COMENIUS UNIVERSITY IN BRATISLAVA

JESSENIUS FACULTY OF MEDICINE IN MARTIN

XXXIX. STUDENT SCIENTIFIC CONFERENCE

PROGRAM and ABSTRACTS

April 25, 2018

Martin, SLOVAK REPUBLIC

XXXIX. Student Scientific Conference
Jessenius Faculty of Medicine in Martin
Comenius University in Bratislava

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PROGRAM AT GLANCE

Date: April 25, 2018

Place: Aula A Novomeského 9, Martin
Aula B Novomeského 9, Martin

Registration: April 25, 2018, 7.30 or before the beginning of your section

Opening ceremony	(Aula A – Novomeského 9)	**08.00 – 08.10**

Aula A

A1: Section of Clinical Disciplines	08.20 – 10.35
- coffee break	
A2: Section of Non-Medical Study Programmes	11.00 – 12.25
- coffee break	

Aula B

B1: Section of Theoretical Disciplines	08.20 – 10.00
- coffee break	
B2: Section of Pre-Clinical Disciplines	10.15 – 11.15
- coffee break	
B3: Section of Molecular Medicine	11.30 – 12.45

Closing ceremony	(Aula A – Novomeského 9)	**13.00**

Duration of lectures: **8 minutes, discussion – 4 minutes**

Language: Slovak, Czech or English

PROGRAM IN DETAILS

„AULA – A“

SECTION OF CLINICAL DISCIPLINES

(8.20 – 10.35)

THROMBIN RECEPTOR AGONIST PEPTIDE AND THROMBIN–INDUCED PLATELET AGGREGATION IS REDUCED IN PATIENTS RECEIVING DABIGATRAN **Linda Soršáková** Tutors: [1]Juraj Sokol, MD, PhD; [2]František Nehaj, MD; [1]Jela Ivanková, MA [1] Department of Haematology and transfusion Medicine, JFM in Martin, CU in Bratislava [2] 1st Department of Internal Medicine, JFM in Martin, CU in Bratislava	**22**
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„AULA – A“ **SECTION OF NON-MEDICAL STUDY PROGRAMMES** (11.00 – 12.25)	
FEAR OF CHILDBIRTH: PSYCHOSOCIAL FACTORS AND ASSOCIATION WITH PREVIOUS CHILDBIRTH EXPERIENCE **Lenka Dendisová** Tutor: Mgr. Zuzana Škodová, PhD. Department of Midwifery, JFM in Martin, CU in Bratislava	**24**

„AULA – B“

SECTION OF THEORETICAL DISCIPLINES

(8.20 – 10.00)

POLYMYXIN B IMPROVES THE EFFICIENCY OF SURFACTANT TREATMENT IN ENDOTOXIN-INDUCED LUNG INJURY **Katarína Maťašová** Tutors: RNDr. M. Kolomazník, PhD. [1, 2], RNDr. J. Kopincová, PhD. [1, 2] [1]Department of Physiology, JFM in Martin, CU in Bratislava [2]Biomedical Center Martin, JFM in Martin, CU in Bratislava	**41**
GENDER DOES NOT INFLUECE COUGH RESPONSE IN GUINEA PIGS WITH MODELLED RESPIRATORY PATHOLOGY **Aleksander Sorkness** Tutor: MUDr. Tomáš Buday, PhD. Department of Pathophysiology, JFM in Martin, CU in Bratislava	**42**
THE EFFECT OF MORIN AND EXPERIMENTALLY INDUCED ALLERGIC INFLAMMATION OF THE AIRWAYS **Dávid Zima** Tutors: assoc. prof. RNDr. Soňa Fraňová, PhD.; Mgr. Ivana Kazimierová, PhD. Department of Farmacology, JFM in Martin, CU in Bratislava Biomedical Center Martin, JFM in Martin, CU in Bratislava	**43**
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CYTOTOXIC EFFECT OF THE APOPTOTIC INHIBITORS IN HUMAN GLIOBLASTOMA CELLS **Sabína Baroniaková** Tutors: doc. RNDr. Jozef Hatok, PhD. Department of Medical Biochemistry, JFM in Martin, CU in Bratislava	**44**

AWARDING AND CLOSING CEREMONY

(13:00)

NOVOMESKÉHO 9, AULA A

ABSTRACTS

All abstracts are available in English at http://www.jfmed.uniba.sk/veda/svoc/

FACTORS INFLUENCING THE RESPONSE TO GROWTH HORMONE THERAPY IN CHILDHOOD

Andrea Ďuranová, Viktória Maťašová

Tutors: doc. MUDr. Miriam Čiljaková,, PhD.; MUDr. Jarmila Vojtková, PhD.

Clinic of Children and Adolescents, Comenius University in Bratislava, Jessenius Faculty of Medicine and University Hospital in Martin

E-mail contacts: miriam.ciljakova@jfmed.uniba.sk; vojtkova@jfmed.uniba.sk
andrejka.duranova@gmail.com; matasovaviktoria@gmail.com

Introduction: Indications for growth hormone (GH) therapy in childhood include GH deficiency, Turner syndome, SHOX gene deficiency or short stature in children born small for gestational age. Short-term hypoglycemia is strong stimulation factor for releasing of GH, so this principle in used in glucagon stimulation test (GST) and insulin tolerance test (ITT) to verify GH deficiency.

Methods: 37 pediatric patients (19 girls,18 boys; age at the begining of treatment 7,7±3,1 years) who were treated with GH during 2017 were enrolled to the study. Data were obtained by retrospective analyse of medical records of all patients. Serum concentrations of minimum glucose, maximum GH and maximum cortisol response were noted in GST and ITT. Basic anthropometric parameters were noted before GH therapy, after every 3 months during the first year of treatment and after the second year of treatment. Hormonal biochemical parameters (IGF-1, IGFBP3, TSH, free thyroxin, vitamin D) were noticed before GH therapy and growth factors also after each year of GH therapy. Children with abnormal concentrations of thyroid hormones or with thyroid diseases were excluded from the study.

Results: During ITT, glycemia was significantly lower compared to GST ($p<0,0001$). Significantly higher response of GH and cortisol were found in GST compared to ITT ($p=0,008$ and $p=0,08$, respectively). Medium negative correlation was found between maximum GH concentration in GST and the patient´s height after the first 3 months and also after the first year of treatment ($r=-0,31$ and $r=-0,26$, respectively). Height increment after the first year of treatment negatively correlated with baseline TSH ($r=-0,27$).

Conclusion: According to our pilot results, greater height increments were found in patients with lower maximum GH concentration in GST (with more serious GH deficiency) and with lower TSH. GST seems to be more safe and effective compared to ITT, even ITT is considered as a gold standard in diagnosis of GH deficiency. Further studies are needed to clarify the role of GST in childhood.

PRESENT STATE OF SURGICAL TREATMENT OF PERITONEAL MALIGNITY IN THE CZECH REPUBLIC

Barbora Fučeková, Matúš Sloviak

Tutor: MUDr. JUDr. Dušan Klos, Ph.D.

1st Department of Surgery, Palacký University Olomouc, Czech Republic

E-mail contacts: barbora.fucekova@gmail.com, matussloviak@gmail.com, dusan.klos@fnol.cz

Introduction: Peritoneal surface malignancies are formed by a wide range of epithelial and mesenchymal tumors. Their incidence is very low. The primary tumors such as pseudomyxoma peritonei and diffuse malignant peritoneal mesothelioma are much more rare than secondary forms. The most common secondary forms are colorectal, gastric and ovarian peritoneal carcinomatosis. The therapy is multimodal and it was developed by Paul Sugarbaker in the 1980's as a combination of cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC).

Material and methods: Retrospective evaluation of patient therapy results after CRS and HIPEC for 2016 at 1st surgical clinic in Olomouc.

Results: There were 13 surgeries performed of peritoneal carcinomatosis by the HIPEC method in the 2016. 9 of which were performed on women and 4 on men. Mortality was 7,7% and morbidity was 7,7%.

Conclusion: HIPEC and CRS are currently performed in the Czech Republic by four clinics – Department of Surgery 1st Faculty of Medicine, Bulovka Hospital, Thomayer hospital and University hospital in Olomouc. In the Czech Republic the main method of treatment is systematic chemotherapy but the treatment results in some types of tumors are so persuasive that HIPEC and CRS will become standard treatment method for certain oncology patients.

ANALYSIS OF THE INFLUENCE OF SELECTED RISK FACTORS ON THE ONSET OF ARTERIAL AND VENOUS THROMBOSIS IN SLOVAK POPULATION

Katarína Chromeková, Kristína Vajdová

Tutor: MUDr. Lucia Stančiaková, PhD.

Department of Haematology and Transfusiology, JFM in Martin, CU in Bratislava

E-mail contacts: katkach15@gmail.com, kikav928@gmail.com,

stanciakova@jfmed.uniba.sk

Introduction: The development of venous thromboembolism (VTE), as well as arterial thrombosis could be associated with inherited and acquired risk factors. However, unfortunately, despite the current progress of the science and research, many questions still remain unanswered. For instance, some patients with several risk factors for VTE will not have a thrombotic event, while the others developed repeated thromboembolic episodes without known risk factor.

Material and methods: The authors analyzed the risk factors and circumstances of the development of thromboembolic events in the patients followed-up in the National Centre of Haemostasis and Thrombosis in Martin taking into accout their thrombophilic states and acquired changes of haemostasis.

Results: In the complex analysis, the authors confirmed that acquired clinical conditions, such as polytrauma, surgical intervention, renal failure, immobilization, treatment, pregnancy, inflammation, travelling or malignancy increased the risk of arterial or venous thrombosis. In the subsequent prospective study of the acquired changes of laboratory parameters in one of these states – in the course of pregnancy, the significant ($p < 0.05$) decrease in the levels of protein S and antithrombin and increase of the coagulation factor VIII activity and D-dimers influencing the risk of thrombosis development was found. In 41 of 61 pregnant patients, the dose of thromboprophylactic drug could be modified according to our results.

Conclusion: Monitoring of prothrombotic changes of haemostasis may be used for the prediction and prevention of the life-threatening thromboembolic episodes. Therefore, results of these laboratory findings could be used for the individualization of the primary or secondary thromboprophylaxis and thus increase the quality of life of affected patients.

Acknowledgements: The authors thank the support of the projects of Scientific Grant Agency Vega 1/0168/16 and Agency for the Support of Research and Development APVV-16-0020.

CHANGES OF SELECTED IMMUNE PARAMETERS DURING SUBCUTANEOUS ALLERGEN IMMUNOTHERAPY WITH HYMENOPTERA VENOM

Alžbeta Kubaľáková

Tutors: doc. MUDr. Miloš Jeseňák, PhD., MBA

Clinic of Children and Adolescents, JFM in Martin, CU in Bratislava, UH in Martin

E-mail contacts: alzbeta.kubalakova@gmail.com; jesenak@gmail.com

Introduction: All stinging insects causing allergic reactions belong to a series of hymenoptera, mostly wasps and bees. Allergic reactions to insect stings can cause broad variety of symptoms from local extreme swelling to systemic anaphylactic reactions. Annually dies in Slovakia on average one patient. The only causal therapy with life-saving preventive effect is subcutaneous specific allergen immunotherapy (SAIT) with the standardized hymenoptera venom.

Material and methods: In our study, we aimed to study the clinical and selected laboratory characteristics of the patients with the history of systemic anaphylactic reactions after hymenoptera sting (wasp or honey bee). We analyzed the tolerance and efficacy of subcutaneous allergen immunotherapy and its effect on selected laboratory markers of allergic inflammation.

Results: Altogether, 21 patients with average age 34±13.5 years were enrolled (7 women and 14 men). 48% of the patients were allergic to wasp and 52% to bee venom. More women were allergic to bees, whereas more men reacted to wasp sting. Regarding the comorbidities, allergic rhinitis was present in 52% and urticaria in 38% of patients. In both cases, after bee and wasp sting, 92% of the patients yielded skin symptoms (hives, generalized pruritus). In 50% of the wasp bites, hypotension prevailed and after bees bites swelling of the oropharynx was more common. 57% of the patients tolerated SAIT without any side effects. One third showed skin reaction at the site of injection administration. During the initial phase of SAIT, eosinophilic cationic protein and total IgE were increasing with subsequent decline during the maintenance phase. During ongoing SAIT, specific IgG4 against both allergens continuously increased in the majority of the patients.

Conclusion: Specific allergen therapy is the only causal therapy for the patients with anaphylactic reaction after hymenoptera sting. In our cohort, SAIT was generally well tolerated and had minimum side effects. Natural exposure of 5 patients during SAIT did not cause anaphylaxis. Moreover, SAIT was accompanied with the beneficial changes of selected laboratory allergic markers.

TONSILLECTOMY VERSUS TONSILLOTOMY IN CHILDHOOD

Adriána Kumorová

Tutors: MUDr. Gabriela Bugová, PhD.; MUDr. Barbora Uhliarová, PhD.

Clinic of Otorhinolaryngology and Head and Neck Surgery, JFM in Martin,CU in Bratislava

E-mail contacts: gaminar@centrum.sk; b.uhliarova@gmail.com;

adriana.kumorova@gmail.com

Introduction: The palatine tonsils are dense compact bodies of lymphoid tissue and occupy the tonsillar fossa between the diverging palatoglossal and palatopharyngeal arches. The medial surface of the tonsils consists of 20 – 30 tonsillar crypts covered by stratified squamous epithelium. Disrupted epithelium of the crypts allows migration of lymphocytes. Lymphocytes bring the antigen information back and participate in the immune response of the organism. Tonsillectomy (extracapsular) is a surgical procedure to remove the tonsils. Tonsillotomy (intracapsular) is a partial excision of the tonsils.

Methods: Forty-eight children with diseases of palatine tonsils (recurrent tonsillitis/ tonsillar hypertrophy) indicated for their surgical treatment were enrolled in the prospective study. Nasopharyngeal and tonsillar swab cultures during their surgery and 3 months after surgery were performed. Postoperative course included dysphagia, odynophagia, need for analgetics, occurence of complications and return to usual activities were investigated.

Results: Before surgery in children with recurrent tonsillitis the isolated pathogenes were Streptococcus pyogenes and Stafylococcus aureus. After surgery predominantly physiological microorganisms were detected. The most common postoperative complications were odynophagia and dysphagia. There were no more problems with snoring and air-way obstruction in children after tonsillotomy. The least occuring complications were bleeding and infection.

Conclusion: The reason children need to have a tonsillectomy might be recurrent tonsillitis, breathing problems related to swollen tonsils, obstructive sleep apnea syndrome or peritonsillar abscess. Due to the very intimate relationship of the tonsils to the large vessels and the airways, life-threatening complications can occur. At present, there is a trend towards less invasive partial performance - tonsillotomy especially in children. In particular the aim is to reduce the incidence of complications. Tonsillotomy is the first line treatment for snoring and apnea syndrome.

THE FIRST EVIDENCE: DETERMINATION OF EDOXABAN CONCENTRATIONS IN HUMAN PLASMA BY AN AUTOMATED ANTI-FACTOR Xa CHROMOGENIC ASSAY

Martin Jozef Pec[1]

Tutors: Michal Mokan, MD, PhD[1]; František Nehaj, MD[1]; Juraj Sokol, MD, PhD[2];

[1]1st Department of Internal Medicine, JFM in Martin, CU in Bratislava

[2] Department of Haematology and Transfusiology, JFM in Martin, CU in Bratislava

E-mail contacts: matopec@hotmail.com; michalmok5@gmail.com; fnehaj@gmail.com; Juraj.Sokol@jfmed.uniba.sk

Introduction: Atrial fibrillation (AF) is the most common cardiac arrhythmia. The risk of AF in patients ≥ 40 years old is estimated at 25%. Stroke is a major complication associated with AF. Patients with AF have a four- to five-fold increased risk of stroke. Currently, the new oral anticoagulant (DOAC) called edoxaban has been approved as alternative to warfarin in patients with AF. Edoxaban is approved for the treatment of deep vein thrombosis, pulmonary embolism, along with prevention of venous thromboembolism in patients with AF. The main outcome of the project is the development of new monitoring method, which will allow rapid assessment of coagulation activity in an emergency situation (major bleeding, thromboembolism and death from any cause).

Material and methods: Patients with non-valvular AF were enrolled. Edoxaban was administered 30 mg or 60mg once-daily dose (at 7:00 AM). Serial blood samples were collected for analysis by the anti-FXa assay before drug dose administration (sample 1, at 7:00 AM) for the assessment of the edoxaban trough level and 2 hours later (sample 2, at 9:00 AM) for the assessment of the edoxaban peak level. Edoxaban equivalent levels were assessed using a commercially available chromogenic anti–factor Xa assay with an edoxaban-specific setup tested by coagulometer BCS-XP Siemens.

Results: The majority of patients were male (n=9, 56%) and the rest were female (n=7, 44%); patients received once-daily edoxaban 60 mg (n=11, 69%) or 30 mg (n=5, 31%). The mean ± standard deviation age was 67.6 ± 10.01.

Conclusion: In this study, an anti-FXa chromogenic assay with edoxaban-specific calibrators and controls demonstrated good accuracy in estimating edoxaban concentrations. Anti-FXa assays for measuring direct oral anticoagulants are clinically useful. This was the first evidence of determination method of edoxaban in plasma levels in Slovak and the Czech Republic.

CLINICAL, RADIOLOGICAL AND LABORATORY PREDICTORS OF SEVERE COURSE OF MULTIPLE SCLEROSIS

Lívia Ridzoňová

Tutors: [1]Ema Kantorová, MD., PhD.; PhD.; [2]Ing. Petra Hnilicová, PhD.;
[1]Prof. Egon Kurča, MD., [3]ass. prof. MSc. Wolgang Bogner, PhD.

[1]Department of Neurology, JFM in Martin, CU in Bratislava
[2]Biomedical Centre, JFM in Martin, CU in Bratislava
[3]TheHigh-Field MR Centre, Medical University of Vienna
E-mail contacts: liviridzonova@gmail.com, kantorova@jfmed.uniba.sk

Introduction: Multiple sclerosis (MS) is a disease, which affects the brain as a whole. MS may cause physical disability and decline of cognitive functions, resulting in severe disease course.

Material and Methods: We included 16 randomly selected MS patients (PAT) and 16 healthy volunteers (CON). All participants underwent magnetic resonance imaging (MR) examination of the brain in “High Field MR Centre” in Vienna. The examination involved volumetric measures of particular brain structures (VOL). All participants underwent a test for cognitive functions – the Single Digit Modality Test (SDMT). Disability of PAT was evaluated by Expanded Disability Status Scale (EDSS). Results of VOL and SDMT were compared between the groups and then correlated with SDMT and EDSS.

Results: PAT and CON differed in results of SDMT (p= 0,047 t-test). In PAT compared with CON, smaller brain volumes were found in nc. accumbens (p=0,04..0,002), left putamen (p=0,029), right thalamus (p=0,018), in cerebellar cortex (p=0,026), and brainstem (p=0,05). EDSS correlated with volume of left nc. caudatus (p=0,01, r= - 0,6) and brain vessels (p=0,05, r=0,049). SDMT in PAT correlated with cerebellar cortex (p=0,03, r= -0,53), but in CON it corellated with left nc.accumbens (p=0,002, r= -0,7) and left pallidum (p=0,01, r= -0,59).

Conclusion: A predictor of a more severe course of SM was a reduction of volume of the subcortical grey, but not white matter. It points out a neurodegenerative component of the disease. The correlation between the volume of vascular structures and the range of disability raises question about circulatory defect in MS. Differences between PAT and CON in correlation between the cognitive function tests and the brain structures require further analyses.

The study was supported by grant VEGA 01/0287/16.

EVALUATION OF ATHLETE'S POSTURAL HABITS AFFECTED BY REGULAR RUNNING THROUGH THE STANDART OVAL TRACK BEND

Anna Selníková

Tutors: Ing. Mgr. Jakub Wrona

Department of Rehabilitation, Faculty of Medicine University of Ostrava

E-mail contacts: selnikova.a@gmail.com, Jakub.Wrona@osu.cz

This bachelor thesis addresses the influence of repeated running through the bend section of a standardized track and field200 meters indoor oval. Variables that affect stressed postural habits e.g. inappropriate loading of lower limbs, foot drop, length and frequency of the step in the curve have been evaluated. These aspects have been analysed by kinesiology assessment that considered parameters of the training oval also from the biomechanical point of view. Twelve athletes specialized in 400 meters track, in the age group 18-22 years have been examined.

Main objective of this thesis is to draw attention of possible injuries that come into existence from one way running to coaches, physiotherapists, athletes and other interested people. Results have shown unilateral overloading of musculoskeletal system in long-term regular training. This topic has the potential for further development in the form of specific studies.

IMPACT OF DECOMPRESSIVE CRANIECTOMY ON DYNAMICS OF TRAUMATIC AND NON-TRAUMATIC INTARCEREBRAL HAEMATOMAS

Jakub Soršák

Tutors: Martin Hanko, M.D.; Assoc. prof. Branislav Kolarovszki, M.D., Ph.D.

Clinic of Neurosurgery, JFM in Martin, CU in Bratislava, University Hospital in Martin

E-mail contacts: jakubsorsak@gmail.com; m.hanko.to@gmail.com;

kolarovszki@jfmed.uniba.sk

Introduction: Postoperative expansion of intracerebral haemorrhagic mass lesions may represent a threatening event in patients after decompressive craniectomy (DC). We aimed to assess the dynamics of intracerebral lesions' volume and its potential relationship to patients' outcome.

Material and methods: We retrospectively reviewed a group of 22 patients with intracerebral haemorrhagic mass lesions who underwent DC at our clinic during years 2015-2017. A control group consisted of 26 patients who were treated in a non-surgical way. Preoperative CT findings were compared with control CT examination that followed after 2±1 days. Patients' outcome was quantified using the Glasgow Outcome Scale. Statistical analysis was performed using non-parametric tests.

Results: In patients with intracerebral haemorrhagic lesions <25 cc the DC decreased the midline shift (p=0.048), increased the thickness of brain oedema (p=0.002) and resulted in increase of intracerebral bleeding volume when compared to preoperative findings (p=0.009) and control group (p=0.013). This was not observed in patients with larger intracerebral lesions. Progression of brain oedema thickness was also significant in patients with intracerebral <25 cc who have not undergone DC (p=0.002). Patients with intracerebral haemorrhagic lesions <25 cc who underwent DC acquired more favourable outcome than patients with larger lesions (p=0.024).

Conclusion: Increase of perifocal brain oedema occurs in patients with intracerebral haemorrhagic lesions <25 cc regardless of whether they undergo DC or not. DC effectively decreases midline shift in patients with intracerebral haemorrhagic lesions <25 cc and tends to increase the lesion's volume. Despite of such findings, volume of intracerebral haemorrhagic lesion <25 cc seems to be a positive prognostic factor in patients undergoing DC.

THROMBIN RECEPTOR AGONIST PEPTIDE AND THROMBIN–INDUCED PLATELET AGGREGATION IS REDUCED IN PATIENTS RECEIVING DABIGATRAN

Linda Soršáková

Tutors: [1]Juraj Sokol, MD, PhD; [2]František Nehaj, MD; [1]Jela Ivanková, MA

[1] Department of Haematology and Transfusiology, JFM in Martin, CU in Bratislava

[2] 1st Department of Internal Medicine, JFM in Martin, CU in Bratislava

E-mail contacts: lsorsakova@gmail.com; juraj.sokol@jfmed.uniba.sk

Introduction: The availability of direct oral anticoagulants has caused a paradigm shift in thrombosis management. The direct thrombin inhibitor dabigatran seems to obstruct tenase complex by inhibiting thrombin generated in the initial phase and feed back to the amplification phase of cell-based coagulation reactions. However, it is still not fully understood if and how dabigatran impact platelet function. This observational study aimed to assess in vitro platelet function in patients with atrial fibrillation receiving dabigatran.

Material and methods: Platelet aggregability was tested with platelet-rich plasma using platelet aggregometry (PACKS-4 aggregometer). Blood samples were stimulated with thrombin receptor agonist peptide and γ-thrombin.

Results: A total of 60 patients with nonvalvular atrial fibrillation were enrolled. The mean age was 71.82 years (range: 50-88 years), 30 patients were women, and the mean CHA2DS2VASc score was 3.6. All patients began treatment with dabigatran as initial anticoagulant treatment. The minimum term use of dabigatran was 18 days. Dabigatran doses were 110 mg (57.14%) or 150 mg (42.86%) twice a day. The TRAP or thrombin-induced platelet aggregation was significantly lower 2 hours after taking dabigatran compared to baseline value (79.39% [13.38] vs 90.14% [10.5]; 8.8% [5.5] vs. 29.3% [20.6]).

Conclusion: The TRAP and thrombin-induced platelet aggregation was reduced in cardiovascular patients 2 hours after receiving dabigatran. Our findings could have some important clinical implications because platelet aggregation and coagulation cascade are affected at the same time.

EXTRACELLULAR DNA AS A PROGNOSTIC AND THERAPEUTIC TARGET IN PATIENTS WITH INFLAMMATORY BOWEL DISEASES

Kristína Tomová[2], MUDr. Zuzana Lešková[1], Prof. MUDr. Tibor Hlavatý[1], PhD., Mgr. Barbora Konečná[2], PhD.

Tutors: Mgr. Janka Bábíčková[2], PhD., RNDr. Ľubomíra Tóthová[2], PhD.

[1]V. Department of Internal Medicine, Faculty of Medicine, CU and UH Bratislava

[2] Institute of Molecular Biomedicine, Faculty of Medicine, Comenius University

E-mail contacts: tomovakristinka@gmail.com, jana.babickova@gmail.com, tothova.lubomira@gmail.com,

Introduction. The incidence of inflammatory bowel diseases is increasing. The exact pathogenesis of this inflammatory disorder remains not well understood. Several studies found that tissue damage and cell death lead to increase in extracellular DNA (ecDNA) content. EcDNA, as a non-cellular component of DNA that is present in plasma, is immunogenic and further might potentiate the course of the disease. The activity of DNase can partly modulate this immunogenic effect.

Aim. The aim of this study was to compare the concentrations of ecDNA in patients with inflammatory bowel disease and healthy subjects and to describe DNase activity in plasma.

Methods. The blood samples were obtained from 39 patients with inflammatory bowel diseases (IBD) and 17 healthy controls. Plasma samples were used for isolation and fluorometric quantification of ecDNA, determination of the concentration of the nuclear and mitochondrial DNA components, and determination of DNase activity. The data were analyzed using one-way ANOVA and ANOVA for repeated measurements. Data is presented as mean + standard deviation. Data were analyzed using GraphPad Prism Software version 6.01.

Results. Collected plasma samples were first divided into two large groups: females and males. Then they were separated according to diagnosis into two groups of patients, ulcerative colitis and Crohn´s disease and healthy controls. No significant differences between the groups in the ecDNA concentration values or in the amount of the nuclear and mitochondrial ecDNA were demonstrated. We observed significantly higher DNase activity in female patients with ulcerative colitis compared to patients with Crohn's disease and healthy controls. For men, such a difference was not recorded.

Conclusion. We found higher DNase activity in female patients with ulcerative colitis. We have not confirmed the hypothesis of increased ecDNA in patients with inflammatory bowel disease (ulcerative colitis and Crohn's disease). Given that this was a pilot study, our results will need to be confirmed after obtaining a larger sample of patients. The collection of new samples is in progress.

FEAR OF CHILDBIRTH: PSYCHOSOCIAL FACTORS AND ASSOCIATION WITH PREVIOUS CHILDBIRTH EXPERIENCE

Lenka Dendisová

Tutor: Mgr. Zuzana Škodová, PhD.

Department of Midwifery, JFM in Martin, CU in Bratislava

E-mail contacts: lenkadendisova.ld@gmail.com, skodova@jfmed.uniba.sk

Aim: Research aim is to explore the association between the level of the childbirth- related fear among pregnant women during the 3rd trimester of gravidity. Research is also focused on differences in the childbirth- related fear depending on age, parity, socio-economic factors, social support and previous birth experience. Another objective of the research was assessing the link between childbirth- related fear and symptoms of depression among pregnant women.

Method: Data collection was carried out at the University Hospital in Martin. The sample includes 136 women (age 29.82±5.68). Questionnaire consists of questions focused on age, parity, socio-economic conditions and social support; Wijma Delivery Expectancy Questionnaire (W-DEQ) was used for assessing the childbirth- related fear; and Edinburg Postnatal Depression Scale was used for assessing the severity of depression symptoms. Descriptive statistics; Student's t-test, ANOVA and correlation analysis were employed.

Results: Results have shown that increased childbirth- related fear (WDEQ>68) occurs in 23.53% of women. Special attention should be paid to the finding that 14.71% women in our sample showed signs of tocophobia (WDEQ>80). Previous birth experience ($F= 0.09$; $p\leq 0.001$), depression ($r=0.44$; $p\leq 0.001$) and social support ($r= -0.27$; $p\leq 0.001$) are significantly related to intensity of childbirth- related fear. Financial situation was the only socio- economic factor statistically significant ($F= 8.49$; $p\leq 0.001$) in relation to childbirth-related fear. There were also differences in level of fear ($t= -2.78$; $p\leq 0.01$) between women, who completed antenatal education and those who didn't.

Conclusion: Results showed that previous birth experience and psychosocial factors such as social support, depression or financial situation are factors which might increase risk of childbirth- related fear, which leads to negative feelings in pregnancy and negatively affects the outcome of birth. Due to negative implications of intensive childbirth-related fear to woman and baby, a relatively high number of women with high level of fear in our sample, as well as a high percentage of women with WDEQ levels indicating tocophobia, is a warning fact.

NURSE'S VIEW ON DIGNITY OF OLDER PEOPLE: DESCRIPTIVE QUALITATIVE STUDY

Laura Chupáčová

Tutor: Mgr. Juraj Čáp, PhD.

Department of Nursing, JFM in Martin, CU in Bratislava

E-mail contacts: juraj.cap@jfmed.uniba.sk; laura.chupacova@gmail.com

Introduction: Old people make up the most numerous group of the patients. At the same time old people represent the most vulnerable group, and therefore it is important to maintain their dignity, as an important part of the nursing care. The goal of the study was to find out how nurses perceive the dignity of old people, and what factors affect it.

Methodology: Qualitative, cross-sectional and descriptive design of the study was chosen. Semi-structured interview for the collection of empirical data and thematic analysis to analyse the data was used. The interviews were realised with 7 nurses in the retirement home for seniors. The inclusion criteria were: achievement of professional competence to practice a nurse's profession, informed consent of respondents, and nursing care of old people for 5 years at least. Before the realisation of interviews the informed consents of the respondents, and the workplace approval were obtained.

Results: We identified the main themes, namely personal dignity, positive and negative factors. Personal dignity included these sub-themes: the life story of patients, to be a necessary and loved, individuality, menschenwürde (human dignity). We identified positive factors which influenced the personal dignity such as: the care factors, support of patients, respect for the personality of patients. As the negative factors we identified: dishonouring communication, personality factors of the patient, the care factors and the physical threat of the patient.

Conclusion: This work can contribute to a deeper reflection on the issue of dignity of the old people, in our socio-cultural context. The results of this work can be used as a base for educational materials for nurses and nursing students, or the management of the workplace. It would be appropriate to realise the research, focused on the patients experience with the dignity, and compare the results with the perspective of the nurses.

SLOVAKIAN MIDWIVES' PERCEPTION OF EMPOWERMENT: NATIONAL SURVEY FROM SLOVAKIA

Eva Vašíčková (rod. Kubenová)

Tutors: PhDr. Mgr. Simona Kelčíková, PhD.

Department of Midwifery, JFM in Martin, CU in Bratislava

E-mail contacts: evakubenova@hotmail.com , simona.kelcikova@jfmed.uniba.sk

Introduction: Midwives are educated to care for women during pregnancy, birth and the postnatal period. The predicted midwifery workforce shortages in our country have serious implications for the care of women. In part this appears to be by a number of factors. For midwives to be able to fulfil their professional role they need to be empowered to do so. The aim of the study was to investigate midwives' perception of empowerment in practice in Slovakia.

Material and Methods: The research has the character of a quantitative cross-sectional study. In September 2017, midwives was sent a questionnaire, which included the Perception of Empowerment in Midwifery scale-R (PEMs-Revised) with demographic questions asked about personal, professional and employment details. Self-administered survey package was distributed to midwives through professional networks in Slovak Republic. Of 2464 eligible midwives, *354* (14,3%) completed the PEMs. For data processing was used the basic descriptive statistics, non-Parametric Kruskal-Wallis test ($p<0,05$) and Spearman**'**s correlation coefficient r(S).

Results: Respondents were predominantly aged 18-49 years and had significant work experience (1-20 years). The Cronbach alpha coefficient was 0.83. Statistically significant differences were recorded comparing scores on all four PEMs-Revised ($p<0,05$) domains. The PEMs showed good psychometric properties with the domains. The highest score was recorded on domains *Skills and Resources* 4.64(±0,78) & *Autonomy* 4.09(±1,08), but only half of midwives (52,55%) in the Slovak Republic perceive autonomy in their work and feel autonomous. The weakest domain are perceived *Manager support* 3.25(±1,34) and *Professional recognition* 3.27(±1,03).

Conclusion: The PEMS showed that, the Slovakian midwives' perception of empowerment at work differed according to midwives' education, age category, division of country, duration of work experience and clinical/ambulant practice. In Slovakia it is necessary to improve *Manager support & Professional recognition* and achieve a better position in the profession of midwife in society. This study supports the psychometric qualities of the PEMs.

SCREENING FOR FALL RISK IN PATIENTS WITH NEUROLOGICAL DISEASE

Jaroslav Madleňák

Tutors: Mgr. Michaela Miertová, PhD.; Doc. Mgr. Ivana Bóriková, PhD.

Department of Nursing, JFM in Martin, CU in Bratislava

E-mail contacts: jaroslavmadlenak@azet.sk; miertova@jfmed.uniba.sk; borikova@jfmed.uniba.sk

Introduction: Patients with some neurological diseases have a predisposition to fall and recurrent falls due to clinical symptomatology. Risk of falling is related to hospitalization in an unknown environment, too. Falls in this patients´ group are due to a combination of several risk factors which can be variety of combine and change during hospitalization and the change of health state of patient. Nurse has an important role in identification of risky patients. For a quick fall risk assessment is recommended to use the screening tool already on admission to hospitalization. The aim of this work was to identify the presence of selected fall risk factors and to realize a fall risk screening.

Material and methods: The sample consisted of 100 patients hospitalized at the Neurological Clinic of University Hospital in Martin. We created a list of selected fall risk factors and used screening tool for fall risk - Morse Fall Scale (MFS) to collect empirical data in adult inpatients.

Results: The sample was consisted of 100 patients (51 men, 49 women) with mean age of 60.0 ± 15.3 (min. 23, max. 92) years. There were fall risk factors: gait and balance disturbance (92%), chronic disease ≥ 4 (80%), pharmacotherapy ≥ 5 drug groups (71%), visual disturbance (61%). Falls history in the past 3 months had 8% patients. The mean score of fall risk by MFS was medium (32.5 ± 16.7, min. 0, max. 75). 26% of patients was at high risk of falling (MFS ≥ 45), mean score by MFS was 55.6 ± 8.0 (min. 50, max. 75).

Conclusion: MFS screening tool is simple and quick for using in nursing practice and allows nurses to identify patients at high risk of falling. Nursing care may be oriented to realization of individualized interventions that reduce this risk.

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EARLY CONTACT OF MOTHER AND CHILD - ATTACHMENT

Andrea Porubská

Tutor: Mgr. Lucia Mazúchová, PhD.

Department of Midwifery, JFM in Martin, CU in Bratislava

E-mail contacts: andrea.porubska2@gmail.com; lucia.mazuchova@jfmed.uniba.sk

Introduction: Safe attachment is one of the most important protective factors for the child's healthy psychosocial development as well as the mental health of women. The aim of this study was to identify the attachment between mother and child, its risk factors and context.

Methodology: There was chosen design of a cross-sectional quantitative study. The study was attended by 200 women, 0-6 weeks postpartum. There was used a postpartum bonding questionnaire (PBQ) (Cronbach´s α = 0,94), which concerned the assessment of four factors: *(1) general factor of attachment quality, (2) rejection and pathological anger, (3) anxiety about the infant, (4) incipient abuse.* The questionnaire was supplemented by questions of its own design, focusing on bonding after birth. The analysis of the obtained data was used for descriptive statistics and induction statistics (Student t-test for two independent selections and analysis of variance - ANOVA).

Results: Correct bonding support following the recommended post-natal procedures was reported by 30,5 % of women. The most frequent reasons for not supporting bonding after birth were the hospital routine, the reluctance and the impatience of health workers. When examining an attachment by a questionnaire PBQ the most high-risk women (9,5 %) were in 1st *general factor,* next in 4th factor *incipient abuse* (5 %), then in 3rd factor *anxiety about the infant* (3,5 %) and least risk women (1,5 %) were in 2nd factor *rejection and pathological anger.* Variable such as *postpartum bonding support* was statistically significant in all factors.

Conclusion: Detection of attachment defects, identification of risk mothers and knowledge of predictors affecting attachment is important for preventing serious health problems in perinatal care, which should be addressed through early intervention. Midwives have an important role to play in developing relationship, providing social support to pregnant women, building the identity of the mother in the period before birth and supporting bonding immediately after childbirth, which has proved to be significant in relation to the attachment.

QUALITY OF LIFE OF PATIENTS WITH THYROID DISORDERS –ThyPRO-39 PILOT STUDY

Bc. Michal Sviatko

Tutors: Mgr. Ivan Farský, PhD.; Mgr. Martina Lepiešová, PhD.

Department of Nursing, JFM in Martin, CU in Bratislava

E -mail contacts: chsmicky@gmail.com; farsky@jfmed.uniba.sk; lepiesova@jfmed.uniba.sk

Introduction: Disorders related to the thyroid gland are common, affecting around 10-15 % of the adult population. Thyroid diseases often require long treatment and control, management of their symptomatology and impact is an integral part of clinical care. Measurement and management of patients' quality of life has become important. The purpose of the study was to evaluate the psychometric properties and validate the Slovak-language version of Quality of Life Questionnaire for Patients with Thyroid Disease ThyPRO-39.

Material and methods: Two independent translators translated English version of questionnaire to the Slovak language and then created reconciled Slovak version of ThyPRO-39. This was sent to the third translator to create back-translated English version. For evaluation of the questionnaire's psychometric properties 56 patients with hypothyroidism due to autoimmune thyroid disease completed Slovak version of ThyPRO-39 and generic instrument WHOQOL-BREF. Statistical psychometric analysis was performed by using IBM SPSS.

Results: The ThyPRO-39 scales have better responsiveness for thyroid disease specific clinical changes than generic instrument WHOQOL-BREF. Results indicated that the ThyPRO-39 has high internal consistency (value of Cronbach's alpha .93; and from .54 to .84 for subscales). All items of questionnaire correlated with total score. Correlations were low to strong, ranging from .27 to .74. Concerning criterion validity, correlations between the ThyPRO39 total score and domains of WHOQOL-BREF were moderate to strong.

Conclusion: The results indicate good psychometric properties for the Slovak-language ThyPRO-39. As compared with full version (85 items), short form ThyPRO-39 offers reduction of respondent burden, potentially increasing response rates. We recommend using ThyPRO-39 in daily clinical practice or in clinical studies among patients with most common benign thyroid diseases.

SATISFACTION OF WOMEN WITH PERINATAL CARE – PSYCHOSOCIAL ASPECTS

Linda Štofaníková

Tutor: Mgr. Lucia Mazúchová, PhD.

Department of Midwifery, JFM in Martin, CU in Bratislava

E-mail contacts: linda.stofanikova87@gmail.com, mazuchova@jfmed.uniba.sk

Introduction: The psychosocial aspects of maternal care are important as well in the psychological as in the somatic area and are an important criterion for women's satisfaction. The aim of the study was to find out the satisfaction of women with care during childbirth considering psychosocial aspects.

Material and methods: For our study was chosen the design of the cross-sectional quantitative study. The study was attended by 360 women after natural birth (average time from birth: 6.22 ± 3.64 SD months). A questionnaire of the CLI-P psychosocial climate questionnaire (Cronbach α = 0,95), validated in the Czech Republic, was used to diagnose the satisfaction of women with care during childbirth and satisfaction considering psychosocial aspects, which assessed 6 factors: (1) empathy of midwives and (2) doctors, (3) superiority and lack of interest, (4) physical comfort and services, (5) woman's control and participation in decision making, (6) reporting of information. Descriptive statistics and ANOVA were used for analysis of received data.

Results: We found out that most women were satisfied with the overall care during childbirth and were satisfied about the psychosocial aspects but about one-third of women were dissatisfied. The worst was the satisfaction with the factor of *woman's* control and participation in decision making, (61.50%) and in the factor of superiority and lack of interest (77.66%). Birth rate and support of post-birth bonding items have been shown to be statistically significant in relation to all examined psychosocial factors.

Conclusions: In spite of the positive outcome, attention should be paid to the psychosocial aspects of health care during childbirth, in particular, to provide emotional support, to change the impersonal and superior approach, to strengthen interventions in the field of involvement of women in codecision, to improve their awareness, to promote bonding and to seek naturalness of birth to be a positive experience for women.

THE EFFECT OF REPERFUSION INJURY ON CALCIUM-REGULATING PROTEINS

Gabriel Brndiar

Tutor: doc. Ing. Zuzana Tatarková, PhD.

Department of Medical Biochemistry, JFM in Martin, CU in Bratislava

E-mail contacts: gabriel.brndiar@gmail.com, tatarkova@jfmed.uniba.sk

Introduction: Calcium (Ca^{2+}) has evolved as global intracellular messenger for signal transduction by reversibly binding to calcium-sensing proteins. In the cardiomyocyte, ion pumps, exchangers and channels keep the cytoplasmic calcium level at rest. The sarcoplasmic reticulum (SR) is an intracellular membrane system in cardiac cells, which plays a pre-dominant role in excitation–contraction coupling and cardiac contractility. Calcium gradient is maintained across the cardiac SR membrane by the Ca^{2+} -ATPase (SERCA2a). SERCA2a actively transports Ca^{2+} into the SR and regulates cytosolic Ca^{2+} concentration, SR Ca^{2+} load and the rate of contraction and relaxation of the heart.

Materials and methods: Isolated Langendorff-perfused rat hearts (6 months old) were subjected to 20 min global ischemia followed by 30 min reperfusion. Temperature and hemodynamic parameters were continuously recorded. Calcium-regulating proteins as well as SERCA2a activity were measured and evaluated in cardiac sarcoplasmic reticulum.

Results: The reperfused hearts showed marked decline in left ventricular developed pressure, maximal rate of contraction (+dP/dt) and relaxation (-dP/dt). SERCA2a expression as well as it's activity was maintained after induced ischemia. Reperfusion induced loss of ryanodine receptor (RyR) in cardiac cells leads to deprivation of Ca^{2} release from SR, which is required for mechanical activity. This was accompanied by potentially protective loss of inhibitory phospholamban. Expression of SERCA2a did not change significantly, but affinity of SERCA2a for Ca^{2+} or ability to bind it, was negatively affected when subjected to higher Ca^{2+}- concentrations.

Conclusion: Since SERCA2a mediated Ca^{2+} transport is responsible for efficient muscle relaxation and maintaining SR Ca^{2+} store, regulation of SERCA2a and its interaction with other Ca^{2+}-related proteins is crucial. These can be modulated by several indirect factors and direct effectors such as protein phosphorylation / dephosphorylation and nitrosylation, thyroid hormones or insulin.

HISTOPATHOLOGICAL CHANGES IN THE RAT BRAIN AFTER FRACTIONATED WHOLE-BRAIN IRRADIATION

Ivana Dlugošová

Tutor: MVDr. Soňa Bálentová, PhD.

Department of Histology and Embryology, JFM in Martin, CU in Bratislava

E-mail contacts: ivka.dlugosova@gmail.com; balentova@jfmed.uniba.sk

Introduction: Ionizing radiation used in the treatment of primary brain tumors and metastases affects neuronal, glial, and endothelial cell population in the brain and lead to significant histopathological and functional deficits. In the present study we investigated radiation-induced histopathological changes in the specific brain regions under experimental conditions.

Material and methods: Adult male Wistar rats received fractionated whole-brain irradiation (fWBI) with a total dose of 40Gy delivered in 5 fractions (dose 8Gy per fraction) once per week in the same weekday during 5 consecutive weeks. Histopathological changes were evaluated by histochemistry, immunohistochemistry, confocal microscopy and image analysis to determine alteration of neurogenesis and glial cell response in 2 neurogenic regions in the brain: the hippocampal dentate gyrus (DG) and the subventricular zone-olfactory bulb axis (SVZ-OB axis).

Results: Image analysis of the brain sections 16 weeks after the exposure showed radiation-induced increase of degenerative Fluoro-Jade C labelled neuroblasts and post-mitotic neurons in both neurogenic regions. Irradiation led to almost total ablation of neuroblasts along the SVZ-OB axis and moderate decrease of astrocytes in both areas.

Conclusion: Our results showed that fWBI led to profound neuronal changes and less obvious glial cell response. Observed histopathological findings reflected subacute radiation-induced changes.

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THE ROLE OF GENE POLYMORPHISMS IN VITAMIN D METABOLISM IN THE DEVELOPMENT OF MULTIPLE SCLEROSIS

Laura Dubová

Tutors: MUDr. Daniel Čierny, PhD., prof. MUDr. Dušan Dobrota, CSc.

Department of Clinical Biochemistry, JFM in Martin, CU in Bratislava

E-mail contacts: dubovalaura@gmail.com, cierny@jfmed.uniba.sk, dobrota@jfmed.uniba.sk

Introduction: Multiple sclerosis (MS) is a demyelinating disease of the central nervous system. Hypovitaminosis D has been found to be one of the important factors related to the development of MS. The production of calcitriol, a biologically active form of vitamin D, is catalysed by 25-hydroxyvitamin-1α-hydroxylase, also known as CYP27B1. The aim of our study was to assess the association of the allele and genotype variants of rs703842 (C/T) in CYP27B1 gene with the risk of MS development in the cohort of Slovak population.

Material and methods: The analysis was performed in 496 MS patients and 521 controls. For genetic analysis, peripheral venous blood samples were taken to EDTA tubes and the genomic was extracted from leucocytes. The DNA was amplified by Polymerase chain reaction (PCR), the products were cleaved by restriction enzyme FspBI and DNA fragments were separated by electrophoresis on 2% agarose gel containing GoodView™ dye. The DNA was visualised by UV light and the genotypes were evaluated.

Results: The results of our study confirmed the role of rs703842 in MS pathogenesis, suggesting the allele C and genotype CC to be protective genetic factors of MS development in Slovaks. The frequencies of the allele C and genotype CC were found to be significantly lower in MS patients when compared to controls.

Conclusion: Our findings showed the association of rs703842 in CYP27B1 gene with MS susceptibility in a cohort of Slovak population, what could be used together with other markers in evaluation of the disease risk in predisposed individuals.

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EFFECT OF INDUCED HYPERHOMOCYSTEINEMIA TO CVS OF LABORATORY ANIMALS

Barbora Oravcová

Tutor: RNDr. Mária Kovalská, PhD.

Department of Histology and Embryology, JFM in Martin, CU in Bratislava

E-mail contacts: oravcova.b364@gmail.com, kovalska@jfmed.uniba.sk

Introduction: Cerebrovascular disease (CVD) is one of the leading causes of morbidity and mortality worldwide. One of the most common form of CVD is ischemic cerebrovascular disease (ICVD). Since, the treatment, prognosis and rehabilitation of ICVD is particular, prevention of ICVD by properly addressing its modifiable risk factors might present the solution. There are several established risk factors associated with ICVD, but a newer modifiable risk factor, hyperhomocysteinemia (hHcy) has created a new window for limiting the occurrence of CVD. hHcy is considered a strong, independent risk factor for stroke and dementia. Homocysteine (Hcy) is potentially vasculotoxic because of its association with endothelial dysfunction and impairment of fibrinolytic system. However, the molecular background underlying these mechanisms is not fully understood.

Material and methods: Global brain ischemia was induced by 4-vessels occlusion. Rats underwent 15 min of ischemia followed by 24 and 72 hours of reperfusion period. hHcy was induced by subcutaneous injection of Hcy (1.2 μmol/g) once a day in duration of 3 weeks. Animals were sacrificed, brain were fixed in 4 % paraformaldehyde and proceed for cryosectioning followed by histological analyses.

Results: We demonstrated occurrence of neurodegeneration in cerebral cortex already 24 hours after reperfusion in groups with combined insult (ischemia + hHcy). The immunohistochemical analyses detected presence of B-amyloid, CD 31 and VEGF even in controls with induced hHcy. The number of immunoreactive cells of above mentioned antibodies increased in time dependent manner with the time of reperfusion.

Conclusion: These findings suggest that global ischemia after induced hHcy could have a neurodegenerative role in rat brain. Our results also indicate that the model of combined insults might lead to progression of ICVD and dementias due to vasculotoxic effect of Hcy.

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ANTI-TUMOR EFFECTS OF CLOVE BUDS IN THE MODEL OF BREAST CARCINOMA

Veronika Sekanová, Monika Beliančinová, Peter Kubatka, Martin Péč

Tutor: doc. RNDr. Peter Kubatka, PhD.

Department of Medical Biology, JFM in Martin, CU in Bratislava

E-mail contacts: veronika.sekanova@gmail.com, kubatka@jfmed.uniba.sk

Chemoprevention, which includes the use of natural substances to reduce the risk of disease, is now becoming an area of intense research. Based on our previous experiments, it seems that cocktail of low-dose phytochemicals present in plant-derived functional foods may be highly effective in mammary carcinogenesis, more than isolated phytochemicals.

The preventive effects of clove buds were evaluated in the model of N-methyl-N-nitrosourea−induced rat mammary carcinogenesis. Cloves were dietary administered at two concentrations of 0.1 % and 1 %. The experiment was terminated 13 weeks after carcinogen administration. At autopsy, mammary carcinomas were removed and prepared for histopathological and immunohistochemical analyses.

Dietary administered cloves caused the dose-dependent decrease in tumour frequency by 47.5% and 58.5% when compared to control. Analysis of carcinoma cells in animals showed bcl-2, Ki67, VEGFA, CD24, and CD44 expression decrease and Bax, caspase-3, and ALDH1 expression increase after high dose cloves administration. MDA levels were substantially decreased in rat carcinomas in both clove groups. The evaluation of histone modifications revealed increase in lysine trimethylations and acetylations (H4K20me3, H4K16ac) in carcinomas after cloves administration. TIMP3 promoter methylation levels of CpG3, CpG4, CpG5 islands were altered in treated cancer cells. An increase in total RASSF1A promoter methylation (three CpG sites) in low dose clove group was found.

Our results clearly demonstrated preventive effect of clove buds in the breast carcinoma model. This is the first mention about the anticancer effects of cloves against cancer stem cells and epigenetic markers in vivo.

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EFFECT OF INDUCED HYPERHOMOCYSTEINEMIA TO CVS OF LABORATORY ANIMALS

Zuzana Sroková[1,2]

Tutors: RNDr. Mária Kovalská, PhD., Doc. Ing. Zuzana Tatarková, PhD.

[1]Department of Histology and Embryology, JFM in Martin, CU in Bratislava

[2]Department of Medical Biochemistry, JFM in Martin, CU in Bratislava

E-mail contacts: zzuzana.srokova@gmail.com; kovalska@jfmed.uniba.sk; tatarkova@jfmed.uniba.sk

Introduction: Risk factor modification remains as the principal aspect of care for cardiovascular disease (CVD) prevention. Understanding of risk factors has advanced and several options are now available to treat modifiable risk factors. However, effective treatment remains a challenging task in clinical practice. Elevated plasma homocysteine (Hcy) concentration is considered a risk factor for CVD. There is also evidence of endothelial dysfunction in patients with mildly elevated plasma Hcy concentrations. Although links have been established between hyperhomocysteinemia (hHcy) and elevated risk for cardiovascular events, the precise role of plasma Hcy in CVD is unclear.

Material and methods: Rats were divided in two groups. One group of animals was treated by subcutaneous injection of Hcy (1.2 μmol/g) once a day in duration of 3 weeks. The second group served as a control. The animals were after treatment sacrificed; the hearts were rapidly excised, placed on Langendorff perfusion system and perfused with the K–H solution for 20 minutes. Afterwards, the hearts were fixed in 10% formalin and prepared for paraffin method according standard protocols. The hearts were cut into semi-thin sections and proceeded for histological as well as immunohistochemical analyses.

Results: We observed significant increase of the perfusion pressure, decrease of the left ventricle end-diastolic pressure (LVDP) and the heart contraction and relaxation indexes (+LVdP/dt and –LV dP/dt). We detected occurrence of changes of cellular volume, cardiomocytes disintegration, swelling and higher amount of connective tissue in hHcy hearts. Immunohistochemical analyses displayed presence of amyloid plaques, VEGF+ endothelial cells and annexin 5+ cells in group treated with Hcy.

Conclusion: These findings suggest that induced hHcy influence not only microcirculation of heart, but also cardiomyocytes themself. These changes resulted in changes not only in the morphological structure, but also in the functional parameters.

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ANTICANCER EFFECTS OF THYME IN EXPERIMENTAL BREAST CARCINOMA

Vladimíra Tóthová, Paulína Turzová, Peter Kubatka, Martin Péč

Tutor: doc. RNDr. Peter Kubatka, PhD.

Department of Medical Biology, JFM in Martin, CU in Bratislava

E-mail contacts: vladka.tothova@gmail.com, kubatka@jfmed.uniba.sk

It is supposed that plant functional foods, rich in phytochemicals, may potentially have preventive effects in carcinogenesis. Based on our previous research, it seems that the mixtures of low-dose phytochemicals present in plant-derived functional foods may be highly effective in mammary carcinogenesis, more than isolated phytochemicals.

The anticancer effects of thyme haulm were evaluated using the chemopreventive model of N-methyl-N-nitrosourea−induced rat mammary carcinogenesis and the 4T1 allograft model of mouse mammary carcinoma. Thyme haulm was dietary administered at two concentrations of 0.1 % and 1 % in both experimental studies. The NMU experiment was terminated 15 weeks after carcinogen administration and the 4T1 model lasted 15 days. At autopsy, mammary carcinomas were removed and prepared for histopathological, immunohistochemical, and molecular analyses.

Dietary administered thyme (1 %) caused the decrease in rat tumour frequency by 53 % when compared to untreated control. Moreover, thyme non-significantly lengthened the tumour latency in rats by 8 days (0.1 %) and 6 days (1 %) compared to controls. In the 4T1 model, the comparison with the control group showed that the thyme significantly reduced tumor volume in mice by 85 % (0.1 %) and 84 % (1 %) respectively ($P < 0.001$ in both treatment groups) in the final 15th day of the experiment. Thyme in both doses significantly reduced the index of mitotic activity and the proportion of necroses in mouse mammary tumor tissue.

Our results demonstrated significant tumour-suppressive effect of thyme haulm in the breast carcinoma model. This is the first mention about the anticancer effects of thyme against experimental breast carcinoma in vivo.

This work was supported by the grant VEGA 1/0108/16.

ANTINEOPLASTIC EFFECTS OF CINNAMOMUM VERUM (ZEYLANICUM) L. IN SYNGENEIC 4T1 MODEL OF BREAST CARCINOMA: PRELIMINARY RESULTS

Paulína Turzová, Vladimíra Tóthová, Soňa Uramová, Peter Kubatka

Tutor: Ing. Soňa Uramová, doc. RNDr. Peter Kubatka, PhD.

Department of Medical Biology, JFM in Martin, CU in Bratislava

E-mail contacts: paulinapaulaturzova@gmail.com, kubatka@jfmed.uniba.sk

Isolated phytochemical administered alone did not show any anti-cancer effects in experimental mammary carcinogenesis in our laboratory. Based on our recent results, it seems that the mixture of phytochemicals with plethora biological activities, present in whole foods, may have additive or synergistic effects against carcinogenesis.

The anticancer effects of *Cinnamomum verum* L. bark were evaluated using the the 4T1 syngeneic (allograft) model of mammary carcinoma in Balb/c female mice. Cinnamomum was dietary administered at two concentrations of 0.1 % and 1 %. The experiment was terminated 15 days after the inoculation of 4T1 cells into animals. At autopsy, mammary carcinomas were removed, measured, and prepared for histopathological analyses.

Compared to control (untreated) group, dietary administered cinnamomum caused dose-dependent decrease of the tumor volume in mice by 10 % ($P>0.05$) and 44 % ($P<0.05$), respectively in the final 15th day of the experiment. Moreover, the index of mitotic activity and the proportion of necroses in mouse mammary carcinoma area are evaluated.

Our result is the first mention about the anticancer effects of cinnamomum in experimental mammary carcinogenesis *in vivo*. This result warrants the follow-up in the oncological research within the preclinical or clinical approach.

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FLIM ANALYSIS OF INTRACELLULAR CHANGES RELATED TO THE DEVELOPMENT OF PARKINSON'S DISEASE IN CELLULAR MODEL

Marek Bašista

Tutor: Mgr. Alžbeta Kráľová Trančíková, PhD.

Department of Pathophysiology, JFM in Martin, CU in Bratislava

E-mail contacts: marekbami@gmail.com; alzbeta.trancikova@jfmed.uniba.sk

Introduction: Parkinson's disease (PD) is the second most common neurodegenerative disorder in the world. Typical pathology of the disease includes the presence of cytoplasmic inclusions called Lewy body (LB), associated with neuronal cell death and more advanced stages of disease. Precise identification of the disease stage at the cellular level presents the critical tool in developing early diagnosis and prevention of PD. The aim of our work is to introduce sensitive microscopic analysis in living cells, focused on initial intracellular changes and thus capable to detect earlier stages of the disease.

Material and Methods: To achieve this goal, a widely used PD model based on the human SH-SY5Y neuronal cell line and rotenone (0-100nM/24h), a validated protein aggregation inducer in both cell and animal PD models, was used.

Conventional confocal microscopy supplemented by Fluorescence Lifetime Imaging Microscopy (FLIM) of a given microscopic image was used to distinguish between early and advanced stages of PD phenotype progression. FLIM, is based on the fact that the lifetime of fluorescence emission is significantly affected by molecules surrounding the fluorophore. Based on the different lifetimes of fluorescence emissions, we can distinguish between fluorophore's free or bound state.

Results: We observed changes in the intensity and lifetime of markers of PD phenotype in living cells. We were able to validate the presence of intracellular inclusions by immunostaining (α-synuclein), exogenous permeable probes (ThS) or endogenous fluorophores capable of binding to protein aggregates (NADH). The observed changes were dependent on the concentration of rotenone, while the fluorescence lifetime showed higher sensitivity in the observed molecules compared to the signal intensity imaging.

Conclusion: The FLIM analysis provided additional information on the presence of intracellular inclusions and, in particular, the potential of this method to produce certain "fingerprints" that could reflect the internal state of cellular environment. In addition, it has highlighted new possibilities for detecting early changes related to the development of PD-like symptoms in the cell model.

THE MODULATION OF CHLORIDE ION CHANNELS ACTIVITY IN EXPERIMENTAL ASTHMA

Christina Forsberg

Tutor: doc. MUDr. Martina Šutovská, PhD.

Department of Pharmacology, JFM in Martin, CU in Bratislava

E-mail contacts: g7jfmed@gmail.com, sutovska@jfmed.uniba.sk

Background: Chloride ion channels, in particular the family of voltage-sensitive calcium-activated chloride channels TMEM16, play a significant role in contributing to the pathogenesis of airway inflammatory diseases. Targeting these ion channels and aiming to modulating them may provide an interesting new approach in the therapy of these potentially fatal diseases.

Methods: This hypothesis we tested on both healthy and ovalbumin-sensitized male Dunkin- Hartley guinea pigs. The ion channels activity was modulated by nonselective (benzbromarone, BE) and TMEM16A-selective (CaCCinh-A01) blockers. *In vivo* airway reactivity, induced by histamine and methacholine, was expressed as specific airway resistance (sRaw) values, number of citric acid-induced coughs was counted using double-chambered bodyplethysmograph and frequency of ciliary beating was *in vitro* assessed by brushing method. For comparative purposes salbutamol and codeine were tested under the same condition.

Results: The results showed significant differences in responses of unsensitized and sensitized airways on both administered TMEM16 blockers. The group of ovalbumin-sensitized guinea pigs treated with CaCCinh-A01 versus BE had noteworthy differences in reduction of cough efforts in favor of nonselective blocker. Significant improvement in sRaw values could be observed in ovalbumin-sensitized CaCCinh-A01-treated subjects compared to BE and salbutamol when challenged with inhalational histamine, and the outcome was only negligible short-term improvement when challenged with methacholine. The ciliary beat frequency was consequentially inhibited in ovalbumin-sensitized subjects treated with selective inhibition of TMEM16A.

Conclusion: The results demonstrated that treatment with blockers of TMEM16 can reduce both cough effort and sRaw but the difference between TMEM16A-selective and nonselective blocking is in favor of BE. It is also worthwhile to notice the impairment of ciliary beat frequency in ovalbumin-sensitized animals treated with CaCCinh-A01and whether it is beneficial to inhibit these channels for airway remodelling prevention at the expense of mucociliary clearance.

POLYMYXIN B IMPROVES THE EFFICIENCY OF SURFACTANT TREATMENT IN ENDOTOXIN-INDUCED LUNG INJURY

Katarína Maťašová

Tutors: RNDr. M. Kolomazník, PhD. [1, 2], RNDr. J. Kopincová, PhD. [1, 2]

[1]Department of Physiology, JFM in Martin, CU in Bratislava

[2]Biomedical Center Martin, JFM in Martin, CU in Bratislava

E-mail contacts: matasova.katka@gmail.com, maros.kolomaznik@uniba.sk

jana.kopincova@jfmed.uniba.sk

Introduction: Intratracheal (*i.t.*) administration of pulmonary surfactant (SF) has been previously shown to mitigate, however not fully eliminate, inflammation caused by lipopolysaccharide (LPS) from membrane of Gram-negative bacteria. An antibiotic drug polymyxin B (PxB) binds to SF phospholipids (PL) and increases resistance of SF to inactivation. We hypothesized that combined therapy with SF+PxB can be more effective in reducing the LPS-induced inflammatory response in the lungs than SF treatment alone.

Material and methods: Adult male rats (Wistar, n=26, b.w. 320±10g) were anaesthetized, tracheotomised and the endotracheal tube was inserted. Lung injury was induced by *i.t.* instillation of LPS (500 μg/kg b.w.; 2.2 ml/kg b.w; *E.coli*, 055:B5). Controls received sterile saline at the same dose. Animals with LPS were further treated *i.t.* with exogenous SF (Curosurf®, 50 mg of PL/kg b.w.) or SF at the same dose with PxB 1% w.w. (SF+PxB). After 5 hrs of artificial ventilation the animals were overdosed by anaesthetics, right lung was homogenized and left lung was lavaged by sterile saline. The markers of inflammation and oxidative damage were determined in homogenized lung (HL) tissue and bronchoalveolar lavage fluid (BALF). Lung oedema was expressed as wet/dry weight ratio.

Results: In comparison to control, LPS increases lung oedema formation ($p<0.001$), oxidative stress ($p<0.01$) and the levels of IL-1β, IL-6, TNF-α and MCP-1 in HL and BALF. In LPS-treated animals, SF administration significantly reduces lung oedema, oxidative stress (both $p<0.05$) in HL and IL-6 ($p<0.01$) in BALF. With exception of lung oedema, this effect is potentiated when PxB is added to SF. In addition, SF+PxB reduces also IL-1β and MCP-1 ($p<0.05$) in BALF and TNF-α and MCP-1 ($p<0.01$) in HL.

Conclusion: Enrichment of exogenous surfactant with PxB potentiates the effect of surfactant therapy in LPS-induced acute lung injury by mitigating lung inflammation and oxidative stress. The results indicate the potential of surfactant preparations to carry the drugs directly to the site of its action.

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GENDER DOES NOT INFLUECE COUGH RESPONSE IN GUINEA PIGS WITH MODELLED RESPIRATORY PATHOLOGY

Aleksander Sorkness

Tutor: MUDr. Tomáš Buday, PhD.

Department of Pathophysiology, JFM in Martin, CU in Bratislava

E-mail contacts: aleksandersorkness@gmail.com, buday@jfmed.uniba.sk

Worldwide epidemiological studies confirm that hypersensitive cough syndrome affects mainly postmenopausal women. Role of female sex hormones is unclear in development in this pathology; however the lack of possible treatment options might be caused by inappropriate translation of results from basic research to clinical practice, as vast majority of basic research is performed only on male animals. Therefore, upon our previous results of pilot study in naïve guinea pigs, we tested the role of gender in guinea pigs with ovalbumin-induced airway hypersensitivity. 20 guinea pigs (Dunkin-Hartley, 10 males and 10 females) were sensitized by intraperitoneal administration of 1% ovalbumin (15μL, with aluminium hydroxide as adjuvant). After 21 days, the results were confirmed by skin prick testing. In animals with positive prick testing, the cough challenges were performed. 15 minutes prior to cough challenge 15μL of 1% OVA was administered to both nostrils to induce symptoms of allergic rhinitis. Cough challenge itself was performed by exposure to tussigen aerosols (0.4M citric acid, 50uM capsaicin, hypertonic saline) for 10min in whole body plethysmograph with simultaneous recording of sounds and pneumotachograph traces for further analysis by two independent observers. Statistical analysis of obtained data did not reveal any significant differences between both genders. Further characterization of cough response of both genders of guinea pigs is necessary in order to develop and validate this model for its utilization in further research.

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THE EFFECT OF MORIN AND EXPERIMENTALLY INDUCED ALLERGIC INFLAMMATION OF THE AIRWAYS

Dávid Zima

Tutors: assoc. prof. RNDr. Soňa Fraňová, PhD.; Mgr. Ivana Kazimierová, PhD.

Department of Farmacology, JFM in Martin, CU in Bratislava
Biomedical Center Martin, JFM in Martin, CU in Bratislava
E-mail contacts: davidenko33@gmail.com; Sona.Franova@jfmed.uniba.sk; Ivana.Kazimierova@jfmed.uniba.sk

Introduction: Asthma is a chronic respiratory disease characterized by airways hyperresponsiveness, inflammation and airways remodelling. Using an experimental model of allergic asthma, the aim of the study was to evaluate the anti-asthmatic potential of flavonol morin after chronic 21 days administration.

Material and methods: The guinea pigs were randomly divided into following experimental groups: a) healthy control group; b) control group sensitized 21 days with ovalbumin (OVA); c) OVA sensitized treated 21 days with morin (30mg/kg/day, p.o.); d) OVA sensitized received 21 days reference antiasthmatics or codeine. In each group we measured the following parameters: the *in vitro* tracheal smooth muscle (TSM) contraction induced by the cumulative doses of histamine (10^{-8}-10^{-3} M); the changes in specific airway resistance (sRaw) to histamine (10^{-6} M) and the sensitivity of a chemically (0,3 M citric acid) induced cough reflex both via an *in vivo* method; the concentrations of inflammatory cytokines IL-4, IL-5 and IL-13 in BALF.

Results: The chronic 21 - days administration of morin had a comparable antitussive efficiency with opioid antitussive codeine. The bronchodilatory efficiency of morin resulted in significant reduction in histamine-induced *in vitro* TSM contractile response. Moreover, the bronchodilatory efficiency of morin defined by sRaw values was by 34 % higher as an effect of long-acting beta2 agonist salmeterol. 21 days morin administration reduced the levels of the inflammatory cytokines IL-4 and IL-13 in BALF. This anti-inflammatory efficiency was comparable with the effect of reference glucocorticoid budesonide.

Conclusion: In conclusion, we can summarize that long-term administration of polyphenol morin revealed significant antitussive, bronchodilatory and anti-inflammatory effects in the experimental model of allergic asthma.

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CYTOTOXIC EFFECT OF THE APOPTOTIC INHIBITORS IN HUMAN GLIOBLASTOMA CELLS

Sabína Baroniaková

Tutors: doc. RNDr. Jozef Hatok, PhD.

Department of Medical Biochemistry, JFM in Martin, CU in Bratislava

E-mail contacts: sabina.baroniakov@gmail.com; hatok@jfmed.uniba.sk

Introduction: The most common primary brain tumors are gliomas, which begin in the glial tissue, of which glioblastoma multiforme (GBM) is a most aggressive in adults. Standard treatment for newly diagnosed GBM consists of surgical resection, radiotherapy and chemotherapy. Tumor resistance to apoptosis is a major obstacle to successful treatment.

Material and methods: The aim of our work was to determine response of human glioblastoma cells (T98G and A172) to selective apoptotic inhibitors (ABT-737, BH3I, MIM-1) and temozolomide (TMZ) as alkylating agent. ABT-737 and BH3I are anti-apoptotic Bcl-2 family members' inhibitors, while MIM-1 is Mcl-1 inhibitor molecule. Viable cells as a marker of cytotoxicity and caspase activation as a marker of apoptosis were determine by combination of two assays: ApoLive-Glo Multiplex and Methylthiazol tetrazolium assays.

Results: Based on the both methods we determine relative resistance of cells to MIM-1, while ABT-737 has inhibition effect even in low concentration (under 20 μM). The data show that the status of p53 (A172 – wild-type vs. T98G – mutated) has no effect of response to TMZ after 48h incubation. However, the T98G showed almost two-fold higher values of IC50 on the all inhibitors compared to the A172. Finally, we estimate caspase activation only in ABT-737 and TMZ treated samples.

Conclusion: Because of diversity in response to inhibiting agents between individual glioblastoma lines our data suggest that with better understanding of the mechanisms, the treatment may have to be customized to individual patients.

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PHENOTYPISATION OF NOVEL HUMAN PANCREATIC DUCTAL ADENOCARCINOMA CELL LINE WITH FLOW CYTOMETRY

Hugo Dumortier[1]

Tutors: [1] Ing.Ján Strnádel, PhD., [1,2] prof.RNDr. Erika Halašová, PhD.

[1]Department of Molecular Medicine, Biomedical Center Martin, JFM in Martin, CU in Bratislava

[2]Department of Medical Biochemistry, JFM in Martin, CU in Bratislava

E-mail contacts: hugo.m.dumortier@gmail.com, strnadel@jfmed.uniba.sk, Erika.Halasova@jfmed.uniba.sk

Introduction: Pancreatic ductal adenocarcinoma (PDAC) represents cancer with extremely poor prognosis. The fact, that the only a limited number of "*in vitro"* models (cell lines) exist for this type of cancer makes it a major limitation for the development of new therapies. Therefore, new "*in vitro"* models are critically needed to gain insights into the pathology of this cancer.

Material and Methods: With the use of protocol and special culture media, developed and previously tested in our lab, we established novel "*in vitro"* model or cell line derived from pancreatic ductal adenocarcinoma tumour. Abbreviated as "PANDA-3" (PANcreatic Ductal Adenocarcinoma, clone-3), cell line is currently being tested in our laboratories. We characterized our cell line by surface CD molecules screening for CD markers typical for PDAC cells, using flow cytometry analysis with last generation FACS ARIA cell sorter.

Results: PANDA-3 showed expression of surface molecules that are typical for commercially available pancreatic cancer cell lines. The expression of CD24, CD44, CD133 and CD326 makes this cell line comparable and also competitive with already established cell lines from ATCC repository. Moreover, we tested the ability of PANDA3 cells to form 3D tumourspheres. We found that PANDA-3 cells form typical spherical tumourspheres. This ability is typical for cancer initiating cancer (stem) cells.

Conclusion: Our novel cell line represents new potential "*in vitro" tumour* tool for PDAC cancer research. The ability of this cell line to grow in 3D makes this cell line attractive for cancer stem cells research field. Currently, a novel nanotechnology approach (patented by collaborator from University of Birmingham, UK) for targeting tumour nucleus is planned to be tested "*in vitro"* using PANDA 3 cell line.

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ASSOCIATION OF GENETIC VARIABILITY IN SELECTED GENES IN PATIENTS WITH DEEP VEIN THROMBOSIS AND PLATELET

Aneta Knazurova

Tutors: [1]Juraj Sokol, MD, PhD; [2]Maria Skerenova, MA, PhD; [1]Jela Ivankova, MA

[1] Department of Haematology and transfusion Medicine, JFM in Martin, CU in Bratislava

[2] Clinical Biochemistry, JFM in Martin, CU in Bratislava

E-mail contacts: anet.knazurova@gmail.com; juraj.sokol@jfmed.uniba.sk

Introduction: The aim of this study was to evaluate the genetic variability of the selected single nucleotide polymorphisms (SNPs) and examine the association between these SNPs and risk for deep vein thrombosis (DVT) in patients with sticky platelet syndrome (SPS).

Material and methods: We examined 84 patients with SPS and history of DVT and 101 healthy subjects. We were interested in two SNPs within PEAR1 gene (rs12041331, rs12566888), two SNPs within MRVI1 gene (rs7940646, rs1874445), one SNP within JAK2 gene (rs2230722), one SNP within FCER1G gene (rs3557), one SNP within PPBP (rs442155), four SNPs within ADRA2A (rs1800545, rs4311994, rs11195419, rs553668), and one SNP within SHH gene (rs2363910).

Results: We identified two protective SNPs within PEAR1 gene and one risk SNP within ADRA2A gene (PEAR1: rs12041331; rs12566888; ADRA2A: rs1800545). A haplotype analysis of 4 SNPs within ADRA2A gene identified a risk haplotype aagc (p=0.003). Moreover, we identified one protective haplotype within PEAR1 gene (AT, p=0.004).

Conclusion: Our results support the idea that genetic variability of PEAR1 and ADRA2A genes is associated with platelet hyperaggregability manifested as VTE. The study also suggests a possible polygenic type of SPS heredity.

SIGNIFICANCE OF ANTIAPOPTOTIC PROTEIN SURVIVIN IN COLON ADENOMAS

Ivana Kumičíková, Katarína Pálušová

Tutor: Prof. Marian Adamkov, MD., CSc.

Department of Histology and Embryology, JFM in Martin, CU in Bratislava

E-mail contacts: ivana.kumicikova@gmail.com, katarina.palus@gmail.com, adamkov@jfmed.uniba.sk

Introduction: Survivin is one of the most important antiapoptotic proteins, because of its different appearence in embryological, normal adult tissues, premalignant and malignant lessions. Survivin plays key role in negative regulation of apoptotic pathway. This protein appears to be localized in different subcellular compartments and there are large quantitative differences in the degree of its expression in malignant tumors on the one hand and in corresponding normal tissues and benign tumors on the other hand.

Method: We studied the role of survivin in group of 50 colon adenomas. We assessed the expression pattern of protein in question with regards to the subcellular location, the intensity of staining and size of polyps. Then, we studied the relationship of survivin expression with degree of dysplasia.

Results: Survivin positivity was expressed in 39 (78%) cases. The positive cases showed variable subcellular localization. Cytoplasmic localization was present in 20 cases (51%). Nuclear and combined nuclear and cytoplasmic reaction was detected in 19 cases (49%). Our adenoma group included 26 (52%) low grade adenomas and 24 (48%) high grade adenomas. Subcellular survivin compartmentalization was statistically associated with adenoma size and dysplasia grade.

Conclusion: Based on our recent results, low grade and smaller (≤5 mm) adenomas are associated mainly with cytoplasmic location, and high grade and larger (>5 mm) adenomas are associated mainly with nuclear or combined location. Thus, survivin and its subcellular localization may represent a promising biomarker in immunohistochemical evaluation in these lessions.

GENETIC MARKERS IN HLA-COMPLEX GENES AT MULTIPLE SCLEROSIS PATIENTS

Lenka Šavelová

Tutor: MUDr. Daniel Čierny, PhD.

Department of Clinical Biochemistry, JFM in Martin, CU in Bratislava

E-mail contacts: lenka.savelova@gmail.com, cierny@jfmed.uniba.sk

Introduction: Multiple sclerosis (MS) is an autoimmune disease of central nervous system characterised by inflammatory reaction and neurodegeneration leading to demyelinisation and axonal damage. Interactions between genetic factors and environmental agents have been shown to be crutial in the ethiopathogenesis of the disease. HLA genetic factors were found to be involved in the antigen presentation and autoimmunity in MS. Our aim was to examine the association of HLA-DRB1*1501 alleles and genotypes with the risk of development of MS.

Methods: Our study group consisted of 496 MS patients and 521 healthy individuals. DNA was isolated from leucocytes in patient's blood by extraction method using the principle of genomic DNA binding to magnetic glass particles. The HLA-DRB1*1501 genetic variants were determined by the analysis of rs31353888 A/G polymorphism. The rs31353888 genotyping was performed by HRMA (high resolution melting analysis). Allelic and genotype frequencies in MS patients were compared to controls.

Results: We found the HLA-DRB1*1501 allele to be present in significantly higher frequency in MS patients when compared to healthy controls. The homozygous and heterozygous genotype for the HLA-DRB1*1501 allele were also present in significantly higher frequencies in patients than in controls.

Conclusion: The results of our study confirm strong association of HLA genetic marker DRB1*1501 with MS susceptibility. The increased risk of MS was shown to be present in individuals with genotypes containing this allele. We suppose that this genetic marker could be used in clinical practice to identify individuals predisposed to multiple sclerosis and improve diagnostic and preventive strategy.

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PREDICTING THE BREAST CANCER RISK USING SNPs IN LOW-PENETRANT GENES: *TOX3, MAP3K1, FGF10*, *FGFR2* AND *CASP8* IN SLOVAK WOMEN

Daniela Vargová

Tutor: RNDr. Zuzana Danková, PhD.

Division of Oncology, Biomedical Center Martin, JFM in Martin, CU in Bratislava

E-mail contacts: daniela23494@gmail.com, Zuzana.Dankova@jfmed.uniba.sk

Introduction: Breast cancer (BC) is the leading cancer type among women worldwide. It is a multifactorial disease caused by a combination of individual, genetic and environmental factors. Recently, there has been a number of attempts to use various genetic variants as a tool to predict the BC risk. The aim of this study was to analyse the predictive ability of five SNPs in low-penetrant genes in association with the BC risk.

Material and methods: We analysed 317 Slovak women: 171 women (57.06±11.60 years) with histologically confirmed BC and 146 women (50.24±10.69 years) as controls. The DNA was extracted from peripheral blood and HRM (High resolution melting) method was applied to detect the genotypes of polymorphisms: *TOX3* rs3803662 *C>T*, *MAP3K1* rs889312 *A>C, FGF10* rs4415084 *C>T*, *FGFR2* rs2981582 *C>T* and *CASP8* rs2293554 *T>G*. The predictive accuracy of our model was measured by the area under the ROC curve.

Results: Risk allele frequency was in all SNPs (except the *CASP8* polymorphism) higher in cases than in controls respectively: *TOX3 T* 0.31 vs. 0.27; *MAP3K1 C* 0.31 vs. 0.21; *FGF10 T* 0.49 vs. 0.45; *FGFR2 T* 0.43 vs. 0.33 and *CASP8 G* 0.07 vs. 0.09. The statistically significant difference of the genotype distribution was observed only in *MAP3K1* (p=0.015) and *FGFR2* (p=0.032). Their odd ratios were as follows: *MAP3K1* 1.76 (95%CI 1.11-2.81, p=0.019) for *AC* and 2.89 (95%CI 1.03-9.57, p=0.048) for *CC*; *FGFR2* 1.77 (95%CI 1.09-2.89, p=0.026) for *CT* and 1.953 (95%CI 1.01-3.83, p=0.049) for *TT*. According to the classification error analysis, the best discriminative ability had again the polymorphisms in *MAP3K1* (42.59%) and *FGFR2* (42.09%). The predictive accuracy of our model had AUC value of 71.8%, specificity of 73.4% and sensitivity of 62.9%.

Conclusion: Our study confirms the statistically significant association of *MAP3K1* rs889312 and *FGFR2* rs2981582 with the risk of BC. These polymorphisms had also the best discriminative ability.

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