.com **Introduction.** In recent years, studies have shown that osteogenesis imperfecta (OI) subjects present more dental problems than the average population. The most noteworthy dental manifestation of OI is Dentinogenesis Imperfecta (DI), but it is not visibly present in every subject affected by OI. It has been studied that if the OI patient is not affected by DI, then orthodontic treatment can generally be conducted routinely. Nevertheless, it is important to raise awareness of the possible underlying structural weaknesses in seemingly unaffected teeth.

Material and methods. Literature searches were performed with "dental" and "osteogenesis imperfecta," as in dental manifestations of OI. Relevant articles were screened, using the examination of the titles and abstracts. Ten literature reviews on this topic were studied, describing different clinical approaches regarding treatment goals and treatment plans.

Results. It is recommended to prioritize the vertical dimension, in lateral open bites, in order to restore posterior occlusal contacts, even if post-treatment, the dentition is to remain in crossbite. For the antero-posterior correction, light intermaxillary elastics may be utilized, as they are less stress-inducing on the dentition and bony structures than a protraction device. The choice of appliances that put heavy stress on teeth and bones, namely a face mask, is strongly discouraged. Clear aligners may prove to be the best alternative in appropriate cases.

Conclusions. Based on the findings of the studies analyzed, it is important that maxillary expansion in OI subjects be handled cautiously, especially in moderate to severe OI. The goal of orthodontic treatment in these subjects is not to correct minor aesthetic imperfections, but to restore a functional occlusion.

The benefits of corticotomy in orthodontic treatment

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Corresponding Author: Crina Ecaterina Pintilie e-mail: crinaecaterina.pintilie@gmail.com **Introduction.** Prolonged orthodontic treatments and the biological limits like gingival retractions, bone resorption, bone deficiency have inconvenienced patients and clinicians alike. To overcome these limitations, simplification of the traditional orthodontic movement many techniques have been implemented and perfected to enhance orthodontic tooth movement and shorten the treatment time, in the literature.

Material and methods. Many electronic databases were searched and abstracts were obtained. Defined inclusion criteria were then applied by an independent examiner for further evaluation of the originally articles. The criteria of selection included human or animal studies, which assessed some aspects of corticotomy assisted orthodontic treatment and/or the biological principles behind it. The quality of the studies was evaluated by the methodological score for clinical trials developed.

Results. Thirteen articles were studied initially, but only ten articles were finally selected for the study. The corticotomy assisted orthodontic treatment was

found to reduce the time required for orthodontic treatment to 1/3 - 1/4 of the time required for conventional orthodontics. Considering corticotomy just as a method to accelerate orthodontic movement would be limitative. The most interesting effect is the osteogenic potential. When combined with bone grafting, this technique may help to expand the basal bone and exhibits no or little risk of root resorption. A localized turnover of alveolar spongiosa and the absence of a hyalinized zone was the acceptable biological explanation of corticotomy.

Conclusions. It is believed that there will be a number of ways to speed up tooth movement without side effects while minimizing surgical invasiveness. Orthodontic microsurgery is associated with minimal morbidity and offers a promising means of improving and simplifying orthodontic therapy in adult patients.

Modifications of the periodontal regenerative potential in autoimmune diseases

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Corresponding Author: Alina Stanomir e-mail: alina.stanomir@yahoo.com **Introduction.** Periodontal mesenchymal stromal cells (MSCs) are important players participating in the complex regeneration and homeostasis network of the periodontium, but little is known about their properties in patients with autoimmune diseases. The aims of this study were to review the scientific literature related to the behavior of MSCs in autoimmune diseases and to evaluate the functionality of MSCs isolated from a systemic sclerosis (SSc) patient from gingiva (SScgMSCs) and apical granulation tissues (SScgtMSCs) in comparison with healthy cells (hMSCs).

Material and methods. PubMed and Scopus databases were searched for the proposed subject. The putative isolated MSCs grown in normal medium and in an experimental medium containing hyaluronic acid (HA) were subjected to two functional tests: Colony-Forming Unit-Fibroblast (CFU-F) assay and migration potential. Comparison between two (HA-treated vs. controls) and three (hMSCs, SScgMSCs, SScgtMSCs) groups was done with the Student t-test and the one-way ANOVA, respectively.

Results. MSCs from autoimmune diseases have impaired proliferation and migration capacity and possibly of the apoptotic rate. The frequency of CFU-F for SScgtMSCs was significantly lower than that of hMSCs (p=0.05) and SScgMSCs (p=0.004) in normal medium, and also markedly lower than that of SScgMSCs (p=0.09) in HA medium. Following HA exposure, both SScgMSCs and SScgtMSCs migrated significantly less (p=0.033 and p=0.005, respectively) than hMSCs.

Conclusions. Both the literature and our research revealed some dysfunctionalities of MSCs derived from SSc as compared to hMSCs.

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Study on the characteristics of cervical preparations for ceramic fused to metal crowns

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Corresponding Author: Mara Ștefania Șimon e-mail: simon.mara@yahoo.com **Introduction.** The study aims to evaluate tooth preparations of the cervical region made by fourth year students during the practical courses of Prosthetic Dentistry within the Faculty of Dentistry, Iuliu Hațieganu University of Medicine and Pharmacy Cluj-Napoca.

Material and methods. Eighty dental cast preparations of the cervical area made for ceramic fused to metal crowns were evaluated according to pre-established criteria found in specialized literature.

Results. Most teeth were insufficiently prepared, especially on the oral and distal surfaces. The location of the prepared tooth was mainly in the lateral areas of the dental arch (80.74%). The design of the finish line was predominantly Chamfer (62.6%), followed by tangential (31%) and Shoulder type (6%). The width of the cervical finish line at the molar level was frequently ≤ 0.5 mm and at the premolar level ≥ 0.5 mm.

Conclusions. The study shows a discrepancy between the theoretical indications and the practical results of the cervical preparations for the metal-ceramic crowns made during the practical courses internships by the students.

The correlation between level of stress and oral manifestations

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Corresponding Author: Mirela Ioana Fluerașu e-mail: mfluerasu@yahoo.com **Introduction.** The last period has generated a collective state of stress related to the epidemiological risk, but also in relation with changes in professional activities, interpersonal relationships and in the usual lifestyle. In the dental practice, the increased level of stress was reflected by the exacerbation of pre-existing pathologies or by the appearance of new lesions, following the general status of the individual, especially among young people.

The aim of the study was to track the statistically significant correlation between the perceived stress level and the alteration of the dento-maxillary apparatus functions, as well as the appearance of certain oral pathologies induced by stress among the young population.

Material and methods. Three hundred seventeen healthy young subjects, males and females, had to answered to a personalized questionnaire. The questionnaire had two parts: the first part analyzed the stress levels of the subject and the second part evaluated the oral and dental status. The data were analyzed using MedCalc Software version 17.4, with statistical significance at p<0.05.

Results. The obtained results indicate an average increase of 20% in the number of cases that presented oral manifestations due to stress, such as: aphthous and ulcerative stomatitis, episodes of awake and sleep bruxism, xerostomia and others, and a significant correlation with the stress score of each subject.

Conclusions. Once again it is proved that stress, this disease of the modern people, is reflected both in the psycho-social status and in the physio-pathological status of the subject, affecting the functions of the whole body, including also the dento-maxillary system.

Strategies for optimizing dental practice during the Covid-19 pandemic

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Corresponding Author: Andreea Kui e-mail: andreeakui@gmail.com **Introduction.** Dental health workers (dentists, assistants, and technicians) are particularly vulnerable to COVID-19 infection because of their close contact with patients and exposure to biological fluids and aerosol/droplet formation during dental procedures. The aim of this research was to evaluate the impact of the Covid-19 pandemic on the knowledge, practices, and expectations of dentists and dental professionals toward digital dentistry and teledentistry.

Material and methods. An online search of scientific literature written in English was performed on the databases Pubmed, Google Scholar, and Science Direct using keywords: COVID-19, digital dentistry, teledentistry, dental practice, infection control, dental care, and telemedicine. Included articles were published between March 2020 and October 2021.

Results. Out of the 62 articles selected, 12 articles were included in the research for further analysis. Traditional impression techniques, in addition to aerosol, saliva, and blood, have been shown to increase the risk of infection in dental treatment. Another issue is the transportation of impressions and fabricated appliances to and from the dental laboratory, as these could be a source of infection for the patient, technician, and doctor. In addition, overall self-reported teledentistry knowledge and practice have increased since the start of the Covid-19 pandemic.

Conclusions. The Covid-19 pandemic had a positive impact regarding teledentistry, as the dentists' interest, knowledge and expectations increased. Also, as the digital impression method speeds up and streamlines the impression process, ensures precision it cuts down on office time, and allows for data transfer without direct touch with potentially contaminated materials. In the context of the Covid-19 pandemic digital technology allows for more efficiency in the production of dental and prosthetic restorations while maintaining the highest level of infection control.

The effects of an experimental green tea based extract on the surface of bleached enamel

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Corresponding Author: Corina Voina-Ionescu e-mail: dr.corinaionescu@gmail.com **Introduction.** Teeth whitening represents one of the most requested noninvasive procedures in esthetic dentistry. Most bleaching substances through their mechanism of action have the effect of increasing the surface roughness of the enamel and therefore, favoring cariogenic bacteria adherence. The aim of this study was to develop an experimental green tea extract and an experimental green tea gel for enamel restoring treatment after bleaching.

Material and methods. The antibacterial effect of the experimental extract against specific cariogenic microorganisms, such as *Streptococcus mutans* (ATCC 25175) was tested. Enamel microstructure was investigated by SEM analysis, and surface details were revealed by AFM.

Results. The inhibition areas around the wells showed evident antimicrobial activity of the experimental extract. The results show that after the whitening process with the experimental gel, surface parameters, similar to healthy enamel were obtained.

Conclusions. The green tea extract solution exerts an important antibacterial effect on *S. mutans* strain, the values of the inhibition diameters having values close to those of the reference antibiotics recommended by CLSI. The experimental group bleached with gel based on green tea extract and carbamide peroxide had a roughness close to that of the control group, untreated due to the protective film of the green tea extract.

Regenerative treatment of a vertical defect caused by an enamel projection in a upper lateral incisor – a case report – 1 year follow-up

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3) Department of MaxilloFacial Surgery and Implantology, Faculty of Dental Medicine, Iuliu Hațieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania Ectopic enamel can lead to attachment loss on the involved tooth and to the formation of a bony vertical defect. The morphology of the defect is related to the size of the ectopic enamel and to the time of diagnosis. A delayed diagnosis can lead to the necessity of tooth extraction with the aesthetic and functional consequences that arise from it. Implant positioning in such a site is difficult – due to the severe bone loss and the necessity of implant site development of hard and soft tissues.

The aim of the presentation is to report the one-year outcome of an innovative regenerative procedure of a vertical defect associated with a case of enamel projection in 1.2.

After full clinical and radiological diagnosis, we performed the antimicrobial therapy in order to decrease the inflammation. A connective tissue graft wall technique



Corresponding Author: Ștefan Adrian Petruțiu e-mail: dr_ady17@yahoo.com associated with Emdogain was used in order to achieve both the regeneration of the vertical defect as well as an aesthetic result. No membrane or bone grafts were used.

The clinical and radiological examinations one year after the surgery show a bone gain in the former vertical defect with a minimum clinical attachment loss associated. Therefore a conservative approach can be used in order to achieve the final esthetic result.

A clinical comparison between lithium disilicate and zirconia crowns

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Corresponding Author: Ana Ispas e-mail: ispas.ana@umfcluj.ro **Introduction.** Dentists have focused on all ceramic restorations lately, but particularly on zirconia and lithium disilicate restorations. These promising dental ceramics are of great interest to dentists because of their excellent biological, mechanical, and optical properties. The aim of this systematic review is to assess the survival rate and complications of lithium disilicate and zirconia crowns.

Material and methods. An electronic search for articles in the English language literature was done using PubMed. This systematic review focused on research articles between 2010 and 2020. All studies, which analyzed the survival and complications of lithium disilicate and zirconia crowns, were included.

Results. The electronic search resulted in 697 articles, of which 28 were included as full text articles, while 21 articles met the inclusion criteria. A significant fracture in the crowns was reported for monolithic lithium disilicate when compared to monolithic zirconia crowns cemented on the lateral area. The biological complications were higher in zirconia crowns when compared to lithium disilicate crowns.

Conclusions. Lithium disilicate restorations had a higher average complication rate than that of zirconia restorations, but the average survival rate of lithium disilicate crowns was higher than that of zirconia crowns.

General anesthesia and dental treatment of uncooperative children

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2) Department of Pedodontics, Faculty of Dental Medicine, Iuliu Hațieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania **Introduction.** In cases with associated general pathologies or syndromes a rigorous management of dental prophylaxis is needed. Unfortunately, there are many cases when the parents are not aware of the importance of treating the temporary teeth and come to the pediatric dentist only when there is already a dental emergency. The aim of this study is to present the therapeutic approach of three patients that have been treated under general anesthesia.

Material and methods. A 3-year-old boy has presented to the pediatric dentistry department with painful complaints because of serous pulpitis at 51 or 52. He suffered a simple coronal fracture by falling. A 4-year-old boy with autism presented a vestibular

Corresponding Author: Meda-Romana Simu e-mail: medaromana@yahoo.com abscess with the starting point 52 and early childhood caries syndrome. A 5-year-old girl with a moderate intellectual disability and receptive and expressive language disorder came for difficulties in alimentation due to 64, 65 mobility based on recurrent infection and pathologic root resorption.

Results. All the patients were completly rehabilitated. The teeth with uncertain prognosis were extracted in order to avoid complications and the need of another intervention.

Conclusions. The general anesthesia is to be chosen only when the behavioral therapies approach didn't have results and the benefits are more important than the risks. For maximizing the results, all these interventions must be carefully prepared starting from a detailed clinical consultations and preoperative radiographies in order to formulate a complete diagnosis and treatment plan. For a good prognostic of the dental treatments the patient should be introduced in a follow up program, with regular dental check-ups for hygiene behaviors reinforcement and for motivating and accompanying the family in the oral care process. A good interdisciplinary collaboration should exist between the pediatric dentist, pediatrician and family to be able to shift the dental management of the patient towards prevention.

The relationship between mineral waters and the bovine dental structure

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Corresponding Author: Nicoleta Claudia Feurdean e-mail: feurdeanclaudia@gmail.com **Introduction.** Water has an important role in the human body, because all chemical reactions take place in aqueous environment. Insufficient water balance can lead to the installation of pathological conditions incompatible with life. The oral cavity has a special situation regarding water consumption, due to the contact of hard and soft tissues with liquids. The ionic composition and pH of the fluids have a direct impact on the oral mucosa and tooth enamel. At the same time, the fluids directly influence the characteristics of the dental materials used in direct or indirect dental restorations, due to their structure (organic matrix-inorganic filling), which allows ion exchange and matrix permeability.

Material and methods. The study was a prospective intervention type, in which 6 mandibular specimens of bovine origin, aged between 1-4 years, were used. The extracted teeth were cured and cleaned of detritus. After tooth numbering, their color was recorded using the Vita Easy Shade @ V spectrophotometer (VITA Zahnfabrik, H. Rauter GmbH & Co. KG). After color evaluation, the teeth were randomly divided into 4 batches and stored at 5° C in alkaline mineral with different conductivities and drinking water. Immersion in distilled water was used for the control samples. After the storage period, the spectrophotometric evaluation with Vita Easy Shade was performed.

Results. The immersion of bovine origin teeth led to a change in the composition of all immersion waters. Statistical analysis (Student's t test) showed that there are no significant differences between ΔE of tooth color in terms of diversity of the type of immersion water used (p = 0.526).

Conclusions. The type of water input and the temperature directly influenced the degree of teeth mineralization and the chemical composition of dental structures. The surface microstructure of the teeth was influenced by the duration of contact with mineral waters.

Traumas of young permanent teeth: incidence, clinical features and diagnosis - a review

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Corresponding Author: Meda-Romana Simu e-mail: meda.simu@gmail.com **Introduction.** Dental and dento-alveolar traumas fall within the category of dental emergency. These occurrences cause serious issues for children, parents and even dentists. A permanent young tooth is a tooth with the root still forming and whose apex is not completely closed, posing a risk of stopping it from evolving if it is traumatized. The goal of this research is to look into the frequency and types of traumas among young permanent teeth.

Material and methods. The current work is based on studies from special literature published in the last 10 years and found in PubMed, Google Academics and the International Journal of Pediatric Dentistry.

Results. Following the research, we have found that the great majority of dental and dento-alveolar traumas are twice as common in boys, as they are in girls in the articles found according to the inclusion criteria. Falls (from 31% to 64.5%), sports activities (40.2%), bicycle accidents (19.5%), circulation accidents (7.8%), but also physical aggression are among the most common causes of these accidents (6.6%). At the same time, research suggest that trauma affects the upper incisors the most, followed by the upper lateral incisors. Patients with class II / 1 occlusions were found to be substantially more prone to dental and dento-alveolar injuries than patients with other classes of occlusions.

Conclusions. The accurate clinical and radiographic diagnosis, the proper immediate therapeutic attitude and long-term monitoring of the injured tooth or teeth are the keys to success in cases of dental trauma.

Early childhood caries – a literature review of prevention and treatment methods

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Corresponding Author: Meda-Romana Simu e-mail: meda.simu@gmail.com **Introduction.** Early childhood caries (ECC) represents a major oral health problem. ECC can be defined as a significant chronic disease found in infants and preschool children worldwide, caused by a multitude of factors. This review focuses on the numerous prevention strategies and on the treatment methods of ECC.

Material and methods. PubMed database was used to drawn from the literature information about the clinical aspects and about the various methods of prevention and treatment of the ECC. This systematic review focused on research articles published between 2010 and 2021, as well as official guidelines.

Results. Some of the risk factors include improper feeding and oral hygiene habits, socio-economic status and a microbiological factor. Good hygiene and feeding habits, the use of fluoridated toothpaste and topical fluoride varnish application are

among the main preventive measures of ECC. The treatment methods can vary, largely depending on the severity of the lesion and of the patient's age and compliance.

Conclusions. There is a lack of knowledge and awareness regarding the disease, prophylactic measures and, generally, oral health in communities. Although it is largely preventable, ECC remains one of the most prevalent diseases in children.

A scanning electron microscopic study of marginal adaptation in milled CAD/CAM crowns

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Corresponding Author: Antonela Berar e-mail: antonela berar@yahoo.com **Introduction.** The current study aimed to evaluate the marginal adaptation of milled CAD/CAM crowns and to investigate the vertical discrepancy at the limit of preparation and prosthetic restoration.

Material and methods. The first maxillary molar was scanned with 3Shape TRIOS® scanner and the polymeric resin abutments were obtained using 3D Asiga printer. Eighteen crowns were designed and milled from three materials: group 1 (IPS Empress CAD, Ivoclar Vivadent), group 2 (Cerasmart, GC) and group 3 (G-CAM, Graphenano Dental). All the crowns were further cemented to the abutments with G-Cem Link Force (GC). The marginal adaptation was observed with a scanning electron microscope, under 45X, 100X, 450X magnification and the gaps were measured employing the morphometric program.

Results. In group 1, the most accurate marginal adaptation was observed, followed by group 2 and 3. There were statistically significant differences between the 3 groups, according to t-test (p<0.5). Nine samples showed marginal gaps at the limit of preparation and crowns. The mean value of gaps in group 1 was 47.09 (\pm 16.93 µm), in group 2 was 18.53 (\pm 14.15 µm) and in group 3 was 21.60 (\pm 14.89 µm).

Conclusions. In this study, differences in marginal adaptation of CAD/ CAM crowns were found. However, the three studied materials (IPS Empress CAD, Cerasmart, G-CAM) presented clinically acceptable limits in terms of marginal discrepancy, suggesting their use as prosthetic restorations.

Study on methods to induce antibacterial effects to denture base materials

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1) Department of Prosthetic Dentistry, Faculty of Dental Medicine, Iuliu Hațieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania **Introduction & Aim.** The presence of the denture in the oral cavity favours the occurrence of oral conditions, mainly as a result of bacterial accumulation. The aim of the study was to induce antibacterial properties to denture base materials.

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Corresponding Author: Cecilia Bacali e-mail: cecilia.bacali@yahoo.com **Material and methods.** A hybrid combination of nanoparticles was added to an acrylic resin for denture bases. Antibacterial effect was tested with and without association of light therapy.

Results. The enhanced resins showed antibacterial effect, the effect depending on the concentration of additives and on the association with different light sources.

Conclusions. New techniques and materials can be associated in order to obtain better antimicrobial effects, with practical importance for the oral health of denture and orthodontic devices wearers.

Modern methods of treatment for the gummy smile

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Material and methods. Studies, articles and case reports were included to comply a comprehensive, general view of 3 methods: botulinum toxin injections, fillers injections and surgical lip repositioning.

Results. Botulinum toxin treatment can target hyperfunctioning perioral muscles, using a dose of 2 to 3 units injected through 1 to 2 sites per side. Efficacity in gummy smile treatment is proven by literature. Fillers can be injected into muscle fibers or superficial to them, and their presence can create a partial hypofunction in muscular activity. This effect can be targeted towards ameliorating gummy smiles. Surgical lip repositioning is a largely unknown treatment modality. It focuses on limiting the lift of the lips. It was designed to be a shorter, less aggressive option to orthognathic surgery. All the techniques can be effective. However, proper case assessment is necessary.

Conclusions. Facial aesthetics are influenced by smile aesthetics, so we can affirm that aspect improvement of gummy smiles has a significant effect on the overall appearance of the patient. All methods and techniques are viable and show promising results. Further data is required to draw definite conclusions on whether some methods are superior to others.

Digital and conventional occlusal analysis in implant supported restorations

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Corresponding Author: Manuela Tăut e-mail: tautmanuela@gmail.com **Introduction.** Even if the importance of occlusal analysis is especially significant in prosthodontics, implantology and orthodontics, the conventional method by means of articulating paper remains the most commonly used method. The new methods of diagnosing dental occlusion have become available, among which the T-Scan Novus v10 computerized occlusal analysis system (Tekscan Inc., South Boston, MA USA) managed to record the distribution of occlusal contacts and sequential occlusal forces. The aim of this study was to determine whether or not the analysis of dental occlusion requires an additional digital method in implant supported restorations using the T-Scan[™] Novus[™] device (TekScan) in comparison with articulating paper.

Material and methods. This pilot study included a number of 10 subjects divided into 2 groups, the first group included patients with at least 10 healthy teeth/ dental arch and the second group included patients with implant-supported restorations. The evaluation methods were the calibrated articulating paper and T-Scan. The following data were collected: contact points in maximum intercuspation, the pairs of teeth performing protrusion and right/left laterotrusion. It was tested if there was a statistically significant difference between the two occlusal diagnostic methods using T test for independent samples. The association magnitude was measured using the Chi-square test (p value).

Results. The difference between the number of contact points between the two types of investigations was not statistically significant when each group was studied: group 1 - T-test p=0.54 and group 2 - T-test p=0.26. There was no statistical significance between the two diagnostic methods regarding protrusion (Chi-square p=0.89), right laterotrusion (Chi-square p=0.87), left laterotrusion (Chi-square p=0.36), respectively.

Conclusions. The analysis of dental occlusion had comparable results in implant supported restorations when using the two examination methods.

Optical properties of layered composite samples: manufacturing methods and color assessment

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Corresponding Author: Elena Bianca Varvara e-mail: bianca.varvara@yahoo.com **Introduction.** When the optical properties of the composite resins are evaluated, it is difficult to standardize the method of samples building and measuring, to mimic the layering method. The aim of this study was: a. to evaluate different techniques of obtaining layered resin composite samples; b. to compare the optical properties resulting when the samples were measured with two different devices: a contact-type dental spectrophotometer and a non-contact spectroradiometer.

Material and methods. Three composite restoration systems (Brilliant Ever Glow-Coltene, IPS Empress Direct-Ivoclar Vivadent, Essentia-GC) were used to build the samples, as follow: single-layered specimens (SLS) (0.5 mm, 1 mm, and

1.5 mm) were obtained using 3 different opacities (opaque, dentin body and enamel), whilst multi-layered samples (MLS) (both 1.5 mm thickness) were created using different shade combination, respecting the anatomical layering technique. The SLS was further overlapped (with and without interposing sucrose solution) to form a final thickness of 1.5 mm. The optical properties of the samples were measured using a spectrophotometer-SFM (Vita Easy Shade-Vita) and a spectroradiometer-SRM (PR-655 Spectra Scan, Photo Research) against A3 shade background. Color differences between SLS and MLS were calculated by Δ the E_{00} formula and compared with the acceptability and perceptibility thresholds (AT₀₀=1.8 and PT₀₀=0.8).

Results. The ΔE_{00} between SLS and MLS ranged 3.52 and 4.53 when SFM was used for measurements, and between 1.89 and 2.60 when SRM was used. The color differences were clinically acceptable ($\Delta E_{00} < 1.55$ units) if a sucrose solution was interposed when overlapping the SLS. Only for one material (IPS Empress), the acceptability threshold was exceeded: $\Delta E_{00} = 2.62$. The color differences were higher when the spectrophotometer has been used for measurements, mainly in the case of SLS superimposed without sucrose.

Conclusion. Within the limitations of the present study, a lower ΔE_{00} between the SLS and MLS has been obtained, when sucrose has been added. The values of ΔE_{00} were higher when the optical properties were measured with the spectrophotometer.

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DOCTORAL SCHOOL

New trends in citation impact: form vs. content

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Corresponding Author: Sorana D. Bolboacă e-mail: sbolboaca@umfcluj.ro The academic publishing world undergoes significant changes related to requirements, volume, speed, and quality. The number of citations and the number of times an article has been cited are seen as a measure of knowledge dissemination in the context of scientific impact in academia (e.g. h-index, i-10 index, etc.). Publishers list different factors linked to the citations: title length and punctuation (shorter the better, no hyphens or "?"); number of authors (smaller the better); preprint publication (more cited); no country name in the title, abstract and keywords; availability of shared data; journal visibility (open access); actively promote your work (conferences, social media - Academia.edu, ResearchGate, Mendeley -, share you full-text and data, link the paper with ORCID or Publons); standardize your name and institutional affiliation; networking (national and international teams); rational length of the paper, number of authors and number of references; etc.

The scite, a tool funded by NSF (National Science Foundation) and NIDA (National Institute on Drug Abuse of the National Institutes of Health), change the way of citation impact by showing the context of citations (mentioning / supporting / contrasting). The scite_ tool shows four metrics: the number of publications citing a particular article, the number of supporting and contrasting citation statements, and the number of mentioning citation metrics. A summary that incorporates the publication type, relationships (self/independent), the authors and the journals, and in which section the citation statement appears are also available. Furthermore, a link to the identified citation statements is also provided in the report. All-in-one, this new tool could change the scientific citation impact, shifting from formal citation (number) to the context of citation statements that quantify the knowledge dissemination impact more appropriately.

Trends in knowledge dissemination at the level of doctoral studies: two academic years study

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3) Department of Toxicology, Faculty of Pharmacy, Iuliu Hațieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania **Introduction.** The research aimed to quantify the main activities related to researchers development at the Iuliu Hațieganu University of Medicine and Pharmacy Cluj-Napoca in two academic years, 2019-2020 and 2020-2021.

Material and methods. The list of PhD students who defended the thesis in the academic years of interest were retrieved from the Doctoral School. The number of publications (indexed in Web of Science or International Databases (IDB) were also extracted from the same source. Furthermore, closely to the defended date, the graduates were asked to provide the following information related to PhD research: the title of the most significant article, participations in international and national conferences and participations in international research training. WoS classification domain, impact factor of the journal, domain and classification for each domain in the 4) Department of Dental Propedeutics and Esthetics, Faculty of Dental Medicine, Iuliu Hațieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania

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Corresponding Author: Sorana D. Bolboaca e-mail: sbolboaca@umfcluj.ro year when the study was published were collected whenever applicable.

Results. One hundred and twenty students defended their PhD thesis, 57 in the 2019-2020 (39 Medicine, 11 Dentistry and 7 Pharmacy) and 63 in the 2020-2021 academic year (45 Medicine, 8 Dentistry and 10 Pharmacy). Significant more ISI publications (p = 0.0049 in 2019-2020 and p = 0.0288 in 2020-2021) and significant lower number of articles indexed in IDB (p = 0.0001 in 2019-2020) were reported by PhD students in Pharmacy. Participations in scientific conferences and international research study visits were reported by 70% of graduates (88% by the 2019-2020 graduates and 54% by the 2020-2021 graduates). Two hundred and eleven participations in scientific conferences (158 by the 2019-2020 graduates and 53 by the 2020-2021 graduates) and 11 international study visits were reported. A tendency to a decreased conference dissemination was observed (~3 by the 2019-2020 graduates and ~2 by the 2020-2021 graduates).

Conclusion. Trends in dissemination of doctoral research are dynamic and somewhat specific to the research field.

RESEARCH CENTERS

Anti CD41 CAR Jurkat cells - therapy against M7-AML DAMI Luc2+ cells

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Corresponding Author: Adrian Bogdan Țigu e-mail: adrianbogdantigu@gmail.com **Introduction.** The treatment of hematological malignancies has progressed significantly in last decades, new therapeutic approaches have been discovered (antibody therapies for specific tumor surface antigens or new compounds that can modulate signaling pathways which can induce tumor cell death). Immunotherapy based on CAR T cells has brough a new alternative to some types of acute leukemias but is still to be applied in acute myeloid leukemia (AML).

Material and methods. Construction of Vector and CAR Jurkat cell transfection: the full length of chimeric antigen receptor was synthesized and subcloned into lentivirus vector. The insert was confirmed by Sanger sequencing.

Co-culture between CAR Jurkat and DAMI cells: the cell lines were cultured and maintained at 37°C in a humidified chamber with 5% CO2. The co-culture was evaluated after 72h by fluorescent microscopy under 40X objective, using the Olympus Confocal Microscope.

D-luciferin evaluation of DAMI cells in co-culture: after 72h of co-culture, the luciferin signal was evaluated using the IVIS machine after adding the substrate over the cells plated at different ratios in a 96 well plate with flat bottom.

Results. The GFP signal for CAR Jurkat cells was maintained during the subculturing steps for all generations and the co-culture was optimized for obtaining the best co-culturing conditions starting from 2000 cells/well. The effect of CAR Jurkat cells was evaluated by the microscopy analysis and the DAMI cells luminescence signal was evaluated by IVIS and various effects were highlighted for the co-cultures.

Conclusions. CAR Jurkat cells might inhibit DAMI cells growth, the inhibitory effect depending on the ratio between the effector and targeted cells.

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Development of an LC-IM-MS approach for analysis of D-amino acids

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 Department of Proteomics and Metabolomics, Research Center for Advanced Medicine – MedFuture, Iuliu Haţieganu University of Medicine and Pharmacy Cluj-Napoca, Romania **Introduction.** Since the discovery of D-serine as an endogenous metabolite, chiral analysis of D-amino acids became relevant for the discovery of diagnostic and prognostic biomarkers in numerous diseases. In biological systems, amino acids are the most notable class of chiral metabolites. It is well known that in mammals the L- enantiomer of amino acids (AA) is naturally occurring. Nevertheless, D-AAs are

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Corresponding Author: Radu-Cristian Moldovan e-mail: moldovan.radu@umfcluj.ro present in very low concentrations (low nM to low μ M range) compared to L-AAs (low μ M to mM range), impeding their detection and quantification. Even though many analytical approaches have been developed, most of them are difficult to implement since they require special infrastructure (2D-LC-MS) or expensive chiral selectors.

The objective of our study was to develop a fast LC-IM-MS method capable to offer baseline enantiomeric resolution (Rs>2) for all proteinogenic amino acids, using the indirect enantioseparation approach. On top, considering that after derivatization with a chiral derivatizing reagent (CDA) the reaction products are diastereomers, ion-mobility spectrometry may offer a complementary degree of separation.

Material and methods. Several observations made in the past were the starting point , where a dependence of chiral resolution on mobile phase pH was documented. Therefore, several qualitative variables were identified and included in the study, such as: CDAs, stationary phase, aqueous phase pH and the nature of organic modifier. Two CDAs were selected: (+)-1-(9-Fluorenyl)ethyl chloroformate ((+)-FLEC) and N-(4-Nitrophenoxycarbonyl)-L-phenylalanine 2-methoxyethyl ester ((S)-NIFE), together with five stationary phases (C18, Polar-C19, PS-C18, Phenyl and F5), two organic modifiers (acetonitrile and methanol) and a pH range between 2 and 8.

Results. After a comprehensive screening of these variables, it was observed that (S)-NIFE and acetonitrile have a positive impact on enantioseparation, as compared to (+)-FLEC and methanol, respectively. A further optimization using design of experiments was carried out for finding the best gradient and for fine tuning the pH of the aqueous phase.

Conclusion. In optimal conditions, baseline chiral separation of all proteinogenic D- and L-amino acids was achieved in less than 20 minutes. Ion-mobility measurements offered complementary information (CCS) which may prove useful for metabolite annotation in complex matrices.

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Abnormal differentiation of hematopoietic MDS92 cells as a result of ATRA treatment in the presence of stroma

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 Department of Hematology, Iuliu Hațieganu University of Medicine and Pharmacy Cluj-Napoca, Cluj Napoca, Romania **Introduction.** Retinoic acid signaling plays a particularly important role in hematopoiesis. Impaired signaling downstream of retinoic acid receptor (RAR) alpha results in acute promyelocytic leukemia, a condition practically cured by forced activation of RA pathway via treatment with all-trans retinoic acid (ATRA). In acute myeloid leukemia (AML) treatment with ATRA has had only minimal clinical benefit in patients with MDS (Myelodysplastic syndrome). Our hypothesis is that HH (Sonic Hedgehog) ligands produced by the MDS clone hijack control of stromal CYP26 and compromise retinoid homeostasis, thus inducing abnormal differentiation of hematopoietic cells and as well as impaired responses to differentiation therapy. We use MDS 92 cell line as a model for AML and OP9 stroma cells to mimic the bone marrow microenvironment.

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Corresponding Author: Diana Cenariu e-mail: diana.cenariu@umfcluj.ro **Material and methods.** MDS 92 cells were co-cultured with OP9 stroma cells in 24 well plates and three different ATRA concentrations (10-6 M, 10-7 M, 10-8 M) were used. Culture plates were maintained at 37°C in a 5% CO2 humidified chamber. We analyzed MDS92 phenotype by flow cytometry and counted clonogenic activity for 2500 isolated MDS92 cells plated in methylcellulose with and without stroma.

Results. CD45, CD38 and CD11b were analyzed by flow cytometry with an expression of CD38 for more differentiated populations within the cell line.

The number of colonies formed in methylcellulose indicate smaller numbers in the ATRA treated variants and higher colony forming in the presence of OP9 stromal cells. The results are validated by the smears obtained from experimental cocultured MDS92 and stromal OP9 cells.

Conclusion. These immature populations of cells decrease in response to ATRA in stroma-free conditions, but they are relatively protected in the presence of MSCs.

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Repositioned 5-Azacytidine therapy impairs lung cancer development via epigenetic reprograming

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Corresponding Author: Diana Gulei e-mail: diana.gulei@umfcluj.ro **Introduction.** Lung cancer remains the leading malignant pathology in terms of incidence and mortality rates for both genders combined. The development of lung cancer brings together genetic, epigenetic and environmental factors that contribute to installation of aberrant signaling networks. In the context of lung cancer heterogeneity, epigenetics could become an advantageous field of study. These types of modifications are reversible and are now considered an individual cancer hallmark. Therefore, demethylation strategies may circumvent issues like tumor heterogeneity and patient ineligibility, reversing the global DNA methylation that sustains the malignant processes.

Material and methods. The present study investigated the therapeutic efficiency of repositioned 5-Azacytidine (5-Aza) (in combination or not with irradiation) in lung cancer in both in vitro and in vivo models. A549 cell line was treated with 2 doses of 5-Aza (IC50 concentration) alone or in combination with 2 Gy gamma radiations. The in vitro modifications were observed via functional tests for cell viability, cell cycle, invasion, and metastasis. In vivo validation was done on subcutaneous and orthotopic immunocompromised mice models of lung cancer grafted with A549 cells.

Results. Data show that 5-Aza induces cell apoptosis and necrosis and is stopping the cell cycle by blocking the cell in the G1 phase independent of irradiation. The clonogenic capacity of lung cancer cells, as well as invasion properties are significantly diminished. When treated with 5-Aza, A549 cells lose their in vivo grafting properties. Moreover, systemic treatment of orthotopic models show complete remission of the primary tumor.

Conclusions. Altogether, the results confirm the therapeutic efficiency of 5-Aza in lung cancer experimental models. Further in-depth studies and also on larger cohorts are necessary for complete evaluation.

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Characterizing the transcriptomic profile of acquired haemophilia using RNA-seq

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Corresponding Author: Rareș Drula e-mail: Drula.Rares@umfcluj.ro **Introduction.** Acquired hemophilia (AH) is a very rare bleeding disorder consisting of the spontaneous alteration of coagulation processes occurring in individuals with no previous hemophilic diagnosis. While classic A or B hemophilia (CH) is usually associated with mutations in the clotting factors genes, AH has a primary autoimmune component, determined by the development of autoantibodies directed against the clotting factors. Most of the underlying mechanisms for the development of AH are largely unknown, especially regarding the factors that might lead to the development of AH in individuals already diagnosed with either solid or hematological malignancies and autoimmune disorders. As such, we sought to characterize the differential transcriptomic profiles of AH patients in comparison with CH patients and healthy individuals using RNA-Seq. We aimed to highlight relevant differentially expressed transcripts associated with AH that might offer reliable biomarker candidates for predicting its development and, additionally, to provide insight regarding the altered pathways and factors involved in the mechanism.

Material and methods. We investigated the transcriptomic signatures in the RNA isolated from the plasma of AH patients (2), patients with different forms of CH (mild and severe, 2 each), and equal numbers of healthy controls for reference. Data regarding dysregulated transcripts were clustered in heatmaps highlighting modifications at fold change level and global comparisons of the alterations were displayed in the form of volcano plots.

Results. We identified a subset of transcripts, both coding, and non-coding, with differential expression levels in the case of AH patients that might act as relevant targets for subsequent future investigations.

Conclusions. We propose RNA-seq as a powerful tool in deciphering the factors involved in AH at the RNA level through the establishment of disease-specific transcriptomic profiles.

Proving the interaction of platinum-based drugs with cellular DNA by means of SERS

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Corresponding Author: Rareş Ştiufiuc e-mail: rares.stiufiuc@umfcluj.ro **Introduction.** The latest improvements in Surface Enhanced Raman Spectroscopy (SERS) allowed the detection of very subtle molecular interactions between different drugs and other biomolecules. In our study, we have used the advantages of this ultrasensitive vibrational method to investigate the interaction of three cell lines with two classes of newly developed drugs containing Pt.

Material and methods. These new classes of Pt drugs were formulated with silica mesoporous nanoparticles, in order to interact with the cell nucleus. The SERS spectra have been acquired on silver solid substrates, synthesized using an original method developed in our laboratory including the purification and concentration by means of tangential flow filtration. The cell lysates (DLD-1, A431, and A2780) were obtained using enzymatic digestion. The measurements were recorded after complete dehydration of the sample (1 μ L) on the solid substrate (created of 1 μ L of purified and concentrated silver nanoparticles). For each cell line, the measurements have been performed on lysates obtained from untreated (control) and treated cells with DGM-Pt1 and DGM-Pt3 drugs.

Results. The SERS spectra of the treated group were able to point out the different interactions of Pt drugs with the cells. The evolution of the vibrational bands assigned to ring breathing vibrational modes of A, G, C, and T can be correlated with the therapeutic efficacy of these two drugs. Our results suggest that DGM-Pt3 has a strong effect on all three cell lines whereas treatment with DGM-Pt1 leads to a noticeable effect only in the case of the A431 cell line.

Conclusions. We strongly believe that our method that implies SER spectroscopy is a valuable tool that enables the analysis of different compounds' effects at the cellular level.

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A new method for DNA methylation assessment using ultrasensitive vibrational microscopy

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Corresponding Author: Rareş Ştiufiuc e-mail: rares.stiufiuc@umfcluj.ro **Introduction.** Raman and its counterpart, Surface Enhanced Raman Spectroscopy (SERS), are one of the most promising techniques capable to investigate nanoscale modifications of biological samples. In our study, we have employed Raman/SER spectroscopy in order to highlight the differences between normal and leukemia DNA samples and to evaluate their methylation pattern.

Material and methods. In order to get spectral information related to DNA bases modifications as methylation, we have developed a new strategy. Our method is based on an incubation step of 4 minutes at 94oC of a mixture of silver nanoparticles and genomic DNA samples extracted from normal and leukemia cell lines. This step allowed a very fast interaction of silver nanoparticles' surface with single-strand DNA. This new method has led to reproducible Raman/SER spectra for all DNA samples.

Results. Raman results emphasized important differences between normal and cancer DNA based on their aggregation behavior induced by the distinct methylation landscape present in the DNA samples. The SER spectra collected on the same DNA samples showed a very intense vibrational band located at 1008 cm-1 assigned to a rocking vibration of 5-methyl-cytosine. The intensity of this band strongly decreases in cancer DNA due to the modification of the methylation landscape occurring in cancers which usually takes place at CpG islands.

Conclusions. We believe that our method could be used as a powerful tool for demonstrating epigenetic changes in cancer, by means of SERS.

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Cellular responses induced by PHGDH inhibition on TNBC cell lines: a proteomic view

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1) Department of Proteomics and Metabolomics, Research Center for Advanced Medicine–MedFuture, Iuliu Hațieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania **Introduction.** Metabolic reprogramming is regarded as a hallmark of cancer that sustains development of malignant cells. The understanding of new metabolic dependences of cancer cells provides tools in the therapeutic approach. Triple negative breast cancer (TNBC) represents an unmet medical which has been relatively stagnant

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Corresponding Author: Ioana Ecaterina Pralea e-mail: pralea.ioana@umfcluj.ro for many years in terms of therapeutic approach. Nevertheless, the de novo serine synthesis pathway (SSP) represents an important source for sustaining the needs of malignant cells by powering several key pathways involved in cell growth and redox homeostasis. Phosphoglycerate dehydrogenase (PHGDH) is the first enzyme in the SSP pathway being responsible for the rate-limiting conversion of glycolysis intermediate 3-phophoglycerate into 3-phosphohydroxypyruvate. According to several large genomic data, PHGDH amplifications were observed in several cancers including breast, cervical, colon cancer and also in melanoma, leukemia, glioma. The role of PHGDH enzyme as potential target for therapy re-emerged following the discovery of two potent inhibitors, namely NCT-503 and CBR-588.

Material and methods. In this study, we employed MS-based approaches to investigate alterations in the protein expression profiles of three TNBC-representative cancer cell lines expressing different levels of the target protein after inhibition of PHGDH by NCT-503. Proteins were extracted from the cell pellet, purified, reduced, alkylated and digested (using trypsin). Purified peptides were analyzed by label-free LC-MS/MS performed using an ultra-performance liquid chromatography system Acquity M-Class (Waters Corporation) coupled with Synapt G2-Si IM-MS (Waters Corporation). Data was processed by the Progenesis QIp software, and functional annotation analysis was performed using PROTEXA (CING-Bioinformatics Group Servers).

Results. Peptides identification were performed using the MSe search and a peptide false discovery rate (FDR)<1%. A total of 19456, 15935 and 12675 peptides were obtained for MDAMB231, MDAMB468 and HS578T respectively. Proteomic profiling of the cell lines resulted in identification of 1854 proteins in MDAMB231, 1604 in MDAMB468 and 1308 in HS578T with a confidence score of >5, sequence length >6 and hits>2. A number of 1016 proteins were identified in all samples. 19, 17 and 14 upregulated proteins (FC>1.5) were found in MDAMB231, MDAMB468 and HS578T respectively. Treatment induced downregulation of 63, 42 and 82 proteins in MDAMB231, MDAMB468 and HS578T. Enrichment analysis performed on proteins showing significant differential expression highlighted as downregulated as expected the serine biosynthesis pathway in all TNBC cell lines (normFC 0.50, 0.63, 0.50) while glycine degradation, pentose phosphate pathways and pentose tRNA aminoacylation were downregulated only in MDAMB cell lines. Specific to HS578T was the underexpression of proteins implicated in the sphingolipid metabolism and glycolysis while overexpression of glycerophospholipid biosynthesis, nucleobase biosynthesis and branched aminoacids catabolism pathways were seen.

Conclusions. Pathway enrichment analysis confirmed serine biosynthesis downregulation and revealed several dysregulated molecular pathways that may be mechanistically involved in TNBC pathology.

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LC-MS based chemical profile and *in vitro* effects of a commercially available herbal preparation

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Corresponding Author: Ioana Ecaterina Pralea e-mail: pralea.ioana@umfcluj.ro **Introduction.** Natural products represent an accessible source of molecules with unique structures and innovative mechanisms of action. Being among the first antineoplastic drugs discovered, phytochemicals are of interest in cancer research. Currently, natural compounds are used in the oncology field in a versatile manner: i. they represent a resource for the development of novel effective drugs; ii. some natural products possess innate antitumor effect and could be used as chemotherapeutic agents; iii. studies emphasized natural compounds with chemopreventive properties; iv. natural products are also used as sensitizers improving the effectiveness of conventional chemotherapy (e.g. in multi-drug resistance cancers).

The aim of this study was to perform a comprehensive characterization of a commercially available herbal preparation, in terms of composition and in-vitro effect on a panel of cancer cell lines.

Material and methods. Phytochemical characterization was carried on a Waters I-Class UPLC instrument coupled with a Synapt G2-Si high-resolution mass spectrometer (Waters, Milford, MA, SUA). Separation was achieved using a BEH C18 stationary phase and gradient elution, while MS data was acquired in the mass range of 50-1200 m/z after negative electrospray ionization. Data processing (peak picking, alignment) was carried using Progenesis QI software (Waters, Milford, MA, USA), using an in-house natural compounds library. Quantitative analysis data was processed with TargetLynx. The effect of the ethanolic extract was investigated using the MTT assay, on a panel of human cell lines (BJ, FR2, LX2 normal cell lines and DLD-1, HCT-116, MCF-7, MDA-MB-231 and SKHEP-1 tumoral cell lines) for the investigation of antiproliferative properties. Cells (96-well flat-bottom plate, 1x104 cells/well) were treated (after 24h incubation) with different concentrations of extract (1.56-400µg/mL) for 48h. The absorbance corresponding to the viable cells was measured at λ =570 nm on a SPARK10M multiplate reader (Tecan, Männedorf, Switzerland).

Results. The phytochemical profiling unveiled twelve major compounds belonging to phenolic acids and flavonoids. The LC-MS quantitative determination revealed 3,5-di-caffeoylquinic and chlorogenic acids as most abundant with a concentration of 4.3 and 2.3 mg/g (m/m DW) respectively. Other high concentration compounds (>0.5 mg/g) were represented by rutin, rosmarinic acid, catechin and luteolin-7-O-glucoside. The extract was screened for antiproliferative effects on a panel of human cell lines, the MTT assay showing accentuated effects on DLD-1, HCT-116 (colon) and SKHEP-1 (hepatic) cancer cell lines, while no antiproliferative effect was observed on the corresponding normal cell lines.

Conclusions. The comprehensive phytochemical profiling revealed twelve major compounds belonging to polyphenols and flavonoids. The major constituents determined were 3,5-di-caffeoylquinic, chlorogenic and rosmanic acids, catechin, rutin and luteolin-7-O-glucoside. The ethanolic extract exhibited antiproliferative effects on several cancer cell lines.

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Minimally invasive approaches in the diagnosis and treatment of lung cancer using NGS technologies

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Corresponding Author: Cecilia Pop-Bica e-mail: cecilia.bica@umfcluj.ro **Introduction.** Lung cancer remains the leading cause of cancer-related deaths in both men and women and is the second most diagnosed cancer after breast cancer according to GLOBOCAN 2020. The use of liquid biopsies represents an alternative to tumor tissue biopsy.

Material and methods. Matched plasma and tumor biopsies samples from 30 patients with stage III and IV lung cancer (21 non-small cell lung cancer (NSCLC) and 9 small cell lung cancer (SCLC)) were used for the NGS experiment. The targeted sequencing protocol was done using the Ion Ampliseq Cancer Panel, including primer pairs for 190 amplicons in 46 cancer genes. Data analysis was performed using the Ion Reporter 5.6 software.

Results. Similarities were identified between the somatic mutations in the tissue biopsy sample and plasma sample from the same patient in a prominent number of patients. *TP53* was the most altered gene in both liquid biopsy and tumor tissue samples, alongside other frequently altered genes such as *PIK3CA*, *KDR*, and *STK11*. We indicated the number of patients identified as harbouring mutated genes for each particular gene emphasizing the alterations identified in tumor tissue also reflected in the liquid biopsy. The comparison between the mutation profiles of the two histotypes revealed differences in the gene alterations frequencies observed in the two groups.

Conclusions. The mutational landscape of lung cancer patients was assessed in plasma samples but also in tumor tissue samples. The comparison between the mutations identified in plasma samples and in tumor tissues allowed the identification of potential genes that could serve as biomarkers for the early detection of lung cancer using minimally invasive techniques.

Bioinformatic approach for the evaluation the prognostic significance of immune response related genes in breast cancer

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Corresponding Author: Cornelia Braicu e-mail: cornelia.braicu@umfcluj.ro **Introduction.** Breast cancer is the most common cancer type in women worldwide. Due to its intricacy in nature, efficacious breast cancer treatment can face many challenges. The development of novel biomarkers or therapeutic targets, has attracted more and more attention in the last years.

Method. Using bioinformatics approaches, we studied the alteration of immune response related genes and its implication on prognostic. Gene expression profiles and clinical data of breast cancer patients were collected from The Cancer Genome Atlas (TCGA) by using UALCAN online interface. Additional using the miRNET it was used to generate the mRNA-miRNA gene interaction network.

Results. Our recent based on breast cancer TCGA datasets revealed downregulation of CXCL1, CXCL2, CXCL3, CCL20, IL6 and IL8. Among these genes, CXCL1, CXCL2, CXCL3 have been correlated with overall survival rate, high



expression of these genes displaying a better prognostic rate. These immune response genes have been interconnected with TGFB1/2, TGFBR1 and EGR1 (genes recognized to be involved in drug resistance). A key element of mRNA-miRNA network was represented by miR-21 a key regulator of oncogenic signaling, overexpressed in most of the solid tumors, including breast cancer.

Conclusions. The findings may offer novel insights into prognostic monitoring of immune-related targets for breast cancer or can be served as reference for the additional investigation and validation of biomarkers.

Assessment of potential biomarkers from liquid biopsy in lung cancer

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Corresponding Author: Liviuța Budișan e-mail: liviuta.petrisor@umfcluj.ro **Introduction.** Lung cancer is the most common cancer in men and the leading cause of cancer death (18.0% of all cancer deaths). Alteration of expression levels of growth factor signaling pathways may contribute to tumorigenesis and disease progression. The aim of this study was to identify whether there are significant differences in expression levels for EGFR, TGF β 1 and IGF-IR in normal and lung cancer serum samples and whether there is a direct correlation between them and the miRNAs targeting them.

Material and methods. We analyzed the serum expression levels of EGFR, TGF β 1 and IGF-IR from a patient cohort comprising 27 lung cancer patients (NSCLC) and a group of 40 healthy subjects. The expression levels of these proteins were determined by the ELISA method. The stained reaction product was measured on an ELISA plate reader (Biotek) at 450 nm. We performed also qRT-PCR for the evaluation of plasma levels of miR-155, miR-181a and miR-21 from the same patient cohort.

Results. EGFR levels in NSCLC patients were significantly lower compared to normal samples (p-value 0.0061). Serum levels of TGF β 1 and IGF-IR in the same patients were not statistically significant compared to normal samples. Using miRNET online tool we proved a interconnection between EGFR, TGF β 1 and IGF-IR proteins expression and miR-155, miR-181a and miR-21expression in liquid biopsies from the same patient cohort. ncRNAs transcripts were proved to be over-expressed in plasma lung cancer patients compared to healthy subjects.

Conclusions. Our data reveal that EGFR, TGF β 1 and IGF-IR could be used in the future as potential biomarkers in NSCLC patients' liquid biopsies, particular when correlated with circulating miRNAs. While at the beginning of their understanding the mechanisms coordinated by miRNAs modulating protein expression could be of high interest if additional studies would be performed in larger patients' cohorts to assist clinicians in making predictive assessment.

Improving the cancer diagnostic methods using cancer cellsderived exosomes

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Corresponding Author: Paul Chiroi e-mail: chiroi.paul@umfcluj.ro **Introduction.** Breast, lung, colorectal and bladder cancers remain the leading cause of incidence and mortality. Early detection and identification of minimally invasive markers require the validation of novel molecules for diagnosis. As they take over some of the geonomic and transcriptomic signature, malignant cell-derived exosomes (MDE) may become the next class of biomarkers.

Material and methods. MDE were isolated by ultra-centrifugation from breast (BT549), lung (H1155), colorectal (HT-29) and bladder (RT4) tumor lines, then characterized by NanoSight NS300. For each line and each type of MDE, NGS (Ion Torrent) was performed on a panel containing the most frequently mutated 46 genes in cancer: *ABL1, AKT1, ALK, APC, ATM, BRAF, CDH1, CDK2A, CSF1R, CTNNB1, EGFR, ERBB2, ERBB4, EZH2, FBXW7, FGFR1, FGFR2, FGFR3, FLT3, GNA11, GNAQ, GNAS, HNF1A, IDH1, IDH2, JAK2, JAK3, KDR, KIT, KRAS, MET, MLH1, MPL, NOTCH, N, PDGFRA, PIK3CA, PTEN, PTPN11, RB1, RET, SMAD4, SMARB1, SMO, STK11, TP53, VHL.*

Results. The common mutations between the malignant cell lines and MDE were highlighted. NanoSight results confirmed the presence of MDE, and NGS allowed the evaluation of the overlap between the mutational profiles of tumor cell lines and MDE. Up to 85.7% of mutations were found common, the frequency of alleles being similar.

Conclusions. Our *in vitro* study highlights the potential of MDE as a non-invasive biomarker for cancer diagnosis, but further evidence is needed for confirmation.

The promising role of lncRNAs in the study of triple negative breast cancer on cell lines

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Corresponding Author: Cristina A. Ciocan e-mail: cristina.ciocan@umfcluj.ro **Introduction.** Long non-coding RNAs (lncRNAs) are entangled in many cellular processes via a transcriptional regulation mechanism of their direct target genes, acting as oncogenes or tumor suppressors. Their deregulation is one of the main obstacles to the effectiveness of chemotherapy, as was observed by our microarray study as an effect of Doxorubicin treatment by multiple dose exposure as described in our recent paper (Ciocan-Cartita CA et al).

Material and methods. The aim of this study was to investigate the effect of Doxorubicin in TNBC cell lines (Hs5678T and MDA-MB-231) and to highlight alterations of the lncRNA pattern after a long exposure to this drug.

Results. The microarray study revealed several altered transcripts, of which 732 upregulated and 785 downregulated lncRNA in Hs578T, and 344 upregulated and 596 downregulated lncRNA in MDA-MB-231, respectively; 73 lncRNA were identified as common signature of the two cell lines. The miRNA-lncRNA network generated with miRNET revealed MALAT1 and LUCAT1 as key elements involved in drug resistance, which are interconnected with miR-181 family members.

Conclusions. The altered lncRNA expression signature revealed by microarray study can be further investigated as effective biomarkers for the prediction response to chemotherapy, including Doxorubicin.



Improvement of peripheral blood stem cell mobilization using human chorionic gonadotropin in addition to current mobilization approaches with granulocyte-colony stimulating factor

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Corresponding Author: Andrei Cismaru e-mail: cosmin.cismaru@umfcluj.ro **Introduction.** The mobilization technique currently represents an essential step in peripheral blood stem cell transplantation (PBSCT) and post-chemotherapy granulocytopenia. However, insufficient mobilization represents one of the most important limitations of the standard approach with granulocyte-colony stimulating factor (G-CSF). Mesenchymal stem cells (MSCs) offer a structural (stromal) and functional (paracrine) support for the physiology and homeostasis of the hematopoietic system and their stimulation could have relevant implications for the current mobilization strategies. Our preliminary results *in-vitro* have shown that human chorionic gonadotropin (HCG) treatment leads to the selection of more primitive and potent MSCs from the bone marrow.

Material and methods. We evaluated HCG as a complementary approach for peripheral blood stem cell mobilization *in vivo* on a rat model. To validate the additional mobilization capability of HCG obtained in the rat model, we validated the effect on a mouse model where we evaluated cell surface markers before and after the addition of HCG to G-CSF.

Results. Our approach showed a superior mobilization capability of HCG+G-CSF than G-CSF alone for the number of monocytes and lymphocytes in the rat model. The effect in the mouse model showed a 9.4% increase in CD34 expression and a 21% increase in CD29 expression. As CD34 is expressed on hematopoietic stem cells and CD29 is widely expressed of monocytes and lymphocytes, the results support our findings on the rat model, confirming an increased capability of HCG to stimulate the additional mobilization of hematopoietic stem cells, monocytes and lymphocytes.

Conclusions. Our findings have relevant clinical implications residing in the potential of improving the outcomes of PBSCT by increasing the mobilization of hematopoietic stem cells and for reducing infectious complications following post-chemoterapy granulocytopenia by mobilizing monocytes and lymphocytes more efficiently. This prompts for the validation of the mobilization capability of HCG+GCSF combination in a proof-of-principle feasibility clinical trial.

miRNAs – the masterminds that regulate colorectal cancer patients' response to therapy

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Corresponding Author: Roxana-Maria Cojocneanu e-mail: roxana.cojocneanu@umfcluj.ro **Introduction.** According to the latest statistic by Globocan 2020, colorectal adenocarcinoma (CRC) is the most frequent type of cancer of the digestive system, ranking third in terms of incidence, and second in terms of mortality across the globe, for both sexes, with the highest number of cases observed in the more developed areas of the world. It is the second type of cancer that affects the female population, and the third in men, with alarmingly high incidence and mortality rates. When diagnosed in its early stages, the success rates of treating colorectal cancer are high, but most patients are usually detected in late stages. Therefore, an essential concern is the identification of the most important molecular mechanisms involved in the response to therapy.

miRNAs have significant roles in all cancer related aspects, from tumorigenesis to progression, including the organism's reaction to treatment. The main objective of our study was the identification of circulating miRNA profiles specific for CRC, for a better understanding of the molecular mechanisms and signaling pathways that motivate the response to therapy and the activation of resistance.

Methods. The microarray experiment was conducted on a total number of 55 CRC plasma samples, of which 17 came from patients who underwent chemotherapy. Additionally, TCGA data on miRNA and gene expression for CRC patients was downloaded from the UCSC platform as a data matrix containing normalized reads, together with pertinent clinical information. Bioinformatics analyses were performed using the GeneSpring GX software, alongside various other local and online tools.

Results. Comparing the profiles of treated versus untreated patients, the analyses revealed a significant number of differentially expressed miRNAs, many of which were consistent with online data regarding CRC development and progression (miR-34a, miR-210, miR-21), while others were involved in drug resistance mechanisms (miR-29b, miR-30c, miR-181a). Additional in silico analyses were performed, including target genes identification, or the most significant gene ontology terms, and signaling pathways.

Conclusions. miRNAs are important overseers of cell fate, integrating all its biological roles, with great potential for cancer management. By integrating our results with the ones presented in literature, we concluded that circulating microRNA profiles give important clues regarding CRC patients' progression and response to therapy.

The functional and molecular effects of Obatoclax mesylate on NSCLC cell lines

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Introduction. Non-small cell lung cancer (NSCLC), is one of the most frequent malignancies in both men and women and is responsible for a high degree of cancerrelated morbidity and mortality. Nonetheless, even with the increased interest towards this disease, there has not been a therapeutic regimen that can reliably cure NSCLC in



Corresponding Author: Maria-Ancuța Jurj e-mail: anca.jurj@umfcluj.ro advanced stages. Thus, more work has to be done in determining what new drugs can be applied in this malignancy. One potential candidate is represented by Obatoclax mesylate, a synthetic small molecule, which modulates the activity of Bcl-2, Bcl-xL and Mcl-1, inducing apoptosis in the malignant cells. Thus, the aim of this study was to determine the effects of Obatoclax mesylate in an *in vitro* setting.

Methods. In this study, we investigated the cytotoxic effect of Obatoclax mesylate through MTT. We further assessed the effects of Obatoclax mesylate on nuclear morphology, adhesion and migratory potential, using fluorescence microscopy. Additionally, we analysed the altered mRNA levels between the experimental conditions using microarray. Bioinformatic tools were used to analyze and identify the main altered transcripts in lung cancer after therapy with Obatoclax mesylate.

Results. Cellular viability and cytotoxicity after treatment with Obatoclax mesylate, were investigated through MTT where the results showed that the therapeutic agent exhibited significant effects on the viability of NSCLC cells. Assessing the frequency of apoptotic events in Obatoclax mesylate treated and untreated cells, we observed a significant increase in the number of apoptotic events in treated cells. Further, we wanted to determine other functional effects of Obatoclax using scratch assay, and we observed that treated cells have a slower migration rate compared to untreated cells. Moreover, to determine the effects of Obatoclax mesylate at a transcriptome level we performed microarray to determine the differences between treated and untreated cells, revealing genes that were significantly up- and down-regulated.

Conclusions. Thus, in the current study we showed that NSCLC cells are affected by Obatoclax which alters important biological processes and molecular pathways. Because of this, it is possible that Obatoclax has the potential to have an effect on murine models of NSCLC and, further down the line, in clinical trials.

miRNAs: patterns in skin cancer

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Introduction. Skin cancer is the most common cancer worldwide, with a rapidly increasing incidence and consistent mortality. The uncontrolled and invasive proliferation of melanocytes, the pigment cells in the basal layer of the epidermis, can lead to the development of melanoma, a very aggressive form of skin cancer. In recent decades, the incidence of this disease has increased considerably, being the most lethal form of all skin cancers. In this context, the discovery of the microRNAs, short sequences of 19-25 nucleotides that do not codify proteins represents a potential molecular source of information for specific malignancy patterns.

Material and methods. Our study comprised 24 malignant melanoma and 8 benign nevi. We used the microarray technology to identify the profiling of miRNAs in both diseases. Based on the bioinformatic analysis we were able to separate three different evaluations based on the level of expression of the miRNAs on melanoma and nevi, but also based on the patients' sexes.

Results. We were able to identify 12 non-coding RNAs known as under expressed and 45 overexpressed, and together with this profiling, we established the sex-specific profile. We aim to identify and validate specific miRNAs that can discriminate between malignancy and nontumoral skin cancers. Together with the IHC

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Conclusion. Significant differences found between cancer cells and nevi and between women and men in microRNA expression profile makes us understand that these short sequences that target a multitude of genes should be considered when tumor samples characterization is estimated by high-throughput methods.

Genetic alterations evaluation in myelodysplastic syndromes

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Corresponding Author: Laura Ancuța Pop e-mail: laura.pop@umfcluj.ro **Introduction.** Myelodysplazic syndrome diseases (MDS) are hematological disorders that are characterized by a phenotypically heterogeneous disease. The main methods used for MDS are morphological dysplasia and cytopenias abnormalities. This disorder is diagnosed mainly in elderly patients and in some cases it can evolve in acute myeloid leukemia. In our study we evaluate the genetic and fusion driver genes alterations in 19 MDS patients.

Material and methods. For the evaluation of the genetic and translocation alterations we used the Oncomine Myeloid Research panel on the Ion Torrent PGM sequencer. This panel evaluates genetic alterations in 40 genes, alterations in expression levels for 5 genes and alterations in 29 fusion driver genes.

Results. From the 19 tested samples, 3 samples presented no alteration, while the rest presented only genetic alterations. We identified mutations in 11 genes and a total of 28 mutations, the more frequently mutated genes were: *TET2*, *SF3B1* and *ASXL1*. Also three genes presented the same mutation in more than one samples, these are: *JAK2* mutation c.1849G>T in 3 samples, *SF3B1* mutation c.2098A>G in 3 samples and *SRSF2* mutation c.284C>A in two samples.

Conclusions. A statistically significant correlation was observed between *TET2* mutations and *JAK2* and *SF3B1* mutations. Patients with *TET2* mutations show a worst overall survival than patients that do not present this type of mutation.

Circulating microRNAs as possible biomarkers for lung cancer

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2) Department of Bronchology, Leon Daniello Pneumophysiology Clinical Hospital, Cluj-Napoca, Romania **Introduction.** Worldwide the high incidence and mortality rates in lung cancer show that this malignancy continues to affect a large fraction of the population, placing 2nd worldwide. Thus, it is imperative to improve the existing diagnosis and, develop minimal invasive approaches for lung cancer patients to benefit from therapy to the highest extent. Recent studies show that circulating miRNAs give important information regarding lung cancer development and progression. In our study, we identified some microRNAs as potential actors for malignity in this pathology. We used bioinformatics tools to identify two new genes related to the miRNAs panel,



Corresponding Author: Lajos-Zsolt Raduly e-mail: lajos.raduly@umfcluj.ro supporting the continuous interplay between coding and non-coding genes.

Material and methods. A total of 89 patients with the diagnosis of lung cancer (NSCLC and SCLC) were enrolled in our study. For the control group, we collected blood, serum, plasma from 30 healthy subjects matched with the plasma samples from patients. We collected from each patient blood, plasma, as well as matched pairs of lung tumors and normal adjacent tissues. The samples were collected and stored according to the hospital protocol (the informed consent and study were approved by the ethical committee of Iuliu Hatieganu UMPh and Leon Daniello Pneumophysiology Hospital).

Results. Three miRNAs (miR-21-5p, miR-181a-5p and miR-155-5p) were analyzed through qRT-PCR on 89 lung cancer plasma samples (n=64 NSCLC and n=25 SCLC) / healthy control plasma samples (n=30 controls for NSCLC/25 controls for SCLC) and 81 matched pairs of tumor and normal adjacent tissues (n=66 NSCLC and n=15 SCLC) fresh frozen.

We identified two new genes targeted by miR-21 and miR-155, CKAP5 and LPGAT1, based on the IPA software analysis.

Conclusions. The qRT-PCR analysis performed compared the lung cancer plasma samples with healthy controls. The three miRNAs showed an altered expression with statistical significance (p-value < 0.05, fold change > 2.0). From these, miR-21-5p and miR-155-5p were up-regulated and miR-181a-5p was down-regulated, in plasma. Similar results were obtained in tissue samples for both miR-21-5p and miR-155-5p, apart from miR-181a-5p that shows an increase in the expression level (the interpretation of the data must be validated in a larger patient's cohort). The miRNAs were further analyzed in what concerns their putative target genes, as well as the canonical pathways in which they are involved. As expected, the most frequently altered biological processes were associated with cancer, cell growth and migration, apoptosis, and inflammation. Based on the bioinformatics analysis we discovered that CKAP5 and LPGAT1 are important genes targeted by all three miRNAs: miR-21-5p, miR-155-5p and miR-181a-5p.

By integrating and interpreting the results obtained in our study with the ones presented in the literature, we concluded that circulating microRNAs have the potential to be used as biomarkers for the diagnosis and characterization of lung cancer.