PhD Tudományos Napok 2013

Semmelweis Egyetem Doktori Iskola
Nagyvárad téri Elméleti Tömb

Budapest, 2013. április 11-12.

Előadáskivonatok

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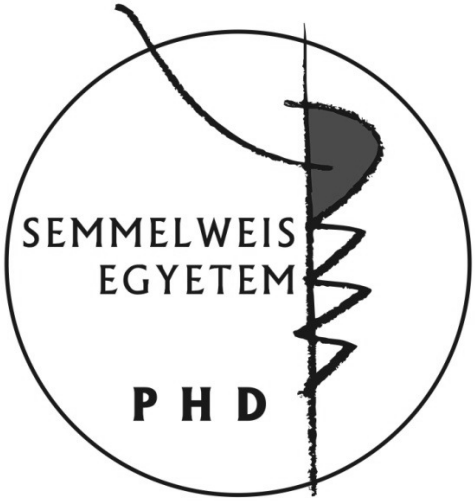

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ELŐSZÓ

Az évente megrendezett PhD Tudományos Napok a Semmelweis Egyetem nyolc Doktori Iskolájában tanulmányokat folytató hallgatók és doktorjelöltek kiemelkedő tudományos fóruma. Jelentőségét a program iránti érdeklődés, az előadások és poszter-bemutatók nagy száma jelzi. A rendezvényen résztvevők a tudományos munka munltidiszciplináris seregszemléjének részesei lehetnek, hiszen az Egyetem különböző tudományos műhelyeiben tevékenykedő PhD hallgatók és doktorjelöltek beszámolóin keresztül a tudományterületek és tudományágak sokasága jelenik meg. A Semmelweis Egyetem Doktori Iskoláinak hallgatóin kívül az előadók sorában az idei évben is örömmel üdvözöljük több hazai egyetem PhD hallgatóit.

A PhD Tudományos Napok immár hagyományos eseménye, hogy a PhD hallgatók és doktorjelöltek tudományos előadásain és poszter-bemutatóin kívül a "Kiváló PhD Oktató" címmel kitűntetett oktatók előadásainak is részesei lehetünk. A tudományos program első részében a 2012. évben "Kiváló PhD Oktató" címmel elismert oktatók közül Dr. Simon Kornél professzor emeritus "*A stresszel való megküzdési stílus, a személyiség és az én-hatékonyság egészségpszichológiai vonatkozásai* " és Dr. Szalay Ferenc egyetemi tanár "*Metabolikus májbetegségek*" címmel tartanak előadást. A tudományos kutatás és oktatás e két kimagasló személyiségének munkássága, tudományos és oktatói elkötelezettsége irányt mutat és példaképül szolgál a tudományos életpályájukat éppen megkezdő fiatalok számára. A rendezvény programjának további részében a Doktori Iskolák PhD hallgatói 7 előadás és 4 poszter szekcióban számolnak be tudományos munkájuk eredményeiről.

Őszintén remélem, hogy 2013. évi PhD Tudományos Napok programja hasznos tapasztalatokkal szolgál és emlékezetes élményt jelent minden kedves résztvevőnek és érdeklődőnek.

Budapest, 2013. április 11.

Dr. Rácz Károly
egyetemi tanár
a Doktori Tanács elnöke

TUDOMÁNYOS PROGRAM

2013. április 11. csütörtök

08.30 - 09.00	Megnyitó: Dr. Szél Ágoston egyetemi tanár, a Semmelweis Egyetem rektora Dr. Rácz Károly egyetemi tanár, a Semmelweis Egyetem Doktori Tanácsának elnöke
09.00 - 09.20	"Kiváló PhD Oktató"-díjas előadó: Dr. Sípos Kornél professzor emeritus A stresszel való megküzdési stílus, a személyiség és az én-hatékonyság egészségpszichológiai vonatkozásai
09.20 - 09.40	”Kiváló PhD Oktató”-díjas előadó: Dr. Szalay Ferenc egyetemi tanár Metabolikus májbetegségek
09.40 – 10.10	*Kávészünet*
10.10 - 13.00	Előadások: E-I/1 – E-I/17
11.00 - 13.00	Poszterek: P-I/1 – P-I/11
13.00 - 14.00	*Ebédszünet*
14.00 - 15.40	Előadások: E-II/1 – E-II/10
15.40 - 16.00	*Kávészünet*
16.00 – 18:30	Előadások: E-III/1 – E-III/15
16.00 - 18.00	Poszterek: P-II/1 – P-II/12

2013. április 12. péntek

08.30 – 10.30	Előadások: E-IV/1 – E-IV/12
10.30 – 11.00	*Kávészünet*
11.10 – 13.00	Előadások: E-V/1 – E-V/11
11.00 - 13.00	Poszterek: P-III/1 – P-III/9
13.00 – 14.00	*Ebédszünet*
14.00 – 15.50	Előadások: E-VI/1 – E-VI/11
15.50 – 16.10	*Kávészünet*
16.10 – 18.10	Előadások: E-VII/1 – E-VII/12
16.10 – 18.20	Poszterek: P-IV/1 – P-IV/16
18.20 - 18.40	*Zárszó, díjkiosztó*

TABLE OF CONTENTS

E/IV ORAL PRESENTATIONS *Chairman: Prof. Dr. József Tímár*		
E/IV-1	**IN VITRO DIFFERENTIATION OF TH17 CELLS** Eszter Baricza, Barbara Molnár-Érsek, Edit Buzás, György Nagy	73
E/IV-2	**GENETIC VARIATIONS IN THE PROMOTER REGION OF THE WFS1 GENE ARE RISK FACTORS OF TYPE 2 DIABETES MELLITUS** Nóra Németh, Zsuzsanna Elek, Suzanne Prokop, Anikó Somogyi, Mária Sasvári-Székely, Zsolt Rónai	74
E/IV-3	**THE PHOSPHOINOSITIDE 3-KINASE B AND Δ REGULATE OSTEOCLAST DEVELOPMENT AND FUNCTION** Dániel Csete	75
E/IV-4	**MODELING THE TEMPERATURE-RELATED AVERAGED ANNUAL RUN OF RELATIVE LB INCIDENCE IN THE PERIOD OF 1998-2012 IN HUNGARY** Attila Trájer, Ákos Bede-Fazekas, János Bobvos, Anna Páldy	76
E/IV-5	**CLINICOPATHOLOGICAL FEATURES OF HEAD AND NECK CANCERS AND THEIR RELATION TO BIOMARKER-EXPRESSION** Kornél Dános, Diána Brauswetter	77
E/IV-6	**EXPLORING CONNEXIN EXPRESSION AND FUNCTIONS IN MELANOCYTIC TUMORS** Gergő Kiszner, Ivett Teleki, Péter Balla, Nóra Meggyesházi, Zsófia Buday	78
E/IV-7	**MODULATED ELECTRO-HYPERTHERMIA CAUSES PROGRAMMED CELL DEATH IN HT29 COLORECTAL CARCINOMA XENOGRAFT** Nóra Meggyesházi, Gábor Andócs, Sándor Spisák	79
E/IV-8	**DIFFERENTIAL CONNEXIN EXPRESSION IN GIANT CELL TUMOUR OF BONE (GCTB)** Péter Balla, Ivett Teleki, Nóra Meggyesházi, Gergő Kiszner, Tibor Krenács	80
E/IV-9	**IN SITU ANALYSIS OF MAMMALIAN TARGET OF RAPAMYCIN (MTOR) COMPLEXES** Noémi Nagy, Ágnes Márk, Sándor Paku, László Kopper, Anna Sebestyén	81
E/IV-10	**THE ROLE OF ALTERED CYTOKINE PRODUCTION IN HHV-7 INFECTIONS** Balázs Stercz	82
E/IV-11	**COMPARATIVE ANALYSIS OF PATIENT DERIVED AND IN VITRO SELECTED VEMURAFENIB RESISTANT MELANOMA CELL MODELS** Tamás Garay, Eszter Molnár, Walter Berger, József Tímár, Balázs Hegedűs	83
E/IV-12	**The author have not agreed the online publication.**	84

E/V ORAL PRESENTATIONS *Chairman: Prof. Dr. Péter Lakatos*		
E/V-1	**COMPARISON OF RAT AND HUMAN ORTHOLOGS OF ORGANIC CATION/CARNITINE TRANSPORTER (OCTN2)** Kitti Szabó, Péter Krajcsi, Zoltán Nagy, Viktória Juhász	**87**
E/V-2	**THE UL54 GENE OF PSEUDORABIES VIRUS MAY BE PART OF THE TRANSCRIPTIONAL INTERFERENCE NETWORK AND MAY SPECIFICALLY REGULATE LATE GENES** Nándor Póka, Péter Oláh	**88**
E/V-3	**MODERATE INHIBITION OF GELATINOLYTIC ACTIVITY BY ILOMASTAT REDUCES INFARCT SIZE IN BOTH ISCHEMIC AND REPERFUSION INJURY IN VIVO** Krisztina Kiss, Péter Bencsik, János Pálóczi, Gabriella F. Kocsis, Anikó Görbe, Judit Pipis, Csaba Csonka, Tamás Csont, Péter Ferdinandy	**89**
E/V-4	**ISOLATION AND ANALYSIS OF LARGE BACTEROIDES PLASMIDS** Viktor Sándor Fenyvesi	**90**
E/V-5	**2-PHOTON LASER MICROSCOPIC ANALYSIS OF PHOTOAGING IN MICE WITH IMPAIRED EPIDERMAL ANTIOXIDANT DEFENSE** Kende Lőrincz, András Bánvölgyi, Dóra Haluszka, Nóra Gyöngyösi, Sarolta Kárpáti, Norbert Wikonkál1	**91**
E/V-6	**BONE FORMATION IS INCREASED WITH ALBUMIN COATED ALLOGRAFTS IN A RAT CRITICAL SIZE DEFECT** Dénes Horváthy, Gabriella Vácz	**92**
E/V-7	**RESISTANCE AGAINST GLUCOCORTICOIDS, CAUSED BY OVEREXPRESSION OF THE GLUCOCORTICOID RECEPTOR B ISOFORM IN CACO-2 CELL LINE** Bence T. Ács, István Likó, Karolina Feldman-Kovács, Henrietta Butz, Károly Rácz, Attila Patócs	**93**
E/V-8	**ROLE OF INTERLEUKIN-24 (IL-24) IN THE PATHOGENESIS OF INFLAMMATORY BOWEL DISEASE (IBD)** Anna Ónody, Erna Sziksz, Leonóra Himer, Domonkos Pap, Beáta Szebeni, Mária Bernáth, Apor Veres-Székely, Krisztián Kovács, Kriszta Molnár, Viktória Ruszinkó, Gábor Veres, András Arató, Tivadar Tulassay, Ádám Vannay	**94**
E/V-9	**A NOVEL ROLE OF INTERLEUKIN-24 (IL-24) IN THE PATHOGENESIS OF CHRONIC KIDNEY DISEASES** Domonkos Pap, Leonóra Balicza-Himer, Anna Ónody, Erna Sziksz, Beáta Szebeni, Apor Veres-Székely, Mária Bernáth, Krisztián Kovács, Tivadar Tulassay, Ádám Vannay	**95**

E/VII-7	**SURFACE COATING EFFECTS ON MORPHOLOGY, MARKER EXPRESSION AND CELL PROLIFERATION OF RAT DENTAL PULP STEM CELLS DURING NEURODIFFERENTIATION** Karola Kalló, Bernadett Gánti, Gábor Varga	**121**
E/VII-8	**GENETIC DETERMINANTS AND HERPES VIRUSES IN THE BACKGROUND OF PERIODONTITIS IN THE HUNGARIAN POPULATION** Péter Stiedl, Csilla Páska, Gabriella Jobbágy-Óvári, Xénia Kelemen, Borbála Soós, Bálint Molnár, Gábor Nagy, Gábor Hullám, Péter Antal, Gábor Varga, István Gera	**122**
E/VII-9	**MODELLIG THE PH REGULATION OF AMELOBLASTS BY NOVEL TWO DIMENSIONAL CELLULAR SYSTEM** Erzsébet Bori, Antonius LJJ Bronckers, Pamela Den Besten, Hidemitsu Harada, Gábor Varga	**123**
E/VII-10	**NEW NON-INVASIVE APPROACH TO EVALUATE IMPLANT STABILITY** Sándor Farkasdi, Katalin Perczel-Kovách, Márta Fülöp Papp, Beáta Kerémi, Bence Szabó, Róbert Rácz, Csaba Dobó-Nagy, József Blazsek, Gábor Varga	**124**
E/VII-11	**SMALL BOWEL ISCHEMIA – A COMPARATIVE EXPERIMENTAL STUDY** Zsolt Turóczi, Zoltán Czigány, Olivér Rosero, András Fülöp, Tibor Kovács, Péter Ónody, Dávid Garbaisz, László Harsányi, Attila Szijártó	**125**
E/VII-12	**LEVOSIMENDAN PROTECTS AGAINST LIVER ISCHEMIC-REPERFUSION INJURY** András Fülöp, Rita Stangl, Péter Ónody, Zsolt Turóczi, Olivér Rosero, Dávid Garbaisz, Zoltán Rakonczay, László Harsányi, Attila Szijártó	**126**
P/I POSTER PRESENTATIONS *Chairperson: Prof. Dr. Lídia Sréter*		
P/I-1	**MULTIFRACTAL ANALYSIS OF NEAR-INFRARED SPECTROSCOPY (NIRS) SIGNALS RECORDED FROM THE HUMAN BRAIN CORTEX** Péter Mukli, Zoltán Nagy, Péter Herman, András Eke	**129**
P/I-2	**SERUM APELIN AS A PREDICTOR OF RIGHT VENTRICULAR DYSFUNCTION** Annamária Kosztin, Gábor Széplaki, Vivien Klaudia Nagy, Gábor Földes, Astrid Apor, Csilla Liptai, Levente Molnár, Endre Zima, László Gellér, Béla Merkely	**130**
P/I-3	**MONITORING BRAIN HEMODYNAMICS AND OXYGENATION WITH NEAR-INFRARED SPECTROSCOPY (NIRS) DURING CARDIOPULMONARY BYPASS SURGERY** Zoltán Nagy, Péter Mukli, Endre Németh, István Portörő, Anita Daragó, Katalin Orbán, Kata Csibi, Klára Ronkay, Edina Wappler, János Gál, András Eke	**131**
P/I-4	**THE EFFECT OF KIDNEY TRANSPLANT PATIENTS' BODY IMAGE CHARACTERISTICS ON THEIR RECOVERY** Melinda Látos, Katalin Barabás, György Lázár, Márta Csabai	**132**

P/III POSTER PRESENTATIONS *Chairpersons: Prof. Dr. Romána Zelkó, Dr. István Antal*		
P/III-1	**ANTHRAQUINONE COMPONENTS OF RUBIA TINCTORUM AS CANDIDATE ANTICANCER AGENTS FOR DRUG TARGETING** Eszter Lajkó, Péter Bányai, Éva Szőke, László Kőhidai	**157**
P/III-2	**SOLUBILITY IMPROVEMENT OF APIGENIN** Zsófia Edit Pápay, Zita Sebestyén, Nikolett Kállai, Krisztina Ludányi, Emese Balogh, István Antal	**158**
P/III-3	**SOMATIC ONCOGENE MUTATIONS IN FINE-NEEDLE ASPIRATION BIOPSY FROM THYROID COLD NODULES** Bálint Tobiás, Bernadett Balla, János P. Kósa, János Horányi, István Takács, Zsolt Nagy, Péter Horváth, Balázs Járay, Eszter Székely, Roland Istók, Tamás Székely, Péter Lakatos	**159**
P/III-4	**RHEOLOGICAL CHARACTERIZATION OF HYDROCOLLOID GELS IN FORMULATION DEVELOPMENT** Enikő Szabadi, Lívia Budai, Mária Hajdú, Imre Klebovich, István Antal	**160**
P/III-5	**THE EFFECTS OF ANGIOTENSIN II ON THE NMDA-TYPE GLUTAMATE RECEPTORS OF THE PYRAMIDAL CELLS IN THE PREFRONTAL CORTEX (PFC)** Adrienn Hanuska	**161**
P/III-6	**THE DEVELOPMENT AND CHARACTERIZATION OF NOVEL KINASE INHIBITORS DESIGNED FOR TARGETED DELIVERY** Zoltán Nemes, Nóra Breza, Csaba-Kis Szántai, Eszter Illyés, Zoltán Horváth, Dániel Erös, Ed E Moret, Péter Horváth, György Kéri, László Örfi	**162**
P/III-7	**ENANTIOSEPARATION OF ASPARTATE AND GLUTAMATE BY CE-LIF IN BRAIN TISSUE SAMPLES** Tamás Jakó, Zsolt Wagner, Tamás Tábi, Gergely Zachar, András Csillag, Éva Szökő	**163**
P/III-8	**EFFECT OF VACUUM-ULTRAVIOLET (V-UV) PHOTOLYSIS TRANSFORMATION PRODUCTS OF DICLOFENAC ON THE PROLIFERATION AND MIGRATORY RESPONSES OF TETRAHYMENA PYRIFORMIS** Júlia Láng, Eszter Arany, Dávid Somogyvári, Krisztina Gajda-Schrantz, Láng Orsolya, András Dombi, László Kőhidai	**164**
P/III-9	**PREPARATION AND CHARACTERIZATION OF FORCESPUN POLYVINYLPYRROLIDONE-IODINE FIBER MAT FOR WOUND DRESSING** István Sebe	**165**

P/IV POSTER PRESENTATIONS *Chairman: Prof. Dr. Gábor Bánhegyi*		
P/IV-1	**THE ROLE OF GLUT10 IN THE ARTERIAL TORTUOSITY SYNDROME** Csilla Németh, Éva Margittai, Marcolongo Paola, Benedetti Angiolo, Gábor	169
P/IV-2	**DEVELOPMENT OF NEW MOLECULAR TOOLS TO MONITOR VARIOUS INOSITOL COMPOUNDS IN STIMULATED HUMAN HEK-293T FIBROBLASTS** József T. Tóth, Gergő Gulyás, Dániel J Tóth, László Hunyady, Péter Várnai	170
P/IV-3	**7H3 IS A NOVEL BURSAL STEM CELL ANTIGEN** Nóra Fejszák, Imre Oláh, Nándor Nagy	171
P/IV-4	**GENETIC RISK FACTORS OF ANTHRACYCLINE CARDIOTOXICITY – RELEVANT POLYMORPHISMS IDENTIFIED IN ENZYMES AND TRANSPORTERS OF ANTHRACYCLINE PHARMACOKINETICS** Nóra Kutszegi, Ágnes F. Semsei, Orsolya Lautner-Csorba, Márta Hegyi, Csaba Szalai, Gábor T. Kovács, Dániel J. Erdélyi	172
P/IV-5	**YAP1 IN THE HIPPO PATHWAY INFLUENCES THE RISK OF ASTHMA** Lili E. Fodor, Ildikó Ungvári, Orsolya Lautner-Csorba, Csaba Szalai	173
P/IV-6	**DEVELOPMENTAL MAPPING OF CD45+ CELLS IN EARLY AVIAN EMBRYO** Dávid Dóra, Imre Oláh, Nándor Nagy	174
P/IV-7	**GRAFTED NEUROCTODERMAL STEM CELLS RESCUE DAMAGED RAT RETINAL GALNGLION CELLS OTHERWISE DESTINATED TO DIE** Péter Balázs Kocsis, Zoltán Fekécs, Antal Nógrádi	175
P/IV-8	**GLYCOGEN DISTRIBUTION IN A HYPERMUSCULAR MOUSE MODEL** Tamás Kocsis, Júlia Baán, Luca Mendler, Anikó Keller-Pintér, László Dux	176
P/IV-9	**THE COMPACT MUTATION OF MYOSTATIN CAUSES A GLYCOLYTIC CHANGE IN THE PHENOTYPE OF SKELETAL MUSCLES** Júlia Baán, Tamás Kocsis, Anikó Keller-Pintér, Luca Mendler, László Dux	177
P/IV-10	**ASIAN-SPECIFIC MITOCHONDRIAL GENOM POLYMORPHISM (9 BP DELETION) IN THE HUNGARIAN POPULATION** Klára Pentelenyi, Viktória Reményi, Gyöngyvér Tömöry, Bernadett Csányi, Anikó Gál, István Raskó, Mária Judit Molnár	178
P/IV-11	**META-ANALYSIS OF BIOMARKER CANDIDATES PREDICTING SURVIVAL AFTER TAMOXIFEN TREATMENT** Zsuzsanna Mihály, Máté Kormos, András Lánczky, Balázs Győrffy	179
P/IV-12	**IONIZING RADIATION INDUCED EFFECT OF GDF-15 AND TGFB1IN MAMMARY CARCINOMA CELLS** Boglárka Schilling-Tóth, Nikolett Sándor, Enikő Kis, Géza Sáfrány, Hargita Hegyesi	180
P/IV-13	**BIOMARKERS OF PLATINUM RESISTANCE IN OVARIAN CANCER** Zsófia Pénzváltó, András Lánczky	181

E/I
ORAL PRESENTATIONS

Chairman:
Prof. Dr. Károly Cseh

E/I-1
COMPARISON OF TWO HINDLIMB ISCHEMIA-REPERFUSION MODELS: THE IMPORTANCE OF RESIDUAL PERFUSION

Rosero Olivér[1], Németh Károly[2], Turóczi Zsolt[1], András Fülöp[1], Dávid Garbaisz[1], András Szuák[2], Mátyás Kiss[2], Ágnes Nemeskéri[2], Attila Szijártó[1]

[1] *I. Department of Surgery, Semmelweis University, Budapest*
[2] *Department of Human Morphology and Developmental Biology, Semmelweis University, Budapest*

Acute limb ischemia-reperfusion (IR) injury may result in limb loss and significant mortality. Rats are the most commonly used animals for studying hindlimb IR injuries. Ischemia performed by arterial clamping causes milder damage than the application of tourniquet due to the presence of residual circulation.

The aim of this study was to evaluate the importance of collateral flow between the two mentioned hindlimb IR models. Male Wistar rats were randomized into three major groups: (A) measurement of ischemic muscle weight (n=10), (B) extension of muscle damage caused by application of tourniquet or infrarenal aortic occlusion (n=20). Blood and muscle samples were taken from group B to assess serum necroenzymes (CK, LDH) and potassium levels, muscle fiber viability and histological examinations and (C) identification of the collateral system between the lower limb and the rest of the body using corrosion casts (n=10).

Results: The use of tourniquet affected lower amount of muscle tissue, but resulted in significantly more severe injury in contrast to the infrarenal aortic occlusion. This difference is reflected in the levels of serum CK ($p<0.001$), LDH ($p=0.047$) and potassium ($p=0.048$). The histological examination and viability assay ($p<0.001$) also confirm these findings. The corrosion casts showed several anastomoses between the arterial systems capable of supplying the lower limb.

This study provides a detailed description of the lower limb arterial collateral network, which explains the discrepancy between the two models regarding the degree of IR injury. These differences should be taken into consideration when designing a hindlimb IR rat model.

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Program: Gastroenterology
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E/I-2
NIM-811 – THERAPEUTIC POSSIBILITY FOR KIDNEY INJURY INDUCED BY LOWER LIMB VASCULAR OPERATION

Dávid Garbaisz[1], Zsolt Turóczi[1], András Fülöp[1], Olivér Rosero[1], Péter Ónody[1], Gábor Lotz[2], László Harsányi[1], Attila Szijártó[1]

[1] *I. Department of Surgery, Semmelweis University, Budapest*
[2] *II. Department of Pathology, Semmelweis University, Budapest*

Introduction: Operation on the infrarenal aorta could cause rhabdomyolysis of skeletal muscle, which may result in myonephropathic metabolic syndrome. NIM-811 (N-metyl-4-isoleucine-cyclosporine) is a mitochondria specific drug, which can prevent ischemic-reperfuison (I/R) injury.

Objectives: Our aim was to reduce damages in skeletal muscle and in the kidney after I/R of the lower limb with NIM-811.

Materials and methods: Wistar rats underwent 180 minutes bilateral lower limb ischemia and 240 minutes reperfusion. Animals were divided into four groups called Sham, IR (I/R+vehicle), NIM-sham (NIM-811+vehicle) and NIM-treated (I/R+NIM-811+vehicle). Serum, urine and histological samples were taken in the end of reperfusion. NADH-tetrazolium staining and muscle Wet/Dry (W/D) ratio was investigated.

Results: In the NIM-treated group has more favourable histological alterations. The serum necroenzyme levels are significantly lower in the NIM-treated group than in the IR group (LDH: $p=0.001$; CK: $p=0.04$). Muscle mitochondrial viability is significantly higher ($p<0.001$) and renal function parameters are better (creatinin: $p<0.05$; FENa: $p=0.015$) in the NIM-treated group. The level of TNF-α is significantly lower ($p<0.05$), IL-6 is lower and W/D ratio is significantly lower ($p=0.04$) in the NIM-treated group.

Conclusion: NIM-811 can reduce the rhabdomyolysis and the damage of the kidney after infrarenal aortic operation.

Doctoral School: Clinical Medicine
Program: Clinical and experimental research in Angiology
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E/I-3
CHANGES IN DYNAMIC BALANCING DURING THE FIRST SIX POSTOPERATIVE MONTHS USING DIFFERENT SURGICAL APPROACHES IN TOTAL HIP ARTHROPLASTHY

Gergely Holnapy[1], Rita M. Kiss[2]

[1] *Department of Orthopaedics, Semmelweis University, Budapest*
[2] *Budapest University of Technology and Economics, Department of Structural Engineering, Budapest*

Aims: The aim of our study was to detect the changes in dynamic balancing –modeled with ultrasound-based sudden perturbation test — during the first six months of the postoperative period in case of different (antero-lateral - AL, direct-lateral - DL and posterior, capsule preserving – P) surgical approaches.

Methods: The dynamic balancing ability_was detected with ultrasound-based sudden perturbation test before total hip arthroplasty, and 6, 12 weeks and 6 months postoperatively in 25 patients with DL-approach, 22 patients with AL-approach and 25 patients with P-approach. The control group was formed by 45 age-matched healthy individuals. The dynamic balancing ability was characterized by the Lehr's damping ratio that was calculated from the results of the measurements data of standing on both-, affected-, and contra-lateral lower extremity.

Result: In the sixth postoperative week, in the case of DL-, and AL approach the Lehr's damping ratio decreased significantly comparing with the preoperative period, but after that it increased continuously. The Lehr's damping ratio calculating from data measured during standing on affected lower extremity was significantly less as well in the sixth postoperative month, comparing to data of healthy individuals. During the postoperative period, the Lehr's damping ratio increased continuously in case of P-approach, and in the sixth postoperative month it was equal to the control group. During the first six postoperative months, the dynamic balancing ability improved at groups operated by DL-, and AL approach, but the dynamic balancing ability of affected side differed from the control group. The improvement of dynamic balancing ability was faster at group with capsule-preserving P-approach than at the other two groups, and in the sixth postoperative month, it didn't differ significantly from the dynamic balancing ability of the control group. To sum it up, we can see that beside improving of muscle forces and the range of motion of hip joint, the improvement of dynamic balancing ability must be taken into consideration too when planning rehabilitation protocols and also in the case of abandonment of crutches.

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E/I-4
EFFICACY OF PRENATAL ULTRASONOGRAPHY IN DIAGNOSING UROGENITAL ANOMALIES IN NEWBORNS

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Objective: Showing a prevalence rate of 0.5-0.8%, urogenital malformations discovered in newborns are regarded relatively common. The aim of this study is to examine the efficacy of ultrasound diagnostics in detecting developmental disorders in the urogenital system.

Study design: We have processed the prenatal sonographic and postnatal clinical details of 175 urogenital abnormalities in 140 newborns delivered with urogenital malformation over a 5-year period. The patients were divided into three groups; Group 1: prenatal sonography and postanatal examinations yielded fully identical results. Group 2: postnatally detected urogenital changes had been partially discovered in prenatal investigations. Group 3: prenatal sonography had failed to detect the urogenital malformation identified in postnatal examinations. Urogenital changes representing part of certain multiple disorders associated with chromosomal aberration were investigated separately.

Results: Prenatal sonographic diagnosis and postnatal results completely coincided in 45%, i.e. 63/140 cases in newborns delivered with urogenital developmental disorders. In 34/140 cases (24%) discovery was partial, while in 43/140 patients (31%), no urogenital malformation was detected prenatally. No associated malformations were observed in 108 cases, in 57 of which (53%) the results of prenatal ultrasonography and postnatal examinations showed complete coincidence. Prenatally, urogenital changes were found in 11 patients (10%), whereas no urogenital disorders were diagnosed in 40 cases (37%) by investigations prior to birth. Urogenital disorders were found to represent part of multiple malformations in a total of 28 cases as follows: prenatal diagnosis of urogenital malformation and the findings of postnatal examinations completely coincided in three patients (11%), partial coincidence was found in 22 newborns (79%) and in another three patients (11%), the disorder was not detected prenatally. In four newborns, chromosomal aberration was associated with the urogenital disorder; 45,X karyotype was detected in two patients, trisomy 9 and trisomy 18 were found in one case each.

Conclusion: In approximately half of the cases, postnatally diagnosed abnormalities coincided with the prenatally discovered fetal urogenital developmental disorders. The results have confirmed that ultrasonography plays an important role in diagnosing urogenital malformations but it fails to detect all of the urogenital developmental abnormalities.

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E/I-5
PREDICTORS OF MORTALITY IN MECHANICALLY VENTILATED PATIENTS OUT OF THE ICU IN THE INTERNAL MEDICAL WARDS

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All over the word, the demands for intensive care beds far exceed their availability. In Israel this shortage has lead to an unbearable situation of mechanical ventilation of patients, out of the ICU, in the internal medical wards. These patients are often rejected from being admitted into the ICU due to their advanced age and poor functional status. Being mechanically ventilated in the internal medical wards increases their morbidity and in hospital mortality.

Aims: To define a group of patients that have the best chance to survive the mechanical ventilation in the medical wards. This information would provide essential tools for better triaging of mechanically ventilated patients from internal medical departments towards the ICU.

Methods: This is a retrospective study, reviewing charts of patients who were mechanically ventilated for the entire period in the internal medical words, from January 1st 2009 to December 31st 2010, in Assaf Harofeh Medical Center, Israel.

Results: A total of 437 mechanically ventilated patients were included, the mean age of which were 81 and in hospital mortality of 72.3%. According to a stepwise logistic regression analysis the factors that independently predicted outcome were: respiratory indications for mechanical ventilation (OR=0.23, P<0.001), tracheostomy usage (OR=0.08, P<0.001), cardiac indication for mechanical ventilation (OR=0.17, P<0.001) creatinine level (OR=0.23, P<1.71), re-intubation (OR=5.34, P=0. 01), duration of hospital stay before intubation (OR=1.14, P=0.006), age (OR=1.04, P=0.005) and had undergone CPR (OR=4.7, P=0.003).

Conclusions: The study suggests that the indication of mechanical ventilation is one of the most important factors in consideration of in hospital mortality. Respiratory and cardiac indications for mechanical ventilation as a favorite outcome whereas undergoing CPR as the worst prognosis. Other variables that have a negative affect are higher creatinine in the first day of admission, longer hospital duration stay before intubation, re-intubation and older age.

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E/I-6
SPINE EXAMINATION OF PRIMARY SCHOOL CHILDREN WITH ZEBRIS ULTRASOUND-BASED MOTION ANALYSING SYSTEM

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Introduction: Since 2005 different motion analysing researches have taken place in the biomechanical laboratory of MÁV Hospital in Szolnok.

A major area of our research is to determine the spinal shapes of primary school children with ultrasound-based motion analysing system.

Aims: The goal of our research is to survey the spinal conditions of children reckoned to be healthy with physical examination and to determine the shape of their spines with ultrasound-based motion analysing system. Another aim is to determine – through a large number of examinations – reference values (kyphosis, lordosis, inclinations) which specify the shapes of spines for different age groups.

Method: Subjects were 210 – from six to twelve years old – children, who were examined every half year for three years. First the subjects were measured in standing position and the spatial coordinates of the processus spinosuses were located with WINSPINE software specially designed for Zebris CM-HS motion analysing system. Than from these data we calculated the changes of thoracal kyphosis, lumbal lordosis and inclinations (total trunk inclination, lateral inclination) both in frontal and in sagittal planes with our own developed Excel software.

Results: After the physical examinations we divided the children into four groups (healthy children, children with bad postures, children with flat backs, and children with scoliosis). In the research we were able to define reference values for every age group.

Through the examinations it revealed that even at healthy-reckoned children posture disorders could be diagnosed which cause no pain or discomfort during childhood, but later could worsen and could be the sources of several rheumatologic and orthopaedic diseases.

From large number of examinations we succeeded to establish a new reference set, which is slightly different from the values used so far.

Table 1.: Values of kyphosis, lordosis, total trunk inclination, lateral inclination and scoliosis at different age groups of 6 to 12 years old children

Age (year)	Diagnosis	Number of Subjects	Kyphosis (Average ±SD*)	Lordosis (Average ±SD*)	Total trunk inclination (Average ±SD*)	Lateral inclination (Average ±SD*)	Scoliosis (Average ±SD*)
6	Healthy	1	32.8	19.6	6.3	0.8	0.0
	Bad posture	6	44.8±11.7	27.9±16.9	3.5 ±2.1	1.5±1.4	0.0
	Flat back	0					
	Scoliosis	5	42.7±3.3	28.1±12.1	2.4±2.0	1.2 ±0.5	0.0
7	Healthy	32	41.4±8.1	34.9±11.2	3.4± 3.1	1.4 ±1.1	0.0
	Bad posture	39	43.7± 8.2	30.0±13.3	3.0 ±2.5	1.2 ±1.0	0.0
	Flat back	7	36.6± 4.3	20.8±12.1	2.4±1.6	1.4 ±1.0	0.0
	Scoliosis	5	42.7 ±3.3	28.1±12.1	2.4 ±2.0	1.2 ±0.5	4.1 ±5.9
8	Healthy	87	42.1± 7.6	30.8±13.0	3.1 ±2.4	1.2 ±1.0	0.0
	Bad posture	58	43.6 ±7.1	33.9±51.4	3.1 ±2.5	1.7± 1.3	0.0
	Flat back	7	32.2 ±8.5	17.8±14.2	3.0 ±2.7	1.4 ±1.2	0.0
	Scoliosis	11	43.3± 6.1	32.4±14.7	2.7± 1.5	1.9 ±1.3	3.1± 6.0
9	Healthy	100	41.1± 8.5	31.6±10.8	3.1 ±2.2	1.2 ±1.1	0.0
	Bad posture	70	42.9 ±7.8	27.0±11.3	3.3 ±2.2	1.7 ±1.3	0.0
	Flat back	7	34.0± 7.3	15.9 ±5.5	4.8 ±3.8	0.6 ±0.5	0.0
	Scoliosis	26	36.7 ±8.5	31.0±10.5	3.5±2.4	1.3 ±1.2	3.1± 3.9
10	Healthy	63	39.1± 8.2	34.3±10.7	3.1± 2.2	1.1± 1.0	0.0
	Bad posture	51	41.2±10.6	30.4±12.9	3.3± 2.2	1.7± 3.3	0.0
	Flat back	8	34.7± 8.4	26.1±10.9	3.4± 2.3	1.0± 0.6	0.0
	Scoliosis	29	38.3± 6.0	30.9±11.6	4.3±2.6	1.0 ±0.9	3.5± 5.7
11	Healthy	40	40.5±10.9	33.6 ±8.7	3.5± 2.8	1.7± 1.2	0.0
	Bad posture	25	42.2± 8.6	30.4± 8.9	3.9± 2.5	1.5 ±1.0	0.0
	Flat back	2	19.6± 6.5	19.1 ±2.0	2.0± 1.5	2.2± 0.6	0.0
	Scoliosis	19	41.8± 7.1	31.2 13.9	4.1 ±2.2	1.9± 1.2	4.3± 6.1
12	Healthy	8	39.1±10.2	31.2 ±8.2	3.8 ±2.1	2.0± 1.4	0.0
	Bad posture	9	45.8 ±7.3	35.7±8.6	3.3 ±3.6	1.7 ±1.5	0.0
	Flat back	0					
	Scoliosis	10	39.7± 9.3	33.0±10.6	3.8 ±2.0	1.9± 1.6	3.7±5.0

**SD= standard deviation*

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E/I-7
EFFECT OF PHOTO-ACOUSTIC STIMULATION PATTERNS ON SALIVA SECRETION

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Objectives: Previous studies demonstrated that photo-acoustic stimulation has a significant effect on human salivary secretion using 8 Hz medium frequenced mixed stimulation patterns. The aim of this study was to investigate if individually created specific photo-acoustic stimulation patterns have pattern specific effect on saliva secretion, and whether it is coupled with phenomenological effects or not.

Methods: 14 healthy volunteers were investigated without any oral pathologies (male: 6, female 8, age: 23-27 yrs). Four patterns of stimulation frequency were studied within a range of 1-15Hz such as increasing pattern; decreasing pattern; increase followed by decrease and decrease followed by increase. Experiments were repeated four times in a self control design.Whole saliva was collected in 5min phases before the stimulation as control value, under administration of specific patterns, under post stimulation phases and after the experiment as last value. The volume of saliva was measured, the flow rate was calculated. Total protein (Bradford) and amylase (starch split) concentration of samples were determined, amylase output and protein output values were calculated. Phenomenological parameters were measured with numerical analogue scales.

Results: The stimulation has a significant effect on salivary flow rate, protein output, amylase activity and amylase output (Friedmann ANOVA $p \leq 0.05$). Stimulation pattern specific effects were found in case of protein output, amylase activity and amylase output as well as in case of trance activity (Wilcoxon test $p \leq 0.05$). Our data confirm previous findigs that photo-acoustic stimulation has a significant effect of on saliva secretion. A specific effect on certain salivary parameters and phenomenology also appeared. Salivary and phenomenological effects seem to be rather independent.

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E/I-8
RESULTS OF A NEW QUESTIONNAIRE TO ASSESS CHILDREN AND ADOLESCENT SLEEP PROBLEMS

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Introduction: Screening of sleep disorders in children is of high importance. In Hungary there is no standardized questionnaire for assessing sleep problems. We evaluated the results of sleep quality scales of our questionnaire and compared the data of healthy and clinical population. We analyzed the correlation between our questionnaire and validated tests and the severity of obstructive sleep apnea (OSA).

Methods: Our questionnaire is designed to estimate sleep hygiene and quality in two age groups (8-14 and 15-18 ys.) by nighttime and daytime symptoms score. Two groups of children were analyzed: 1. healthy group (n=2020), 2. children with sleep problems (n=66). The second group filled out two validated tests, Modified Pediatric Epworth Sleepiness Scale (MP-ESS), Conner's Rating Scales-Revised (CRS-R) and underwent polysomnography. Severity of OSAS was characterized by Apnea-Hypopnea Index (AHI) and Oxigen-Desaturation Index (ODI).

Results: Children underwent polysomnography had significantly higher score both on nighttime and daytime symptoms scale than healthy children. Correlations were: score of nighttime symptoms scale and CRS-R score (r=0.441; p=0.001), score of daytime symptoms scale and MP-ESS score (r=0.389; p=0.001). Children in the highest quartile of nighttime symptoms scale had significantly higher AHI (mean±SD: 0.62±1.07 vs. 5.97±11.39; p=0,04) and ODI (mean±SD: 0.49±0,53 vs. 6.23±12,07; p=0.02) than children in the lowest quartile.

Conclusion: Our questionnaire can be potentially useful in evaluating sleep problems in children and give more information about sleep problems than other tests. However validation of the questionnaire is still needed.

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E/I-9
IN VIVO EVALUATION OF SKIN GLYCATION BY THE USE OF TWO-PHOTON MICROSCOPY

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Two-photon excitation fluorescence microscopy is a novel system for monitoring the morphology and physiological processes in the skin. The near infrared laser light (650-1300 nm) allows imaging of deeper layers of the skin down to 500-1000 μm. The epidermis and dermis contain numerous endogenous chromophores, such as NADH, melanin, collagen, elastin, that can be efficiently excited in the near infrared spectral range by two-photon absorption. Glycation is a nonenzymatic modification of proteins, resulting from reactions between glucose and primary amino groups. The advanced glycation endproducts are the group of chemically modified proteins, that can accumulate within the tissue and they can cause diabetes-related complications.

Aims: In our study, we optimized the in vivo imaging by using two-photon microscopy combined second harmonic generation to investigate the glycation-induced changes within the skin of ob/ob knockout and wild type (B6) mice.

Results: Morpologic and spectroscopic differences were found investigating the skin of ob/ob knockout and wild type mice.

Our study suggests that the second harmonic generation imaging could be used for in vivo noninvasive visualizing and diagnosis in dermatology.

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E/I-10
SIMULTANEOUS ANALYSIS OF SERUM INFLIXIMAB AND ANTI-INFLIXIMAB ANTIBODY LEVELS IN THERAPY RESISTANT PEDIATRIC PATIENTS WITH CROHN'S DISEASE

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Anti-TNF-alfa infliximab (IFX) therapy plays a significant role in the treatment of paediatrics Crohn's disease (CD). The process of the long-term treatment reduces the efficacy, in which the inadequate serum levels and anti-infliximab antibodies (ATI) play a key role. The current method for detection of ATI is a double-antigen ELISA, however, in this assay serum IFX interferes with ATI during the measurement. The rate of the interference can be reduced with the usage of the new Homogeneous Mobility Shift Assay (HMSA).

Aim: Our aim was to determine the serum levels of IFX and ATI in children with CD treated with IFX, and to examine correlation between these parameters and clinical response.

Study population and methods: IFX and ATI were measured in 230 serum samples from 71 CD patients (age 7-21)(Group I) using HMSA and compared to the clinical status of the patients characterized by the Pediatric Crohn's Disease Activity Index and the serum CRP. Furthermore, in 31 out of the 71 patients an average of 6 samples were available during the length of the treatment (Group II), which gave the opportunity to follow up ATI and IFX levels.

Results: ATI were positively detected in 29.6% (21/71) of the patients and in 20.4% (47/230) of serum samples. In Group II ATI appeared in the serum of 8 patients. In the ATI positive cases the IFX median value was 0 μg/ml, the ATI negative patients median value was 2.55 μg/ml. At the 45% of the ATI negative serum samples the IFX levels were >3 μg/ml. In Group II linear regression analysis was performed showing reduction in CRP value at 88% of those cases whose serum IFX levels were more than 3 μg/ml.

Conclusion: Lower IFX and higher CRP levels were measured in ATI positive CD patients. Monitoring IFX and ATI may improve therapeutic decisions.

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E/I-11
THE PLASMA LEVEL OF MYELOPEROXIDASE IN HEALTHY AND DIABETIC GROUPS

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Myeloperoxidase (MPO) is a heme enzyme stored in the primary granules of mononuclear cells and is involved in the production of bactericidal free radicals during phagocytosis. However when released from the cell it can damage the extracellular components and thus play a role in the pathogenesis of various diseases. The aim of our work was to find out if the plasma concentration of MPO is associated with the cyclic changes of sex hormone levels and the existance of certain free radical mediated diseases (diabetes mellitus).

Methods: Fasting venous blood was obtained from healthy men and women and patients with type 1 diabetes (T1DM) and gestational diabetes (GDM). The plasma concentration of MPO was assessed with mass spectrometry. The plasma testosterone and estradiol levels of healthy men and women was also measured, respectively.

Results: Mean MPO level (pmol/L) of healthy groups: 1. women at the time of estradiol peak (n=23, estradiol: 257.63 pg/mL): 208.47; 2. women at the time of estradiol minimum (n=27, estradiol: 47.59 pg/mL): 265.9; 3: men (n=23, testosterone: 486.79 ng/dL): 332.32.

Mean MPO level (pmol/L) of diabetic groups: I. GDM treated with diet (n=11): 269.0; II. GDM with multiple pregnancy (n=8): 259.75; III. T1DM with preganancy (n=4): 320.67; IV. non-diabetic women with pregnancy (n=16): 208.75; V. T1DM women without pregnancy (n=10): 310.67; VI. T1DM men (n=9): 386.56.

MPO levels were significantly higher in group 2. compared to group 1., and MPO levels of group 3. were significantly higher than those of goups 1. and 2. MPO concentration in group VI. was significantly higher compared to most diabetic and healthy groups.

Discussion: According to our results MPO levels are higher in healthy women at the time of estradiol minimum, and even more elevated in healthy men compared to women at the time of estradiol peak. Thus the higher level of estradiol can be protective against free radical mediated diseases through the reduction of MPO. The diabetic state enhances MPO plasma levels in the case of the moderate GDM and even more in T1DM. So the measurement of MPO levels might be useful in prognosing the development of diabetic complications.

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E/I-12
PHARMACOKINETICS AND PHARMACOGENOMICS OF HIGH-DOSE METHOTREXATE TREATMENTS IN PEDIATRIC ALL

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High-dose methotrexate (HD-MTX) is an important component of the consolidation therapy of childhood acute lymphoblastic leukemia (ALL).

Aim: Our objectives were to perform a detailed comparative study of pharmacokinetics and toxicity of methotrexate (MTX) and 7-hydroxy-methotrexate (7-OH-MTX) after HD-MTX treatments and to analyze their relation with common and rare polymorphisms in genes of folate metabolic pathway, transporter molecules and transcription proteins.

Methods: Data of 65 children treated with 5 g/m^2/24h and 88 children treated with 2 g/m^2/24h HD-MTX according to ALL-BFM 95 and ALL IC-BFM 2002 protocols were collected [mean age: 6.4 years (1.0-17.9 years)]. Totally 583 HD-MTX infusions were analyzed. Hepato-, nephro- and bone marrow toxicities were evaluated. 63 single nucleotide polymorphisms (SNP) of 14 genes were genotyped. Random forest and regression trees were used for variable selection. Linear mixed models were established to prove the significance of the selected variables and to estimate effect sizes.

Results: 5 g/m^2/24h treatments resulted in higher serum and CSF MTX and 7-OH-MTX levels ($p < 0.001$). CSF penetration rate of MTX was independent of given dose [0.023 (95% CI: 0.017-0.025) vs. 0.028 (95% CI: 0.024-0.03)]. CSF MTX concentration correlated with 24h serum MTX level. Slightly more but reversible side effects were seen after 5 g/m^2/24h MTX. SNPs (rs4948502, rs4948496, rs4948487) of ARID5B gene were associated with serum levels of MTX ($p < 0.001$), serum levels and AUC of 7-OH-MTX ($p < 0.001$) and with hypoproteinaemia ($p < 0.001$). The rs4149056 of SLCO1B1 showed also significant association with the serum levels of MTX ($p < 0.001$).

Conclusions: Therapeutic serum and CSF MTX concentrations can be achieved more reliably with 5 g/m^2/24h treatments. We confirmed the association of ARID5B gene and MTX plasma levels however the exact role of this gene on MTX levels needs further investigations.

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E/I-13
AGE AT DIAGNOSIS <40-YEARS IS NOT AN ACCURATE PREDICTOR OF DISEASE OUTCOME IN PATIENTS WITH CROHN'S DISEASE

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Background: An age <40-years at diagnosis has been identified as a marker of disabling Crohn's disease (CD) disease in previous studies. The aim of this study was to analyze the predictive value of age at onset <40-years to predict the evolution of disease behavior, need for resective surgery, time to azathioprine(AZA) or steroid exposure in the population-based Veszprem province database.

Methods: Data of 506 incident CD patients were analyzed (median age at diagnosis:31.5;SD:13.8years). Both in- and outpatient records were collected and comprehensively reviewed.

Results: Patients with an age at diagnosis >40 years presented more frequently with colonic (48.2% vs 32.6%,p<0.001) and complicated (50%, vs 41.1%) disease compared to patients with an age at diagnosis <40 years. In contrast, in a Kaplan-Meier analysis the probability to develop complicated (< 40-years:54.6% and 65.8% vs >40-years:59.2% and 60.4% after 5- and 10-years), penetrating disease (< 40-years:36.8% and 49.1% vs >40-years:31% and 37.7% after 5- and 10-years, pLogRank=p=0.15) or need for surgery (< 40-years:13.6%, 33.3% and 44.8% vs. >40-years:15.9%, 33% and 43.3% after 1-, 5- and 10-years, pLogRank=0.97) was not significantly different in patients with an age at onset < or > 40-years. In a Kaplan Meier analysis, the probability of AZA use was significantly more higher in patients with an age at diagnosis < 40 years (32.8%, 39.2% and 51% vs >40-years:17.1%, 25%, 31.1%, pLogRank=0.001, HR: 1.89, 95%CI: 1.27-2.82) after 1-, 5- and 10-years of disease duration

Conclusions: Despite subtle differences in disease phenotype at diagnosis, age at diagnosis <40-years was not associated with clinically important disabling. The association between age at diagnosis and drug exposures (e.g. need for or time to AZA, anti-TNF or steroids) rather represents a difference in treatment strategy and should not necessarily be interpreted as a disabling outcome.

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E/I-14
ACCURACY OF PATTERN-BASED INNER MACULAR THICKNESS PARAMETERS OF THE RTVUE OCT TO EARLY DETECT GLAUCOMATOUS PROGRESSION

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Aims: To investigate the ability of different parameters of the RTVue-100 Fourier-domain OCT to detect early structural glaucomatous progression.

Methods: One eye of 68 patients (17 controls and 51 perimetric glaucomas) was examined prospectively at 6-months interval for 1.5 to 3 years. Progression was determined by Octopus normal G2 visual field progression criteria (Hodapp criteria).

Results: In 10 of the 51 glaucoma eyes functional progression found based on visual field criteria. Median visual field mean defect (MD) change was -0.300 dB/ year for the controls, -0.120 dB/ year for all glaucoma eyes ($p=0.461$ vs. controls) and 1.231 dB/ year for the 10 functionally progressing glaucoma eyes ($p<0.001$ vs. controls). When the glaucoma group and the control group were compared for progression rates, no ONH, RNFLT and average GCC (Ganglion Cell Complex) parameters differed significantly. In contrast, both GCC-Focal Loss Volume and GCC-Global Loss Volume showed significantly greater progression rates in glaucoma group than in control eyes ($p=0.004$ and $p=0.001$, respectively).

Conclusion: Early structural progression of glaucoma may be better detected with pattern-based GCC parameters of the RTVue-OCT than any ONH, RNFLT and average GCC parameters of the same instrument. Increase of GCC-FLV and GCC-GLV may indicate progression even when functional progression is mild.

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E/I-15
INVESTIGATING THE CLINICAL CONSEQUENCE OF TRANSITION-SPECIFIC KRAS MUTATIONS IN LUNG ADENOCARCINOMA

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Background: Platinum-based chemotherapy is the most common treatment in advanced lung adenocarcinoma. However, the identification of patients who are likely to benefit is rather challenging. So far there is no strong evidence for the predictive effects of KRAS mutations on the clinical outcome of chemotherapy. However, most of these studies did not take into account the specific transitions in the KRAS gene.

Methods: For this very reason we studied a cohort of 505 stage III-IV lung adenocarcinoma patients with known KRAS mutational status who were treated at the the National Koranyi Institute of TB and Pulmonology. Formalin fixed paraffin embedded histological samples were subjected to restriction fragment length based KRAS codon 12 and codon 13 mutation screen. All mutant cases then were subjected to direct sequencing. Next, the correlation of various specific transitions with the clinicopathological characteristics including smoking status, progression-free and overall survival, response rate to platinum based treatments was analyzed.

Results: In our cohort 338 non-KRAS mutant (67%), 147 codon12 mutant (29%) and 20 codon13 mutant (4%) patients had been identified. We found no significant differences among the different KRAS mutation groups in progression free or in overall survival. Importantly, we found that G12V transitions were significantly more frequent in the never-smoker patients than in ever-smoker patients (26% versus 6%, $p=0.023$). Furthermore, they tended to have a higher response rate (66% versus 47%, $p=0.072$). There was also a modest increase in the median overall survival from 559 to 638 days in the G12V subgroup of patients.

Conclusions: While KRAS mutation status per se may not be a prognostic or predictive biomarker in lung adenocarcinoma, the transition specific analysis may indeed identify clinically very important subgroups of patients that ultimately may influence the treatment decisions during therapy.

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E/I-16
CAROTID INTIMA-MEDIA THICKNESS IN CHILDREN AFTER RENAL TRANSPLANTATION – CROSS SECTIONAL STUDY

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Introduction: Cardiovascular (CV) morbidity is increased in end-stage renal disease and even after successful renal transplantation (RTX). Surrogate markers should be assessed to characterize CV damage in this population. Carotid intima-media thickness (cIMT) and central pulse wave velocity (PWV) are known as markers of arterial stiffness, predicting CV morbidity and mortality in adults. Our aim was to investigate IMT and PWV, and to assess their determinants in RTX children.

Material and Methods: 54 RTX (16.9±4.5 years, 36 males) children were involved in the study. cIMT was investigated by B mode ultrasonography, PWV was measured by applanation tonometry. 24 hour ambulatory blood pressure monitoring was performed, body composition was assessed by multifrequency bioimpedance measurement. Standard laboratory parameters were measured by routine laboratory methods.

Results: IMT exceeded the 95th percentile in 21/54 children. IMT SDS showed bimodal relationship with serum 25OH vitamin D ($p<0.05$) and negative correlation with serum HDL-cholesterol level (-0.42, $p<0.05$). PWV exceed the 95th percentile in 15/54 children. PWV correlated with serum total cholesterol level ($r=0.39$, $p=0.005$). Children who spent more than 2 years on dialysis had higher PWV SDS values (1.74 (-1.04 – 4.03) vs. 0.64 (-1.01 – 3.12), $p<0.05$)).

Conclusions: Subclinical atherosclerosis is present in pediatric renal transplant recipients. After RTX lipid-lowering therapy could have great importance to halt the progression of atherosclerosis and adequate vitamin D supplementation could reduce the CV risk.

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E/I-17
RISK OF COLORECTAL CANCER IN CD PATIENTS WITH COLONIC INVOLVEMENT AND STENOSING DISEASE. RESULTS FROM A POPULATION-BASED STUDY

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Background and aims: Since data are limited our aim was to study the risk of colorectal cancer (CRC) in patients Crohn's disease (CD) presenting with stenosing colonic lesions in the population-based, Veszprem province database, which included incident patients diagnosed between January 1, 1977 and December 31, 2008.

Methods: The data of 506 incident CD patients were analyzed (age-at-diagnosis: 31.5, SD: 13.8 years). Both hospital and outpatient records were collected and comprehensively reviewed.

Results: CRC was diagnosed in total 5 CD patients (total follow-up: 5758 person-years) during follow-up. 47 patients presented with colonic/ileocolonic disease and a stenotic lesion in the colon. The total follow-up was 502 person-years (mean: 10.6 SD 7.1 years). CRC developed in 3 patients (6.3%), equalling 0.6 /100 person-years. In a Kaplan-Meier analysis the probability of developing CRC was 4.7% after 5-years and 7% after 10-years of disease duration. In a sensitivity analysis, we included all patients who presented with colonic/ileocolonic disease and a stenosing colonic lesion at diagnosis or during follow-up (n=66, total follow-up: 734 person-years, mean: 11.2 SD 8.3 years). The prevalence of cancer was overall 4.5% (0.4/100 person-years). In a Kaplan-Meier analysis the probability of developing CRC was 3.3% and 5.1% after 5- and 10-years of disease duration.

Conclusions: The risk to develop CRC in colonic CD patients presenting with or developing a stenotic lesion in the colon is high already after relatively short disease duration suggesting the need for careful surveillance of these patients.

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E/II
ORAL PRESENTATIONS

Chairman:
Prof. Dr. István Bitter
Dr. Pál Czobor
Dr. Róbert Bódizs

E/II-1
GENETICS OF SUICIDAL BEHAVIOR: ROLE OF THE MICRORNA SYSTEM

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Suicide is the most devastating outcome of the psychiatric disorders, its possible risk factors have been studied intensively. Recent studies reported an association between the executive functions and suicidal behavior that has been replicated repeatedly and was independent from the psychiatric diagnoses. The genetic architecture of the executive functions is still unclear, however, the microRNA (miRNA) system has been implicated by multiple studies. The miRNAs play a vital role in neurodevelopment and synaptic plasticity, influencing the executive functions. The objective of our study was to examine the gene-based associations between the suicidal behavior and miRNA genes differentially expressed in the dorsolateral frontal circuitry among subjects with major depressive (MDD) and bipolar disorder (BD).

Samples from NCBI GAIN BD (n=999) and MDD (n=1753) case-control datasetswere analyzed. Suicidal behavior was defined by having severe suicidal ideation, or lifetime suicide attempt, control subjects were non-suicidal BD or MDD cases. Genes were selected by using the EBI Gene Expression Atlas, 53 of the 91 miRNA genes were sufficiently covered. Gene-based association tests were assessed with VEGAS and were validated with KGG. Datasets were combined in a random effect meta-analisis and population stratification was corrected with the genomic inflation factors. Multiple comparisons was corrected by using permutaion with 1000,000 cycle.

Nominal significant p-values were detected for DICER1 (p=0.0042) and MIR765 (p=0,0253) genes, and DICER1 remained significant after the correction for multiplicity (p=0,048).

The product of the DICER1 gene is a rate limiting factor in the biosynthesis of the miRNAs and suggested to have a significant effect on the executive functions. The statistically significant association between the DICER1 gene and suicidal behavior found in this study in both the MDD and bipolar sample corroborates the link between executive functions and suicide cutting across DSM-IV diagnoses and may contribute the better understanding of the etiology.

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E/II-2
THE ATTITUDE OF DRUG USERS ABOUT DEATH

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Drug-related deaths directly due to drug use, shortly after consumption patterns mean death. Health problems into account, in particular the use of injectable may result infections (AIDS, hepatitis C), while most of the high value of mortality due to overdose, suicide and violence that may occur due to a victim, and infectious diseases as well. (Rácz, 1999)

In 2011, 14 occurred directly related to illicit drug use, 29 indirectly drug-related deaths have been reported in Hungary. (EMCDDA, 2011c) The year before, 12 deaths reported a significant increase in direct comparison with a case, behind the increase is presumably the development of the collection methods.

Aims: of the research is to assess whether a statistically significant sample search of death among opiate users in relation to the abstinent population. It could get meaning in the first line of prevention work, and the close up of drug using, and in the achievement of long-term abstinence. The research subject was from the Kozma str. Prison in Budapest – inside of the Judical Monitoring and Psychiatrical Institute (IMEI). In the prison context – in front of view the selection of drug users is justified of available abstinence which is complusion of prison and the veridiction of answers on questionnaires has been helped by the fact that it is not a question of delinquency.

Method: Addiction Severity Index (Bácskai, Gerevich, Rózsa, 2001), Multidimensional Fear of Death Scale (Zana, 2006), Caldwell Social Support Scale (Caldwell 1987, Kopp 2000), short version of Beck's Depression Scale (Rózsa 2001), other items (Smudla, 2010), participants observation

Results: the common of previous studies is that drug users experiences about death is belittled, in the background is often an unfinished grief-work, or the total negation of death - multiple overdose survived, it's omnipotence experience, which is also charachteristic of the opioid mechanism of action.

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E/II-3
PERSONALITY TRAITS AND TOBACCO USE: AFFECTIVE TEMPERAMENTS AND THEIR RELATIONSHIP WITH SMOKING PATTERNS. A CROSS-SECTIONAL STUDY

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Background: Affective temperaments determine the emotional core of personality and may play a role in the initiation of addictive behaviours influencing the success of discontinuation. The aim of our study was to determine the role of affective temperaments in tobacco use and to explore gender differences.

Methods: 467 chronically ill outpatients (123 current smoker, 123 former smoker and 221 cigarette naïve patients) were collected from primary care practices from Hungary. The self-rating version of the Temperament Evaluation of Memphis, Pisa, Paris and San Diego questionnaire was used to measure point scales and dominant forms of affective temperaments. Chi-square test and Mann-Whitney U test was performed to compare affective temperaments, gender and smoking status.

Results: Smokers were younger (55±14 years) than quitters (61±13 years) or cigarette naïve patients (59±15years) ($p=0.005$) and males were more likely to try cigarette during their lifetime ($p=0.018$). Dominant depressive and anxious temperament was more prevalent among current smokers comparing with former smokers ($p=0.019$ respectively) and depressive temperament revealed to be more important in males ($p=0.023$) while anxious temperament in females ($p=0.041$). Dominant irritable temperament showed strong association with current smoking when compared with cigarette naïve patients ($p=0.019$). In contrast to never smokers, current smoker males scored higher on depressive ($p=0.013$), cyclothymic ($p=0.025$) and irritable ($p=0.07$) temperament subscales while current smoker females on cyclothymic ($p=0.005$) and irritable ($p<0.0001$).

Conclusion: Affective temperaments show different patterns among current, former and never smokers. Higher scores on cyclothymic, irritable and (in males) depressive temperament are related to the initiation of tobacco use, while the absence of dominant depressive and anxious temperament may promote cessation.

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E/II-4
ERROR-RELATED BEHAVIORAL INDICATORS IN PATIENTS SUFFERING FROM ADULT ATTENTION DEFICIT/HYPERACTIVITY DISORDER (ADHD)

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Background. Attention deficit/hyperactivity disorder (ADHD) is a common neurodevelopmental disorder defined by the behavioural symptoms of inattention, hyperactivity and impulsivity. A growing body of evidence shows that patients with ADHD exhibit deficits not only in executive funcioning, but also in emotional regulation[1]. Thus, investigation of the behavioural characteristics of error monitoring and emotional regulation deficits have both become a prominent field of research.

Objective: Our primary aim was to investigate whether ADHD patients differ from healthy control subjects with respect to the error-related behavioral markers of commission and omission errors and post-error slowing (PES). Additionally, we wanted to examine to what extent arousing emotional picture stimuli interfere with executive functioning, as indexed by errors of commission in subjects with and without ADHD.

Method: Thirty-one ADHD patients and thirty-two individually matched healthy controls performed an emotional behavioral inhibition (go/no-go) task. The task was performed by using pictures of the International Affective Picture System (IAPS). Participants were asked to respond as quickly and as accurately as possible to each stimulus, and to withhold their response to the second instance of any stimulus that is repeated.

Results: Consistent with available literature, a pronounced difference was found in commission and omission error rates, with ADHD patients performing significantly more poorly. Additionally, significant PES differences were found between the two groups. Analyzing the commission error rates by high and low arousal levels, we found that while the control subjects performance showed a pronounced difference depending on the valence of the picture, this effect could not be found in ADHD patients.

Conclusion: Consistent with previous findings our results indicated that error monitoring and related behavioral adaptation are impaired in adult ADHD. Furthermore, our data suggest that disturbances in emotional processing may interfere with executive functioning, and may therefore account for impairments in life functioning.

[1] Differential diagnosis of adults with ADHD: the role of executive function and self-regulation. Barkley RA. Department of Psychiatry, Medical University of South Carolina, Charleston, SC, USA.

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E/II-5
HEALTH CONDITION OF GYPSIES

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In 2004 has written a study (by Csaba Dupcsik), and we can see that there is a large difference between the health of gypsies and non-gypsies in Hungary. In some cases the difference is unbelievable. Iron-deficient anaemia 14,7 times, tuberculosis 12,9 times, asthma 6,6 times, stomach and duodenal ulcer 5,7 times the difference, and every time is onto gipsies' harm. However if we see the previous dates of researches (1978 and 1993), the results are not so dramatic, at then the dates show a relative well balanced situation.

What happened during the last genaration?

The last two genaration of gypsies' history can divide three parts. The first one is up to '61, the second is to '89, and the last one is up to now. And it seems, while during the middle period the health of gypsies has got similar to non-gypsies, after the change of political transformation happened something that changed the life of gypsies, and because of it, the health of gypsies deteriorated dramatically. Why is it? It is because of the difference of living conditions. The gypsies lost there jobs in the early '90 years, and in this way started a process leading to this situation nowadays.

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E/II-6
DIFFERENCES AND SIMILARITIES BETWEEN THE FAMILY THERAPY OF MALE AND FEMALE PATIENTS WITH ANOREXIA NERVOSA

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Formerly eating disorders were regarded as the disorders of white Western women ("3W"). At present this is not valid any more, as the prevalence of eating disorders is increasing among non-white people, in non-Western countries and among males. Males with eating disorders have been reported since 1689. According to the DSM-IV TR the ratio of male eating disorders is 10%.

Males with an eating disorder are less fearful about gaining weight and becoming fat or heavy than eating disordered females. Predisposing factors and characteristics of male eating disorders differ from those of females. For example females try to lose weight continuously, but males stop losing weight at a low but not life-threatening body weight.

Family therapy one of the major therapeutical methods in the treatment of eating disorders. This presentation will summarize the main characteristics of the family therapy of four male patients with anorexia nervosa, restrictive type (age range: 19-30 years). The therapeutical process is more or less different from that of females. The separation-individuation process of the anorectic males is difficult because their attachment to the mother is strong, even in the early adult years. The anorectic symptoms symbolize the fear of adulthood. There is an interesting phenomenon among young adults called postadolescence, which was first published by Keniston in 1970. It is more frequent among males than females.

The patients presented were older than the classical restrictive anorectic females. In the development of their eating disorder the postadolescence may be an essential factor.

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E/II-7
BEHAVIORAL TREATMENT OF OBESITY

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Introduction: Obesity is a global epidemic condition with serious health consequences for individuals. Behavior therapy is one of the evidence based methods in the treatment of obesity. Standard behaviour therapy for obesity was extended with self-help. The aim of our study was to determine the feasibility and the results of such a setting.

Methods: The 24-week weight loss program involved 39 participants (10 men and 29 women) between 21-65 years of age (M= 39,9, SD=11,25) Patients's mean BMI was 37,4 (SD=8,06). The overweight participants were mentally sine morbo. Exclusion criteria were psychiatric disease and chronic physical illness. The effectiveness of this therapy was assessed by measuring the body weight of participants, and by participants filling in questionnaires before the first session and after the 8th, 16th and 24th sessions. We used the following measures: Three-Factor Eating Questionnaire, Rosenberg Self-esteem Questionnaire.

Results: Respondents reported average weight loss to be around 9.9 kg (SD=5,87 range: 2,0-27,0 kg;), which corresponds to 8,8% (SD=4,31%, range: 2,1-19,1%) of baseline weight. 90% of participants achieved the normative of a 5% minimum weight loss during treatment. 28% attained 10% weight loss. Significant relationships ($p<0,001$) and large effect sizes were found regarding changes of eating behaviour (such as uncontrolled eating, emotional eating, cognitive restraint) (Cohen's d =1,80-3,04). Significant relationship was found between the increase of cognitive restraint ($r=0,51$; $p=0,002$) and the decline of emotional eating ($r=0,38$; $p=0,021$) in respect to the rate of weight loss during treatment. A tendency was found between the decline of uncontrolled eating and the rate of weight loss ($r=0,31$; $p=0,058$). Weight loss was associated with improvement of global self-esteem ($\beta=0,43$; $p=0,009$), which remained significant even when controlling for background variables ($\beta=0,34$; $p=0,033$).

Conclusion: Our results suggest that standard behavioral therapy extended with self-help elements can be a cost - efficient method to help obese patients reduce weight. Treatment has significant benefits in changing maladaptive eating behaviours into adaptive ones, and these changes resulted in bigger weight loss during therapy. Intentional weight loss has a favourable effect on mental health, which is shown by the relationship between weight loss and global self-esteem.

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E/II-8
SOCIOCULTURAL AND ETHNICAL DIFFERENCES IN THE RISK FACTORS OF SERIOUS SUICIDE ATTEMPTS IN HUNGARY

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Objective: The suicide rate in Hungary is one of the highest in the European Union. The aim of the study was to explore psychosocial and cultural risk factors of suicide attempters with different ethnicity in Borsod-Abaúj-Zemplén county, and in Budapest.

Method: Semi-structured interviews were conducted among 151 suicide attempters hospitalized at the Toxicology Departments of Miskolc County Hospital and the Péterfy Sándor Hospital in Budapest for self-poisoning. Patients were asked about their demographics, social and marital status, physical and mental illnesses. Detailed data regarding the circumstances, the reason and the method of their attempt were also recorded. Patients completed the Shortened Beck Depression Inventory, the Social Support Questionnaire, and the Hopelessness Scale. Suicide attempts regarding seriousness were classified based on the MONSUE (Monitoring Suicide Behavior In Europe) registration form.

Results: As a cause of self-poisoning, patients mentioned interpersonal conflicts, financial problems, grief, sleeping disturbance, and physical illness. Members of the Roma minority (N=61) reported previous suicide attempts more frequently, and had fewer planned attempts (p=0.003). Although there was no significant difference in the level of depression, hopelessness, and social support, there were more serious attempts among the non-Roma group with real intent to die (p=0.003). High educational attainment increased the odds of serious suicide attempts among the Roma patients by 35 times. Hopelessness was associated with a 1.5 times higher odds of serious suicide attempt in the non-Roma group.

Conclusion: Significant differences in the risk factors of suicidal behaviour were identified between Roma and non-Roma patients. High educational level as a risk factor in the Roma group requires further research considering socioeconomic changes and social transition. Suicide prevention strategies should take these differences into consideration to ensure more effective intervention.

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E/II-9
EFFECTS OF ORGAN DONATION ATTITUDE AND FAMILY APPROACH ON ORGAN DONATION ACTIVITY

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Introduction: The number of cadaver organ donors is influenced by ICU staffs' attitude, knowledge, and the acceptance of brain death (BD) criteria, meanwhile the involvement in the donation process influences the attitude of the personnel. The family approach is mainly affected by the understanding of BD, timing of request, and skill of the individual making the request. The aim of this research is to investigate the Hungarian ICU personnel attitude regarding organ donation.

Method: Family approach questionnaires were collected for 15 months (n=188), with validated, 46 questions. The questionnaire was filled when first signs of BD were identified and family was approached. 329 **attitude questionnaire**s with 48 questions were collected at the National Anaesthesiology Congress.

Results: One family interview happened in 105 cases, more in 82 cases. They last for 17 minutes in average. Mainly one medical doctor informed the family. 15 of the 26 initial family refusals were changed during the communication. One communication occurs 8 hours before the certification of the BD, while in the other group, the first started 18 hours before the BD declaration.

99% of health care professionals support organ donation in general, 88,5% would offer their organs, but only 46% practice presumed consent consciously. 56% are satisfied with their hospital's donation activity, but only 38% have experience in donor report, 40% in family approach, and 50% in donor management.

Discussion: In order to increase the effectiveness of the organ donation process, it is necessary to learn the methodology how to communicate with donor families, and to ensure appropriate environment, timing and input. Further evaluation of family refusals can identify the most common reasons behind refusals, and by knowing that we can prepare ourselves better for these meetings. Public knowledge and special education for medical doctors may collectively decrease family refusal rates.

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E/II-10
PSYICHOSOCIAL AND FAMILY DYNAMICS STUDY OF EPILEPTIC PATIENTS AND PATIENTS LIVING WITH CHRONIC SPINAL PAIN

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Objective: In our research we examine **the psychosocial and health-related quality of life** of epileptic patients and as a control group, patients with chronic spinal pain by using a **self-completed Psychosocial Health Check Battery**. In the second part of the research, we analyse the social support and background **family dynamics context** influencing the quality of life with using self-completed questionnaires and projective technics. By the dimensions mentioned above our research enables us to compare the two chronic patient groups, the psychosomatic and the non-psychosomatic one.

Theoretical Background: The treatment of epilepsy (EP) raises not only medical but **psychosocial questions**. (J. Békés, 2009). From the first epileptic seizure, the disease becomes a psychosocial issue causing **difficulties in emotional-social adaptation.** (Békés, Halász, 2009). Epileptic patients are very vulnerable to psychosocial problems, and the risk of occurrence of psychopathologic diseases is higher. (T. Mirnics, 2001). According to Strine's (2009) examinations, one can declare that EP patients are more likely to suffer from psychological stress including serious mental disease, they are more inactive physically, they report physical illness, and generally they do not have employment, are single and often lonesome. Based on Harald Breivik's (Breivik et al., 2006) extensive epidemic research, concerning the psychological and social status of persons living with chronic pain, one can declare that **chronic pain has a significant effect on the person's living, psychological status and on the evolution of the person's relationships. Chronic pain influences the physical, mental, emotional, social, nutritional and spiritual aspects of life.** (Farrugia, Fetter, 2009).

Methodes: The tests used in Psychosocial Health Check Battery are generic and disease-specific measuring methods related to international HRQOL examinations. Self-administered questionnaires of 100 epileptic patients and, as a matched control group, 80 patients with chronic spinal pain were analysed. Patients were involved from clinics of two hospitals and from the Psychoterapic Department of the National Centre for Spinal Disorders. A comparative analysis examines the psychosocial background, the psychological well-being (WHO), the level of satisfaction with life (Diener) and of anxiety (HAS) as well as depression (Beck), the sense of self-esteem (Rosenberg) and of self-efficacy (Scwartzer), the subjective perception of the illness (IPQ), coping strategies (FKV-LIS) and in case of EP patients the quality of life, as well, using a disease-specific questionnaire (for EP patients: SHE, LSSS, Quolie-31; in case of patients with spinal disease: VAS). Besides, in case of epileptic patients, the quality of life is examined by epileptologic datas, as well, thus in function of types, frequency and severity of epileptic seizures as well as neurotoxic effects of the used medications.

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E/III
ORAL PRESENTATIONS

Chairman:
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E/III-1
VGLUT3-CONTAINING RAPHE NEURONS REPRESENT A NEW MODULATORY POSSIBILITY

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Nucleus raphe medianus (MR) provides a strong serotonergic input to the hippocampus, whereas almost half of the projecting MR cells including some serotonergic ones express the vesicular glutamate transporter VGluT3. Previously, we reported VGluT3-containing MR-fibers as forming synapses on hippocampal interneurons. Stimulation of this pathway resulted in fast, temporally focused activation of postsynaptic cells, mediated by ionotropic glutamate receptors. This effect raises the possibility of a novel type of modulatory control within the raphe-hippocampal system, as well as the question whether VGluT3-containing cells form a distinct subgroup of MR neurons.

Aims: We registered the firing of MR neurons and hippocampal activity simultaneously in urethane-anesthetized Wistar rats. Recorded cells were labeled with Neurobiotin for further anatomical identification; serotonin- and VGluT3-content were also determined. Dendritic arbor of some neurons was reconstructed as well. In electrophysiological analysis, we focused on changes of firing behavior during hippocampal state transitions.

Results: Recorded and identified cells were grouped into four subpopulations: serotonin-immunopositive, VGluT3-immunopositive, double positive and double negative cells. Serotonergic neurons were slow firing regardless of VGluT3-expression. In contrast, non-serotonergic VGluT3-immunopositive cells fired significantly faster and in a more complex manner than the serotonin-containing populations indicated by high interspike interval variability. Importantly, the firing pattern of VGluT3-immunopositive cells changed more significantly during hippocampal state transitions compared to the serotonergic subgroups. Morphological analysis unraveled profusely branching dendritic tree with shorter dendrites of serotonergic cells whereas the dendrites of both VGluT3-immunopositive and double positive neurons were longer with minimal number of branches. Taking together, VGluT3-containing neurons form a distinct subpopulation in the MR potentially contributing to state transitions.

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E/III-2
METABOLIC CHANGES DURING DIFFERENTATION OF NEURAL STEM CELLS

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According to previous results[1], neural stem cells survive at much lower oxygen supply than neurons, both *in vivo* and *in vitro*. In order to understand the diverse O_2-demand, metabolic analyses were carried out on one-cell derived populations of neural stem cells representing progenitors of the neural plate /early neural tube (NE-4C[2]) and the adult neurogenic zones (HC_A and SVZ_M)[3]. The embryonic (E9) neuroectoderm derived NE-4C neural stem cells displayed very low O_2 consumption, and it was further decreased by starvation. Differentiating NE-4C progenies on the other hand, increased O_2 consumption in response to starvation indicating that neural precursors gain energy from catabolizing own cellular material. Depending on origin and developmental stages, different stem cells displayed different responses in response to supplementing the "starvation" medium with single metabolites (glucose, lactate, β-OH-butyrate, amino acids). Non-differentiated NE-4C cells increased O_2-consumption in response to any of the metabolites. In contrast, neuronal derivatives of NE-4C cells decreased O_2-consumption and increased H^+ production in response to glucose, indicating that glucose is not used for mitochondrial energy production by these cells. Adult-derived non-differentiated neuronal stem cells also decreased O_2-consumption in response to glucose. In these cells, addition of amino acids resulted in a sudden but transient increase, while ketone bodies caused a slow but permanent increase of oxygen consumption. The data indicate that the basic metabolism shifts with the advancement of neural differentiation, and the metabolic profile reflects the origin and stage of differentiation of distinct neural stem/progenitor populations.

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E/III-3
EFFECT OF UNILATERAL AND BILATERAL STN STIMULATION AND LEVODOPA ON DISTAL AND PROXIMAL ALTERNATING MOVEMENT OF THE UPPER LIMB IN PARKINSON'S DISEASE

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Introduction: Bilateral deep brain stimulation (DBS) of the nucleus subthalamicus (STN) effectively improves bradykinesia in Parkinson's disease. We investigated the effect of unilateral and bilateral stimulation on proximal and distal movement of the upper extremity.

Methods: Eleven patients (age: 61,7±9,54years, disease duration:18±6,11years) with Parkinson's disease were recruited one year after bilateral STN-DBS implantation. They performed 14 seconds of finger tapping (FT), hand grasping(HG) and pronation-supination of the arm (PS) as quickly as possible in five conditions (BOTH-ON, BOTH-OFF, CONTRA-ON, IPSI-ON and BOTH-ON-MED-ON) after 12 hours levodopa withdrawal. A motion sensor consisting of a three-dimensional gyroscope and accelerometerwas worn on the index finger to measure limb movement in each condition. Speed as root mean square angular velocity and amplitude as root mean square excursion angle were calculated from the signal of the gyroscopes and compared with ANOVA for repeated measures ($p < 0.05$).

Results: Contralateral and bilateral stimulation increased the speed and amplitude of FT and HG equally and significantly more than ipsilateral stimulation. These parameters were similar during ipsilateral stimulation and the BOTH-OFF state. Speed of PS was improved significantly by contralateral stimulation, but significantly less than by bilateral and significantly more than by ipsilateral stimulation.PS speed did not differ during ipsilateral stimulation and in the BOTH-OFF state. Contralateral stimulation had a similar effect on the amplitude of PS to that of bilateral stimulation; they were significantly greater than the effects in IPSI-ON and BOTH-OFF states. Levodopa intake did not change the speed or amplitude more than bilateral stimulation in either movement.

Conclusion: Contralateral and bilateral stimulation increase the speed and amplitude of finger and hand movement similarly. To reach satisfying improvement in the speed of more proximal arm movements, bilateral stimulation is necessary. Levodopa intake did not change the speed and amplitude of the distal and proximal movements during bilateral stimulation.

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E/III-4
MEASURING FUNCTIONAL CHARACTERITICS OF THE ATHLETE'S HEART WITH TDI

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Introduction: Tissue Doppler Imaging (TDI) is a very useful method in identifying pathological features of the heart. It has been introduced to the sports medicine investigations as well, however findings are controversial. As TDI measurements are less dependent on preload and heart rate, and are free of pseudonormalisation effect, it was suggested that they might be better indicators of cardiac function than traditional Doppler measurements.

Aim of our study was to summarize the data of our TDI measurements and find out if they give better and more exact results and prognose in the functional characteristics of the athlete's heart

Method: Data of 411 measurements were analyzed (131 women(w) and 280 men(m), age between 18-35 ys.). Subjects were divided into 3 groups in both sexes: 1: competetive 1st class athletes, 2: 2nd class and leisure time athletes, 3: sedentary people (N(w): 1: 78, 2: 29, 3: 24; N(m): 1: 218, 2: 35, 3:27). Functional characteristics of the athlete's heart were measured with TDI echocardiography. Diastolic function was described with the E/A ratio and the mitral lateral E/E' ratio. Systolic function was characterised with EF, VCF and mitral lateral S' velocity.

Results: The sedentary group in women was a bit older than the 1st. (Age: 1: 22,75±1,94ys vs 3: 25,79±2,11ys p=0,029). There were no differences in the body size and diastolic function in both sexes. The muscular quotiens and left ventricular muscle mass is greater in athletes than sedentary people. VCF and Ejection fraction was smaller in athletes than in the 3rd group (VCF: 1: 1,108±0,084 vs 3: 1,235±0,085 p=0,0203 and 2: 1,112±0,095 vs 3 p=0,0249; EF: 2: 69,291±2,29 vs 3: 72,836 ±1,85 p=0,047), but lateral S' velocity showed no difference.

Conclusion: TDI measurements seem to be less important than traditional Doppler in characterising the athlete's heart and showing small differences between good and better, than in differentiating pathological features from normal findings.

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E/III-5
FLUID OVERLOAD AND ADVERSE OUTCOMES FOLLOWING PEDIATRIC CARDIAC SURGERY

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Introduction: Fluid overload is associated with hemodynamic instability and acute kidney injury in critically ill pediatric patients. This study investigated the relationship between postoperative fluid overload and mortality in pediatric patients undergoing cardiac surgery.

Methods: We have retrospectively analyzed the data of 1,520 consecutive pediatric patients undergoing cardiac surgery between January 2004 and December 2008. In the first 72 hours, daily fluid balance was calculated as percentage equal to (fluid in [L] - fluid out [L])/(admission weight [kg]) x 100%. Urine output was also recorded and calculated for body weight. Primary end point was in-hospital mortality. Demographic parameters, intraoperative characteristics were also recorded.

Results: Sixty-three patients (4.1%) died. 332 (21.8%) patients had postoperative cardiac failure and 99 (6.5%) patients needed dialysis. Table 1 shows the association between degree of fluid overload and outcomes, which remained after adjusting for demographic and intraoperative variables.

Conclusion: Our results indicate that fluid overload in the early postoperative period is associated with mortality. Monitoring fluid balance and early correction of fluid overload should be standardized in the pediatric cardiac surgery setting.

Outcome		**Urine (ml/kg)**		**Fluid balance (ml/kg)**	
		OR (95% CI)	p	OR (95% CI)	p
Dialysis	DOS	0.981 (0.968-0.994)	**0.004**	1.014 (1.004-1.025)	**0.007**
	Day 1	0.978 (0.967-0.989)	**<0.001**	1.002 (0.991-1.013)	0.751
Cardiac	DOS	1.004 (0.997-1.011)	0.243	1.017 (1.010-1.024)	**< 0.001**
	Day 1	1.001 (0.994-1.007)	0.862	1.004 (0.997-1.012)	0.261
Mortality	DOS	0.996 (0.983-1.009)	0.515	1.016 (1.005-1.027)	**0.003**
Cumulative	DOS	1 (0.998-1)	0.975	1.01 (1.005-1.018)	**< 0.001**
	Day 1	0.998 (0.991-1.004)	0.502	1.004 (0.996-1.012)	0.363

Table 1 – Association between adverse outcomes and degree of urine output and fluid balance. DOS:day of surgery, OR:odds ratio, CI:confidence interval

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E/III-6
REDUCED NEURAL BAROREFLEX-SENSITIVITY IS RELATED TO ENHANCED ENDOTHELIAL FUNCTION IN PATIENTS WITH END-STAGE LIVER DISEASE

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Introduction: Reduced cardiovagal baroreflex-sensitivity (BRS) was found to be an independent predictor of mortality in end-stage liver disease, but the underlying mechanism of impaired baroreflex function is not known. BRS consists of two components: the mechanical component (mBRS) is determined by the distensibility of the baroreceptor vessel walls and the neural component (nBRS) reflects the sensitivity of the neural signal processing. In animal models nitric oxide (NO) modulates neural responsiveness of the baroreflex arch elements in a dose-dependent manner. Increased endothelial NO production in end-stage liver failure might decrease nBRS. Therefore, we investigated if (i) the reduction of mBRS and/or nBRS is responsible for the impaired baroreflex function (ii) enhanced endothelial function influences nBRS.

Subjects and methods: We enrolled 20 patients with end-stage liver disease and 17 age- and gender-matched controls. BRS was determined by ECG and beat-to-beat blood pressure recordings. mBRS was characterized by the distensibility coefficient (DC) of the common carotid artery. nBRS was estimated by the ratio of BRS and DC. The endothelial function was quantified by flow mediated dilation (FMD) of the brachial artery.

Results: BRS was markedly reduced in patients compared with controls ($8.5 \pm 2.7^{*}$ vs. 13.5 ± 9.3 ms/Hgmm). The mBRS was not different in the two groups (2.5 ± 0.8 vs. 2.4 ± 0.8 10^{-3}/Hgmm), while nBRS showed significant reduction in patients ($3.6 \pm 1.5^{*}$ vs. 5.5 ± 3.0 ms/10^{-3}). FMD was higher in patients with end-stage liver disease ($9.9 \pm 4.0^{\dagger}$ vs. 5.9 ± 1.3 %). FMD and nBRS was inversely related in patients ($r = -0.51^{*}$), but directly related in controls ($r = 0.62^{*}$). (mean $\pm$ SD; *:$p < 0.05$; †:$p < 0.01$)

Conclusions: Reduced BRS in end-stage liver disease can be explained by the deterioration of nBRS, and mBRS appears to be preserved. Endothelial NO may enhance BRS in healthy subjects, however, central, endothelial overproduction of NO possibly contributes to the reduction of nBRS in patients with end-stage liver disease.

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E/III-7
MEASUREMENT OF PLATELET SPREADING AND ADHESION ON HUMAN PLATELETS WITH IMPEDIMETRY

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Purpose: Thrombogenesis has been recently focused in cardiology. Numerous methods exist for the assessment of platelet aggregation, but there is no well standardized and generally accepted technique for the isolated measurement of platelet adhesion. Impedimetry is a real-time technique for the dynamic measurement of cell adhesion, proliferation, viability and cytotoxicity. In this work we propose this novel method as a candidate for the measurement of platelet adhesion.

Methods: The effect of activators (epinephrine, ADP and collagen) and unfractionated heparin on human platelets isolated from healthy individuals under no current drug therapy was investigated. For these experiments the xCELLigence SP system (Roche) was used, where the platelets adhere to golden electrodes placed at the bottom of the wells. The change of electric impedance on the electrodes is in direct correlation with the number and the level of spreading of the adhering platelets. For the measurement of adhesion, platelets were introduced into wells that the drug had already been added to. For the measurement of spreading, platelets were seeded onto the electrodes and the drug was administered afterwards.

Results: Both epinephrine and ADP increased platelet adhesion, 10 uM epinephrine caused 5.42 fold ($p=0.002$), 5 uM epinephrine caused 5.34 fold ($p<0{,}001$), 10 uM ADP caused 11.9 fold ($p<0.001$) and 5 uM ADP caused 9.89 fold ($p<0.001$) increase in slope; collagen showed no significant effect on platelet adhesion. Unfractionated heparin decreased platelet adhesion on pharmacological concentration, 250 IU/mL unfractionated heparin caused 0.48 fold ($p=0.001$) decrease in slope, on lower concentrations there was no significant effect. Platelet spreading was increased by ADP: 10 uM ADP caused 16.12 fold ($p=0.011$) and 5 uM ADP caused 10.89 fold ($p=0.007$) increase in slope. Epinephrine and collagen had inhibitory effects on the spreading of platelets.

Conclusions: Platelet adhesion proved to be qualitatively and quantitatively well detectable by impedimetry. Characteristic slopes of data measured have a good correlation with the effect of substances used as laboratory reference and drugs of medical therapy. The novel method is offered as a useful technique for the more detailed evaluation of platelet function and the following of antithrombotic drug therapies.

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E/III-8
EFFECTS OF LEVOSIMENDAN-CATECHOLAMINE COMBINED TREATMENT ON HAEMODYNAMICS AND VENTRICULAR ARRYTHMIAS IN CANINE HEART FAILURE MODEL

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Introduction: Calcium sensitiser levosimendan has become the first-line treatment in acute heart failure (AHF) besides catecholamines (CA), which are limited by increasing oxygen demand and arrhythmogenic effects.

Objectives: Present study aims to evaluate haemodynamics and arrythmogenic effects of levosimendan (LEVO) administered together with catecholamines: dobutamine (DOB), dopamine (DA) and arterenol (ART) in canine heart failure model.

Methods: Heart failure (n=7) induced by rapid right ventricular pacing (240/min) occured 22±4 days after pacemaker implantation. Development of heart failure was monitored with echocardiography and biomarkers (proANP, endothelin-1). Pacing was continued until acute cardiac decompensation. Effects of LEVO and CAs were investigated on anesthetized animals, applying constant infusion (0.1 μg/kg/min) of LEVO alone and increasing doses of catecholamines (DOB, 3-6-12 μg/kg/min; DA, 4-8-16 μg/kg/min; and ART, 0,04-0,08-0,16 μg/kg/min). On-line monitoring of mean blood pressure (MBP), left ventricular end-diastolic pressure (LVEDP), contractility (dP/dtmax), relaxation (dP/dtmin) and ECG was performed. Incidence of ventricular premature beats (VES), coupled VESia (bigeminy, trigeminy) and ventricular tachyacardias (nsVT, VT) were analysed.

Results: Under LEVO infusion MBP (112±27 vs 121±18mmHg p=0,074), LVEDP (26,8±7,5 vs 20,7±9,1mmHg, p=0,178) did not change significantly. dP/dtmax (2391±987 vs 2979±946mmHg/s, p=0,006) and dP/dtmin (-2306±830 vs -3062±1012 mmHg/s, p=0,002) were significantly increased. At combination of LEVO and single CAs, both of dP/dtmax and dP/dtmin were increased, greatest elevation was observed with DA (2391±987vs 4283±1248 mmHg/s, p<0,0001; and -2306±830 vs -3551±1206 p<0,0001, respectively). MBP was just slightly increased by catecholamines. We could observe significant decrease in LVEDP (26,8±7,5 vs 16,4±7,7 mmHg, p=0,029) with co-admission of LEVO and DOB. Ventricular tachyarrhythmias, or significant increase in VES occurrence could not be observed, even at high doses of LEVO and CAs.

Conclusion: Levosimendan-catecholamine combined treatment had beneficial effect on haemodynamics and did not lead to malignant arrythmias or increase in arrythmogenic activity in our heart failure model.

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E/III-9
NT-PRO-BNP SERUM LEVEL IS AN INDEPENDENT PREDICTOR OF INTIMA-MEDIA THICKNESS OF THE COMMON CAROTID ARTERY IN ASYMPTOMATIC PATIENTS OF A PRIMARY PREVENTION STUDY

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Purpose: Determination of novel biomarkers of subclinical vascular diseases is a main target of primary prevention efforts. NT-pro-BNP represents a well-known prognostic marker in both systolic and diastolic heart failure. Recently, its association with coronary atherosclerosis and incidence of vascular events in symptomatic patients with peripheral artery disease has been confirmed. The aim of this study on asymptomatic patients was to analyse factors predictive to increased intima-media thickness of the common carotid artery (CCIMT), a widely used marker of subclinical atherosclerosis. Relationship between CCIMT, traditional risk factors and NT-pro-BNP serum level was analysed.

Methods: Carotid ultrasound and offline semi-automatic measurement of CCIMT were performed and medical history, anthropometric data and laboratory test results were collected in 559 subjects with preserved left ventricular ejection fraction (EF≥55%), without echo signs of diastolic dysfunction and without any symptoms of cardiovascular disease. The mean, maximal and minimal value of CCIMT was determined at a segment of 200 (±10) measurement points of the common carotid artery 1 cm proximal to the carotid bifurcation at both sides. Results were correlated with serum NT-pro-BNP levels determined by an immunochemistry method.

Results: The mean age was 52.3 (± 14.4) the proportion of males was 41.5%. CCIMT values were categorised as normal (<0.9 mm) or increased (above 0.9 mm). NT-Pro-BNP plasma levels were significantly higher in the group with increased carotid intima-media thickness ($p<0.001$) and NT-pro-BNP level showed correlation with average CCIMT ($r=0.3$; $p<0.001$). Regression analysis including risk factors such as age, gender, body mass index, hypertension, diabetes mellitus, hypercholesterolemia, smoking habits, showed an independent association of CCIMT with higher log NT-pro-BNP levels ($p=0.04$).

Conclusions: Serum level of NT-pro-BNP is an independent predictor of increased CCIMT in asymptomatic patients with normal left ventricular ejection fraction. Therefore determination of NT-pro-BNP serum level may serve as an additional biomarker in the screening of subclinical carotid artery disease.

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E/III-10
FIBRINOLYTIC ACTIVITY OF HUMAN BONE MARROW MESENCHYMAL STEM CELLS

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Plasmin is the key enzyme of fibrinolysis but also plays a role in a number of other proteolytic processes which are required eg. in angiogenesis.

In our experiments we wanted to evaluate the fibrinolytic/proteolytic activity of human bone marrow mesenchymal stem cells (MSC). We used human endothelial cells as controls.

MSC and human brain capillary endothelial cells (HBEC) were kept under standard culture conditions. Samples were collected at 24 hours after fresh medium change. Plasmin generation on cell surface and medium was measured by plasmin specific chromogen substrate. The expression of tissue- and urokinase-type plasminogen activators (tPA and uPA) was detected by in situ cell surface ELISA and their inhibitor PAI-1 in medium by sandwich ELISA.

We found that MSC generate plasmin on the cell surface (extinction: 0.080 ± 0.013). Plasmin generation was detectable in MSC culture media (0.173 ± 0.02). We also found that MSC exert tPA and uPA activity on the cell surface (0.423 ± 0.03 and 0.488 ± 0.05 respectively). In comparison, plasmin generation on HBEC surface was 0.410 ± 0.15, plasmin generation in culture media was 0.246 ± 0.03, tPA and uPA expression on HBEC were 0.678 ± 0.03 and 0.769 ± 0.03 respectively. We could detect PAI-1 in MSC cell culture media (98 ± 9.4 ng/mL).

We were able to detect the presence and activity of fibrinolytic proteins in MSC however on a lower level then in HBEC.

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E/III-11
RED CELL DISTRIBUTION WIDTH IS ASSOCIATED WITH MORTALITY IN KIDNEY TRANSPLANT RECIPIENTS

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Red Cell Distribution Width (RDW), a parameter routinely reported as part of the complete blood count (CBC), is associated with increased morbidity and mortality risk in different patient populations. No published data are available about the association between RDW and mortality in kidney transplant recipients.We collected socio-demographic, clinical parameters, medical and transplant history and laboratory data at baseline in 723 prevalent kidney transplant recipients between June and October 2008 (mean age 51 ± 13 [SD] years, 56% men, 21% diabetics). Associations between baseline RDW values and all-cause mortality over 3 years were examined in unadjusted and adjusted models.Increasing RDW was associated with increased mortality in both unadjusted ([$HR_{1\%\ increase}$ = 1.63; 95% CI: 1.41-1.89] and [$HR_{>median}$ = 2.74; 95% CI: 1.68-4.48]) and fully-adjusted models ([$HR_{1\%\ increase}$ = 1.60; 95% CI: 1.27-1.89] and [$HR_{>median}$ = 1.33; 95% CI: 0.76-2.35]). In reclassification analyses RDW improved the predictive value of all-cause mortality prediction models [the net reclassification improvement (NRI) was (NRI=0.189; $p<0.001$)].RDW, a cheap and readily available but largely neglected parameter independently predicts mortality in prevalent kidney transplant recipients and could potentially been used in everyday risk assessment of kidney transplant recipients.

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E/III-12
LEFT VENTRICULAR UNTWISTING IN ATHLETE'S HEART: KEY ROLE IN EARLY DIASTOLIC FILLING?

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Left ventricular (LV) untwisting contributes to LV filling through suction generation. Reduction of untwisting velocities are indicative of diastolic dysfunction in numerous diseases. The aim of our study was to investigate LV diastolic function and untwisting dynamics in different forms of LV hypertrophy: in athlete's heart and in hypertrophic cardiomyopathy.

Elite athletes (EA) in kayaking, canoeing and rowing (n=28, mean age 26.1±8.4 years), patients with hypertrophic cardiomyopathy (HCM, n=15, 32.9±14.4) and healthy sedentary volunteers (NC, n=13, 30.2±5.2) were compared. Left ventricular volumes, maximal end-diastolic wall thickness-to-volume index ratio (MWT-to-EDVi) were assessed by cardiac MRI. After conventional and tissue Doppler echocardiography, untwist (UT) and untwist rate (UTR) were determined by 2D speckle tracking echocardiography.

MWT-to-EDVi describing LV remodeling was significantly higher in HCM patients, but similar in EA and NC (EA vs. HCM vs. NC: 0.107±0.019 vs. 0.271±0.091 vs. 0.104±0.012 mm×m²/ml, mean±SD, $p<0.001$). Mitral lateral annulus e' velocity referred to diastolic dysfunction in HCM (15.3±3.6 vs.7.9±3.3 vs.15.0±3.0 cm/s, $p<0.01$). At the timepoint of mitral valve opening, UT and UTR were significantly different in the three groups: the highest values were measured in EA, whilst the lowest values were found in HCM (UT: 51.3±19.1 vs. 11.6±10.4 vs. 35.9±16.3%; UTR: -32.5±13.0 vs. -10.6±10.8 vs. -23.0±7.7 °/s, $p<0.05$). UT and UTR correlated with E/A, e', E/e' and left ventricular volume indices.

The athlete's heart is characterized by increased early diastolic untwist and untwist rate, which can aid diastolic function. Evaluation of untwisting dynamics may help to distinguish between physiological and pathological hypertrophy.

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E/III-13
COMPARATIVE INVESTIGATION OF DIABETIC CARDIOMYOPATHY IN RAT MODELS OF TYPE-1 AND TYPE-2 DIABETES MELLITUS

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Diabetes mellitus (DM) is associated with characteristic structural, molecular and functional changes of the myocardium, termed diabetic cardiomyopathy. We investigated whether type-1 or type-2 DM lead to different characteristics in cardiac dysfunction, histological and molecular changes.

Methods: Experiments were performed in rat models of type-1 (streptozotocin induced) and type-2 DM (Zucker Diabetic Fatty rats). Detailed characterization of left ventricular (LV) function was performed using a pressure-volume (P-V) conductance catheter system. The slopes of the end-systolic (ESPVR) and end-diastolic pressure-volume relationship (EDPVR) were calculated as load independent indexes of LV contractility and stiffness, respectively. Additionally, TUNEL assay was performed for detection of DNA-strand breaks. Myocardial gene expression analysis was performed by qRT-PCR, expression of proteins was investigated by western blot and immunohistochemistry.

Results: When compared to control, type-1 DM was associated with decreased LV systolic pressure, maximal dP/dt, Ees (1.04 ± 0.07 vs 2.23 ± 0.20 mmHg/μl) and cardiac and stroke work indexes. In type-2 DM, systolic indexes were altered only to a lower extent and the increase of LV stiffness was more pronounced (slope of EDPVR: 0.058 ± 0.004 vs 0.019 ± 0.004 mmHg/μl). Histological examination showed hypertrophy and degeneration of cardiac tissue. DNA-damage, nitro-oxidative stress, overexpression of c-fos and c-jun and downregulation of eNOS were more pronounced in type-1 DM. On the other hand TGF-β1 and ANF mRNA-levels were markedly upregulated in type-2 DM.

Conclusions: Diabetes is characterized by decreased systolic performance and delayed active relaxation (mainly in type-1 DM), accompanied by increased diastolic stiffness (mainly in type-2 DM). Correspondingly a different pattern and severity of myocardial structural and molecular changes could be documented between the two models.

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E/III-14
CARDIAC EFFECTS OF ACUTE EXHAUSTIVE EXERCISE IN A RAT MODEL

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Background: The role of physical exercise in the prevention and treatment of cardiovascular diseases has been well-described, even though elevations in cardionecrotic biomarkers after prolonged exercise (i.e. ultramarathon running) were observed. We aimed to establish and validate a rat model of acute exhaustive exercise and determine the biochemical, molecular biological, structural and functional alterations in the heart.

Methods: Rats of the exercise group were forced to swim for 3h with 5% body weight (workload) attached to the tail, control rats were taken into the water for 5min. 2 hours after completion of swimming we performed left ventricular (LV) pressure-volume analysis using a pressure-conductance microcatheter to investigate LV function and mechanoenergetics. Additionally, blood and myocardium samples were harvested for biochemical and histological examination. Alterations of gene expressions were detected using qRT-PCR.

Results: When compared to controls, elevated plasma levels of cardiac troponin T (0.131 ± 0.022 vs. 0.025 ± 0.006ng/ml), creatine kinase, transaminases and lactate dehydrogenase were detected after exhaustive exercise. Histological analysis showed sporadic fragmentation of myocardial structure and leukocyte infiltration. The relative myocardial expression of the anti-apoptotic bcl-2 was decreased (0.73 ± 0.06 vs. 0.97 ± 0.04), while the oxidative stress marker thioredoxin, as well as matrix metalloproteinase-2 (1.41 ± 0.14 vs. 1.04 ± 0.07), a marker of remodeling induced by oxidative stress injury showed increased expression. We observed increased end-systolic volume, decreased ejection fraction (48 ± 5 vs. 59 ± 3%), impaired contractility (E_{es}: 0.60 ± 0.07 vs. 0.90 ± 0.05mmHg/μl) and mechanical efficiency (47 ± 1 vs. 58 ± 2%) of LV in the exercise group.

Conclusions: Excessive physical activity has an adverse effect on the heart. Enhanced oxidative stress and apoptotic signalling could underly the elevation of myocardial necrotic markers. The characteristic molecular and histological alterations are associated with functional impairment.

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E/III-15
CORRELATION OF CLINICAL FINDINGS AND CLOT ULTRASTRUCTURE IN ARTERIAL THROMBI

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Background/Aim: Thrombus architecture is an important determinant in the outcome of preventive and therapeutic interventions in arterial thrombosis, but it is hardly accessible for evaluation in clinical practice. Here we address the correlations between clinical data and structure of thrombi removed from coronary and large arteries.

Methods: Thrombus samples removed by PCI-thrombus aspiration (n=101) or thrombend arterectomy (n=50) in a heterogeneous group of patients (aged 36-98 years, male-female ratio 6:4) were processed in two parallel ways: scanning electron microscopy and indirect immunostaining for fibrin and platelet-receptor GpIIb/IIIa. Images taken with both microscopic techniques were analyzed morphometrically to determine fibrin fiberdiameter, relative occupancy by fibrin, platelet, red blood cells (RBC), white blood cells (WBC). The correlation between the measured ultrastructural characteristics and selected clinical parameters (age, sex, vascularlocalization, blood cell counts, haematocrit, plasmaC-reactive protein (CRP), ECG findings, anti-platelet medication, accompanying diseases) was assessed using multiple hypothesis testing and regression analysis.

Results: Fibrincontent of peripheral thrombi showed positive correlation with CRP and male sex ($P=0.014$, $P=0.04$, respectively), but no such dependence was observed in coronary thrombi. Thrombus platelet content correlated stronger with hematocrit ($P=3x10^{-12}$,$R^2=0.75$ coronary; $P=0.02$,$R^2=0.238$ peripheral) than with blood platelet count ($P=2x10^{-4}$,$R^2=0.20$). Aspirin premedication increased the dependence of thrombus platelet content on systemic platelet count ($P=4x10^{-7}$,$R^2=0.54$) and the negative correlation between fiber diameter and blood RBC count ($P=0.009$,$R^2=0.16$ non-treated; $P=0.003$,$R^2=0.29$aspirin-treatedgroup). No such effects were found for clopidogrel. Sorting thrombi by their vessel of origin revealed lower values of fibrin-platelet ratio in the coronaries than in the ilio-femoro-popliteal region ($P<0.023$ for various combinations of subgroups). In line with this observation, platelet content was significantly higher in left anterior descending coronary thrombi than in the ilio-femoral subgroup ($P=0.037$). In terms of platelet content and fibrin-platelet ratio coronary thrombi were similar to those of aorticorigin. Impact of ECG findings and accompanying diseases could be revealed only by using complex regression models.

Conclusion: Individually tailored therapautic strategies could be developed on the basis of these findings.

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E/IV
ORAL PRESENTATIONS

Chairman:
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E/IV-1
IN VITRO DIFFERENTIATION OF TH17 CELLS

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Background: The Th17 helper T lymphocytes represent a subset of T cells, that produce inflammatory cytokines (Interleukin-17A, -17F, -21, -22, and tumor necrosis factor (TNF)). Increased Th17 cell differentiation have been observed in rheumatoid arthritis (RA) and in several other autoimmune diseases. IL-17 increase inflammation and promote osteoclast differentiation in RA.

Aims: We are investigatning the human Th17 cell differentiation. Our further purpose is to compare the differentiated Th17 cells from healthy volunteers with cells from RA patients.

Methods: CD4 positive T cells were separated by magnetic method from peripheral blood mononuclear cells (PBMC) of healthy volunteers. The cells were activated with anti-CD3 and anti-CD28 antibodies and treated with TGF_{β}, IL-6 and IL-1 cytokines. The IL-17 production was measured by ELISPOT and RORc expression was measured by real-time PCR method. Cell viability was monitored by Trypan blue staining and by AnnexinV externalization.

Results: After 5-10 days differentiation we could detect a pronounced increase in the RORc expression and IL-17 production. Our present data suggest that CD3/CD28 treatment effectively promotes IL-17 differentiation, even in the absence of IL-1, IL-6 and TGF_{β}. Further work is needed to clarify the regulation of Th17 differentiation.

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E/IV-2
GENETIC VARIATIONS IN THE PROMOTER REGION OF THE WFS1 GENE ARE RISK FACTORS OF TYPE 2 DIABETES MELLITUS

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WFS1 codes the wolframin, which plays an important role in maintaining the homeostasis of the ER. Loss-of-function mutations of the *WFS1* gene are responsible for the Wolfram-syndrome (diabetes insipidus, diabetes mellitus, optic atrophy and deafness), while polymorphisms are examined as possible risk factors of diabetes mellitus.

Aim: In this study we investigated if genetic variations in the promoter region of the WFS1 gene were genetic components of diabetes mellitus. Following *in silico* analysis by dbSNP and TransFac DNA samples of 452 patients and 484 healthy controls were genotyped. Statistical analysis was carried out using khi-square statistics, linkage analysis was done by the Haploview software. Region of interest was cloned in pGl3b reporter vector, different haplotypes were prepared by site-directed mutagenesis.

Results: 4 single nucleotid polymorphisms (rs4273545, rs71537681, rs71537683, rs71524386) and an insertion/deletion variant (rs148797429) were investigated. Genetic analysis revealed that 3 SNPs were not polymorphic in our population (rs71537681, rs71537683, rs71524386). The rs4273545 G/T SNP showed a significant association with type 2 diabetes, even after correcting for Bonferroni (p = 0.00034, OR = 1.343). Allele frequency of the insertion/deletion variant was defined (MAF = 0.408). Between the SNP and the ins/del linkage analysis revealed linkage disequilibrium (D' = 0.97; R^2 = 0.78), moreover a combined analysis of the two loci demonstrated that the rs4273545T–rs148797429ins haplotype showed an increased risk for T2DM (p = 0.0004, OR = 2.410). *In vitro* functional analysis is in progress.

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E/IV-3
THE PHOSPHOINOSITIDE 3-KINASE B AND Δ REGULATE OSTEOCLAST DEVELOPMENT AND FUNCTION

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Background: Osteoclasts are bone-resorbing cells of myeloid origin. Phosphoinositide 3-kinases (PI3K) have crucial roles in regulating a variety of cellular functions, but their role in osteoclast biology is poorly understood. Here we tested the role of PI3Kβ and PI3Kδ in osteoclast development and function using combined genetic and pharmacological approaches.

Materials and methods: Murine bone marrow cells were isolated from long bones of wild type, $PI3K\beta^{-/-}$, $PI3K\delta^{KD/KD}$ and $PI3K\beta^{-/-}PI3K\delta^{KD/KD}$ mice and differentiated into osteoclasts *in vitro* in the presence of recombinant M-CSF and RANKL. Isoform specific PI3K inhibitors TGX221 and IC87114 were used as selective inhibitors of PI3Kβ and PI3Kδ, respectively. Osteoclast differentiation and function were examined by osteoclast-specific TRAP-staining and resorption of artificial hydroxyapatite surface.

Results: Differentiation of progenitors to multinucleated osteoclasts and their resorption activity was impaired in the $PI3K\beta^{-/-}$ cultures and in the presence of the PI3Kβ inhibitor. Both the inhibition and the disruption of PI3Kδ resulted in impaired osteoclast development and function. Osteoclast differentiation and function was nearly completely blocked by the combined pharmacological inhibition of PI3Kβ and PI3Kδ and in the $PI3K\beta^{-/-}PI3K\delta^{KD/KD}$ double mutant cultures.

Conclusion: Our results indicate that PI3Kβ and PI3Kδ play a critical but overlapping role in osteoclast development and function. This can be important in development of isoform specific inhibitors to cure diseases caused by hyperactive osteoclasts.

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E/IV-4
MODELING THE TEMPERATURE-RELATED AVERAGED ANNUAL RUN OF RELATIVE LB INCIDENCE IN THE PERIOD OF 1998-2012 IN HUNGARY

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Ixodidae ticks, -the main vectors of *Borrelia burgdorferi*-, take only one or a few very large blood meal per life stage to develop. The development highly depends on the ambient temperature. Between both the interstadial development rates of ticks and the daily questing can be described by non-linear relationships with temperature. It is important for modeling that ticks vary their questing activity in response to their immediate climatic conditions**.** Our aim was to model the Lyme season using a population dynamics model. The weekly incidence of LB data for the period 1998-2012 were retrieved from the Hungarian National Epidemiological and Surveillance System. We handle the country as a homogenous unit. The daily mean temperature data were derived from the European Climate Assessment & Dataset. Our approach was that the relative (percentage) weekly LB-incidence is the function of a temperature-dependent activity factor of ticks– the tick activity positively correlates with the outdoor temperature –, and the potentially questing ratio of tick population. Secondly we expected, that there is a start whole hungry nymph and adult tick population before the tick season. These population starts to decrease in the first week and to the end of the season only low percentage of the start population remains. The model calculate the next week's percentage population iteratively from the same week's calculated activity and the previous week's remained population. We found that this model can well describe the observed Lyme season.

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E/IV-5
CLINICOPATHOLOGICAL FEATURES OF HEAD AND NECK CANCERS AND THEIR RELATION TO BIOMARKER-EXPRESSION

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Introduction: Prognosis of head and neck squamous cell carcinomas (HNSCCs) is considerably poor (5-year overall survival: 50%). Though these tumors belong to the same histopathological entity, they posess different clinicopathological characteristics. In our study, we compared the biomarker-expressions of HNSCCs arising from different anatomical localizations and evaluated their correlations with the clinical parameters.

Methods: 226 patients having HNSCCs were enrolled into our study. We prepared Tissue Microarrays (TMA) made from the patients' tissue samples and used immunohistochemical staining for detecting the biomarkers (Ki67, p53, EGFR, p16ink4, Collagen XVII). The histological evaluation was performed on computers using the Panoramic Viewer software. Expressions were considered positive when more than 25% of tumor cells were stained.

We performed Chi-square tests and Kaplan-Meier survival analysis.
We compared the biomarker-expressions according to conventional anatomical classification of the tumors then performed comparisons by and between subsites.

Results: Among supraglottic tumors, the p16ink4-, Ki67- and EGFR-expression rates were sigificantly higher than those among other laryngeal and hypopharyngeal tumors. Ki67-expression rates of the tonsillar tumors were significantly higher than those of the oral and other oropharyngeal tumors.

The survival rate of patients with p16-negative cancer was significantly lower than that of patiens with p16-positive disease. The Ki67-positivity was associated with worse prognosis and a higher rate of lymph node metastasis.

Factors such as T and N stage, diameter of the tumor and the histological grade significantly affected the prognosis.

Conclusions: We considered proven that the HNSCCs cannot be regarded as a homogeneous entity based on their biomarker-expressions. Regarding the close correlation between p16-expression and HPV infection, we assume that HPV plays a role not only in tonsillar carcinogenesis, but in the development of supraglottic cancers, too.

Additionally, we can declare that the supplementation of the conventional TNM-system with biomarker-profile could lead to a more precise prognostic score.

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E/IV-6
EXPLORING CONNEXIN EXPRESSION AND FUNCTIONS IN MELANOCYTIC TUMORS

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Background: Connexin proteins (Cx) form gap junction transmembrane channels which can transport small (< 1.8 kDa) hydrophilic signaling molecules including Ca^{2+}, IP3, cAMP and other metabolites between adjacent cells. They can also function as hemichannels that can release regulators to the extracellular space and interact with intracellular regulatory proteins (non-channel functions) of cell replication, cell death and maintenance of multicellular homeostasis.

Methods: We have tested the expression of connexin isotypes in cutaneous melanocytic tumors using immunohistochemistry in tissue microarrays of 15 common and 53 dysplastic nevi and 56 primary and 21 metastatic malignant melanomas as well as in human melanoma cell lines HT199 and A2058.

Results: Cx43/GJA1 expression was observed as punctuate membranous plaques in 60% of nevi and as strong cytoplasmic immunostaining in both of melanoma cell lines and in 88% of melanomas. Cx30.3/GJB4 reaction was punctuate and cell membrane associated in the superficial regions of 70% of nevi including atypical nests and cytoplasmic in 28% of melanoma tissues. The cell lines proved to be negative. Cx36/GJD2 perinuclear, cytoplasmic or membranous immunostaining was observed in 54% of nevi, 29% of melanomas and in both cell lines. All melanocytic tumors expressed Cx26/GJB2 protein. The reaction was diffuse and cytoplasmic in 33% of melanomas and in both cell lines and paranuclear in most nevi (77%). All these expression differences between nevi and melanomas were statistically significant ($p < 0.001$). Detailed analysis of further Cx isotypes (Cx46/GJA3, Cx50/GJA8, Cx32/GJB1, Cx31/GJB3, Cx25/GJB7, Cx45/GJC1) we found in melanocytic tumors are still under way. So as the functional dye transfer experiments to test impaired channel functions suggested by the dominantly cytoplasmic localization of connexins in melanomas.

Conclusion: Our results demonstrate that several previously undetected connexin isotypes can be found in melanocytic tumors. Most tested connexins are significantly down-regulated in melanomas, which possibly contributes to their malignant phenotype.

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E/IV-7
MODULATED ELECTRO-HYPERTHERMIA CAUSES PROGRAMMED CELL DEATH IN HT29 COLORECTAL CARCINOMA XENOGRAFT

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Background: Modulated electro-hyperthermia (mEHT) is a non-invasive complementary technique for targeted tumor treatment. The mEHT generated capacitive impedance-coupled modulated radiofrequency selectively accumulates in the tumor tissue without major effect in the surrounding normal tissues. We have studied the molecular mechanism of action of mEHT related tumor damage.

Methods: HT29 human colorectal carcinoma cell line was xenografted into both femoral regions of BalbC/nu/nu mice. A single shot mEHT treatment (LabEHY, Oncotherm Ltd, Hungary) for 30 minutes was applied when the xenografts reached ~1.5 cm. Samples were collected at 0, 1, 4, 8, 14, 24, 48, 72, 120, 168, 216 h in 3 mice each group by keeping 5 animals untreated. Treatment related mRNA expression was tested using Human genome U133 Plus 2.0 Arrays in 4h post-treatment and 24h untreated samples. A Proteome profiler Human Apoptosis Arrays were also used on 8, 14 and 24h treated samples. Histomorphologic, immunohistochemical and TUNEL assay results were analyzed semi-quantitatively in digital slides.

Results: In HT29 xenografts mEHT caused programmed cell death starting from the tumor centre. The mRNA array chip results showed the differential expression of 48 genes upon treatment, including heat shock protein 70 and hsp90. Immunohistochemistry confirmed elevated hsp70 and hsp90 expression in the morphologically intact peripheral parts of treated tumors. In the apoptosis arrays TRAILR2 and FADD apoptosis receptor proteins and some of their related downstream pro-apoptotic regulatory proteins (Bax, SMAC/Diablo and HTRA2/Omi) were upregulated 8h post treatment. Immunohistochemistry proved activation related mitochondrial translocation of Bax 8-14h post-treatment. In line with this cytochrome-c release from mitochondria to the cytoplasm between 8-14h post-treatment and nuclear translocation of AIF between 14-24h were observed. The massive TUNEL positivity 24-48h post-treatment confirmed DNA fragmentation.

Conclusion: In HT29 colorectal cancer xenografts mEHT causes TRAILR2 mediated programmed cell death which follows a caspase independent and AIF dependent subroutine.

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E/IV-8
DIFFERENTIAL CONNEXIN EXPRESSION IN GIANT CELL TUMOUR OF BONE (GCTB)

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Intercellular communication through connexin (Cx) channels is known to regulate cell homeostasis and play crucial roles in promoting signals and nutrients between osteoblasts and osteocytes. Giant cell tumour of bone (GCTB) is an aggressive osteolytic lesion, in which neoplastic stromal cells drive osteoclastogenesis. Here we tested if Cx expression correlates with GCTB progression.

Tissue microarrays of 94 primary and 82 recurrent GCTB cases were immunostained for connexin isotypes and the results were scored in digital slides including image quantitation.

Cx37 and Cx40 were detected only in endothelial cells and Cx23, Cx26, Cx43 and Cx46 were found primarily in mononuclear cell fraction. Double labelling revealed connexins both stromal and monocytic lineage cells. Cx23 was also seen consistently and Cx46 occasionally in giant cells. None of the Cx isotypes showed statistical preference between primary and recurrent cases, though Cx43 displayed a tendency for upregulation in recurrent cases. Concerning clinico-radiological stage, only Cx26 showed significantly elevated ($p < 0.05$) expression in aggressive compared to active GCTB cases.

Though a wide range of connexins can be detected in GCTB, some of them have not been published in osteoblasts, stromal cells or monocytes, their expression is not statistically lined with GCTB progression/recurrence.

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E/IV-9
IN SITU ANALYSIS OF MAMMALIAN TARGET OF RAPAMYCIN (MTOR) COMPLEXES

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Analysis of intracellular functions and mechanisms is becoming extremely important. Measuring the expression, activation and localisation of proteins is necessary for these studies. We set out to examine the regulation of the mTOR signalling pathway. mTOR kinase forms two distinct complexes (C1/C2), which play important roles in the regulation of cellular metabolism, proliferation and survival. Many aspects such as the amount and activity of these complexes are highlighted in tumor biology. Immuncytochemistry and –histochemistry were used to study the expression of the elements in these protein complexes in situ. Moreover, the appropriate quantitative evaluation of these techniques is highly subjective.

We established a new method, Duolink, which allows quantitative in situ analysis of phospho-proteins and protein-protein complexes in cell lines in vitro and human biopsies as well. The method requires two different primary antibodies to detect different proteins or different epitopes of the same protein. The binding of these antibodies at an appropriate distance allows sensitive detection of the hybridization and amplification of special Duolink secondary antibodies conjugated to oligonucleotides. Discrete signals can be quantitatively evaluated by computer software.

We applied this method for detecting phosphorylated ribosomal S6 protein to measure mTOR activity, and confirmed the sensitivity and specificity of this technique to detect changes in mTOR activity in mTOR inhibitor treated cell cultures. We tested several antibodies and fixation methods to analyse mTOR-Rictor and mTOR-Raptor expression in complexes. We established this quantitative method to measure mTORC2 expression in human cells based on our experiments, and different mTORC2 expression was also confirmed in certain cell lines. We started to establish this technique in formalin fixed paraffin embedded human tissues. Our results suggest that the Duolink system is a useful method for the studies of signalling mechanisms in situ.

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E/IV-10
THE ROLE OF ALTERED CYTOKINE PRODUCTION IN HHV-7 INFECTIONS

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Human herpesvirus 7 (HHV-7) plays a role in several diseases. It can be the causative agent of pityriasis rosea and pediatric febrile conditions, or can be a cofactor for example in socks and gloves syndrome, pemphigus, psoriasis, cytomegalovirus disease of renal transplant patients. Due to infecting a limited range of cell types, their pathogenicity cannot be attributed to direct tissue damage, rather to indirect ways via mediators produced by infected immune cells.

Aims: We studied the alteration in cytokine pattern of lymphoid cells infected by HHV-7. Our aim was to extrapolate these findings to the different clinical manifestation of HHV-7 infection.

Methods: We infected SupT1 cell line and human peripheral mononuclear cells (PBMC). PBMC was isolated from seronegative and seropositive individuals, to model primary and secondary infections, respectively. Heat inactivated (HI) and UV-irradiated (UVI) preparations were used, beside the infectious HHV-7. The treatment of cells was made at high multiplicity of viral inoculums in the presence and absence of mitogens. Cytokine gene expression and protein secretion was monitored upto 72h post infection (pi). Messenger RNAs were analysed by RT-PCR and Northern blot. The amounts of secreted proteins were quantitated by ELISA.

Results: IL-4 and IL-6 synthesis of PBMCs was not affected by HHV-7 infection. In contrast, TNF-α and IL-1β release was induced. Mitogens augmented IL-1β output. Production of IL-2 and IFN-γ shows different pattern in uninfected and infected cells. Their mitogen-elicited mRNA and protein production was augmented in primary, diminished in secondary infections. IL-10 mRNA level was independent of serostatus and TNF-α, protein output was higher in seronegative cases. HI-HHV-7, LPS, PHA also activated IL-10 production. SupT1 cells produced high level IL-10, GM-CSF mRNA and proteins, but no IL-1β, IL-2, IL-6.

Conclusions: In contrast to the known immunosuppressive effect of HHV-6, cytokine pattern altered by HHV-7 is balanced and results in a self-limited primary infection (pityriasis rosea). Reactivated HHV-7 hardly affects humoral immunity. Lymphocyte activation by simultaneous microbial infections diminishes cellular immunity.

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E/IV-11
COMPARATIVE ANALYSIS OF PATIENT DERIVED AND *IN VITRO* SELECTED VEMURAFENIB RESISTANT MELANOMA CELL MODELS

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Background: The recent introduction of vemurafenib, a selective inhibitor of mutant BRAF had a huge impact on the treatment of BRAF mutant melanoma patients that accounts for about 60% of the cases. However, both primary and secondary therapy resistance is quite observed and the underlying molecular mechanisms are far from understood. Accordingly, we seek to characterize melanoma cell cultures that developed resistance during in vitro treatment or in vemurafenib treated patients.

Materials and methods: *In vivo* sensitive-resistant pairs of cell lines were isolated from the same melanoma patients before and after the treatment with vemurafenib., In the *in vitro* pairs, resistant cell lines were established by long-term culturing of the parental cell lines in media containing vemurafenib up to 10μM. Cell viability, migration and sphere forming ability of the corresponding pairs of sensitive and resistant cell lines were determined.

Results: Most of the initially sensitive melanoma cultures became resistant against vemrafenib *in vitro*. However, in cell lines with initially low sensitivity the grade of resistance did not change considerably. Importantly, resistant cells showed higher migratory activity compared to their sensitive pairs. Vemurafenib treatment clearly impaired the sphere forming ability of sensitive cell lines but not of the resistant ones.

Conclusion: Our investigations did not reveal considerable differences between *in vitro* established and patient derived resistant-sensitive pair of cell lines. Thus both models are comparably suitable for the further investigation of the molecular mechanisms of resistance. Our finding of increased cell migration in resistant cell cultures supports the observation that relapsing BRAF mutant melanomas show a more aggressive clinical phenotype.

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E/IV-12
The author have not agreed the online publication.

E/V
ORAL PRESENTATIONS

Chairman:
Prof. Dr. Péter Lakatos

E/V-1
COMPARISON OF RAT AND HUMAN ORTHOLOGS OF ORGANIC CATION/CARNITINE TRANSPORTER (OCTN2)

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Membrane transporters play a crucial role in ADMETox (Absorption – Distribution – Metabolism – Excretion –Toxicity) / pharmacokinetic properties of drugs. Therefore, testing of interaction of candidate drugs with transporters is compulsory in drug development. OCTN2 („novel organic cation/carnitine") membrane protein was shown to be responsible for sodium dependent renal transport of L-carnitine (3-hydroxi-4-N-(trimethylamino)-butyrate. Expression of OCTN2 is ubiquitous as L-carnitine has many physiological roles, such as mitochondrial transport of fatty acid catabolism to allow β-oxidation, a process common to many tissues and cell types. OCTN2/Octn2 has been postulated to be a specific transporter of L-carnitine and related compounds. While it is not a general drug transporter, its role in drug pharmacokinetics has been clearly shown. Correlation analysis of the rat and human orthologs is important to see if the *in vivo* rat models are applicable for pharmacodynamic, pharmacokinetic and toxicity studies.

Utilization of immortalized cell lines overexpressing the rat or the human orthologs is the most straightforward approach for correlation studies and, thus, we are presenting species specificity studies of rat Octn2 and human OCTN2 expressed in CHO cells.

Aims: (1) Characterizing L-carnitine uptake/influx of Octn2 and OCTN2 transporters, (2) scanning and examining drugs influencing L-carnitine uptake, (3) investigating inhibitors as potential substrates of Octn2/OCTN2, (4) characterizing the uptake/influx transport of the drugs behaving as substrates, (5) correlation analysis of the rat and human orthologs.

Results: (1) Several pharmacologically important drugs affect L-carnitine transport by Octn2/OCTN2, (2) differences in the function of rat and human Octn2/OCTN2 transporters were experienced in many cases.

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E/V-2
THE UL54 GENE OF PSEUDORABIES VIRUS MAY BE PART OF THE TRANSCRIPTIONAL INTERFERENCE NETWORK AND MAY SPECIFICALLY REGULATE LATE GENES

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Since the genome of the Pseudorabies virus (PRV) is compact, genes are very close to each other, and are often nested within each other. Due to this transcriptional interference occurs between these genes, giving opportunity to regulate expression without a complicated machinery. Interference also occurs between genes facing or diverging each other. Together we call these the Transcription Interference Network (TIN). We believe that the product of UL54 gene takes part in this network by facilitating the expression of nested genes by aiding the recognition of cryptic polyA singals at the end of "outer" genes. The UL54 gene encodes for the protein ICP27, which has multiple roles during viral infection for example: mRNA trafficking, transcription regulation, protein etc. It may also have role in the switch between the expression of early and late genes and.

Aims: We sought to characterize a UL54 insertional null mutant virus, with special focus on the switch between late and early genes, and the activation of nested genes.

Results: Initial results confirm, that replication of the mutant virus is severely impaired. We found out that with some exceptions, the expression of immediate-early and early genes are not heavily affected in general. The late genes also seem to have a slight activation at 4h post infection, but they lag behind the expected expression level at 6h p.i. Further work is needed to fully understand how ICP27 modulates gene expression, and to find out whether it is truly part of the Transcription Interference Network.

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E/V-3
MODERATE INHIBITION OF GELATINOLYTIC ACTIVITY BY ILOMASTAT REDUCES INFARCT SIZE IN BOTH ISCHEMIC AND REPERFUSION INJURY *IN VIVO*

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Activation of matrix metalloproteinases (MMPs) is involved in the pathology of acute ischemia/reperfusion injury. Therefore, pharmacological inhibition of MMPs is a promising target for acute cardioprotection.

Aims: In the present study we investigated if the non-selective MMP inhibitor ilomastat given before ischemia or before reperfusion is able to reduce infarct size in vivo.

Results: Infarct-size limiting effect of ilomastat (0.3 - 6.0 μmol/kg) was tested in an in vivo ratmodel of myocardial infarction induced by 30 min coronary occlusion/120 min reperfusion. Ilomastatat 0.75 and 1.5 μmol/kg decreased infarct size significantly as measured by standard TTC staining, when administered 5 min before the on set of ischemia as compared to vehicle (DMSO) treated group. When administered 5 min before the on set of reperfusion, ilomastatat6.0 μmol/kg significantly reduced in farct size. Area at risk was not affected by ilomastat treatments. To further assess the cytoprotective effect of ilomastat, primary cardiomyocytes isolated from neonatal rats subjected to 240 min simulated ischemia followed by 120 min of reoxygenation were treated with ilomastat (5 nM-5 μM). Ilomastatat 0.5 μM and 5.0 μ M significantly increased cell viability when compared to vehicle treated group. To assess the in situ MMP inhibitory effect of the cytoprotective dose of ilomastat (0.5 μM), in separate experiments in situ zymography was performed. Ilomastat showed a moderate (approximately 25%) inhibition of MMP-2 inischemic/reoxygenated cardiac myocytes.

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E/V-4
ISOLATION AND ANALYSIS OF LARGE BACTEROIDES PLASMIDS

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The species of *Bacteroides* genus are important symbionts and commensalists in the gut, but among certain circumstances they may become pathogenic. In this genus and in its relatives the mobile genetic elements are widely spread. These are insertion sequence elements, mobilizable and conjugative plasmids, transposons, mobilizable and conjugative transposons which may participate in the spread of antibiotic resistance genes or insert into the genome and activate or boost the transcription. The plasmids have two size category: the small (2,7-11 kb) and the large (> 11 kb).

Aims: Our aims were to compare the homologies amongst the type plasmids with already known sequences, to get knowledge about their evolution, to find a suitable method for their isolation and to screen a collection of Bacteroides strains for their large plasmid content. Additionally, we wished to gain information about their roles based on their nucleotide sequences and sites of origin.

Results: During our investigations we have isolated 11 different large plasmids from 37 strains in a wide size range (18 to 180 kb). Using restriction enzyme (BglII and HindIII) digestions and Southern hybridization with pBF9343 we detected homologous plasmids to this latter one from our collection; there were two strongly and three faintly hybridizing plasmids, and from the former we have chosen two for full nucleotide sequence determination. During the process we determined the nucleotide sequences of some smaller (2,7-5,6 kb), a medium-sized (12 kb) and a large plasmid (37 kb, homologue of pBF9343) Additionally, we have identified the constitutively excised circular form of the MTn4555 mobilizable transposon (B. fragilis 76240) which harboured the cefoxitinase (cfxA) gene.

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E/V-5
2-PHOTON LASER MICROSCOPIC ANALYSIS OF PHOTOAGING IN MICE WITH IMPAIRED EPIDERMAL ANTIOXIDANT DEFENSE

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Photoaging is a process of aging of the skin attributed to continuous, long-term exposure to oxidative stress inducing UV radiation. The mitochondrial manganese superoxide dismutase enzyme is vital in elimination of reactive oxygen species. Mice deficient for MnSOD in their epidermis are viable, nevertheless they show an impaired antioxidant defense. In our study, we investigated the effects of extensive UVA irradiation on epidermally homozygous MnSOD knockout mice. A group of hairless mice with normal enzyme activity were used as a controls.

Aims: We performed 2-photon laser microscopic and histological analysis to observe differences in photoaging of the two groups as a result of increased oxidative stress. Wrinkling and epidermal thickening were also measured and statistically compered among animals with various genotypes.

Results: The degree of wrinkling and thickening of the skin were significantly higher in MnSOD deficient mice. Laser microscopic and histologic analyses verified our clinical findings, both techniques revealed the presence of achantotic epidermis and destructed collagen structures in knockout mice.

Our results suggest that MnSOD is necessary to protect skin against increased oxidative stress. When MnSOD function is lacking in the epidermis the photoaging process is markedly aggravated and accelerated.

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E/V-6
BONE FORMATION IS INCREASED WITH ALBUMIN COATED ALLOGRAFTS IN A RAT CRITICAL SIZE DEFECT

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Blood serum fractions such as platelet rich plasma or activated serum are known adjuvants in bone replacement therapies with an unclear mode of action. In previous experiments we have shown that serum albumin coating on bone allografts can significantly increase stem cell number in vitro, raising the possibility that albumin alone may be an effective proliferative agent in bone remodelling. In the present experiment, we investigated the bone formation by filling critical size defects with serum albumin coated allografts in rat cranial defect model. Bone formation was followed by computed tomography at 1,3,5,7,9,11 weeks postoperatively. The area of the remaining defect and densitiy were calculated. At five weeks significant difference was seen between the control groups and the albumin-coated group in the size of the remaining bone defect (no graft control 62.1± 7.8%, uncoated graft 63.4 ± 12.8 %, albumin coated graft 15.2 ± 6.6 %). In the albumin-coated group every bone defect healed completely by the 9th week. In addition, from the 5th week the albumin-coated group showed significantly higher bone density values compared to both controls. By the 11th week the defects treated with the albumin-coated graft reached over 1000 Hounsfield unit, while controls remained below 700. In conclusion, the present investigation shows that implanting serum albumin coated allografts significantly reduce healing time in a critical size defect. These results may be explained by the idea that albumin coating provides a convenient milieu for stem cell function and proliferation, resulting in faster remodeling of the graft.

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E/V-7
RESISTANCE AGAINST GLUCOCORTICOIDS, CAUSED BY OVEREXPRESSION OF THE GLUCOCORTICOID RECEPTOR B ISOFORM IN CACO-2 CELL LINE

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Introduction: Glucocorticoid acts through the glucocorticoid receptor (GR). Two isoforms differing in their C-terminal region the GRα and GRβ have been identified. The beta isoform does not bind ligands, it inhibits the GRα's transactivation properties. Elevated level of GRβ has been reported in steroid resistant states.

Aims: To develop an in vitro model in order to evaluate the GRβ related transcriptional regulation in the development of steroid resistance.

Material and Methods: GRß stable expressing cell line (Caco-Grβ) was created from Caco-2 intestinal cell line. GRß was cloned form the GRα isoform into mammalian expression pcDNA3.1-V5-His-TOPO vector. The expression of GRβ was confirmed by quantitative real time PCR and Western blot analyses. The glucocorticoid-mediated signaling transduction pathway was evaluated using pGRE-SEAP (Clontech) system after treatment of the basic Caco-2 and Caco-GRβ cell lines with dexamethasone (Dex, 100 nmol). Agilent44K cDNA microarrays were used to detect gene expression profiles of both the basic Caco-2 and the Caco-2-GRß in basal condition and after Dex. treatment. Pathways affected by differentially expressed genes were evaluated by Ingenuity pathway analysis (IPA).

Results: The mRNA level of GRα/GRβ ratio was 1:0.6 vs. 1:0.001 in Caco-2GRβ cells compared to the basic Caco-2 cells. Luciferase activity measured after Dex treatment in Caco-GRβ cell lines was approximately 50% of that measured in basic Caco-2 cells. Dex treatment affected the expression of 151 (88 up and 63 down) in basic Caco-2 and only 16 transcripts in Caco-GRβ cells. 1182 transcripts were differentially (279 under- and 903 over-) expressed in Caco-2-GRß cells compared to the basic Caco-2 cell line. IPA revealed that these transcripts are involved in pathways: "cell death and survival", "cell morphology", "cancer", "cell-to-cell signaling", "connective tissue disorders", "cell mediated immune response", "gastrointestinal and endocrine and immunological diseases".

Conclusions: GRβ may possess a dominant-negative effect of GRα-mediated gene transcription in Caco-2 cells similarly to HeLa cells, making this cell line a valid model for studying glucocorticoid resistance. However, the network and pathway analysis using the differentially expressed genes may suggest that forced expression of GRβ may affect the sort of cells through GR-independent mechanisms.

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E/V-8
ROLE OF INTERLEUKIN-24 (IL-24) IN THE PATHOGENESIS OF INFLAMMATORY BOWEL DISEASE (IBD)

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Background: The exact pathomechanism of inflammatory bowel disease (IBD) is not fully understood; its medication is not solved. Targeted therapies to cytokines belong to interleukin (IL)-10 family came into focus and are under drug development. Our recent target molecule IL-24 is a new member of the family, which function is less known. Based literature it can be hypothesized that IL-24 may be involved in the regulation of inflammation and tissue regeneration, however its role in IBD is not clarified.

Aims: The aim of our study is to better understand the pathomechanism of IBD and to find new potential therapeutic applications. We plan to examine the expression and distribution of IL-24 and its receptor in children with Crohn's disease (CD) ulcerative colitis (UC) and investigate its effect on processes involved in the pathomechanism of IBD such as proliferation or fibrosis.

Methods: Colonic biopsy samples were collected from children with CD (n=17), UC (n=12) and controls (n=20). The mRNA expression and localization of IL-24 and a common element of its heterodimer receptor complex (IL-20RB) were determined using real-time RT-PCR and immunofluorescent staining, respectively. In vitro HT-29 colonic epithelial cells were treated with recombinant IL-24 and ERK1/2, JNK1/2 specific inhibitors. Phosphorylation of ERK1/2 and JNK1/2, and the amount of tumor growth factor (TGF-ß) and platelet-derived growth factor (PDGF-ß) were analyzed by flow cytometry.

Results: The mRNA expression of IL-24 was significantly elevated in the colonic mucosa of children with IBD (CD and UC) compared to controls ($p < 0.05$). Strong immunopositivity of IL-24 and IL-20RB were detected in colonic epithelial cells and subepithelial fibroblasts in children with IBD compared to controls. Increased phosphorilation of ERK1/2 and JNK1/2, and elevated level of PDGF-β and TGF-β were observed in HT-29 cells following IL-24 treatment. After administration of ERK1/2 and JNK1/2 inhibitors number of PDGF-β and TGF-β positive cells decreased.

Conclusion: Elevated level of IL-24 suggests its involvement in the pathomechanism of IBD. Its effect on PDGF-β and TGF-β may refer to its potential role during fibrotic processes in IBD mediated by ERK1/2 and JNK1/2 signaling pathways. However further studies are needed we suggest that IL-24 may be a potential therapeutic target in the future.

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E/V-9
A NOVEL ROLE OF INTERLEUKIN-24 (IL-24) IN THE PATHOGENESIS OF CHRONIC KIDNEY DISEASES

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Aim: The target molecule of our investigations is the recently discovered cytokine IL-24 which is a member of the interleukin (IL)-10 gene family. IL-24 was demonstrated to selectively induce growth suppression and apoptosis of diverse human cancer cells. The role of IL-24 in chronic kidney diseases (CKD) remains unknown. Our previous microarray studies showed that IL-24 mRNA levels were significantly increased in the fibrotic kidneys. The aim of our study is to clarify the role of IL-24 in chronic renal diseases leading to the development of fibrosis.

Method: To study the development of renal fibrosis we applied the unilateral urether obstruction (UUO) induced mouse model of renal fibrosis. Confocal microscopy was used to determine tissue localization of IL-24 and its receptor IL-20Rβ in the kidney. After the onset of UUO the level of IL-24 and IL-20Rβ in the proximal tubular epithelial cells (PTECs) were determined by flow cytometry (n=6). We investigated the effect of TNF-α and TGF-β treatment on IL-24 and IL-20Rβ expression in HK-2 proximal tubule epithelium cell line (n=6). The effect of IL-24 on HK-2 cells was analyzed by proliferation assay (n=6).

Results: The level of IL-24 and IL-20Rβ were elevated in PTECs from the second of the initiation of UUO. In the HK-2 cells TNF-α or TGF-β treatment increased the level of IL-24 and IL-20Rβ. IL-24 induced the proliferation of HK-2 cells *in vitro*.

Conclusion: We demonstrated increased level of IL-24 and its receptor in the PTECs in a mice model of renal fibrosis. Our data demonstrates that the early macrophage derived cytokines, such as TNF-α or TGF-β may induce the expression of IL-24 and IL-20 Rβ. Investigating the effect of IL-24 on the tubular epithelial cells we demonstrated that IL-24 may induce the proliferation of HK-2 cells. Our data suggest that increased level of IL-24 may play a role in the pathomechanism of CKD. However further experiments are needed to elucidate the precise role of IL-24 in the renal fibrosis.

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E/V-10
THE ANTIDEPRESSANT FLUVOXAMINE IS PROTECTIVE AGAINST RENAL ISCHEMIA/REPERFUSION INJURY

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Introduction: Ischemia/reperfusion (IR) injury induced acute renal failure is a severe complication of various clinical situations. Previously we showed that pretreatment with the antidepressant fluvoxamine (FLU) improves postischemic survival and results in milder deterioration of renal function and kidney damage. In heart IR injury FLU has been shown to be protective through activating the Sigma-1 receptor (S1R) – nitric-oxide synthase (NOS) system, however there is no data concerning the kidney. To determine the role of the S1R-Akt-NOS signaling pathway in the renoprotection of FLU here we studied the intrarenalvasoregulatory effect in vivo and measured protein levels after pretreatment with FLU or FLU and various NOS blockers.

Methods: Male Wistar rats were subjected to 50 minute renal ischemia followed by 24 hours of reperfusion. 30 min prior to the ischemic procedure groups were treated i.p. either with (1) vehiculum (VEH); (2) FLU (20 mg/bwkg; FLU); (3) FLU+ S1R antagonist NE-100 (1mg/bwkg; FN); (4) FLU+ non-selective NOS blocker L-NAME (10mg/bwkg); (5) FLU + selective endothelial (e) NOS blocker L-NIO (20mg/bwkg); (6) FLU and selective neuronal (n) NOS blocker 7-NI (25mg/bwkg). Sham-operated animals served as controls (C) (n=10/group). Renal S1R, Akt, eNOS and nNOS protein levels were measured by Western blot, while the alteration of renal capillary diameters were determined in vivo using muliphoton microscopy.

Results: IR induced renal vasoconstriction, which was ameliorated by FLU (C: 9.86 ± 1.23 μm; VEH: 8.29 ± 1.29 μm; FLU: 10.64 ± 2.53 μm; FN: 7.88 ± 1.67 μm). This

increase was neutralized by all NOS blockers. After 24 hours of reperfusion all measured protein levels increased in treatment groups vs healthy controls. S1R levels were similar in all treatment groups. Akt and eNOS levels were lower, while nNOS levels were higher in the FLU treated group compared to VEH and FN . The acute vasodilatative effect of FLU 30 minutes after treatment was suspended by L-NAME and 7-NI and even reversed by L-NIO (FLU+L-NAME Δd=0.23 μm; FLU+7-NI Δd=0.86 μm; FLU+L-NIO Δd=-0.57 μm vs. FLU Δd=2.18 μm). S1R, Akt and eNOS protein levels were elevated 30min after FLU treatment, while nNOS levels remained unchanged.

Discussion: The S1R agonist FLU – used as an antidepressant chronically without notable side-effects – is renoprotective in IR. FLU pretreatment improves postischemic renal perfusion through the activation of S1R – NOS system in a time and NOS isoform specific manner. Based on this data one can hope to find a new therapeutic target in the treatment of renal IR damage through the modulation of the S1R.

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E/V-11
BIOMECHANICAL COMPARISON OF HARD TISSUE ENGINEERING POTENCY OF MICRO- AND NANO PARTICULATED BONE AUGMENTATION MATERIALS EXAMINED IN OSSI MODEL

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Objectives: Nowadays nano-particulate (NP) biomaterials are in the center of attention due to their outstanding properties over traditional micro-particulate(MP) materials. Our study focuses on measurements of the strength of fixation of implants surrounded by NP or MP materials.

Methods: Female Wistar rats (Crl(Wi)Br, Charles River; 250-370 g) were used (ethical permission for animal experiments No: 1799/003/2004).The surgical procedure was performed according to the OSSI model (Blazsek et al., PatholOncol Res, 2009). At the level of caudal C4-C5 joint vertebrae a circular incision was made on the skin. After the skin retraction the vertebrae were dissected under sterile conditions. In the exposed joint surface of C4, the axial cavity (2.0x3.5mm) for screw type titaniumimplant placement was formed (Full-Tech Ltd, Hungary). The study included five groups, named after the used biomaterial (nHA, mHA, nβTCP, mβTCP, control). Evaluation: 8, 12 and 16 weeks after the surgery implants were removed using pull-out testexpressed in Newtons (N). Following the removal of the implants, the vertebrae were fixed in 10% formalin. Histological analysis and micro-CTevaluation were used for morphometric measurements.

Results: In general, extraction force increased gradually by time. At week 8 nHA ($36,7 \pm 8,3$) and nβTCP($25,3 \pm 4,2$) reached higher biomechanical property than mHA($15 \pm 4,4$) and mβTCP($6 \pm 1,3$). The procedures of new bone formation and remodeling were quicker using NP biomaterials. Nano-particulate HA($36,7 \pm 8,3$) did not set back new bone formation compared to control ($41,1 \pm 7,5$). But mβTCP ($6 \pm 1,3$) significantly ($p < 0.05$) retarded the osseointegration compared to control ($41,1 \pm 7,5$) and nHA($36,7 \pm 8,3$) at week 8. The evaluation of micro-CT and histological results showed the expansion of bone trabecules and the reduction of intra-trabecular space. Consequently, bone density growth was detected.

Conclusions: The outcome of this study is that the particle size of implantation material has an effect on the duration and quality of new bone formation process. NP augmentation materials may help to obtain a better bone neogenesis in every aspect.

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E/VI
ORAL PRESENTATIONS

Chairpersons:
Prof. Dr. Éva Szőke
Prof. Dr. Kornélia Tekes

E/VI-1
IN VITRO AND CELLULAR STUDY OF BENZOTHIOPHENE-3-CARBOXAMIDES AS INHIBITORS OF AURORA KINASE FAMILY

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Serine/threonine kinases Aurora A, B and C play essential role in mitotic process, cytokinesis and maintaining the genomic integrity of normal cells. Aurora A and B kinases are often overexpressed in various tumor types and their inhibition results in mitotic arrest and eventually in apoptosis of the tumor cells. Up till now several Aurora inhibitor agents are in clinical development for the treatment of solid and blood cancers.

Applying *in vitro* recombinant kinase assay we identified novel benzothiophene-3-carboxamide derivatives as potent Aurora A and B kinase inhibitors in the molecular library of Vichem Chemie Ltd. Whether these compounds inhibit cell cycle and induce apoptosis on tumor cells, we compared them to clinical aurora kinase inhibitors in further recombinant kinase and cell-based assays.

For *in vitro* tests we utilized the IMAP fluorescent recombinant kinase assay. The antiproliferative effects were screened on colon carcinoma cell lines (Aurora overexpressing HCT-116 and HCT-15 with normal expression level of Aurora kinases) using the MTT assay. Mitotic arrest and induction of early and late apoptosis were assessed by flow cytometry on the same cell lines. Inhibition of Aurora A and B kinase activity was proved by SDS-PAGE and immunoblotting.

Most of the compounds tested inhibited either Aurora A or B kinases *in vitro*. However only a subset had antiproliferative effect on cell lines. These selected compounds indeed caused G2 arrest, and inhibited cytokinesis, what resulted in polyploid, multinucleated cells. Moderately elevated level of apoptotic cells occured only after longer incubation with these coumpounds. However, all results were comparable to the effect of the reference compounds.

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E/VI-2
DAPOXETIN AND ITS METABOLITES: SYNTHESIS AND ENANTIOSEPARATION BY CYCLODEXTRIN-MODIFIED CAPILLARY ELECTROPHORESIS

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Dapoxetine (Dpx), (*S*)-N,N-dimethyl[3-(naphthalen-1-yloxy)-1-phenylpropyl]amine hydrochloride, Priligy®) is a novel short acting selective serotonin reuptake inhibitor that is being developed specifically as an on-demand oral treatment of premature ejaculation. Dpx has been marketed and approved in more than 50 countries. The eutomer (*S*)-Dpx is 3.5 times more potent SSRI than (*R*)-Dpx and most of the synthetic procedures bear the possibility of chiral contamination, a fast and reliable enantioseparating method is essential for the analysis of the compound. Moreover, this drug is also a target for adulteration as other active pharmaceutical ingredients for the treatment of sexual disorders. A wide range of synthetic procedures were developed to synthesize racemic and enantiopure Dpx. The enantiomeric excess in these procedures were verified solely by chiral HPLC.

Dpx is extensively metabolized via the glucuronidation, *N*-oxidation, hydroxylation, sulfation and *N*-demethylation pathways leading to multiple metabolites. The *N*-demethylated derivatives are pharmacologically active.

Aims: Our aim was to synthesize the racemic and enantiopure Dpx and its active metabolites. The development of a chiral separation method was also planned.

Results: The synthesis of Dpx and its *N*-didemethyl derivative was accomplished by modified literature data. The synthesis of *N*-demethyl dapoxetine resulted in the formation of an unexpected compound. The structure of this byproduct, along with the mechanism of the reaction was elucidated using 2D NMR and MS-TOF techniques. Further heterocyclic compounds were synthesized utilizing this new synthetic pathway.

Cyclodextrin-hosted diastereomeric complexation and concomitant enantioseparation of dapoxetine and its metabolites were carried out. The parameters of the most promising system, using randomly methylated-*γ*-cyclodextrin as chiral selector was further optimized in terms of selector, buffer and organic modifier concentrations, pH, temperature and applied voltage.

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E/VI-3
THE LONG TERM EFFECT OF HORMONAL IMPRINTING INDUCED BY INSULIN AND SEROTONIN ON CELL PHYSIOLOGICAL PARAMETERS OF TETRAHYMENA

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In unicellular *Tetrahymena pyriformis*, the production of hormones characteristics for vertebrates, and their specific effects on cell physiological parameters were demonstrated. The first encounter with a hormone can induce the phenomenon of hormonal imprinting, by which the altered responsiveness of imprinted cells is transmitted also to their offspring.

In our present work the durability of the hormonal imprinting induced by insulin and serotonin in 10^{-15} and 10^{-6} M concentrations was measured up to generations 500 and 1000 by testing essential physiological indices: (i) insulin binding, (ii) endogenous serotonin content, (iii) cell growth, (iv) chemotaxis, (v) swimming behavior of imprinted and control cells.

In 500^{th} and 1000^{th} generations the insulin binding and serotonin content were detected with flow cytometer. To evaluate growth rate CASY TT system was applied. The chemotactic activity was assessed by capillary chemotaxis assay. For characterizing the swimming behavior the mean velocity and the tortuosity of swimming tracks were determined by tracking module of AxioVision Rel 4.7.1. software.

According to our results in generations 500 and 1000, the reactions of imprinted cells were quantitatively different from the control (non-imprinted) group. The insulin binding and endogenous serotonin content were reduced in generation 500 in both concentrations of insulin and serotonin imprinting. The 10^{-6} M serotonin imprinting significantly elevated the growth rate in generations 500 and 1000. The pretreatment with serotonin in both concentrations decreased the chemotactic response of progeny generations 500 and 1000; the re-treatment with serotonin could further improve this chemorepellence. The imprinting with 10^{-6} M insulin and serotonin resulted in higher swimming velocity than the control, while the re-exposure with hormones independently of their concentrations initiated slow, winding swimming behavior.

In summary, the responses of Tetrahymena were transgenerationally modified by hormonal imprinting, which points to the formation of durable memory and raises the possibility of the development of an epigenetic inheritance in the eukaryotic ciliate model.

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E/VI-4
SYNTHESIS OF 6B-ACYLAMINO AND HYDROXYLAMINE DERIVATIVES OF MORPHINANS

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During the last half century, medicinal chemists have been searching for improved opioid analgesics. Thousands of compounds have been synthesized and tested for improvements over alkaloids obtained from the opium poppy (*Papaver somniferum).*

The N-acyl-substituted derivatives of C-6 naltrexamine epimers have substantial effect on μ- and κ-opioid receptors. The most important compound of this series is β-funaltrexamine, which is an irreversible μ-opioid receptor antagonist. 6β-Acylamino derivatives of morphine, the principal drug of the opioid family have not been reported in the literature. Our aims were to systematically design and synthesize series of 6β-acylamino derivatives of morphine and its congeners. 6β-Aminomorphine, 6β-aminocodeine and 6β-aminodihydrocodeine were synthesized by means of Mitsunobu-reaction. 6β-Aminodihydromorphine was synthesized by the reduction of 6-azidodihydromorphine. The 6β-amines were acylated with a series of substituted benzoyl and cinnamoyl chlorides.

The biological activity of the novel 6β-acylaminomorphinans was studied *in vitro* and *in vivo;* results indicate that the novel 6β-acylamino derivatives have strong μ-opioid receptor binding and possess significant analgesic properties.

Furthermore, 6-oxo morphinans (naltrexone, naloxone and oxycodone) were reacted with *O*-methylhydroxylamine hydrochloride in ethanol, and the resulting oxime ethers were subsequently reduced. The reduction resulted in C-6 α- and β-epimers which were reacted with benzoyl chloride. The products were separated with column chromatography, their structure and absolute configuration were determined by means of HRMS, ^{1}H-, ^{13}C-NMR, chiroptical spectroscopy and quantum chemical computations.

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E/VI-5
RADIOLABELED MONOCLONAL ANTIBODIES AND PEPTIDE ANALOGS FOR CANCER IMAGING IN SPONTANEOUS DISEASED ANIMAL MODELS

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Background: Animal models have long been applied for cancer research such as human - murine xenografts and different transgenic animals. The relatively high incidence rate of some cancers, similar biological behaviour, large body size, comparable response to chemotherapeutic agents, shorter overall lifespan and shorter latency period are the factors that contribute to the advantages of the companion animals as a model for human neoplastic diseases. Spontaneous tumours in dogs and cats share a wide variety of epidemiologic, biologic, and clinical features with human cancer.

Materials and methods: Monoclonal antibodies designed against various antigens or receptors associated with specific tumour types serve as targeted carriers of radionuclide to malignant tumours overexpressing either antigens or receptors. These specific antibodies and peptide analogs radiolabeled with positron (68Ga) or gamma (99mTc, 111In) emitting isotopes are suitable for detection of cancer. The same specific carriers labelled with beta radiating isotopes (177Lu, 90Y) can be designed for anti-cancer treatments.

Results: In our whole body 3D SPECT/CT examinations we used altogether 6 referred dog and 2 cat patients with spontaneous tumours. Two dogs with thyroid carcinoma and oral melanoma were examined with ^{177}Lu-nimotuzumab (EGFR receptor targeting monoclonal antibody). The tested radiopharmaceutical showed clear uptake in thyroid carcinoma (150x90x85 mm) and its lung metastases (3 – 8 mm in diameter) 2 hours post injection. No relevant tumour uptake was observed in the dog with oral melanoma.

A 99mTc-labeled recombinant human TSH analog peptide was also investigated in two cat and 2 dog patients with thyroid cancer and in 2 dogs having other type of head and neck cancers. The TSH analog showed high specific uptakes in the thyroid carcinomas both in the cats and the dogs but only low, non-specific uptakes in the other head and neck carcinomas. The tumourous animals tolerated well the radiopharmaceutical applications; neither acute nor chronic side-effects were detected.

Conclusion: On the base of our preliminary results different spontaneously occurring tumours in companion animals proved to be useful in radiopharmaceutical research because of the high degree of similarity.

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E/VI-6
ENANTIOSEPARATION OF ALOGLIPTIN BY CYCLODEXTRIN-MODIFIED CAPILLARY ELECTROPHORESIS

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Alogliptin (Nesina®) is an orally available, selective dipeptidyl peptidase-4 inhibitor approved for the treatment of type II diabetes in Japan (2010) and in the USA (2013). Alogliptin has two enantiomers, however only the *R* isomer is in clinical use. As the optical purity is a general requirement of Pharmacopoeias and Regulatory Authorities in the case of single enantiomer drugs, development of sensitive enantioseparation methods is necessary.

Besides HPLC, capillary electrophoresis (CE) is widely used for chiral separations. During the electrophoretic runs the selector cyclodextrin (CD) and the analyte enantiomers form diastereomeric host-guest inclusion complexes enabling the separation. Our aim was to develop a CE-based separation method for alogliptin enantiomers using cyclodextrins.

As a first step in method development, CE-pH titration was conducted to determine the acid dissociation constant of alogliptin. The fast enantioseparation screening with 2 native, 5 uncharged and 6 charged cyclodextrin derivatives clearly showed that RAMEγ and HPγ-CD can partially, native γ, SPEβ and γ, SBEβ and γ-CD can completely separate alogliptin enantiomers. In addition, cavity size dependent enantiomer migration order reversal was observed: the *R* enantiomer migrates faster with γ-CD derivates and the *S* enantiomer migrates first with β-CD derivates due to the different complexation affinity of the enantiomers. To detect trace enantiomer impurity even below 0.1%, buffer components and concentration, pH, CD concentration, applied voltage, temperature and injection parameters were optimized for an alogliptin-SBEβ-CD (DS ~ 6.3) system.

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E/VI-7
THE COMPLETE MICROSPECIATION OF OVOTHIOL, THE SMALLEST TETRAFUNCTIONAL BIOMOLECULE

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Thiol-disulfide equilibria in amino acids, peptides and proteins (e.g. cysteine, glutathione, oxytocin, vasopressin, somatostatin, insulin, *N*-acetylcysteine) are essential in maintaining the redox balance, protecting thus the living organisms against oxidative stress.

To the best of our knowledge, the smallest, yet most-faceted thiol-contating biomolecule is ovothiol, which occurs as three differently methylated derivatives at the amino group. Ovothiol A, B, and C are mercaptohistidine derivatives first observed in marine invertebrate eggs. These molecules are among the most potent antioxidants found in nature, due to their remarkably low thiolate basicity.

Although the redox and acid-base equilibria of ovothiol A have been described, the site-specific characteriziation of this small molecule with as many as four basic moieties (thiolate, carboxylate, amino and imidazole nitrogen) is yet to be elucidated.

A deductive method was designed in order to elucidate the entire microspeciation of ovothiol A, by examining three derivative compounds (ovothiol A amide, *S*-methyl ovothiol A, *S*-methyl ovothiol A amide) that model the minor microspecies of ovothiol A. The synthesis of these model compounds was described for the first time. By conducting NMR-pH titrations followed by regression analysis, the macroscopic protonation constants of the model compounds were determined, which in turn were used to calculate the microscopic protonation constants of ovothiol A.

Our results include the entire microspeciation scheme of ovothiol A (32 site-specific protonation constants for 16 microspecies) calculated by two independent methods using ^{1}H NMR-pH titration data, these calculations were confirmed with UV-pH titration and ^{15}N NMR-pH titration data. We also determined the interactivity parameters between the proton-binding sites of ovothiol A, along with the standard chemical shift change values of all the nuclei in or near the basic centers.

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E/VI-8
PREPARATION AND CHARACTERIZATION OF ELECTROSPUN POLYMER FIBERS CONTAINING AMORPHOUS FAMOTIDINE

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Electrostatic spinning is a fast and gentle, solvent-based, continuous technology originating from the textile/filtration industry. The method is capable of producing very thin polymer fibers via extremely fast evaporation of the solvent. Recently, many medicine-related fields, including pharmaceutical technology, show notable attention towards this technique, as various active pharmaceutical ingredients (API-s) can often be incorporated in the fibers in amorphous form. This, combined with the large surface-area of the fibers, results in enhanced dissolution properties. Famotidine is an important H_2 histamine antagonist drug with very limited literature information about any amorphous forms or preparation. Moreover it possesses poor solubility in the small amount of saliva available in the mouth.

Aim: The aim of this work was the preparation and thorough characterization of famotidine 'orally dissolving web' system (ODW), that is, thin polymer fibers containing API in amorphous form, possessing fast and complete oral dissolution.

Methods: Morphology of samples was characterized by polarization microscopy and scanning electron microscopy. Effectiveness of amorphization and physical stability were studied by differential scanning calorimetry, powder X-ray diffraction, micro-Raman- and solid-state NMR spectroscopy, while chemical stability was tested by solution NMR and LC-MS. Dissolution properties were studied at pH 6.8 with both the conventional and a new, small-volume method for a better modeling of intraoral conditions.

Results and conclusion: Electrostatic spinning was suitable for preparing and stabilizing famotidine in amorphous form. Thin polymer fibers were prepared with diameter predominantly in the 1-2 μm range and the incorporated API was fully amorphous. The samples showed no crystallinity even after 12 months and thermal stability of API increased within the fibers. Dissolution of the incorporated API was almost immediate; moreover small-volume dissolution revealed significant solubility-increase when compared to the two polymorphic forms as well as to physical mixtures with the polymer, thus showing properties of an ODW formulation.

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E/VI-9
PRECLINICAL FORMULATION DEVELOPMENT OF A CARRIER SYSTEM FOR NANOPARTICLE ALBUMIN BOUND VORICONAZOLE

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In recent years human serum albumin (HSA) is instrumental in the development of new carrier system of active pharmaceutical ingredients (API). Intravenous liquid dosage form development of drugs or drug candidates that show high plasma protein binding and poor water solubility can be addressed by using human serum albumin due to its advantageous properties, such as its biocompatiblity and tolerability. Since voriconazole, a new generation of antifungal triazole, exhibits poor water solubility and high binding affinity to HSA it is a very promising candidate for the dosage form development using HSA.

Aim: The main objective of this study was to prepare an injectable liquid formulation comprising voriconazole using nanoparticle albumin-bound technology (NAB-technology), a technology based on the formation of HSA nanoparticles.

Results: Voriconazole-loaded nanoparticles were developed by high pressure homogenizer (Emulsiflex B15, Avestin, Canada). Process parameter optimization led to the elaboration of the optimal settings: six homogenizing cyles at 1800 bar pressure. The physicochemical features, such as particle size distribution and polydispersity index of the formulated nanoparticles was investigated by Zetasizer Nano S (Malvern, United Kingdom). The average size in the optimized product was 48.78 ± 9.41 nm which is optimal for parenteral administration. Furthermore, NAB-voriconazole particles resulted in the solubility enhancement of the drug by at least twofolds. An in vitro dissolution modell was adapted and proven to be suitable for predicting the release behavior of the voriconazole from the nanoparticles. In our study half the amount of the totally encapsulated voriconazole was liberated in less than an hour. The concentration of the API was determined by HPLC-UV following the sample preparation, which was developed specifically for the samples and included precipitation and centrifugation.

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E/VI-10
SITE-SPECIFIC GLYCOSYLATION ANALYSIS OF PLASMA PROTEINS

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Introduction: Glycosylation is one of the most common post-translational modification of proteins. Glycosylation has many roles, like transport of proteins, communication between cells, immune response, therefore its study is of great importance. In the literature, two main types of glycosylation studies can be found. Most studies are focusing on the determination of 'average' glycosylation patterns. In these worksglycans are removed from the proteins with an exoglycosydase enzyme, and all glycans are analyzed together, therefore information about attachment sites of glycans is lost. In contrast, using 'site-specific'analysis, glycosylation sites and the site-specific distribution of glycans can be determined. Proteins are digested with endoproteinases, and resulting glycopeptides are analyzed. Site-specific glycosylation patterns of most plasma proteinsare not available in the literature, however they are carrying relevant biological information.

Methods: Our recently developed complete workflow allows the determination of site-specific glycosylation pattern of proteins from complex biological mixtures (e.g. plasma). The method includes: depletion of two high-abundant abundant proteins, pre-fractionation of the remaining proteins with RP-HPLC, in-solution digestion, nanoLC-MS/MS and nanoLC-MS analysis of peptides and glycopeptides and data evaluation. The optimization of each steps were carried out using both standard proteins and plasma samples.

Results: Characterization of site-specific glycosylation of several high-abundant proteins and also minor components from human plasma (healthy donor) were carried out successfully. Distribution of sugar components, commonly observed glycan structures and novel site-specific glycosylation patternswith potential biological importance have been determined.

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E/VI-11
PREDICTION OF THE ORAL DISINTEGRATION TIME OF FAST DISINTEGRATING TABLETS AFTER OPTIMIZATION

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The fast disintegrating tablet dosage form is widely used around the pharmaceutical market. In the course of the characterisation of these tablets it is important to determine their oral disintegration times. Since these tablets contain active ingredients which can dissolve in the mouth, therefore an *in vitro* method is appropriate to test large number of tablets. The texture analysis method is one of the suitable *in vitro* methods for disintegration time determinations, since the tool is able to follow softening of tablets during sinking into a fluid medium. Texture analysis measurements were carried out on five types of different tablets in order to quantitatively characterise the method. The instrument recorded load - displacements curves which were indicative of the structure of the tablets.

Aims: Optimization of the method was carried out by changing different parameters of the measurements (e.g. test speed, polymer composition of the medium, polymer concentration of the medium) in factorial experiments. Based on the obtained regression equations computer optimization was performed. The oral disintegration time values were predicted from an empirical equation after the optimization.

Results: Two experiments were performed and the efficiency of the optimization was evaluated using independent tablets. In the case of the second experiment successful optimization was attained for seven types of different tablets of high *in vitro in vivo* correlation.

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E/VII
ORAL PRESENTATIONS

Chairman:
Dr. Gábor Békési

E/VII-1
FLUVOXAMINE PRETREATMENT AMELIORATES THE DEPRESSION OF DIABETIC ANIMALS: THE ROLE OF THE *BRAIN-DERIVED NEUROTROPHIC FACTOR*

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Introduction: The decreased level of the *Brain-derived neurotrophic factor* (BDNF) in the serum and hippocampus plays a pivotal role in the patomechanism of diabetes associated depression. Sigma-1 receptor (S1R) increases the expression of BDNF which might be protective against the development of depression. It has been recently described that besides its serotonin reuptake inhibitor effect, the antidepressant fluvoxamine is also a potent S1R agonist. Here we analyzed the development of depression and the alteration of neuronal BDNF and Sigma-1R in diabetic and fluvoxamine treated animals.

Methods: Five weeks after streptozotocin (65mg/bwkg, *i.p.*) induced diabetes male Wistar rats were treated orally either with fluvoxamine (20 mg/bwkg/die) or fluvoxamine + S1R antagonist NE-100 (1 mg/bwkg/die) for 2 weeks. Vehicle-treated diabetic and non-diabetic animals served as controls (n=8/group). The depressive behaviour was evaluated with forced swim test. Hippocampal BDNF and S1R protein levels were measured by Western blot.

Results: Diabetic rats showed depressive behaviour which was ameliorated by fluvoxamine treatment. The lower protein level of hippocampal precursor and mature BDNF of diabetic animals was increased by fluvoxamine pretreatment. The S1R antagonist NE-100 did not suspend the effects of fluvoxamine. Hippocampal S1R protein level remained unchanged in diabetes vs. controls; while increased after fluvoxamine pretreatment which was neutralized by NE-100.

Discussion: In diabetic animals the hippocampal Sigma-1R – BDNF signaling pathway plays a role in the development of depression. The activation of this cascade could represent a novel therapeutic target for the antidepressant fluvoxamine.

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E/VII-2
RAT SPINAL CORD TRANSECTION MODEL - PRELIMINARY EXPERIMENTS FOR STUDIES ON THE EFFECT OF STEM CELLS OF DENTAL ORIGIN

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Dental stem cells were shown to have high plasticity and immunomodulatory effects. Spinal cord injury models are useful to study neuronal survival and axonal regeneration. We aimed to establish a rat spinal cord injury model to investigate the possible neuroprotective and regenerative effects of human dental stem cells.

Adult Wistar rats were anesthetized with ketamin/xylazine. After laminectomy the spinal cord was transected with a stainless steel blade at the L4 spinal cord segment. Wounds were closed, animals received antibiotic treatment and were kept in individual cages. Then we attempted to identify motoneurons in the lumbar enlargement of the spinal cord using a retrograde tracer, FluoroGold. In anesthesia the right peroneal nerve was exposed and labeled by immersion into FluoroGold solution. Three weeks later, rats were perfused with formaldehyde, spinal cord was sectioned into longitudinal slices to count surviving labeled motoneurons. We also aimed to measure noradrenaline (NA) release from isolated spinal cord. The tissue was removed, tissue slices were labeled with 5 μCi/ml ^{3}H-NA, then put into superfusion chambers. After preperfusion, the effluent was collected. Supramaximal electrical field stimulation was applied and ^{3}H-NA in the fractions and in tissue was measured by liquid scintillation counting. Fractional release was calculated.

The spinal cord injury model became reproducible with high survival rates when a minimally invasive approach and sterile surgical conditions were applied. Motoneurons were successfully labeled through the peroneal nerve with FluoroGold. Their number substantially decreased following spinal cord injury induced inflammatory response and tissue degeneration. As expected, baseline fractional ^{3}H-NA release ($0.9 \pm 0.1\%$) increased considerably by EFS ($1.7 \pm 0.1\%$), in a reversible manner ($n = 16$). Repeated stimulation yielded similar results.

In this preliminary work we developed new protocols to monitor the structural and functional changes following spinal cord injury that may later serve to study immunomodulatory and anti-inflammatory effects of dental stem cells.

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E/VII-3
THE RENIN RELEASE IN ISCHEMIA/REPERFUSION KIDNEY INJURY; GENDER DIFFERENCES

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Ischemia/reperfusion (I/R) kidney injury is one of the most important risk factors for chronic allograft nephropathy. The course and severity of I/R kidney injury differs in the two genders. Our studies focused on the role of renin in I/R kidney injury. The juxtaglomerular apparatus (JGA) is the key anatomical site, where renin is synthesized and released on the contrary the collecting duct (CD) is a newly described localization of renin release. We have investigated *in vivo* the effect of I/R kidney injury on renal renin system in male and female rats.

Left renal pedicles of mature male and female Wistar rats were clamped for 50 minutes followed by 2, 8, 16, 24 and 48 hours of reperfusion, sham-operated rats served as controls. Paraffin sections of the excised kidneys were stained with periodic acid-Schiff reagent and the kidney injury were evaluated. We applied fluorescence-activated cell sorting (FACS) analysis for quantitative measurements and used multi-photon imaging to directly and quantitatively visualize the intact kidney, monitor the basic parameters of kidney function *in vivo* including (pro)renin content and release.

The histological analysis confirmed I/R kidney injury. Applying FACS analysis we have detected decrease in both JGA and CD renin content in the first 8 hours of reperfusion, however, following the 16th hour of reperfusion renin content increased in both localization. These results were further supported by a state-of-the-art method, the intravital multi-photon microscopy and as a result of the local renin activation vasoconstriction was found in the kidney.

In summary, our studies revealed first that there is a subacute renin response to I/R injury not only in the JGA but in the CD segment too. We could visualize the renin content and release *in vivo* even in this new localization and reveal that renin release is more explicit in males than in females.

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E/VII-4
RENIN-ANGIOTENSIN-ALDOSTERONE SYSTEM BLOCKERS IN DIABETIC NEPROPATHY: THE ROLE OF EPITHELIAL TO MESENCHYMAL TRANSITION

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Introduction: In diabetic nepropathy (DN) the over activated renin-angiotensin-aldosteron system (RAAS) induces the epithelial to mesenchymal transition (EMT). During EMT, which is a key element of fibrotic transformation, epithelial cells start to express mezenchymal proteins like α smooth muscle actin (αSMA) and platelet-derived growth factor (PDGF). Here we investigated the development of renal EMT in diabetes and after various RAAS inhibitor treatments.

Methods: After 5 weeks of streptozotocin (65mg/bwkg ip) induced diabetes, male Wistar rats were treated for 2 weeks with angiotensin I convertin enzyme (ACE) inhibitor *enalapril* (40 mg/bwkg/day) or *ramipril* (10 mg/bwkg/day), angiotensin II receptor blocker (ARB) *losartan* (20 mg/bwkg/day) or aldosterone-antagonists *spironolactone* or *eplerenone* (50-50 mg/bwkg/day). Untreated diabetic and healthy animals served as controls (n=6/group). Mesangial matrix expansion and tubulo-interstitial fibrosis were analyzed on periodic acid-schiff and Masson stained kidney sections. Human kidney 2 (HK2) proximal tubular cell line was cultured with normal (5,5 mM) or high glucose solution (35 mM) or mannitol (35 mM) as osmotic control. Renal and HK2 αSMA and PDGF protein level was examined by Western blot or fluorescence-activated cell sorting and renal localization of αSMA and PDGF receptor was analyzed by immunoflourescent staining.

Results: Diabetes induced mesangial matrix expansion and interstitial fibrosis were ameliorated by each RAAS blocker. The increased renal αSMA and PDGF level in diabetes was lowered by RAAS inhibitors. While in controls αSMA was only visible around the vessels, in diabetes intraepithelial and glomerulal signal was also detectable. The staining of the tubulo-interstitialy localized PDGF receptor was more intensive in diabetic rats than in controls. RAAS blockers minimized changes in αSMA and PDGF receptor staining. High-glucose treatment increased the level of αSMA and PDGF of HK2 cells, while no change was observed in mannitol treated cells.

Conclusion: EMT is a key feature in the development of diabetes induced renal fibrosis. Inhibition of this process could serve as a new therapeutic target of RAAS blockers. Moreover, the changes in EMT are likely to be due to the presents of hyperglycemia than to glucose induced hyperosmolarity.

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E/VII-5
COMPARISON OF DENTAL PULP STEM CELLS AND MG-63 OSTEOBLAST TUMOR CELLS OSTEOGENIC DIFFERENTIATION TIME COURSE

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Since their discovery in 2000, several work groups attempted to characterize dental pulp stem cells (DPSC). In this study, we compared the cell biological characteristics of DPSCs and the MG-63 osteoblast tumor cell line during osteogenic differentiation.

Dental pulp was isolated from human impacted wisdom teeth. Dental pulp cell cultures were differentiated for 21 days with ascorbic acid-2-phosphate, dexamethasone and β-glycerophosphate. Cell viability was assessed by measuring mitochondrial dehydrogenase activity. Cell numbers were determined by measuring DNA content, and alkaline phosphatase (ALP) activity was also studied. Expression of stem cell markers [STRO-1, c-Kit, CD-90], a mesenchymal protein [Vimentin], and osteogenic markers [osteonectin, bone sialoprotein] was investigated by immunocytochemistry. Quantitative data were analyzed by non-parametric ANOVA. Mineralization was followed by von Kossa staining.

Viability assay of both cell types, measured weekly, showed an increase during osteogenic differentiation, viability of DPSCs being consistently higher than that of MG-63 cells. Similar difference was observed in cell numbers between the two cell types. The difference in ALP activity between the two cell types was more prominent. DPSCs had 3 to 4 times higher activity than MG-63 cells had over the 21 days. Significant difference was also detected by von Kossa staining, MG-63 cells remained negative over the 21 days, while DPSCs stained positive on day 14. The immunophenotypes of the two cell types were similar initially, both DPSCs and MG-63 cells expressed all of the examined markers. However, during osteogenic differentiation, the proportion of STRO-1 positive cells was greater and the expression of the osteogenic markers was much reduced in MG-63 cells compared to DPSCs.

We conclude that DPSCs proliferate and accumulate calcium deposits in conventional osteogenic medium, but the same medium does not induce mineralization of MG-63 cell cultures.

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E/VII-6
THE FIRST FAMILY WITH *NPHS2* HOMOZYGOUS P.R229Q AND FAMILY MEMBERS WITHOUT STEROID-RESISTANT NEPHROTIC SYNDROME: THE MISSING EVIDENCE

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NPHS2 is the most frequently mutated gene in steroid-resistant nephrotic syndrome (SRNS) in both child- and young adulthood. Its mutations are inherited in an autosomal recessive fashion. Patients with *NPHS2* mutations typically develop SRNS during the first decade of life. A later onset can be associated with the c.686G > A (p.R229Q) variant. The p.R229Q allele has been reported to be pathogenic in association to an *NPHS2* mutation. However, it is difficult to assess the pathogenicity of homozygous p.R229Q. Several studies have identified homozygous p.R229Q in patients with late-onset SRNS and reported these patients as *NPHS2*-associated, suggesting that homozygous p.R229Q can cause SRNS in itself.

A 37-year-old patient with focal segmental gomerulosclerosis progressing to end-stage renal disease at the age of 33 was found to carry the *NPHS2* p.R229Q variant in homozygous state by direct sequencing. The allele frequency of p.R229Q was ascertained in 212 Hungarian controls and found to be 3% (13/424), giving a chance of 1 in 1100 for finding a homozygous p.R229Q accidentally. However, both the father and the brother were homozygous for p.R229Q with no proteinuria at the age of 59 and 40 years ($< 2 mg/m^2/hour$), proving the lack of its pathogenicity.

A detailed ophthalmological evaluation has been performed and a morning glory anomaly was detected. Therefore, the *PAX2* gene has been sequenced, and a de novo, truncating mutation (c.76dupG) was detected. This mutation explained the phenotype of the patient, proving again the lack of pathogenicity of homozygous p.R229Q. The identification of the causative mutation made possible to personalize the immunosuppressive regime after renal transplantation.

We conclude that the homozygous variant p.R229Q should not be considered pathogenic in late-onset SRNS.

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E/VII-7
SURFACE COATING EFFECTS ON MORPHOLOGY, MARKER EXPRESSION AND CELL PROLIFERATION OF RAT DENTAL PULP STEM CELLS DURING NEURODIFFERENTIATION

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Objectives: Although our group developed a protocol for neural differentiation of human dental pulp stem cells, it is not completely applicable for rat dental pulp stem cells (rDPSC). Our aim was to optimize the neurogenic differentiation protocol of rDPSC cultures.

Methods: Cells were isolated from rat lower incisors, and cultivated under standard conditions. To induce neural differentiation, first we activated PKA and PKC signalling and treated the cells with growth factors. Cells were maintained for two more weeks with bFGF and retinoic-acid containing media. Differentiation was performed on fetal calf serum (FCS), laminin (LA), poly-L-lysine (PLL), poly-L-lysine/laminin (LYLA), ornithin/laminin (ORLA) and on untreated surface (NTC). Marker expression was studied with Q-PCR and proliferation with WST-1 test.

Results: Within 24 hours, cells attached to the surface displaying similar morphologies. We observed three different cell types: fibroblast-like cells, epitheloid cells, and large, flat cells. In the first differentiation step cells formed ridges on FCS coating, but spread out on other surfaces. During the induction, the proportion of cells with neural morphology increased, but during the first maturation stage it decreased. By the second maturation stage neuronal-like cells were visible on LYLA, ORLA and PLL surfaces. At the end of the differentiation, the expression of the neural markers NFM and NSE increased six fold and two fold, respectively on LYLA and ORLA surfaces compared to NTC. Proliferation rate decreased during differentiation.

Conclusion: Neural morphology was more evident and neural markers elevated when rat pulp cells were cultured on lysine-laminin and ornithin-laminin surfaces. By the end of differentiation proliferation decreased, cells assumed a neural-like morphology and some cells underwent cell death.

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E/VII-8
GENETIC DETERMINANTS AND HERPES VIRUSES IN THE BACKGROUND OF PERIODONTITIS IN THE HUNGARIAN POPULATION

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Objectives: Periodontitis is a complex multifactorial disease: genetic factors, pathogenic bacteria, environmental factors and herpes viral infections have been shown to be involved in its etiology. We investigated 16 single nucleotide polymorphisms *(IL-1α-889A/G, IL-1β+3954C/T, IL-1β-511G/A, IL-10-1082T/C, TNFα-308A/G, TLR4-299A/G, TLR4-399C/T, VDR-1056A/G, TNFα-1031C/T, IL-10-597T/G, IL-6-1363G/T, CD14-260A/G, COX2-8474A/G, ASPORIN-9659C/T, MMP8-799A/G, ANRIL)* and 5 herpes viruses *(HSV1-2, VZV, CMV, EBV)* in patients with several forms of periodontal disease in the Hungarian population.

Methods: DNA was isolated from buccal scrapings from 355 patients. They were classified according to clinical parameters into healthy control, gingivitis, chronic and aggressive periodontitis groups. SNPs were identified by Genotyping Realtime PCR, viruses were detected by nested PCR. Group-wise differences were calculated by logistic regression, Chi2 probe, and were further analysed by Bayesian multilevel statistical analysis.

Results: We observed significant differences in allele frequencies of the *IL-1β-511, IL-6-1363, TNFα-1031 and CD14* SNPs and in the genotype distribution of polymorphisms within the *IL-1α-889, IL-1β-511, IL-6-1363, TNFα-1031, CD14, Asporin* and *Anril* genes. VZV showed higher incidence in aggressive periodontitis compared to controls. Viral mono and coinfections showed a group and age specific distribution. By the Bayesian method we created a possible dependency model of the investigated SNPs and viruses in the background of periodontitis in the Hungarian population (Figure 1.)

Conclusions: Among the SNPs investigated CD14-260 was the only central factor in the development of periodontitis in the Hungarian population, through which *TNFα-1031* and the two *TLR4 SNPs* acted, while herpes simplex viruses have an independent effect. Complex dependencies between SNPs could be investigated only by Bayesian statistical approach, an emerging method to investigate the background of multifactorial diseases. The use of our model may result in novel diagnostic and therapeutic approaches in periodontology.

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E/VII-9
MODELLIG THE PH REGULATION OF AMELOBLASTS BY NOVEL TWO DIMENSIONAL CELLULAR SYSTEM

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Epithelial ameloblasts are responsible for enamel formation and have important roles in the pH regulation of the mineralization space. During the maturation stage of amelogenesis large number of protons are liberated as hydroxiapatite crystals rapidly grow. Without pH regulation this could stop mineralization, resulting in hypomineralized enamel. Transporters typical in electrolyte secreting epithelia such as anion exchangers (Ae2, Pendrin), Na^+/HCO_3^- cotransporter (Nbce1) and Cl^- channel (Cftr) have been found in ameloblasts by expressional studies, but functional methods have not been available so far to strengthen these findings.

We aimed to establish a new *in vitro* ameloblast model suitable for functional studies.

We used the Hat-7 ameloblast cell line. Cells were differentiated on polyester membranes with different pore sizes (0.4 and 3μm) in different culture media: DMEM/F12 as control (Control medium, CM) and two differentiation media (Differentiation medium, DM and Hepatostim medium, HM). We monitored transepithelial resistance (TER) as an indicator of tight junction (TJ) formation. Expression of transporters and TJ proteins was measured by RT-PCR. Bicarbonate transport was estimated by microfluorometry.

Hat-7 cells formed polarized monolayers on the filters with 0.4μm pore size. We obtained the highest TER values by HM (5th day: CM: 283 ± 28 Ωcm^2, DM: 462 ± 55 Ωcm^2, HM: 1798 ± 291 Ωcm^2, $n=4$). We detected the gene expression of key transporters: Nhe1, Ae2, Ae3, Nkcc1 and Cftr, and TJ proteins: Zonula occludens 1, 2, Occludin and Claudin 1, 4, 8. By microfluorometry we found basolateral bicarbonate uptake which was sensitive to 1mM acetazolamide (carbonic anhydrase inhibitor) and 500µM H_2DIDS (AE/NBC inhibitor) (pH_i increase after HCO_3^-/CO_2 exposition: 0.14 ± 0.02 and 0.26 ± 0.01 versus 0.43 ± 0.06 pH unit/min of control, $n=8, 4, 13$, respectively).

Our new model may serve for studies of electrolyte transport across ameloblast-like cells and can be useful for functional studies on the molecular mechanism of amelogenesis.

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E/VII-10
NEW NON-INVASIVE APPROACH TO EVALUATE IMPLANT STABILITY

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Osseointegration is a rigid fixation of implant within the bone. Non-invasive and invasive methods are available to measure implant stability. We developed an experimental model, named OSSI, to evaluate osseointegration. Until recently, we could only measure tangential fixation force when using the OSSI. In the past few months we succeeded in the adaptation of OSSI model to a non-invasive method - resonance frequency analysis (RFA).

Materials and methods: We used the harvested C4-C1 vertebrae of Wistar rats (ethical permission No: 1799/003/2004) for implant placement and stability examination. Axial cavities were created for the placement of titanium implant. Implant stability was measured using a non-invasive system utilizing RFA (Osstell, Sweden). Stability was described by a value called ISQ (Implant Stability Quotient) which could fall between 0 and 100, where a larger ISQ indicates higher stability. Biomechanical properties were further characterized by a pull-out test, measuring the maximum extraction force (expressed in Newtons (N)) using a Tenzi device (TENZI Ltd., Hungary). We then calculated the strength of primary fixation per surface area. After primary stability evaluation we imitated "osseointegration" (secondary stability) in an in vitro environment using phosphate cement to fix implants in vertebrae. We used Wilcoxon test to compare values and Spearman's correlation test to estimate correlation.

Results: We found a strong correlation between non-invasive and invasive implant stability evaluation methods ($r=0.704$). We observed statistically significant differences between primary stability and secondary stability ($p<0.05$). The average values of primary fixation of implants were 0.61 ISQ/mm^2 using RFA and 0.06 N/mm^2 using the pull-out test. One N was found to correspond to 10.16 ISQ.

Conclusions: We successfully adapted resonance frequency analysis non-invasive measurements in the OSSI model. We found correlation between RFA and pull-out test. We successfully calculated the value of titanium implant fixation with bone surface.

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E/VII-11
SMALL BOWEL ISCHEMIA – A COMPARATIVE EXPERIMENTAL STUDY

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Introduction: Serious small bowel injuries can occur during superior mesenteric artery (SMA) occlusion. Nevertheless significant damage of the small intestine can be observed following lower limb vascular occlusions as well as a systemic consequence of local ischemic-reperfusion (IR) injury of the muscles and might be due to the redistribution in systemic circulation. There are limited data available on the examination of the degree of injury after lower limb vascular operations.

Aim: To evaluate the effects of lower limb ischemia and SMA ischemia on small intestinal injury, and to compare the obtained result.

Materials and Methods: Male Wistar-rats (n=30) underwent in one group (n=10) 3 hours of bilateral lower limb ischemia achieved by infrarenal aortic occlusion. In another group of rats (n=10) 1 hour of mesenteric ischemia was induced. The length of reperfusion was standardized in 6 hours in both groups. Sham operated groups were created for each IR group (n=2x5). For analysis of redox-homeostasis (*free-radical- content*, *antioxidant-levels*) and for histological assessment (Chiu-score), samples were taken from specified sections (jejunum and ileum) of the small intestine.

Result: Free-radical-content has increased significantly after SMA (jejunum: $p=0.025$ ileum: $p=0.029$), as well as after infrarenal occlusion (jejunum: $p=0.014$ ileum: $p=0.010$) int he small intestine, compared to the Sham-operated groups. The levels of tissue antioxidants were significantly ($p<0.05$) reduced in both IR-injured groups in comparison with the Sham-groups. Except for the jejunum SH-group values there were no significant alterations between the two IR-injured groups regarding the redox-state parameters ($p>0.05$). Considering the histological evaluation of intestinal injury no significant differences were detected between the two occlusion groups with the Chiu semiquantitative score ($p>0.05$).

Conclusion: In this study we demonstrated that sublethal mesenteric IR-injury and 3 hours of bilateral lower limb ischemia can induce similar extent of small bowel damage.

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E/VII-12
LEVOSIMENDAN PROTECTS AGAINST LIVER ISCHEMIC-REPERFUSION INJURY

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Introduction: Temporary occlusion of the hepatoduodenal ligament leads to ischemic-reperfusion (IR) injury of liver. Levosimendan is a new positive inotropic drug, which is able to induce preconditioning-like adaptive mechanisms due to opening of mitochondrial K_{ATP} channels. The aim of the present study was to examine possible protective effects of levosimendan in a rat model of hepatic IR injury.

Material and methods: In male Wistar rats, in two subgroup – 1 (early) or 24 (late) hours before operation – levosimendan pretreatment was used followed by 60 minutes segmental liver ischemia. The microcirculation of liver was monitored by laser Doppler flowmeter. After 24 hours of reperfusion liver, and blood samples were taken for histology, immuno- and enzyme-histochemistry (TUNEL; PARP; NADH-TR), and laboratory tests. Furthermore liver antioxidant state and HSP72 expression were measured.

Results: In both levosimendan pretreatment group significant improvement ($p<0.05$) of the hepatic microcirculation was observed compared to the analogous IR groups. Severity of histological damage was also reduced after administration of levosimendan. This observation was supported by the significantly lower level of serum ALT ($p_{early}=0.02$; $p_{late}=0.005$), AST ($p_{early}=0.02$; $p_{late}=0.004$) and by the moderate DNA damage indicating TUNEL ($p_{early}=0.05$; $p_{late}=0.034$) and PAR positivity ($p_{early}=0.02$; $p_{late}=0.04$). Both levosimendan pretreatments resulted in significant improvement of liver redox homeostasis. Furthermore, significantly better mitochondrial function was detected in the late pretreatment animals ($p=0.003$). However, HSP72 expression was not affected by either levosimendan pretreatment.

Conclusion: Levosimendan pretreatment – administrated 1 or 24 hours before operation - can induce hepatoprotection and would be useful before extensive liver resection.

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P/I
POSTER PRESENTATIONS

Chairperson:
Prof. Dr. Lídia Sréter

P/I-1
MULTIFRACTAL ANALYSIS OF NEAR-INFRARED SPECTROSCOPY (NIRS) SIGNALS RECORDED FROM THE HUMAN BRAIN CORTEX

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$1/f$ noise has been found ubiquitous in natural processes. This fractal pattern can be modeled in the frequency domain as $|A|^2 \propto 1/f^{\beta}$ where β (spectral index) captures the scale-free behavior of power amplitudes (A) within the scaling range (SR) of frequencies (f). Using multifractal formalism, the global distribution of the fractal measure can be revealed in a singularity spectrum, $D(h)$. Previously, we reported that NIRS-signals did spontaneously fluctuate in the human brain cortex as monofractal processes [1]. Our aim was to investigate if these hemodynamic signals have multifractal properties.

NIRS-signals (sampled at 2 Hz, length: 8192 s) were obtained from the prefrontal cortex of healthy volunteers (4 groups with n = 5 in each: young male - M1, young female - F1, aged male - M2, aged female - F2). Relative hemoglobin concentration time series were calculated by the modified Beer-Lambert law. The analyzing algorithm was the differential Multifractal Detrending Moving Average method operating in the time domain. Its performance was found reliable for stationary signals, so our non-stationary signals needed to be differentiated. A multifractal variable, P_c, was calculated from characteristic measures of $D(h)$ as the end-point of multifractal analysis.

Fractal measures	F1	M1	F2	M2
Monofractal (β)	1.10 ± 0.25	1.16 ± 0.13	1.63 ± 0.35*	1.01 ± 0.35*
Multifractal (P_c)	0.03 ± 0.03	0.03 ± 0.02	$0.15 \pm 0.15^{\#}$	$0.02 \pm 0.01^{\#}$

Table 1. Results are shown as mean ± SD (, #: $p < 0.05$)*

Fractal measures pertinent to SR were obtained for β and P_c (Table 1.). Significant differences (two-way ANOVA, Bonferroni post-hoc test) were found between F2 and M2 groups both in β and P_c.

To conclude, we demonstrate that (i) multifractal temporal structuring is present in hemodynamic fluctuations recorded from the human brain cortex, (ii) in the post-menopause age groups, gender has an impact on both mono- and multifractality, which can be explained by vascular (age-related stiffening of cerebral vasculature) or neural factors (declining neural activity).

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Reference

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P/I-2
SERUM APELIN AS A PREDICTOR OF RIGHT VENTRICULAR DYSFUNCTION

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Background: Apelin is the endogenous ligand for G protein-coupled receptor, APJ. The role and changes in its expression in chronic heart failure has already been demonstrated. In preclinical studies, different biologically active apelin fragments reduce preload, afterload, and increase cardiac contractility. However, these results are still controversial in clinical settings and need to be further investigated.

Aims: We have previously shown the predictive value of impaired right ventricle function on mortality and prognosis of patients with cardiac resynchronization therapy (CRT). Our aim was to determine the association of apelin and right ventricular dysfunction in severe heart failure patients.

Methods: In this study we studied 111 CRT-D/P implanted patients with chronic systolic heart failure. Serum apelin was determined by competitive ELISA (Raybiotech). Left ventricular function, geometry and right ventricular tricuspid annular plane systolic excursion (TAPSE) were evaluated. Additionally right ventricular longitudinal strain was measured with spackle tracking strain echocardiography.

Results: Baseline parameters were: ejection fraction 29.09%, 66 patients with ischaemic cardiomyopathy, 90 men, NYHA II: 17 patients, NYHA III-IV: 131 patients, TAPSE: 18.02mm. We found significant lower serum apelin levels and decreased TAPSE (cut off <14mm) in patients with right ventricular dysfunction (serum apelin, mean$\pm$SD: 765 $\pm$ 363 ng/ml vs. 1099 $\pm$518 ng/ml, $p=0.0042$). The right ventricular longitudinal strain and other left and right ventricular and functional parameters were not associated with baseline apelin concentrations. Apelin level was not associated with outcome in this cohort.

Conclusions: Based on our results, apelin is associated with right ventricular dysfunction in the patient population. It might be a prognostic factor of right ventricular heart failure, which also influences the prognosis of patients with severe systolic heart failure to a great extent.

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P/I-3
MONITORING BRAIN HEMODYNAMICS AND OXYGENATION WITH NEAR-INFRARED SPECTROSCOPY (NIRS) DURING CARDIOPULMONARY BYPASS SURGERY

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Even routine surgery can challenge the brain, not to mention open-heart surgery with its multiple stressors. In particular, postoperative cognitive disfunction frequently emerges when non-pulsatile extracorporeal heart pump is used. In its etiology, impaired pressure autoregulation with an elevated lower autoregulatory threshold can be considered. Thus a lower than adequate mean arterial pressure (MAP) sustained by the non-pulsatile pump may lead to cerebral hypoperfusion and hypoxia. Hence our aim in this study was to caracterise the cerebral hemodinamic status by novel parameters which can aid in personalising the surgical protocol.

Eleven patients (65±9 years, 5 female and 6 male) underwent non-pulsatile heart-lung pump assisted (NP-CPB: 2.4 L/min/m^2, 98±28 minute pump time, 50-70 Hgmm MAP) open-heart surgery. With NIRS the relative change in HbO and HbR compartments were continuously recorded. From that, regional saturation (rSat), vascular reactivity index (r_{VRI}) – the coefficient of correlation between the low frequency fluctuation of blood pressure and blood volume (HbO+HbR) – and the correlation coefficient of hemoglobin compartments (r_{Hb}) were calculated for 15 minute steady state periods before (*M), on (M) and after (M*) heart pump. Ranges $r_{VRI} \leq 0$, and $r_{Hb} << 0$ indicate physiological conditions: effective pressure autoregulation at the input and impacting neuronal activity at the output of the cerebrovascular system, respectively.

	*M	M	M*
rSat	0.42±0.04	0.32±0.06 #	0.42±0.08
r_{VRI}	0.03±0.14	0.20±0.25 #	0.04±0.09
r_{Hb}	-0.44±0.30	0.11±0.15 #	-0.48±0.17

*Table 1. Results are shown as mean±SD. Significant differences (one-way ANOVA, Newman-Keuls post-hoc test) were found between *M and M similarly to M-M*. (#:$p < 0.05$)*

Increase in r_{Hb} indicates that the demand-regulated distribution of oxygen in the monitored regions becomes supply-regulated on heart pump (Table 1). Due to changes in pathological direction, the overall oxygen supply to the brain tissue becomes inadequate as shown by decreased Sat. The coordinated changes seen in r_{VRI}, r_{Hb} and rSat offer the basis for future personalization of NP-CPB protocol for an optimal target MAP.

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P/I-4
THE EFFECT OF KIDNEY TRANSPLANT PATIENTS' BODY IMAGE CHARACTERISTICS ON THEIR RECOVERY

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There is an increasing body of evidence proving that transplanted patients' perceptions of their disease and their body have an important influence on their recovery.

Aims: The aim of this study is to determine whether kidney transplantation is associated with body image disturbance, and whether body image charecteristics predicts poor renal outcomes in both crosssectional and prospective analyses.

Methods: The data were collected a three-year period from December 2009 to December 2012 at the Surgery Clinic, University of Szeged. We tested 51 kidney transplant patients with a combination of five instruments. Mental representation of the body and the illness were measured with a projective drawing test between the postoperative 5th and 10th days. Besides assessment of illness perceptions, we tested patients with the Spielberger's State and Trait Anxiety Scale and the Beck's Depression Scale. Parameters of kidney function (serum creatinine level and acute and/or chronic graft rejection) were registered after the transplantation and one years follow-up.

Results: The results of the logistic regression analysis showed that complexity of the drawing test, the size of the body in the projective test and pre-discharge serum creatinine were able to predict graft rejection during one year after transplantation.

Conclusion: In conclusion, body image disturbances and higher pre-discharge plazma creatinine level are strong predictors of a poor long-term outcome. The findings of this study suggest that drawings provided important information about patients' representation of their body, and perceptions of kidney function.

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P/I-5
THREE DIMENSIONAL HISTOLOGICAL EXAMINATION OF DENTAL ROOT CEMENT: A METHODICAL INNOVATION APPROACH

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Aims: The goal of our team was the development of „true three-dimensional (3D) transparent intravital microscopy". At first, we established the basis of real 3D imaging in microscopy and constructed a prototype of a 3D vital microscope. Recently, we have been dealing with the improvement of clearing solutions, that were able to make the soft tissues (e.g.: liver, small intestine, salivary gland) transparent. In our recent experiment we intended to investigate the clearing effect of these materials on hard tissues, specially teeth.

Material and Methods: We prepared cross sectional and vertical slices of extracted human teeth and investigated the clearing effect of one of our newly developed physiologic solution. For the inspection we applied the above mentioned 3D vital microscopy. We documented our observations by means of 3D photographs.

Results: The newly developed solution was able to clear the hard dental structures. Acellular cement has rather granular structure; meanwhile the cellular cement looks like to have lamellar structure. In the cellular cement, we were able to detect coal black, dendritic cells, without the usage of any histochemical staining. It was quite frequent, that we detected such form of cell groups, where there was a centrally oriented pyramid-like cementocyte, encircled by cells in wreath. The processes of these latter cells contacted with each other, creating a web like impression. We had the opportunity to observe some typical cell forms just like pyramid, roundabout, polyhedron, ovoid and cylindrical. At the end of the processes we quite often recognized butt-like flares or rod-like ramifications. In case of the cellular cement, the periodontal fibers anchored in between the superficial crests, meanwhile by the acellular cement they could pass a little deeper among the granules.

Conclusion: Our newly developed system is suitable to clear and investigate not only the soft tissues, but the more challenging hard tooth structures as well, promoting real 3D qualitative and quantitative histological observations, which are of great importance regarding the functional and clinical consequences.

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P/I-6
THE EFFECT OF METFORMIN ON GLYCOTOXIC INTERMEDIATES IN PATIENTS WITH TYPE 2 DIABETES

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Background: Hyperglycaemia increases the formation of intracellular reactive oxigen species and glycotoxic intermediates. Methylglyoxal (MG) is a highly potent glycatic agent that is throught to contribute to late diabetic complications either as a toxic agent or as a precursor for advanced glycation end products. Metformin, a biguanide, binding MG, was studied in a prospective non randomized trial in 12 patients with type 2 diabetes with respect of its effects on MG levels, intracellular activity of glyoxalase-1 (GO-1), the GSH dependent enzyme for MG detoxification.

Aims: The patients were educated for a low energy diet and treated with metformin (2000 mg/day) for 24 weeks. Glycaemic control was determined by glucose and HbA1C. Plasma MG was detected by high-performance liquid chromatography. The glyoxalase system was measured by enzyme assays in peripherial blood mononuclear cells and red blood cells. Plasma *N-Epsilon-(Carboxymethyl)-Lysine* (CML) modified protein concentration was determined by ELISA.

Results: At baseline MG levels correlated with GO-1, but not GO-2 activity. Metformin treatment in addition to life style intervention reduced significantly fasting glucose from 7,7 to 6,3 mmol/l ($p=0,02$), HbA1c from 7,1 to 6,3% ($p=0,04$) while body weight and BMI was only marginally reduced during the 24 week trail. Treatment reduced significantly MG ($p=0,015$) and subsequently also levels of CML ($p=0,04$). The reduction of MG was paralleled by a significantly increased activity of GO-1 in peripheral blood mononuclear cells ($p=0,002$) and red blood cells ($p=0,03$), while no effect was observed on GO-2 activity. Most importantly multivariate analysis showed that neither glucose, nor HbA1c nor changes in body weight influenced on MG levels. The only significant interaction was found with respect to metformin treatment.

Conclusion: Metformin might beneficial influence on the glycotoxic intermediate-methylglyoxal-metabolism in type 2 diabetes. Based on these data it is likely that metformin might affect MG plasma levels via restoring glyoxalase-1 activity.

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P/I-7
INVESTIGATION OF METHYLATED CFDNA FRACTION CHANGES IN PATIENTS WITH COLORECTAL CANCERCOMPARED TO IBD, ADENOMA AND HEALTHY CONTROLS

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Introduction: DNA methylation is a well known epigenetic regulation of genes functions and its alteration can be observed by investigation of plasma circulating cell free DNA (cfDNA) during cancer development.

Aims & Methods: Our aim was to detect the methylation pattern changes of cfDNA isolated from peripheral blood of healthy, IBD, colorectal adenoma and cancer patients. We investigated 50-50 patients in each group. CfDNA was isolated from the plasma with QIAamp Circulating Nucleic Acid Kit (Qiagen). From each sample 50-100 ng extracted DNA was assembled in each groups and pooled DNA was applicated for further sequenci alanalysis (SOLiD sequencing). After matching native plasma samples to the reference genome, coverage and pile up diagrams were defined. We sought for positions at least twenty five times covered and also shows differencies between healthy and cancer samples.

Results: Region between 92075 and 92115 derived from SEPT9 gene has shown 6200 times higher number of readsin CRC samplesin 50-50% from reverse and forward direction to ensure that is not artifact. This position is exactly matched with region detected by Epi Pro Colon Kit (Epigenomics) based on the enrichment of methylated fragments. It is already proven that methylated SEPT9 (mSEPT9) is present 94,7% in CRC patients. The coverage of mSEPT9 was 245 times higher in adenoma and only 8 times higher in healthy patients plasma sample. SFRP1, SFRP2, MAL and PRIMA1 genes proceeds the same result which means that enrichment of methylatedregionsin CRC were significantly higher than in the other groups.

Conclusion: General hypomethylation and local hypermethylation is characteristic in tumours that is reflected in cfDNA content. The detection of these specific epigenetic changes from peripheral blood can be important step to develop screening and diagnostic assays. Our results show that investigation of epigenetic changes is possible from native plasma sample as well.

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P/I-8
CHARACTERISTIC MIRNA EXPRESSION ALTERATIONS IN COLORECTAL CANCER

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Background: Analysis of miRNA plays important roles in fields of functional and biomarker discovery in recent years. Expression profiles of miRNA altered along tumour formation, furthermore these miRNA may spread into tumour microenvironment.

Aims: Our primary aim was to identify the alteration of miRNA expression pattern in colorectal cancer (CRC) formalin-fixed-paraffin-embedded tissue (FFPET) samples. Our further aim was to analyse the alteration of the circulating miRNA profile in C38/ C57BL/6 mouse tumour model.

Methods: miRNA was isolated from formalin-fixed CRC samples (n=3) and from normal tissues (n=3). miRNA expression was measured by Exiqon qPCR. Circulating miRNA was isolated from plasma samples which were collected twice a week over 45 days using C57BL/6-C38 tumour model. Affymetrix GeneChip miRNA array platform was used for screening of the altered miRNA profile and results were validated by qPCR.

Results: Our Human Panel study results showed that 200 miRNA were detected in the normal samples, 216 individual miRNA were expressed in CRC samples, and 284 miRNA were expressed in both normal and tumorous samples. The expression level of 253 miRNA (hsa-miR-92a, hsa-miR-21) were increased in CRC in contrast to 31 miRNA (hsa-423-5p, hsa-145*), were down-regulated in the same sample type. All together 94 miRNA were detected in the plasma samples of healthy animals, 161 miRNs in early and 176 miRNA in late tumour stages. During the tumour progression 25 miRNA were identified, which showed increased expression as compared to the healthy samples. miR-676 and miR-92a showed increased expression level in plasma samples by qPCR, that was consistent with the microarray results.

Conclusion: Characteristic tissue miRNA patterns were determined in CRC that were also detected in peripheral blood. As based on our results, it seems that many miRNA originate from healthy cells, further investigations are required to understand the communication process between cancer and host cells.

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P/I-9
ALTERATION OF DNA METHYLATION PATTERN IN COLORECTAL ADENOMA-CARCINOMA SEQUENCE

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Background: Several epigenetic modifications, including DNA hypermethylation, play an important role in the development of colorectal cancer (CRC). A subset of CRC, commonly found in the proximal colonis abundant in hypermethylated genes. However, the methylation status of the more frequent distal tumors has not been thoroughly studied.

Aims: Our aims were to analyse DNA methylation alterations of 96 genes during colorectal carcinogenesis and to compare the metylation profile of different cancer stages focusing on CpGmethylator phenotype (CIMP) negative, microsatellite stable (MSS) cancers.

Materials, methods: A total of 59 endoscopically removed colonic biopsy samples (19 healthy, 12 LGD, 10 HGD, and 18 CRC) were examine for their methylation status using EpiTect Methyl qPCR Array System. Immunohistochemistryfor MLH1, MSH2, MSH6and mutation analysis of BRAF/V600Eand KRAS were performed to define microsatellite and CIMP status. Furthermore, to confirm our results, LGD samples from 5 patients were compared to their matched CRC pairs.

Results: Based onimmunohistochemicalstainings, all biopsies were MSS, and 25% of the samples showed KRAS, 10% exhibited BRAF/V600E mutation. Interestingly the number of methylated genesand degree of methylationwere higher in precancerous lesions, as compared to CRC. DNA methylation of 6 genes have shown altered methylation pattern through adenoma-dysplasia-carcinoma sequence, and using this panel, precancerous and cancerous lesions can be distinguished from healthy tissue. In addition, we identified higher level of DNA methylation in LGD than in CRC samples in regulation regions of 9 genes.

Conclusion: In this study a characteristic methylation pattern of distal, CIMP negative, MSS cancers and their precursor lesions were identified. Based on this methylation profile, CRC can be distinguished from healthy control. Interestingly more hypermethylated genes were observed in LGD than in CRC samples, that needs to be further studied.

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P/I-10
MONITORING OF THE ADHESION OF CREVICULAR FLUID CELLS AND ITS MODIFICATION BY OLIGOTUFTSIN DERIVATIVES

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Objective: Gingival sulcus is a preformed, 1-2mm deep physiological space between gingiva and teeth. Gingivitis, periodontitis etc. cause characteristic changes in sulcus depth as well as in the cellular composition of crevicular fluid (CF), therefore this space and its elements are also in the focus of prevention of periodontitis, caries and plaque formation. The objectives of the present work were: (i) whether impedance based techniques are available to detect adhesion of CF-cells; (ii) do members of oligotusftsin library (Tp5-Tp55) have significant effects on CF-cell adhesion; (iii) is there any difference in responsiveness in samples representing different diseases; (iv) is there any correlation between cell populations/CD markers and responsiveness of CF-cells?

Methods: Members of the tested oligotusftsin library were representing oligomer peptides composed of [TKPKG] sequence derivatives. Cell adhesion of CF-cells was monitored in a real-time mode (24h) by xCELLigence SP (Roche). CD marker profiling (CD3, 11b-c, 14, 16, 18, 45, 49d, 62L, HLA-DR) of samples of CF-cells was carried out by direct immunocytochemistry and evaluation was done by flow cytometry (FACSCalibur, Beckton Dickinson). Samples of 120 patients were analysed. ANOVA test was used for statistical evaluation.

Results: Strong cell adhesion of CF-cell samples was detected on 1 μl/cm^2 fibronectin coated surfaces, which property was influenced/blocked by the Tp5-Tp55 oligotuftsin derivatives, out of which Tp45 10^{-6}M was the most effective. Diverse responsiveness was detected in samples of different pathological backgrounds (periodontitis, gingivitis, dental plaque, caries, cancer).

Conclusions: (i) some oligotuftsin ligands are able to modulate cell adhesion of CF-cells in a disease dependent way; (ii) the effect of oligituftsins is dependent on the molecule length; (iii) it is presumed that differences in expression of surface molecular structures are responsible for diversities in cell adhesion (e.g. CD49d) and in effector functions (CD11b and c) characteristic to clinical conditions.

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P/I-11
THE METHYLATION STATUS OF HUMAN DNA DETERMINES THE AUTOLOGACTIVATION OF TLR9 PATHWAY ON HT29 COLORECTAL CANCER CELLS

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Background: Toll-like receptor 9 (TLR9)recognisescytosin-guanine dinucleotides from bacteria, fungi, prokaryotes and viruses and synthetic oligodeoxynucleotide (ODN) sequences.Till today no evidence exists,that the human DNA released thorough apoptosis, necrosiscan act throughTLR9signaling in a paracrine way.

Aims: Examine the gene expression level changes of TLR9 and genes on TLR9 signal transduction pathway on the mRNA level after thetreatment by unmethylated DNA, and methylated DNA isolated from HT29 cells on HT29cells. Toanalyse the expression of DNA methyltransferase expressionchanges before and after DNA treatment.

Materials and methods: Genomic DNA for the treatment was isolated from HT29 cells and partially consequtivelymethylated byNew England BiolabsCpGMethyltransferase (M.SssI). Subsequently, $0.5x10^6$ HT29 cells were treated with 15μg of DNA in 2 ml RPMI 1640 without BSA for6 hours. The cells were harvested and total RNA was isolated both before and after DNA treatment using QiagenRNeasy Mini Kit. Expression levels of genes were examined by RT-PCR for IL-8, MYD88A, NFκB, TLR9 RP 11, TRAF6,Immunocytochemistry was performed for TLR9, DNA methyltransferases (DNMT1, DNMT3a, DNMT3b), proliferation and differentiation factors (CDX2, CK). At immunocytochemistry the cells from DNA treated and untreated samples were divided into 4 groups (strongly positive, meanly positive, weakly positive and negative).

Results: TLR RP 11 level was significantly increased after the treatment by non-methylated DNA, ($p < 0.05$). MYD88A, TRAF6, IRAK2 genes showed significant overexpression at the treatment by the non-methylated DNA ($p < 0.05$).Treatment by methylated DNA showed significant proinflammatory response mediated by high level of NFκB, IRAK2, IL-8 ($p < 0.05$).CK expression was significantly increased for DNA treatment(32,2%, 17,4%, 46,1%, 4,3%) as compared to the control(0,0%, 3,4%, 36,8%, 59,8%)($p <= 0,0001$).

DNA methylation activity could be induced by DNA treatmentas it was shown by DNMT3a IHC (0,0%, 0,0%, 17,5%, 82,5%) as compared tountreated control(0,0%,0,0%, 1,8%, 98,2%)($p <= 0,0001$).

Conclusions: Human DNA can react on paracrine way on cancer cells through TLR9 activation. DNA treatment resulted significant overexpression of CK and DNMT3a. The DNA treatment increased the differentation and the methyltransferase activity. The methylation rate of the released DNA is reflected in the cell's response. Released human DNA is not only a biomarker for cancer detection, but also biologically activemolecule in a local context.

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P/II
POSTER PRESENTATIONS

Chaipersons:
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Prof. Dr. Dóra Perczel-Forintos
Dr. Lajos Simon

P/II-1
STRESS AT WORK: PSYCHOSOCIAL RISK AND PROTECTIVE FACTORS AMONG EDUCATION AND HEALTHCARE PROFESSIONALS

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Objectives: We analysed workplace related psychosocial risk factors and protective factors in education and healthcare to investigate what are the similarities and the differences between the two professions.

Methods: We used the Hungarian version of the COPSOQ II Questionnaire, a scientifically validated tool, measuring 7 dimensions and 28 factors related to work stress. Factors are scored from 0-100, on certain factors higher values indicate higher risk, while on other factors higher values indicate lower risk, they are protective factors. A voluntary sample of 193 persons (education (Ed) N=75, healthcare (Hc) N=118) completed the on-line questionnaire. We used descriptive statistics and Independent Sample T-tests.

Results: We found significant differences between the two professions in the following factors: Quantitative demands, Work pace, Emotional demands, Social support from colleagues, Social community at work. The COPSOQ profiles shows Hc workers had higher values in Emotional demands (Hc=68 / Ed= 58) and Work pace (Hc=60 / Ed=51). Hc workers also experienced less Influence at work (Hc=39 / Ed= 45) and less Justice and respect (45/46), while they rated higher the Social community (Hc=75 / Ed=66) which is an important protective factor. There were no significant differences in Health outcome we found moderate to high values in both professions: Burnout (Ed= 52 / Hc= 48); Stress (Ed=43 / Hc=44), Sleeping troubles: (Ed=33 / Hc= 30).

Conclusions: These results show many similarities in psychosocial risk factors of the two professions, with significant differences in two dimensions: Demands and Collaboration and leadership. Despite experiencing higher levels of psychosocial stress, Health outcomes did not differ significantly. This might suggests that good social community at work as protective factor may compensate higher stress load.

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P/II-2
THE SURVEY OF PROTECTIVE ELEMENTS OF COMMUNITIES, THE ATTITUDE OF HUNGARIAN AND ITALIAN ADOLESCENTS TO RELIGION, RELIGIOUS COMMUNITIES

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Belonging to a community, religion, spirituality are such values and protective resources that are determining to the people's physical, social and mental health. The research of these protective factors in the light of values are extremely important in the case of adolescents, as the results are to be considered when forming the preventive activities.

Aims: In a Hungarian-Italian comparative survey the way adolescents approach religion is analysed and the fact of belonging to a community and their values.The aim is to know what values the youth consider important, how much religion and spirituality is important for them. What is the proportion of young people belonging to a religious community and also what is the importance of that in their values?

We also want to know that in a difficult situation, how much the resources of the survey are involved in decision-making/problem-solving.

What kind of solutions can we see that are typical to adolescents and are either protecting or endangering their health?

Methods and sample: We are making a comparative survey in Hungarian and Italian languages among students going to high schools in Budapest and in Rome. The students are 16-18 years old.

The questionnaire is given to students of grade 11 and 12, n=800. In the first part we are curious about the adolescents' values, the place of religion in this hierarchy. In the second part we want to know how they solve problems in a critical situation.

The poster shows the conception of the research and the results of the pilot-survey ending in March 2013 connected with the first part of the research.

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P/II-3
EMPATHIC RESPONSE TO OTHERS' PAIN IN BORDERLINE PERSONALITY DISORDER: STRESSING THE IMPORTANCE OF MULTICOMPONENTIAL ANALYSIS

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Introduction: Results concerning empathic abilities in Borderline Personality Disorder (BPD) are so far contradictory. One explanation for this might lie in the dissociation between the various components constituting the capacity. Studies acknowledging this multicomponentiality focus mainly on the ability to discriminate and infer others' mental states, with little attention being paid to the intrapersonal processes elicited by the observation of others' distress that can and should also be decomposed to understand the behavioral reactions.

Our study aimed to investigate 'empathic response' to others' pain in borderline patients and matched healthy controls, taking into account its multidimesional nature and the role of attentional focus in shaping the reaction.

Methods: We presented 23 female BPD patients and 23 healthy controls with 24 video-clips displaying either accidental injuries (18) or self-harm (6), once with an instruction aiming to facilitate the enmeshment of self-other boundaries (self-focus), once with one intending to help emotional detachment and focus on the other's experiences (other-focus). Ratings were asked for self-experienced pain, distress, bodily sensations, feelings of being overwhelmed by emotions and sympathy/empathic concern towards the other, after each video-clip.

Results: Patients reported more intense bodily sensations of pain in self-focus ($p < 0.001$) and experienced their emotions to be more manageable in other-focus ($p < 0.05$) compared to controls while viewing accidental injuries. Experience-level differences may have been masked by self-reported difficulties in identifying own emotions. Upon observing self-harm, patients gave more intense emotional reactions, with ratings being more elevated in self-focus (personal distress-$p < 0.001$, feelings of loss of control over emotions-$p < 0.001$, sympathy-$p = 0{,}06$; bodily sensations of pain-$p < 0.001$).

Conclusions: Results indicate enhanced emotional response to others' pain in BPD at a non-reflective, somatic level, in situations facilitating the enmeshment of self-other boundaries, that is, however, not present at the subjective level. Focusing on the other's experiences may help borderline patients' affect-regulation in interpersonal situations.

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P/II-4
FACILITATING THE IMPLEMENTATION OF MEDICATION RECONCILIATION

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Introduction: According to published literature medication errors impose a great risk to patients and worsen the quality of health care. To minimize patient harm in hospitals several approaches were suggested. For medication safety improvement medication reconciliation was proven to be an effective, transferable method. Hungarian expert panel discussions showed lack of knowledge on medication reconciliation.

Aim: Gaining a better understanding of the process of reconciling medicines. Mapping the driving and restraining forces of introducing medication reconciliation in foreign countries to support Hungarian implementation.

Methods: A search of the literature was conducted. A relevant search string was built using the PICO technique. 19 databases (including MEDLINE, CINAHL and PsychINFO) were searched using 7 different search engines. Grey literature was also scanned. Results were deduplicated. The relevance of the papers was rated on a four grade scale by two independent experts and the grades were multiplied. Articles reaching 8 or more points were selected for extraction. Additional relevant articles were added by hand search. Data was extracted based on a previously compiled extraction tool.

Results: Merging the redundant data 230 articles were scanned by the experts. Only one-third was selected for data extraction. Often mentioned implementation obstacles were: communication issues, disengagement of the leaders, unpredictable resources and competence problems. Recommendations mainly consisted of process redesign techniques, communication of cost-effectiveness data, special training and hiring extra staff. Designing an implementation toolkit was shown to have great impact.

Conclusion: For improvement of medication safety in Hungarian hospitals implementing medication reconciliation should be considered. Preparation of a concise and ready-to-use toolkit containing the results would facilitate change. For the toolkit to be extensive and feasible further research is planned.

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P/II-5
SOCIOCULTURAL ASPECTS OF EATING DISORDERS WITH SPECIAL FOCUS ON MEDIA USE TV – INTERNET – MAGAZINES

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Introduction: According to the bio-psycho-social model of eating disorders in the development of these disorders many contributing factors are participating. There is no single cause of eating disorders. The bio-psycho-social model suggests that complex interactions are between social, environmental, psychological, and biological factors (Sigman, 2003).

In western societies a great emphasis is placed on shape, weight and more generally on bodily appearance. The sociocultural factors manifest on different levels and influence body weight regulation indirectly. Media has utmost importance in shaping values and norms (Grabe et al., 2008; Túry & Pászthy, 2008).

Methods: In the study we implemented a single-occasion, cross sectional design. Self-administered instruments and demographic data are collected via single online assessment among Hungarian college and university students in Budapest. Instruments measure media use, eating disorder related symptomatology and related factors.

Hypothesises:

1. It is hypothesized that magazine reading (fashion/beauty & health/fitness/diet magazines), appearance related Internet content browsing and television watching has correlations with the drive for thinness and slim body internalization.

2. It is hypothesized that those who read more fashion/beauty & health/fitness/diet related magazines or browse more fashion/beauty and health/fitness/diet related internet content or watch such television programmes are more dissatisfied with their bodies and have lower self-esteem.

3. It is hypothesized that there are mediator factors (e.g.: social & appearance comparison, thin body internalization, drive for thinness) between media use and disordered eating behaviours.

Conclusion: The final results of the study would provide more insights in the nature of media use among Hungarian youth who might be at risk or already have/had eating disorders. Therefore we will be able to initiate a powerful Hungarian media literacy prevention program.

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P/II-6
MIDWIVES' ROLE IN CHANGING SMOKING PATTERNS AMONG WOMEN WHO SMOKE IN PREGNANCY

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Introduction: Smoking is associated with ill health for a woman and her baby during pregnancy and later on. What midwives believe on their role in helping people to quit, the level of their qualification in this matter, effectiveness of their efforts in case they interact with smokers is not clear. The aim of this study is to investigate all these points.

Methods: 203 midwives (mean age 41,6 +/- 10,2 years, average working experience 16,9 +/- 11,1 years) were recruited into the study in four counties of Hungary in 2012. A self administered questionnaire of 96 items partially based on some questionnaires published was used before they participated on a training on smoking cessation. Statistical analysis: SPSS v.14. (khi square test, Mann-whitney test, Spearmann correlation).

Results: Almost all (96%) midwife assesses smoking habits at first visit, 64% repeats it on following visits, 71% informs the pregrant women about short/long term consequences of smoking. These parameters were independent from length of consultation, place of residence and midwivfe's smoking status (current smoker 7%, ex-smoker 19%). There was significant difference concerning assessment of the partner's or others smoking habits (chi square (12)=29,87, p=0,003), which showed correlation with qualification (r:0,162, p: 0,023), preventing relapses (r:0,197, p:0,005) and offering help to quit (r:0,234, p: 0,001). 41% of subjects reported lack of knowledge of helping people to quit.

Conclusions: Midwives believe that helping people to quit is part of their job. There is a lack in the assessment of passive smoking circumstances and informing patients wich are probably linked to insufficient knowledge on cessation. Training on smoking cessation for midwives is needed.

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P/II-7
THE SITUATION OF CHILDREN RETURNED FROM THEIR ADOPTIVE FAMILY TO THE CHILDCARE SYSTEM

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My **purpose** is to learn about the situation of those children who had been adopted in early stages but, due to familial crisis, loss, serious educational difficulties or inaptitude of the parents, had to leave their adoptive families after the legal validation of the adoption. The study constitutes basic research; no similar survey has been conducted in Hungary to date. The research examines all affected minors nationwide.

Aims: I search for basic demographical data of the affected adopted children, their adoptive parents and want to learn about the main reasons behind the crisis in their cases. My long term goal is to work out those methods and means that are able to help the adoptive families effectively. There is no mandatory helping or monitoring system of the adoptive families in Hungary, and many adoptive families turn for help only when their situation is lost and irreversible, or they see the only solution in having the child removed from the family.

Results: There are only preliminary results by now. There are many factors on the side of the parents that can undermine the child's situation in the family: divorce, death of one of the parents, birth of biological children, serious financial problems of the family. There are some causes of disruption that cannot be predicted or prevented. However, there are other factors that can be influenced. By identifying shortcomings on the system level, I want to demonstrate that most cases could be prevented by adequate preparation or constant professional support.

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P/II-8
EXAMINING DYSKINESIA IN CHILDREN WITH ADHD

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Background. Attention-Deficit/Hyperactivity Disorder (ADHD) is one of the most prevalent child psychiatric disorder. Methylphenidate is one possible treatment of ADHD. Based on several studies methylphenidate is safe and effective. Among its adverse effects, dyskinesia is scarcely investigated. However, we indicated in our previous study that children with ADHD, who are under methylphenidate treatment, has a higher level of dyskinesia than healthy children.

Aims. The aim of our study is to investigate the impact of methylphenidate on dyskinesia in treatment-naïve children.

Method. The study takes place at the Vadaskert Child Psychiatry Hospital. We investigate three groups (aged 6-18 years): 1) healthy control children; 2) treatment-naïve children with ADHD 3) children with ADHD, who had received methylphenidate treatment before the study. The Mini International Neuropsychiatric Interview Kid is used for establish the diagnosis of ADHD, the Abnormal Involuntary Movements Scale is used for evaluate dyskinesia. The methylphenidate administration of the involved children is in accordance with the dose prescribed by their therapist.

Results. At this phase of the study the data collection is in progress: we completed the data collection of two groups: 1) healthy control children; 2) treatment-naïve children with ADHD; the data collection of the third group, 3) children/adolescents with ADHD, who received methylphenidate treatment before the study is in progess. According to the preliminary data, there is no significant difference in the overall rate of having dyskinesia between the healthy control children and the treatment-naïve children with ADHD (Chi-Square=0.553; df=1; p=0.457)

Discussion. We found no significant difference between the control and the treatment-naïve groups. The furter research focus on the question whether there is difference in the level of dyskinesia in the treatment-naïve group and the group of children with previous methylphenidate treatment. The results implicate major clinical importance.

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P/II-9
OBSTRUCTIVE SLEEP APNEA WITHOUT EXCESSIVE DAYTIME SLEEPINESS IN KIDNEY TRANSPLANT RECIPIENTS

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Introduction: Obstructive sleep apnea (OSA) increases cardiovascular risk, thus the timely diagnosis and effective therapy for OSA is important. The most characteristic daytime symptom of OSA is excessive daytime sleepiness. OSA is frequent in chronic kidney disease, suprisingly however, in kidney transplant recipients OSA may not be accompanied by daytime sleepiness according to our clinical experience.

Methods: 100 kidney transplant recipients were included in the study (57 males, 43 females, mean age 51±13 years, BMI 27±5 kg/m^2, GFR 52±19ml/min). OSA was diagnosed by one night polysomnography (PSG); OSA severity was defined by the apnea-hypopnea index (AHI). Daytime sleepiness was measured by the Epworth Sleepiness Scale (ESS). Statistical analysis was performed by STATA 12.0 software.

Results: OSA was present in 43% of patients, mild (5<=AHI<15): 18%, moderate (15<=AHI<30): 11%, severe (AHI>=30): 14%. There was a strong, negative correlation between AHI and the average oxigen saturation during sleep (r=-0.585; p<0.001). BMI was positively correlated with AHI (r=0.452; p<0.001), so were abdominal and neck circumference. AHI was also positively correlated with hemoglobin level (r=0.240; p=0.016). Suprisingly AHI showed a weak negative correlation with ESS (r=-0.218; p=0.029). The median ESS scores were: 5 (5) in non-OSAS, 4 (5) in mild, 4 (5) in moderate and 4.5 (7) in severe OSAS subgroups. In multivariable linear model the correlation of AHI and ESS was not significant after correction for gender, age, kidney function and BMI. BMI remained an independent predictor of ESS in the multivariable model (β:-0.263; p=0.024).

Conclusion: Among kidney transplant recipients excessive daytime sleepiness is not associated with OSA. Additionally as BMI increases, which is a known risk factor for OSA, the subjective sleepiness decreases. Our results highlight the fact that in kidney transplant recipients PSG should be performed if OSA is suspected even if there is a lack of daytime sleepiness.

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P/II-10
SOCIO- DEMOGRAPHIC CHARACTERISTICS OF RELIGIOUS COMMUNITIES

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Introduction: The lack of communities, a long lasting deficiency of advanced societies has been dealt with by several scientists during the last decades. The decreasing tendency for community, as a result of the strenghtening of individualization and the weakening of cohesive ties between social groups prevent the sustenance of social cohesion and is ultimatly an obstacle in the development of trust. The role of small religious communities as the subject of the present reseach is significant not only as a mean of re-creating religious communities, but also as a value integrating process of society.

Aims: The goal of this investigation was to determine the socio- demographic characteristics of the examined communities, with regard to educational level and social status in particular.

Method: Sampling took place in one of the main Eastern Hungarian cities, in a multiconfessional area. Seven communities from the Roman and Greek Catholic, the Calvinist and the Baptist churches were involved. These groups have been chosen by random sampling. For data collection a survey of 61 variables has been edited. In this presentation we have applied cluster analysis.

Result: The outcomes confirmed that though religious communities cannot be considered homogeneous, a dominance of those with higher education and higher social status can be determined. Thus our earlier hypothesis that the improvement of objective living conditions is bringing forward the aim for assosiations seems to be confirmed. Analyzing the age factors we can state that the highest proportion is that of the youngest and the eldest groups and in case of other cohorts a lower level of activity can be determined. This might be explained by stage of life effect.

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P/II-11
GENDER DIFFERENCES IN SLEEP EEG CORRELATES OF SUPERIOR IQ

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Introduction: Sleep EEG spectra are individual characteristics with a strong hereditability and biological foundation, therefore they may be connected to IQ. It is unclear if superior IQ compared to normal is related to similar biological differences as low IQ to average. Alternatively, studies found gender differences in wakefulness EEG correlates of high IQ.

Methods: Sleep EEG spectra were calculated from 17 Hungarian Mensa members and 17 controls. Power spectraof REM and NREM sleep were compared binwise. both between the two groups as awhole and group members of each gender.

Results: Gender-independent differences between the two groups are modest in both REM and NREM sleep. In Mensa females NREM alpha and REM beta powers are significantly increased. Mensa males show significantly increased REM theta activity around 6 Hz, and a tendency of higher NREM theta and sigma activity.

Discussion: Superior IQ does not appear to have a general effect on sleep EEG, but differences appear in gender-separated comparisons. Location of higher activity in Mensa males corresponds to frequencies usually connected to higher learning and memory performance. There is less clarity about the observed high alpha and beta activity in Mensa females, which is usually a sign of sleep disturbances.

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P/II-12
THE ROLE OF SOCIAL SUPPORT IN PATIENTS WITH MALIGNANT MELANOMA TREATED WITH ADJUVANT LOW-DOSE INTERFERON – 1 YEAR FOLLOW-UP

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Objectives: Cancer has severe psychosocial impact involving not only the patients, but their relatives and caregivers, as well. Psychosocial support is necessitated by the ever increasing incidence of melanoma, well demonstrated by the annual 400 new cases diagnosed in the National Institute of Oncology (Budapest).

According to chronic stress-related mechanisms and other neurobiological aspects, the deeper psychological contents, like coping mechanisms, general psychological preparedness, social support, etc. may have an influence on tumor progression.

Methods: In a longitudinal study with tumor-free, high risk melanoma patients treated with adjuvant interferon the possible relationship between the psychological constructs and the primary tumor characteristics and the progression rate was examined.

Results: In our sample (N= 49) increased level of distress (Beck Depression Inventory and State Trait Anxiety Inventory) were found. The extent of social support and the thickness of primary tumor (Breslow-scale) showed significant negative correlation ($p < 0,05$), just like the trait-anxiety and the thickness ($p < 0,05$). We also found significant negative correlation between social support and illness intrusiveness, and the level of anxiety ($p < 0,05$). There were significant ($t = 2,789$, $p < 0,01$) differences in the anxiety patterns of men and women, but in other psychological constructs no differences were found.

Conclusion: Treatment may result in longer symptom-free survival providing better quality of life. Social support may be an important field of psychological intervention. Exploration of the possible role of psychosocial preparedness requires further long term research.

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P/III
POSTER PRESENTATIONS

Chairpersons:
Prof. Dr. Romána Zelkó
Dr. István Antal

P/III-1
ANTHRAQUINONE COMPONENTS OF *RUBIA TINCTORUM* AS CANDIDATE ANTICANCER AGENTS FOR DRUG TARGETING

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The drug delivery systems bearing synthetic anthraquinone derivatives (e.g. doxorubicin) have been already used in tumor therapy to diminish the toxic side effects of the conjugated drugs. The alizarin and purpurin – the 1-hydroxyanthraquinone compounds of *Rubia tinctorium* – were reported to have antitumor effect without any genotoxic properties.

Our objectives were to study the (i) antiproliferative/cytotoxic activity, (ii) the cell adhesion modulator effects of alizarin and pupurin as well as an extract of *Rubia tinctorum* and (iii) to analytically characterize this extract in order to find an ideal anthraquinone for design drug delivery systems.

The *Rubia tinctorum* hairy root culture was extracted with distillated water for 24 h. The identification of compounds in the extract was achieved by HPLC and ESI-MS. The cytotoxicity was evaluated by MTT-assay after 24, 48, 72 h of incubation with 10^{-8}-10^{-5} M anthraquinones in two melanoma cell lines (A2058, HT-168/M1) with different metastatic character. The effect of the anthraquinones on cell adhesion was measured by impedimetry (xCELLigence SP).

According to our results the concentration dependent cytotoxic effects of purpurin was more significant in the less invasive A2058 than in HT-168/M1 cells. On the contrary, the alizarin elicited a proliferation inducer activity in both model cells. Regarding the cell adhesion the purpurin had a positive effect in A2058 cells at 10^{-5} M, while the adhesion of HT-168/M1 cells was decreased at 10^{-7} M. The extract proved to be more cytotoxic than the pure compounds in equimolar concentrations, but failed to affect the melanoma cell adhesion. In the extract, the munjistin was identified as the main component.

In summary, the effective inhibitory activity of anthraquinones of *Rubia tinctorum* towards melanoma cells, and the presence of moiety suitable for conjugation in the compounds (e.g. munjistin) of the extract suggested their application in drug targeting model experiments.

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P/III-2
SOLUBILITY IMPROVEMENT OF APIGENIN

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Flavonoids are polyphenolic compounds that occur ubiquitously in plant foods. Flavonols and flavones are subclasses of flavonoids, may play a prominent role in cancer prevention. Apigenin is a 4',5,7-trihydroxyflavone which can be found in parsley *(Petroselinum crispum L.*) in high quantities. It has been stated that apigenin posesses free radical scavenging, antiinflammatory and anticancer activities. The bioavailability of flavonoids has been shown to be influenced by their chemical form in foods, the food matrix and the consumer's microbial flora. Apigenin belongs to the BCS (Biopharmaceutical Classification System) II group which means high permeability but low solubility.

Aims: The objectives of this study were to enhance the solubility of apigenin and to improve the extraction efficiency from parsley leaves. We applied different types of cyclodextrins to obtain the most appropriate complex. The parameters of the complex formations were evaluated. As pharmaceutical carrier system multiparticulates were used in fluid-bed. The critical parameters of the fluidization were determined. The appearance of pellets were analyzed by stereomicroscopy and image analysis. The apigenin containing pellets were filled into hard gelatine capsules for better dosing and their drug release was tested.

Results: The solubility of apigenin was improved significantly in the presence of cyclodextrins in the rank order of HP-β-CD > Y-CD > β-CD > α- CD. The extraction efficiency from parsley leaves can be enchanced by cyclodextrins as well. Furthermore we developed a carrier system for this flavonoid. The physical characteristics of pellets as well as the drug release from hard gelatine capsules were adequate.

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P/III-3
SOMATIC ONCOGENE MUTATIONS IN FINE-NEEDLE ASPIRATION BIOPSY FROM THYROID COLD NODULES

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Cold nodules are quite frequently detected on thyroid scans. Five-ten % of originally benign nodules will become malignant with time. Our aim was to examine somatic genetic alterations related to differentiated thyroid cancers in fine-needle aspiration (FNA) samples. These alterations included single nucleotide polymorphisms (SNP) (BRAF, HRAS, NRAS, KRAS) and genetic translocations (RET/PTC1, RET/PTC3, PAX8ex7/PPARgamma, PAX8ex9/PPARgamma) as well. SNPs were tested using real-time PCR with fluorescence melting curve analysis and rearrangements were detected by Taqman probe-based quantitative real-time PCR method. Alltogether, 792 FNA samples were collected and patients have been followed up – at present – 2 years.

Having reached the 2nd year of follow-up, we analyzed 250 consecutive FNA samples. We found 14 different genetic alterations (4 BRAF, 1 NRAS, 7 HRAS, 1 KRAS mutations and 1 RET/PTC3 rearrangement). During the 2 years, we have identified 13 patients with papillary cancer. Out of these 13, genetic alteration was seen in 5 (4 BRAF mutations and 1 RET/PTC3 rearrangement). In 9 cases carrying mutations, no sign of malignancy could be observed at present. The sensitivity of the gene set used by us is 96.2% for differentiated thyroid cancers. No PAX8/PPARgamma rearrangement was demonstrated in the 250 samples. These data are not in complete accordance with published information. This fact might be due to several factors including the differences in iodine supply in different geographical areas. Cytological examination completed with genetic data may support the more accurate diagnosis of thyroid malignancies.

Keywords: thyroid cancer, fine-needle aspiration, RAS, BRAF, RET/PTC, PAX8/PPARgamma

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P/III-4
RHEOLOGICAL CHARACTERIZATION OF HYDROCOLLOID GELS IN FORMULATION DEVELOPMENT

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Coherent gelling polymers gain more and more significant role in pharmaceutical and cosmetical industry as carrier systems. There is a huge progress in development and research of gels, especially seeking proper connection between physical properties and structure how they influence release. Absorbing and keeping great amount of liquid is typical attribute of gels. Their volume can be materially biased by changing environmental factors as well as combining the excipients. Connection can be seen between the formulation and rheological properties which allows also the modulation of drug release.

Aims: The aim of the investigation was to characterize the rheological behaviour of hydrocolloid-type gels (e.g. chitosan, Carbopol® 934) at different pH environment and in the presence of electrolytes or other ingredients (e.g. mannitol).

Methods: The influence of several physichochemical factors (pH, temperature etc.) and applied electrolite intermediates (buffer, ions) were studied on the gelling process and structure of gels. Thixotropy, flow curve, yield stress, temperature dependence and viscoelastic modulus were tested by Kinexus (Malvern Instruments Ltd.) rheoviscometer to characterize the rheological behaviour of gels.

Results: Carbopol® was found to be more thixotropic than chitosan at the studied conditions. Chitosan seems to be more advantegous over Carbopol® considering the viscoelastic behavior.

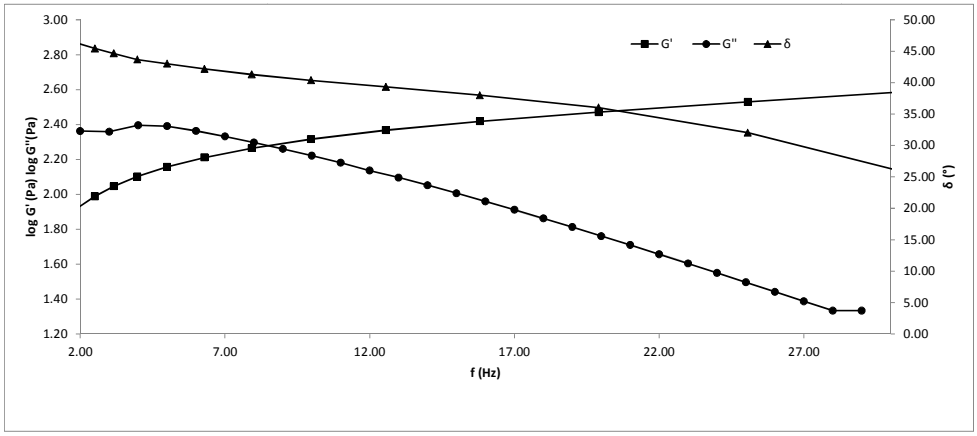

Figure 1. - Viscoelastic behaviour of chitosan

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P/III-5
THE EFFECTS OF ANGIOTENSIN II ON THE NMDA-TYPE GLUTAMATE RECEPTORS OF THE PYRAMIDAL CELLS IN THE PREFRONTAL CORTEX (PFC)

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PFC and its pyramidal cells have an important role in learning and behavior. Angiotensin II (AT) influenced learning and memory in behavioral tests. Our aim was to study the effects of AT on NMDA receptors of pyramidal cells in PFC with patch clamp.

Whole-cell voltage-clamp access was establishedin pyramidal cells of brain slices prepared from 10-11 days old rats. The cells were perfused with artificial cerebrospinal fluid (ACSF) (2,5-3ml). NMDA (30 μM) applied 3 times for 1.5 min with 10-min intervals between applications, induced inward currents (T1-3). Effects at T3 were presented as T3/T2. More than ±15% change at T3 compared to T2 was considered as an effect.For statistical analysis we used one-way ANOVA and Bonferroni correction ($p < 0,05$). AT was given 5 minutes before and during T3,AT1 receptor antagonist eprosartan (1μM) was in the ACSF all along.

0,3μM AT enhanced NMDA currents in a subpopulation of the cells, in the rest there were no effects. 1μM AT enhanced the currents in50% of the cells, inhibited them in 25%, in the rest it was ineffective. Eprosartan reversed the enhancement in both concentrations. 3μM AT either inhibited the currents or it was ineffective. Eprosartan did not influence these effects.

Thus AT has dual effect: 0,3-1μM AT enhances the currents in a subpopulation of the cells, which are reversed by eprosartan. These currents are probably AT1 receptor mediated. 1-3μM AT reduces the currents in another subpopulation, which are not influenced by eprosartan.

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P/III-6
THE DEVELOPMENT AND CHARACTERIZATION OF NOVEL KINASE INHIBITORS DESIGNED FOR TARGETED DELIVERY

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Introduction: Sunitinib is exceptional among the FDA approved kinase inhibitors. Although originally it was registered for the treatment of renal cell carcinoma and imatinib resistant gastrointestinal stromal tumor, it has been investigated in fibrosis and diabetes mellitus as well. The extensive applications are due to Sunitinib's multi kinase target profile.

Aim: Our goal was to develop new Sunitinib analogue kinase inhibitors, designed for peptide based drug delivery which can lead to organ specificity, and increased efficiency.

Methods: We have docked 100 virtual molecules into all available RCSB co-crystal structures (VEGFR2-PDB code: 4agd; c-Kit-PDP code: 3g0e; CDK2-PDB code: 3ti1; ITK-PDB code: 3miy; PHKG2-PDB code: 2yj7) containing Sunitinib, using YASARA Structure software.

We have validated our docking results *in vitro*, measuring the IC_{50} value of Sunitinib on VEGFR2.

To predict that the free drug would be able to penetrate through the membranes, we have calculated the logP values of the proposed compounds using the 3DNET4W program.

Based on the *in silico* screening results, we have selected and synthesized the most promising 20 molecules, bearing a carboxylic function, which offers the possibility of the conjugation of drug carriers via a peptide bond to obtain organ specific delivery.

We have synthesized the ester derivatives of the free drugs as well with the aim of testing the *in vitro* uptake, and to predict the effect of the free drugs. The purity of the compounds was determined using HPLC-MS and ^{1}H NMR techniques.

We have determined the IC_{50} values of our compounds on VEGFR2, using TranScreener ADP2 assay.

Results: The *in silico* calculations showed good correlation with the *in vitro* biochemical results. Based on the IC_{50} and LogP values we were able to select the best candidates for targeted delivery. Our future perspective is to test the ester derivatives *in vitro*. Furthermore, based on the *in vitro* results, select the best free drugs and bind them to peptide based delivery systems such as RGD peptides.

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P/III-7
ENANTIOSEPARATION OF ASPARTATE AND GLUTAMATE BY CE-LIF IN BRAIN TISSUE SAMPLES

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Glutamate and aspartate are the two major excitatory neurotransmitters in the CNS, playing central role in learning processes and memory formation. While the function of glutamate is widely investigated, the role of aspartate is less well understood. It is also known, that D-Aspartate occurs naturally in the CNS, and it is claimed to have an effect on the regulation of neurotransmission, neurogenesis and neuronal plasticity.

Due to its outstanding separation efficiency capillary electrophoresis is perfectly suitable for enantiomer separation. When coupled to laser induced fluorescence detector it also possesses an excellent sensitivity appropriate for the analysis of brain tissue samples.

In our work a capillary electrophoresis method has been elaborated in order to achieve chiral separation of fluorescently labeled aspartate and glutamate. Separation conditions have been optimized to achieve short analysis time using reverse polarity mode in coated capillary. To reach appropriate chiral and chemical selectivity a dual cyclodextrin system has been developed and validated. Its analytical performance has also been demonstrated by analyzing brain tissue samples. D-Asp concentration has been found to be in the range of 0.2-0.3 μM in the striatum of one day old domestic chickens. These results confirm that the elaborated method is appropriate to further study the role of D-Asp in the CNS.

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P/III-8
EFFECT OF VACUUM-ULTRAVIOLET (V-UV) PHOTOLYSIS TRANSFORMATION PRODUCTS OF DICLOFENAC ON THE PROLIFERATION AND MIGRATORY RESPONSES OF *TETRAHYMENA PYRIFORMIS*

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Advanced oxidation processes (AOPs) are promising water purifying techniques that may allow enhanced removal of pollutants (e.g. pharmaceuticals) resisting to conventional water treatment methods.

Diclofenac is the most frequently detected drug in water bodies, the removal of which is pretty low (20 – 40 %) at wastewater treatment plants (WWTPs). Diverse AOPs could degrade diclofenac efficiently; however, little is known about the ecotoxicity of the degradation products.

In the present study our aims *were* to i) describe the formation of degradation products of diclofenac (10^{-4}M in PBS) during the V-UV photolysis using different operating conditions (O_2 saturated or O_2 deprived milieu); ii) to characterize the effects of the photolysis samples taken at different times on the *proliferation* and *migratory responses* of the eukaryotic ciliate *Tetrahymena pyriformis*.

Our results showed that the same two major aromatic byproducts could be detected during photolysis in O_2 saturated and O_2 deprived milieu. However, the kinetics of degradation product formation was slightly different in the two cases. Biological effects of photolysis samples collected between 0 - 60 min of treatment were significant. Samples of the O_2 deprived condition had slight proliferation inhibiting effect (about 25%) in the later phase of the treatment (7.5 - 60 min) at 25 V/V%. O_2 saturated condition samples had similar impact regarding the intensity but only in case of samples of 5 - 30 min. Chemotactic response of Tetrahymena was also altered by the samples in wide concentration range (0.0001 – 1 V/V%); the elicited responses -if significant- were predominantly chemorepellent (Chtx. Ind. > 45%).

In summary diclofenac was degraded efficiently by V-UV photolysis though operating conditions impact the biological effects of treated samples. Bioassays such as *Tetrahymena* proliferation and migration assay are useful tools when assessing environmental impact of transformation products.

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P/III-9
PREPARATION AND CHARACTERIZATION OF FORCESPUN POLYVINYLPYRROLIDONE-IODINE FIBER MAT FOR WOUND DRESSING

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In the course of our experiments poly(vinylpyrrolidone)/poly(vinylpyrrolidone-vinylacetate)/ iodine (PVP 25/PVP 64/iodine) fiber mat of different polymer ratios (1:0, 2:1, 1:1, 1:2, 0:1) and of 0.4-20 μm average fiber diameters were successfully prepared by high-speed rotary spinning technique.

Aims: To explore the relationship between the structure and the iodine binding capacity of different fiber composites. The obtained fiber mats were subjected to detailed physical-chemical and microbiological analysis. The thickness and the surface morphology of the fibers were characterized by Scanning Electron Microscopy (SEM) and Atomic Force Microscopy (AFM). Positron Annihilation Lifetime Spectroscopy (PALS) provided specific information about the free volume distribution and consequently the supramolecular structure of fibers, which were in close connection with the amount of released iodine. FT-IR spectroscopy was applied to confirm the real composite ratios. The iodine binding capacity of the fiber samples was determined by in vitro dissolution study and microbiological assay was carried out to test their effect on the bacterial growth. Prototypes suitable for wound dressing were prepared from samples of the best properties and antibacterial activity.

Results: The prepared PVP micro- and nanofiber mats demonstrated their ability to store and release drugs to wounds. The PALS results, both the o-Positronium (o-Ps) lifetime values and distributions, revealed the changes of the free volume of fibers as a function of their composition and the presence of iodine. The PALS enabled the tracking of the changes of the microstructure as a function of the fiber composition.

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P/IV
POSTER PRESENTATIONS

Chairman:
Prof. Dr. Gábor Bánhegyi

P/IV-1
THE ROLE OF GLUT10 IN THE ARTERIAL TORTUOSITY SYNDROME

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Arterial tortuosity syndrome (ATS, OMIM 208050) is a monogenic heritable connective tissue disorder characterized by elongation and generalized tortuosity of the major arteries, hyperextensible skin and joint laxity. ATS is caused by loss of function mutations in the gene encoding glucose transporter GLUT10 (SLC2A10).

Our hypothesis – which is based on the previous results of our laboratory – is that GLUT10 is an ascorbate transporter in the endoplasmic reticulum, and transports dehydroascorbate (the oxidized form of ascorbate) towards the lumen, where it acts as a cofactor for the hydroxylation of proline and lysine, a biochemical reaction crucial for collagen/elastin maturation/folding.

Upon the examination of subcellular localization of GLUT10 it was found that the expression of the protein is more relevant in the liver of species unable to synthesize ascorbate (human, guinea pig), than in rodents (mouse, rat). GLUT10 was mainly found in the microsomal fraction of the liver, which corresponds to the endoplasmic reticulum. Immunocytochemistry of human fibroblasts and smooth muscle cells also revealed a reticular localization of GLUT10 transporter.

The GLUT10-dependent dehydroascorbate transport was examined on plasmamembrane permeabilized cells derived from control and ATS patients, where the luminal uptake of the oxidant was stimulated. We found that patients with ATS syndrome showed negligible dehydroascorbate transport respect to control cells. The total collagen synthesis however was not decreased in fibroblast cells where we knocked down GLUT10 protein.

The work will be continued with the examination of hydroxylation state of collagen/elastin, and the distribution of intracellular ascorbate. The possibly results might clarify the pathomechanism of ATS.

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P/IV-2
DEVELOPMENT OF NEW MOLECULAR TOOLS TO MONITOR VARIOUS INOSITOL COMPOUNDS IN STIMULATED HUMAN HEK-293T FIBROBLASTS

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In recent years it became clear that phosphoinositides (PI) are not only structural lipids in membranes, but they also have important roles in several cellular functions ranging from mediating signalling cascades through regulation of ion channels to cell movements. Their levels in the plasma membrane, endomembranes and in the cytoplasm can influence these processes, thus measuring the level of PIs in living cells can help us to better understand their distinct functions.

Our aim was to develop a highly sensitive method which enables us to follow the dynamic change of these lipids in living cells. We performed bioluminescence resonance energy transfer (BRET) measurements between various luciferase-labeled PI-binding domains and a plasma membrane-targeted Venus in HEK-293T cells. To monitor the inositol lipid pools the following domains were used: the PH domain of PLCδ1 for PIP_2, the 2xPH domain of OSH2 for PI4P and the PH domain of BTK for PIP_3. To measure cytoplasmic IP_3 level a recently developed intramolecular BRET sensor, based on the ligand binding domain of the type-1 IP_3 receptor, was used.

As expected, stimulation of the cells expressing type-1 angiotensin receptor resulted in a transient response including the decrease of the plasma membrane PI4P and PIP_2 level, and increase of the cytoplasmic IP_3 concentration, but no change of the PIP_3 level. In contrast, more robust, sustained responses could be recorded if carbachol was applied to stimulate cells expressing M3 muscarinic acethylcholine receptors indicating that cells are able to synthetize huge amount of PI4P and PIP_2. Stimulation of the cells expressing EGF receptor resulted in a sustained increase of the PIP_3 and a slowly developing IP_3 signal. Both PI4P and PIP_2 levels were decreased, but in contrast with Gq-activating hormones, decrease of the PI4P pool was continuous and significantly higher compared to the transient decrease of the PIP_2 level.

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P/IV-3
7H3 IS A NOVEL BURSAL STEM CELL ANTIGEN

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The avian embryo provides an excellent model system for studying the development of lympho-myeloid organs because it is amenable to in vivo experimental manipulation throughout embryogenesis. A further advantage of avian model is the B-cell development takes place in a separate organ, the bursa of Fabricius. As an effort to learn how lympho-myeloid cell diversification is regulated in the birds we have produced a large panel of monoclonal antibodies (mAbs) by immunizing mice with cell suspension of spleen and bursa of Fabricius of guinea fowl (Numida melegaris).

One of these mAbs (clone: 7H3) was found to recognize a cell surface antigen (molecular weight: ~ 70 kDa) expressed by CD45+ hematopoietic cells in the early embryo. In bursa of Fabricius, spleen, and thymus from embryonic day 16, nearly all lymphoid progenitor cells carried the 7H3 antigen. By the end of the embryonic period, double immunolabeling proved that all B cells of embryonic bursa expressed the 7H3 antigen. However, after hatching the 7H3 expression in both the cortex and medulla of the follicles gradually diminished, and it was lost, except a subpopulation of cortical B cells and CD3+ T cells. Other cells of lympho-myeloid origin, macrophages, dendritic cells, granulocytes did not react with 7H3 mAb.

According to previous cell transplantation experiments, the postnatal bursa of Fabricius may contain an undifferentiated B cell population (called bursal stem cells) which regenerates the bursal follicles after B cell depletion. On the base of the embryonic expression of the 7H3 antigen we hypothesized that our mAb could be a candidate marker for these bursal stem cells. To examine the ontogeny of 7H3+ cells during bursal regeneration we induced B cell depletion in 10 week old birds with cyclophosphamide (Cy) treatment. Three days CY treatment caused virtual absence of bursal lymphoid cells and later, destruction of the normal bursal architecture. Two weeks after treatment, bursal recovery starts by infiltration of 7H3+ cells in the cortex and 15 days later followed the medulla.

Taken together, these data suggest that 7H3 mAb is a novel hematopoietic cell marker, which recognizes bursal stem cells of the adult bursa of Fabricius.

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P/IV-4
GENETIC RISK FACTORS OF ANTHRACYCLINE CARDIOTOXICITY – RELEVANT POLYMORPHISMS IDENTIFIED IN ENZYMES AND TRANSPORTERS OF ANTHRACYCLINE PHARMACOKINETICS

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Aims: The main dose limiting side-effect of anthracyclines is late cardiotoxicity. Survivors of anticancer therapy have increased risk for cardiovascular problems and have higher such mortality. Subclinical changes may become crucial in case of later accompanying diseases affecting the cardiovascular system, or these changes can precede severe late onset cardiac failure. Identifying patients with altered tolerance to anthracyclines would provide great clinical benefit.

Methods: We studied 164 paediatric acute lymphoblastic leukaemia (ALL) patients who had been treated with ALL BFM protocols. They had cardiac ultrasound scans with a mean follow up of 6.4 years after anthracycline therapy. Left ventricular function was assessed as fractional shortening (LVSF). Germline genotypes of 19 single nucleotide polymorphisms (SNPs) in the *ABCC1*, *CBR1*, *CBR3* and *AKR1A1* genes were measured. Logistic regression analyses were performed to test for associations.

Results: Patients with *ABCC1* rs246221CT/TT genotype had lower LVFS at the time of the latest echocardiography compared to CC patients (38.4% and 40.7% respectively, $p=0.027$). Those with *AKR1A1* rs2088102CC genotype had lower LVFS than those harbouring at least one T allele (36.9% and 39.1% respectively, $p=0.013$). Further SNPs showed no association with left ventricular function.

Conclusion: Our results suggest that the *ABCC1* rs246221 and the *AKR1A1* rs2088102 variations are associated with altered left ventricular function in late survivors of childhood acute lymphoblastic leukaemia. The identified early subclinical changes may contribute to a polygenic disorder that evolves over a longer time and manifests in congestive heart disease later.

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P/IV-5
YAP1 IN THE HIPPO PATHWAY INFLUENCES THE RISK OF ASTHMA

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Asthma is an inflammatory disorder of the lungs. The main aim of this study was to identify new asthma susceptibility genes within the Hippo pathway. The Hippo pathway is responsible for organ size control, and is an important pathway that mediates survival and apoptosis of immune cells that play a role in asthma.

The expression of seven genes in the Hippo pathway was studied on RNA isolated from induced sputum oftwentyasthmatics and twelvenon-asthmatics. TaqMan gene expression assays were used in order to find a new gene to play a role in asthma. Furthermore, six, single nucleotide polymorphisms (SNPs) in the promoter region of *YAP1* were genotyped on 110 asthmatics and 123 controls using KASPar genotyping, in order to find a susceptibility allele within this gene.

As a result, *YAP1* gene expression levels were found to be significantly different between the two groups studied ($p=0.044$), hence indicating *YAP1* as a novel gene in the Hippo pathway to play a role in asthma susceptibility. Additionally, correlation studies showed a significant positive correlation between *YAP1* mRNA level and sputum macrophage percentages ($p=0.034$), which confirms that *YAP1* gene expression increases in asthmatic progress, as well as the macrophage count increasing, leading to inflammation of the lungs in asthma. Additionally, *YAP1* mRNA level also showed significant differences between the control, the mild asthmatic and the moderate to severe asthmatic groups ($p=0.035$). On the other hand, there were no significant differences in *YAP1* SNP genotype counts between cases and controls.

To conclude, in this study a new gene was identified within the Hippo pathway that may play a role in asthma contributing to the existing knowledge on the pathogenesis of asthma.

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P/IV-6
DEVELOPMENTAL MAPPING OF CD45+ CELLS IN EARLY AVIAN EMBRYO

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Almost every organ contains stellate-shaped cells expressing CD45 hematopoietic marker and MHC class II antigen. The embryonic origin of these cells, how they colonize a given organ primordium, and their tissue distribution and phenotype are virtually unknown. The avian embryo is well suited for studying the origin, differentiation and tissue specific colonization of hematopoietic cells. The accessibility of the embryo allows manipulations not feasible in mammalian systems.

The aim of our study was to determine the embryonic origin of the chicken CD45+ cells in the different embryonic tissue and their differentiation in loco. In the chicken embryo the first CD45+ cells emerge in the blood island of the yolk sac at 48 hours of incubation, which is followed by their accumulation in the intra-aortic cells clusters about 12-16 hours later. The circulating CD45+ cells are round or ovoid shaped, but in the mesenchyme scattered, stellate-shaped, CD4+ cells also occur. By 120 hours of incubation stellate-shaped CD45 positive cells colonized all organ rudiments, even they appear in the mesenchyme of the limb buds. The round-shaped CD45+ cells are concentrated around the aorta and in the splanchnic mesenchyme, and form a "sheath" around the splanchnic arteries. In the mesenchyme, the CD45 hemopoietic cells co-express MHC class II antigen, which makes them capable for antigen presentation.

To study whether the CD45+ stellate-shaped cells of the avian embryo can be considered a different subpopulation of the circulating CD45+ cells, or instead they have common stem cells originating from the extraembryonic blood islands, yolk-sacs without embryos were cultured in the egg for additional 48 hours and the dissected embryos were cultured in vitro in three-dimensional collagen gel matrix. In the case of cultured yolk sacs, large number of CD45+ stellate cells differentiated, while in the explanted embryos only CD45+ cells with round-morphology developed.

It is concluded that the hemopoietic stem cells for the stellate CD45+ cell series originate from some source other than the intraembryonic round CD45+ cells, and that this source must be extraembryonic, namely the yolk-sac blood island. On the base of the embryonic expression of the CD45 antigen we hypothesize, that yolk-sac derived CD45+ stellate precursor cells actively migrates through the embryonic mesenchyme, and colonizes each organ primordia to differentiate into CD45 and MHC class II double positive stellate cells.

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P/IV-7
GRAFTED NEUROCTODERMAL STEM CELLS RESCUE DAMAGED RAT RETINAL GALNGLION CELLS OTHERWISE DESTINATED TO DIE

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Purpose: Gradual deterioration of vision and progressive retinal ganglion cell loss are the fatal features of glaucoma in human. Our aim was (a) to determine the progressive retinal ganglion cell layer (GCL) loss in an experimental rat glaucoma model and (b) to investigate the neuroprotective effect of intravitreally grafted immortalized murine neuroectodermal stem cells.

Methods: All together 20 (100-150 g, 8-10 w/o) female Sprague-Dawley rats were used. The majority of episcleral veins and the perilimbal venous plexus were thermocoagulated except a 40-50° segment at the nasal limbus. The right eye was left untreated (intact eyes). Rats that developed corneal or refractive media opacity or severe inflammation were excluded. Transplanted rats (n=5) received neuroectodermal stem cell grafts (500.000 cells/2-3 μm/eye) intravitreally 3 weeks after injury and were allowed to survive for further 6 weeks. Control animals received no graft after the injury and survived for 3, 6 and 9 weeks respectively (n=5 in each group). Intra ocular pressure (IOP) was measured before and after treatment, and then twice a week until the end of the survival period. The operated and intact eyes of all animals were removed at the end of the survival period and the numbers of retinal ganglion cells and optic nerve axons were determined. The locations of the stem cell derivatives were mapped and their phenotype was immunohistochemically characterized.

Results: IOP significantly elevated after injury but returned to normal levels by 6 weeks after the ocular damage. The number of ganglion cell showed a gradual decrease: 3 weeks: 80.4 % ± 3.1 %; 6 weeks: 75.2 % ± 2 % and 9 weeks: 62.8 % ± 0.6 %. In the transplanted group of animals grafted with stem cells prevent cell death by approximately 50% (surviving ganglion cells: 83.4 %). This finding was confirmed by the number of remaining myelinated axons in the optic nerve: 62.1 % ± 0.8 % in the 9 week control group vs. 80.9 % ± 4.6 % in the transplanted group. (All values are mean ± SEM)

Conclusion: Our results suggest that, grafted neuroectodermal stem cells rescue retinal ganglion cells destinated to die due to glaucoma-like injury.

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P/IV-8
GLYCOGEN DISTRIBUTION IN A HYPERMUSCULAR MOUSE MODEL

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Signaling pathways playing role in the determination of organ size are poorly understood. The TGF-beta member myostatin is the main negative regulator of skeletal muscle mass and it has systemic metabolic effects (e.g. involving adipose tissue) as well. The *Compact* mice carry a naturally occurring 12-bp deletion in the propeptide region of the myostatin precursor, and additional modifiers are involved in determining the full expression of the hypermuscular phenotype.

Aims: Morphological and morphometrical analysis of the *Compact* mice, focusing on the glycogen content and distribution of m. tibialis anterior (TA) and liver samples.

Materials and methods: Frozen sections were stained by PAS to visualize glycogen and immunohistochemistry to detect the different muscle fiber types, respectively. Fiber type specific glycogen content was analyzed densitometrically on serial sections. The total glycogen content of TA and liver samples was measured by spectrophotometry.

Results: The absolute weight of TA and liver significantly increased in *Compact* animals compared to wild type; however, the liver weight normalized to body weight significantly decreased. The whole glycogen content significantly increased either in TA (43.6 ± 2.4 vs. $28.7 \pm 0.7681 * 10^{-2}$ mg, $p < 0.01$) or liver (103 ± 9.6 vs. 19.1 ± 4.9 mg, $p < 0.0001$) of *Compacts*. The *Compact* mutation had no effect on the glycogen content of the different fiber types. Among the fast fibers, the type IIB fibers contained the most glycogen in both *Compacts* and wild type animals. The average glycogen concentration in the TA samples of *Compacts* was significantly lower (3.72 ± 0.23 vs. 5.52 ± 0.24 mg/g, $p < 0.01$); however, in case of the liver it increased significantly (52.06 ± 3.8 vs. 14.45 ± 3.1 mg/g, $p < 0.0001$).

Conclusion: The *Compact* mutation has opposite effect on the relative weight and glycogen concentration of skeletal muscle and liver. The decreased glycogen concentration of *Compact* muscle can play a role in the lack of proportionate muscle force increase observed previously.

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P/IV-9
THE *COMPACT* MUTATION OF MYOSTATIN CAUSES A GLYCOLYTIC CHANGE IN THE PHENOTYPE OF SKELETAL MUSCLES

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Myostatin is an important negative regulator of skeletal muscle growth. *Compact (Cmpt)* mice, similar to the myostatin knock out animals, are characterized by hypermuscularity. The *Cmpt* mutation comprises a 12-bp deletion in the propeptide region of myostatin, however, modifier genes are also involved in the full penetration of the phenotype. Previously, we demonstrated that in contrast to myostatin knock out mice, hypermuscularity of *Cmpt* mice was caused exclusively by fiber hyperplasia without any hypertrophy.

Aims: To analyze the possible effects of the *Cmpt* mutation on the fiber type composition (i.e. the ratio of slow oxidative I, fast oxidative IIA, fast glycolytic-oxidative IIX and fast glycolytic IIB fibers), immunostaining of the different Myosin Heavy Chain (MHC) isoforms was carried out in the tibialis anterior (TA) muscles of ten-week old male *Cmpt* and wild type (BALB/c) mice. Moreover, transcript levels of MHC isoforms was investigated by isolating total RNA from the contralateral TA muscles followed by qRT-PCR analysis using Hprt (hypoxantine guanine phosphoribosyl transferase) as an internal control.

Results: Immunohistochemical analysis revealed a significant increase in the number of the glycolytic IIB fibers (80,3%±3,3 vs. 50,3%±3,3, mean±SEM) and a significant decrease in the number of the more oxidative IIX and IIA fibers (IIX: 19%±3,2 vs. 46,4%±2,6, IIA: 0,65%±0,05 vs. 3,3%±0,09) in *Cmpt* mice showing a glycolytic shift in the muscle phenotype compared to the wild type. Similarly, MHCIIB mRNA levels were significantly increased, while MHCIIX and IIA transcript levels significantly decreased in *Cmpt* animals compared to BALB/c ones. These results suggest that the glycolytic shift in TA muscle is primarily regulated at the level of MHC transcription.

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P/IV-10
ASIAN-SPECIFIC MITOCHONDRIAL GENOM POLYMORPHISM (9 BP DELETION) IN THE HUNGARIAN POPULATION

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Objectives: Severalpolymorphismsin the mitochondrial genome have population-genetically and anthropologically interest. The 9 bp deletion is anthropological marker for people of East-Asian origin.

Methods: Themitochondrial A8344G mutation was investigated by PCR-RFLP, performed on DNA samples isolated from blood and postmitotic muscle biopsy specimens. The mitochondrial COII/tRNS^{Lys} and hypervariable regions were sequenced bidirectionally.

Results: From 890 patients we found 13 cases with 9 bp deletion (CCCCCTCTA) in the mitochondrial hipervariable non-coding region. Among them in 11 cases the 9 bp deletion was present with homoplasmic C8270T substitution. Their coexistence determines the M haplogroup. In one family (3 patients) beside these alterations we found a new heteroplasmic A8332G mutation in the tRNA^{Lys} gene, wich was absent in 150 normal controls.

Conclusion: M haplogroup is in European populations very rare. It is mainly present in Asia, America and Australia, because of the human migration directions, these populations migrated eastwards. The frequency of 9 bp deletion in the Hungarian population is 1,5%. This polymorphism can be explained by the Westward migration of Hungarians from Siberia (in the matriarchal lineage). The deletion induce instability of this mitochondrial DNA-region like enough, and provoke the conformation other pathogen mutations.

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P/IV-11
META-ANALYSIS OF BIOMARKER CANDIDATES PREDICTING SURVIVAL AFTER TAMOXIFEN TREATMENT

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Background: To date, three molecular markers (ER, PR and CYP2D6) have been used in clinical settings to predict the benefit of the anti-estrogen tamoxifen therapy. However, even ER, the most effective of these can only identify half of the patients responding to endocrine therapy. Our aim was to validate new biomarker candidates, that predict response to tamoxifen treatment, by evaluating the meta-analysis of available microarray datasets with known treatment and follow-up information.

Methods: Data sources: published biomarker candidates were identified in Pubmed (2007-2012) and in the 2010-2012 ASCO and SABCS abstracts. Breast cancer microarray datasets were downloaded from GEO and EGA. Study eligibility criteria, participants and interventions: from the biomarker candidates, only those identified or already validated in a clinical cohort were eligible. From the transcriptomic datasets relapse-free survival data of tamoxifen treated patients and overall survival data of endocrine treated patients were used. Synthesis methods: the raw microarray data was re-processed and integrated into two databases. Relapse free survival (RFS) up to 5 years was used as endpoint in a ROC analysis. In the EGA dataset, Kaplan-Meier analysis was performed for overall survival (OS).

Results: Altogether 60 biomarker candidates were identified. The transcriptomic datasets included 584 GEO-based and 1208 EGA-based microarrays. Among these, the best performing genes were: PGR (AUC=0.64, p=2.3E-07), MAPT (AUC=0.62, p=7.8E-05), SLC7A5 (AUC=0.62, p=9.2E-05) and TP53 (AUC=0.60, p=1.2E-03). Further genes significantly correlated to relapse-free survival include BTG2, HOXB7, DRG1, CXCL10, BCL2, TPM4, IGF1R and SMC3. PGR (HR=0.67, p=1.7E-04), MAPT (HR=0.7, p=7.2E-04) and SLC7A5 (HR=1.6, p=1.6E-05) genes correlated significantly to overall survival as well.

Discussion: According to our meta-analysis two genes – MAPT and SLC7A5 – could be used as a predictor of Tamoxifen treatment efficacy in breast cancer patients.

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P/IV-12
IONIZING RADIATION INDUCED EFFECT OF GDF-15 AND TGFB1IN MAMMARY CARCINOMA CELLS

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It is well established, that nuclear also mitochondrial (mtDNA) damage occurs by elevated reactive oxygen species release after ionizing radiation. Delayed removal of this damaged mitochondria due mitophagy produces significant amount of free radicals leading up to a self-supporting constitutive oxidative stress in the cell. Our study is focused on the harmful influence of GDF-15 on the ionizing radiation caused mitochondrial DNA damage. The GDF-15 is a member of the TGFb family, its own receptor is recently unknown, supposed to act on the TGFb receptor. We want to demonstrate the hypothesis based on our previous study, that the GDF-15 is an anti-apoptotic element of a molecular network attenuating the mtDNA damage due inhibition of Tumor Growth Factor beta 1 (TGFb1).Human epidemiology studies verify the bad prognoses in gliomas,oral cell carcinoma (OSSC)and prostate cancerwith increased amount of GDF-15 in the serum, but the exact role of the gene is still unclear. Inducing apoptosis by inhibition of GDF-15 is previously described in mammary carcinoma cells therefore the amount of this cytokine in the serum can indicate on the radiation resistance of the breast carcinomas.

In our recent work the radiation induced mitochondrial common deletion (CD), the expression of GDF-15 and TGFb1, the changes in TGF-b1 protein amount were measured.CD was quantified by real-time (RT-PCR) from total DNA. Expression changes of GDF-15 and TGFb1 were analyzed by RT-PCR. ELISA assay were investigated for TGFb1 protein examination.

We demonstrated an elevated expression of GDF-15 after 2 Gy exposure in all cell lines, which effect decreases to normal level after time, this results are consistence with the GDF-15 expression level in breast cancer patients after radiation therapy in our former study. An earlier activation of the TGFb1 gene was measured depending on the GDF-15 expression. After radiation a dose dependent accumulation of CD were observed, dependent on dose, and time.

Our data suggest that decreased level at GDF-15 activates earlier TGFb1 response, so we demonstrate an inhibition of TGFb through GDF-15.

In conclusion our datasuggest, that elevated level of GDF-15 in breast cancer indicates due inhibiting the mtDNA damage an effect of radiation resistanceby delaying the programmed cell death.

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P/IV-13
BIOMARKERS OF PLATINUM RESISTANCE IN OVARIAN CANCER

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Background: Ovarian cancer is the most lethal gynecological cancer. Besides surgery, taxol and platinum chemotherapy represent the primary treatment options. Platinum resistant cancer recurs in 25% of patients within six months. In our present study we aimed to identify biomarkers of platinum therapy response.

Methods: We set up a databank of publicly available ovarian microarray datasets containing treatment and response information. We searched GEO and TCGA to identify datasets suitable for the analysis of the effect of the genes on therapy response. We performed receiver operating characteristic (ROC) analysis for all genes and ranked them based on the area under the curve (AUC) values. We selected the eight most promising candidates for in vitro functional validation including JRK, CNOT8, RTF1, CCT3, NFAT2CIP, MAP2K1, FUBP1 and CSDE1. We preformed gene silencing with simultaneous 48 h carboplatin administration in four ovarian cancer cell lines (SKOV-3, CAOV-3, ES-2, and OVCAR-3). The efficacy of the silencing was validated by qRT-PCR. The change in the cell resistance was measured by MTT tests.

Results: We identified 1267 patients in 8 datasets meeting our criteria in GEO and TCGA. The average progression free survival is 24.8 months with 731 progressions. 1152 patients received a platinum-based chemotherapy. The ROC values of the selected genes were JRK (0.625), CNOT8 (0.610), RTF1 (0.620), CCT3 (0.620), NFAT2CIP (0.612), MAP2K1 (0.611), FUBP1 (0.608) and CSDE1 (0.605). The expression change of JRK ($p=0.0002$), MAP2K1 ($p=0.0117$) and CNOT8 ($p=0.0036$) were significantly correlated with progression free survival. JRK was not expressed in the cell lines. The silencing of RTF1, FUBP1, CSDE1, CNOT8 and MAP2K1 caused significant sensitization in each of the investigated cell lines (p values respectively: $4*10^{-8}$, $7*10^{-7}$, $3*10^{-9}$, $3*10^{-7}$, $7*10^{-6}$).

Discussion: We identified and in vitro validated five potential biomarkers correlated to platinum resistance in ovarian cancer.

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P/IV-14
INHIBITION OF AUTOPHAGIC CELL DEATH AND RADIOSENSITISATION WITH SILENCING OF TP53INP1 IN HUMAN FIBROBLAST CELLS

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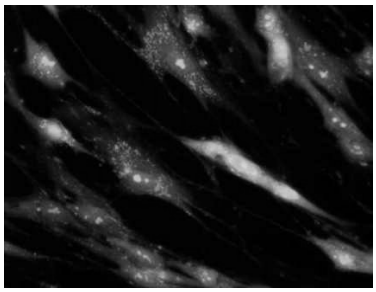
Tumor protein 53-induced nuclear protein-1 (TP53INP1) takes part in p53-mediated cell death and cell cycle arrest in response to stress, and its transcription is activated by p53. Overexpression of this gene promotes apoptosis and cell cycle arrest in many cases. Moreover, TP53INP1 interacts with p53 thus modifies the transcriptional activity of p53 on several other genes.

Aims: In present study we assess what radiation-induced cell responses the TP53INP1 take plays a role in.

The importance of TP53INP1 expression for radiation responses was investigated using F11hTERT (hTERT immortalized human fibroblasts) knockout for TP53INP1 with TP53INP1 shRNA. We examined the following areas in the modified cells related to normal fibroblast: cell cycle distribution (by flow cytometry), the autophagy and senescence (with Acridine Orange and SA-β-Gal), the expression of interested genes (by real-time PCR), and the kinetic of repair of double strand breaks by γH2AX staining. Irradiated fibroblast and bystander cells were compared for survival, by the colony-forming assay and amount of mitochondrial DNA deletion.

Results: We demonstrated that TP53INP1 deficient cells showed resistance of the G2-delay, and the proliferation rate was higher compared with the F11hTERTcells. Furthermore the lack of TP53INP1 gene function results in autophagy decline following irradiation, while it has not effect on the senescence. TP53INP1 enhances ionizing radiation induced elevation of CDKN1A and GDF-15. At DNA repair we found that in gene silenced cells the reparation was delayed. Bystander effect decrease was also observed with arrested TP53INP1. Finally, we show that TP53INP1 proficiency is important for clonogenic survival after radiation.



(*autophag vacuoles in human fibroblast)*

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P/IV-15
METABOLIC SYNDROME INFLUENCES CARDIAC GENE EXPRESSION PATTERN AT THE TRANSCRIPT LEVEL IN MALE ZDF RATS

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Aims: Metabolic syndrome is a prominent risk factor for cardiovascular morbidity and mortality, however, its effect on cardiac gene expression pattern is unclear. Therefore, we examined the possible alterations in cardiac gene expression pattern in 25 wk old male Zucker Diabetic Fatty (ZDF) rats, a model of metabolic syndrome.

Results: Fasting blood glucose, serum insulin, cholesterol and triglyceride levels were significantly increased, glucose tolerance and insulin sensitivity were impaired in ZDF rats compared to leans. At week 25, total RNA was isolated from the myocardium and assayed by rat oligonucleotide microarray for 14921 genes. Expression of selected genes was confirmed by qRT-PCR. As compared to lean controls, 36 genes showed significant up-regulation and 49 genes showed down-regulation. Genes with significantly altered expression in the heart due to metabolic syndrome includes functional clusters of metabolism, structural proteins, signal transduction, stress response, ion channels and receptors. Moreover some other genes with no definite functional clusters were also changed. The differentially expressed genes were submitted to DAVID bioinformatics system and database to perform gene ontology analysis which revealed several significantly enriched functional inter-relationships between genes influenced by metabolic syndrome.

Conclusion: Metabolic syndrome significantly alters cardiac gene expression profile which may be involved in the development of cardiac pathologies in the presence of metabolic syndrome.

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P/IV-16
PROSTAGLANDIN D2 RECEPTOR (PTGDR) GENE HYPERMETHYLATIONIN COLORECTAL ADENOMA-CARCINOMA SEQUENCE

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Background: Dysregulated gene expression can be caused by DNA methylation alterations, that can contribute to the formation of colorectal cancer (CRC). In the promoter region of prostaglandin D2 receptor (PTGDR) gene three CpG island can be predicted.

Aims: our aims were to analyse the DNA methylation status of the gene in colorectal cancer samples and to correlate these results with mRNA and protein expression levels.

Materials and methods: PTGDR gene was selected on the basis of whole genome expression data (Affymetrix HGU133 Plus 2.0 microarrays) from healthy colonic (n=49), colorectal adenoma (n=49) and left-sided CRC (n=49) biopsy samples and also from laser microdissected (LCM) epithelial and stromal cells from healthy (n=6) and CRC (n=6) samples. CpG island prediction was performed with EMBOSS CpG Plot. DNA methylation analysis was performed on macrodissected (n=10) and LCM (n=5) healthy colonic, adenomatous biopsy (n=10) and LCM (n=5), macrodissected (n=10) and LCM (n=5) left-sided colorectal cancer samples using bisulfite-sequencing PCR (BS-PCR) followed by pyrosequencing. Prostaglandin D2 receptor protein level was analyzed by immunohistochemistry.

Results: PTGDR gene showed decreasing expression ($p \leq 0{,}01$) in adenoma and carcinoma biopsy samples and its mRNA level was found to be significantly downregulated ($p \leq 0{,}01$) in the tumor epithelial cells, whereas no DNA methylation difference could be found in stromal cells of normal and tumor samples. Hypermethylation of the gene could be observed in 20 % (2/10) of adenoma biopsies and 50% (5/10) of macrodissected tumor samples. The pyrosequencing results of laser microdissected colonic epithelial cells confirmed increased methylation levels in tumor epithelial cells. The prostaglandin D2 receptor protein level was found to be lower in adenoma and tumor samples compared to healthy controls.

Conclusion: PTGDR was found to be hypermethylated in colorectal cancer samples predominantly in the epithelial cells that can result in reduced mRNA and protein levels during tumorigenesis.

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(LISTED UNDER THE CORRESPONDING DOCTORAL SCHOOLS)

BASIC MEDICINE DOCTORAL SCHOOL

E/III-5 FLUID OVERLOAD AND ADVERSE OUTCOMES FOLLOWING PEDIATRIC CARDIAC SURGERY
Daniel János Lex
Program: Physiology and clinics of the heart and coronary diseases

E/III-6 REDUCED NEURAL BAROREFLEX-SENSITIVITY IS RELATED TO ENHANCED ENDOTHELIAL FUNCTION IN PATIENTS WITH END-STAGE LIVER DISEASE
Domonkos Cseh, Alexandra Pintér, Tamás Horváth, Adrienn Sárközi, Zsuzsanna Gerlei, Márk Kollai
Program: The mechanisms of normal and pathologic funcions of the circulatory system

E/III-7 MEASUREMENT OF PLATELET SPREADING AND ADHESION ON HUMAN PLATELETS WITH IMPEDIMETRY
Lívia Polgár
Program: Physiology and clinics of the heart and coronary diseases

E/III-8 EFFECTS OF LEVOSIMENDAN-CATECHOLAMINE COMBINED TREATMENT ON HAEMODYNAMICS AND VENTRICULAR ARRYTHMIAS IN CANINE HEART FAILURE MODEL
Vivien Klaudia Nagy, Eszter M. Végh, Endre Zima, Tamás Bárány, Balázs Sax, Annamária Kosztin, Violetta Kékesi, Béla Merkely
Program: Physiology and clinics of the heart and coronary diseases

E/III-9 NT-PRO-BNP SERUM LEVEL IS AN INDEPENDENT PREDICTOR OF INTIMA-MEDIA THICKNESS OF THE COMMON CAROTID ARTERY IN ASYMPTOMATIC PATIENTS OF A PRIMARY PREVENTION STUDY
Loretta Kiss, Zsolt Bagyura, Réka Vadas, Pál Soós, Lívia Polgár, Béla Merkely, Zsolt Szelid
Program: Physiology and clinics of the heart and coronary diseases

E/III-10 FIBRINOLYTIC ACTIVITY OF HUMAN BONE MARROW MESENCHYMAL STEM CELLS
Kinga Lakatos, Edit Gara, Éva Szigetfű, Béla Merkely, Judit Skopál
Program: Physiology and clinics of the heart and coronary diseases

E/III-11 RED CELL DISTRIBUTION WIDTH IS ASSOCIATED WITH MORTALITY IN KIDNEY TRANSPLANT RECIPIENTS
Ujszászi Ákos
Program: Fluid and electrolyte balance in health yand diseased regulation of blood pressure and circulation

E/III-12 LEFT VENTRICULAR UNTWISTING IN ATHLETE'S HEART: KEY ROLE IN EARLY DIASTOLIC FILLING?
Attila Kovács
Program: Physiology and clinics of the heart and coronary diseases

E/III-13 COMPARATIVE INVESTIGATION OF DIABETIC CARDIOMYOPATHY IN RAT MODELS OF TYPE-1 AND TYPE-2 DIABETES MELLITUS
Csaba Mátyás, Attila Oláh, Balázs Németh, László Hidi, Ede Birtalan, Sevil Korkmaz, Gábor Szabó, Béla Merkely[1], Tamás Radovits[1]
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E/III-14 CARDIAC EFFECTS OF ACUTE EXHAUSTIVE EXERCISE IN A RAT MODEL
Attila Oláh, Csaba Mátyás, Balázs Németh, László Hidi, Ede Birtalan, Dalma Kellermayer, Mihály Ruppert, Béla Merkely, Tamás Radovits
Program: Physiology and clinics of the heart and coronary diseases

P/I-1 MULTIFRACTAL ANALYSIS OF NEAR-INFRARED SPECTROSCOPY (NIRS) SIGNALS RECORDED FROM THE HUMAN BRAIN CORTEX
Péter Mukli[1], Zoltán Nagy[1], Péter Herman[1,2], András Eke[1]
Program: The mechanisms of normal and pathologic functions of the circulatory system

P/I-2 SERUM APELIN AS A PREDICTOR OF RIGHT VENTRICULAR DYSFUNCTION
Annamária Kosztin, Gábor Széplaki, Vivien Klaudia Nagy, Gábor Földes, Astrid Apor, Csilla Liptai, Levente Molnár, Endre Zima, László Gellér, Béla Merkely
Program: Cardiovascular disorders: physiology and medicine of ischaemic circulatory diseases

P/I-3 MONITORING BRAIN HEMODYNAMICS AND OXYGENATION WITH NEAR-INFRARED SPECTROSCOPY (NIRS) DURING CARDIOPULMONARY BYPASS SURGERY
Zoltán Nagy[1], Péter Mukli[1], Endre Németh[2], István Portörő[1], Anita Daragó[1], Katalin Orbán[1], Kata Csibi[1], Klára Ronkay[2], Edina Wappler[2], János Gál[2], András Eke[1]
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CLINICAL MEDICINE DOCTORAL SCHOOL

E/I -1 COMPARISON OF TWO HINDLIMB ISCHEMIA-REPERFUSION MODELS: THE IMPORTANCE OF RESIDUAL PERFUSION
Olivér Rosero [1], Károly Németh [2], Zsolt Turóczi [1], Fülöp András [1], Dávid Garbaisz[1], András Szuák[2], Mátyás Kiss[2], Ágnes Nemeskéri[2], Attila Szijártó[1]
Program: Gastroenterology

E/I-2 NIM-811 – THERAPEUTIC POSSIBILITY FOR KIDNEY INJURY INDUCED BY LOWER LIMB VASCULAR OPERATION
Dávid Garbaisz[1], Zsolt Turóczi[1], András Fülöp[1], Olivér Rosero[1], Péter Ónody[1], Gábor Lotz[2], László Harsányi[1], Attila Szijártó[1]
Program: Clinical and experimental research in Angiology

E/I-3 CHANGES IN DYNAMIC BALANCING DURING THE FIRST SIX POSTOPERATIVE MONTHS USING DIFFERENT SURGICAL APPROACHES IN TOTAL HIP ARTHROPLASTHY
Gergely Holnapy, Rita M. Kiss
Program: Physiology and pathology of the musculoskeletal system

E/I-4 EFFICACY OF PRENATAL ULTRASONOGRAPHY IN DIAGNOSING UROGENITAL ANOMALIES IN NEWBORNS
Fanni Rebeka Erős, Artúr Beke, István Szabó, Barbara Pete, Éva Görbe
Program: Reproductive medicine

E/I-6 SPINE EXAMINATION OF PRIMARY SCHOOL CHILDREN WITH ZEBRIS ULTRASOUND-BASED MOTION ANALYSING SYSTEM
Mária Takács, Ervin Rudner, Rita M. Kiss
Program: Physiology and pathology of the musculoskeletal system

E/I-7 EFFECT OF PHOTO-ACOUSTIC STIMULATION PATTERNS ON SALIVA SECRETION
Anita Beck
Program: Dental research

E/I-8 RESULTS OF A NEW QUESTIONNAIRE TO ASSESS CHILDREN AND ADOLESCENT SLEEP PROBLEMS
Zsófia Lendvai
Program: Fetal and neonatal medicine

E/I-9 IN VIVO EVALUATION OF SKIN GLYCATION BY THE USE OF TWO-PHOTON MICROSCOPY
Dóra Haluszka, Kende Lőrincz András Bánvölgyi, Nóra Gyöngyösi, Attila Kolonics, Róbert Szipocs, Sarolta Kárpáti, Norbert Wikonkal
Program: Dermatology and venerology

E/I-10 SIMULTANEOUS ANALYSIS OF SERUM INFLIXIMAB AND ANTI-INFLIXIMAB ANTIBODY LEVELS IN THERAPY RESISTANT PEDIATRIC PATIENTS WITH CROHN'S DISEASE
Dolóresz Szabó, Nóra Judit Béres, Kriszta Molnár, András Arató, Winter S. Harland, Gábor Veres
Program: Prevention of chronic disease in childhood

E/I-11 THE PLASMA LEVEL OF MYELOPEROXIDASE IN HEALTHY AND DIABETIC GROUPS
Júlia Stark, István Marczell, Zoltán Takáts, Gábor Békési
Program: Hormonal regulatory mechanisms

E/I-12 PHARMACOKINETICS AND PHARMACOGENOMICS OF HIGH-DOSE METHOTREXATE TREATMENTS IN PEDIATRIC ALL
Katalin Csordás , Orsolya Lautner-Csorba, Márta Hegyi, Ágnes Félné Semsei, Andrea Harnos, Olivér Eipel, Dániel Erdélyi, Csaba Szalai, Gábor Kovács
Program: Clinical Haematology

E/I-13 AGE AT DIAGNOSIS <40-YEARS IS NOT AN ACCURATE PREDICTOR OF DISEASE OUTCOME IN PATIENTS WITH CROHN'S DISEASE

Petra A. Golovics, Barbara D. Lovász

Program: Molecular genetics, Pathomechanism and clinical aspects of metabolic disorders

E/I-14 ACCURACY OF PATTERN-BASED INNER MACULAR THICKNESS PARAMETERS OF THE RTVUE OCT TO EARLY DETECT GLAUCOMATOUS PROGRESSION

Farzaneh Naghizadeh, Anita Garas, Péter Vargha, Gábor Holló

Program: Ophthalmology

E/I-15 INVESTIGATING THE CLINICAL CONSEQUENCE OF TRANSITION-SPECIFIC KRAS MUTATIONS IN LUNG ADENOCARCINOMA

Zoltán Lohinai, Mihály Cserepes, Gyula Ostoros, Tamás Barbai, Erzsébet Raso, Judit Moldvay, Ilona Kovalszky, József Timár, Balázs Hegedűs, Balázs Döme

Program: Pulmonology

E/I-16 CAROTID INTIMA-MEDIA THICKNESS IN CHILDREN AFTER RENAL TRANSPLANTATION – CROSS SECTIONAL STUDY

Arianna Dégi, Andrea Kerti, Éva Kis, Orsolya Cseprekál, Attila J Szabó, Péter Sallay, Horváth Tamás, Pintér Alexandra, Kollai Márk, György S Reusz

Program: Prevention of chronic diseases in shildhood

E/I-17 RISK OF COLORECTAL CANCER IN CD PATIENTS WITH COLONIC INVOLVEMENT AND STENOSING DISEASE. RESULTS FROM A POPULATION-BASED STUDY

Barbara Dorottya Lovász, Petra Anna Golovics

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E/V-5 2-PHOTON LASER MICROSCOPIC ANALYSIS OF PHOTOAGING IN MICE WITH IMPAIRED EPIDERMAL ANTIOXIDANT DEFENSE

Kende Lőrincz, András Bánvölgyi, Dóra Haluszka, Nóra Gyöngyösi, Sarolta Kárpáti, Norbert Wikonkál[1]

Program: Dermatology and Venerology

E/V-6 BONE FORMATION IS INCREASED WITH ALBUMIN COATED ALLOGRAFTS IN A RAT CRITICAL SIZE DEFECT

Dénes Horváthy[1,2], Gabriella Vácz[1]

Program: Physiology and Pathology of the musculoskeletal system

E/V-7 RESISTANCE AGAINST GLUCOCORTICOIDS, CAUSED BY OVEREXPRESSION OF THE GLUCOCORTICOID RECEPTOR B ISOFORM IN CACO-2 CELL LINE

Bence Tamás Ács[1,2], István Likó[3], Karolina Feldman-Kovács[1,2], Henrietta Butz[2], Károly Rácz[2], Attila Patócs[4,5]

Program: Hormonal regulations

E/V-8 ROLE OF INTERLEUKIN-24 (IL-24) IN THE PATHOGENESIS OF INFLAMMATORY BOWEL DISEASE (IBD)

Anna Ónody[1], Erna Sziksz[2], Leonóra Himer[2], Domonkos Pap[1], Beáta Szebeni[2], Mária Bernáth[1], Apor Veres-Székely[1], Krisztián Kovács[1], Kriszta Molnár[1], Viktória Ruszinkó[3], Gábor Veres[1], András Arató[1], Tivadar Tulassay[1,2], Ádám Vannay[2]

Program: *Prevention of chronic diseases in childhood*

E/V-9 A NOVEL ROLE OF INTERLEUKIN-24 (IL-24) IN THE PATHOGENESIS OF CHRONIC KIDNEY DISEASES

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Program: Prevention of chronic diseases in childhood

E/V-10 THE ANTIDEPRESSANT FLUVOXAMINE IS PROTECTIVE AGAINST RENAL ISCHEMIA/REPERFUSION INJURY

Ádám Hosszú[1,2], Nóra Fanni Bánki[1,2], Zsuzsa Antal[2], Sándor Kőszegi[1,2], László Wagner[3], Lilla Lénárt[1,2], Ádám Vannay[4], Attila Szabó[2], Tivadar Tulassay[2], Andrea Fekete[1,2]

Program Prevention of chronic diseases in childhood

E/V-11 BIOMECHANICAL COMPARISON OF HARD TISSUE ENGINEERING POTENCY OF MICRO- AND NANO PARTICULATED BONE AUGMENTATION MATERIALS EXAMINED IN OSSI MODEL

Márta Fülöp Papp, Katalin Perczel-Kovách, Beáta Kerémi, Sándor Farkasdi, Bence Szabó, József Blazsek, Csaba Dobó-Nagy, Gábor Varga

Program Dental research

E/VII-1 FLUVOXAMINE PRETREATMENT AMELIORATES THE DEPRESSION OF DIABETIC ANIMALS: THE ROLE OF THE BRAIN-DERIVED NEUROTROPHIC FACTOR

Lilla Lénárt[1,2], Nóra Fanni Bánki[1,2], Sándor Kőszegi[1,2], Judit Hodrea[1,2], László Wagner[3], Ottó Pintér[4], Tivadar Tulassay[2,5], Andrea Fekete[1,2]

Program: Prevention of chronic diseases in childhood

E/VII-2 RAT SPINAL CORD TRANSECTION MODEL - PRELIMINARY EXPERIMENTS FOR STUDIES ON THE EFFECT OF STEM CELLS OF DENTAL ORIGIN

Zoltán Borbély, Krisztián Benedek Csomó

Program: Dental research

E/VII-3 THE RENIN RELEASE IN ISCHEMIA/REPERFUSION KIDNEY INJURY; GENDER DIFFERENCES

Rózsa Csohány

Program: Prevention of chronic diseases in childhood

E/VII-4 RENIN-ANGIOTENSIN-ALDOSTERONE SYSTEM BLOCKERS IN DIABETIC NEPROPATHY: THE ROLE OF EPITHELIAL TO MESENCHYMAL TRANSITION
Sándor Kőszegi[1,2], Nóra Fanni Bánki[1,2], Lilla Lénárt[1,2] , Ádám Hosszú[1,2], László Wagner[3], Ádám Vannay[4], Tivadar Tulassay[2,4], Andrea Fekete[1,2]
Program: Prevention of chronic diseases in childhood

E/VII-5 COMPARISON OF DENTAL PULP STEM CELLS AND MG-63 OSTEOBLAST TUMOR CELLS OSTEOGENIC DIFFERENTIATION TIME COURSE
Katalin Perczel-Kovách, Krisztina Nagy, Orsolya Hegedűs, Gábor Varga
Program: Dental research

E/VII-6 THE FIRST FAMILY WITH *NPHS2* HOMOZYGOUS P.R229Q AND FAMILY MEMBERS WITHOUT STEROID-RESISTANT NEPHROTIC SYNDROME: THE MISSING EVIDENCE
Andrea Kerti[1], Rózsa Csohány[1], Eszter Jávorszky[1], László Wagner[2], Erika Maka[3], Tivadar Tulassay[1,4], Kálmán Tory[1]
Program: Prevention of chronic diseases in childhood

E/VII-7 SURFACE COATING EFFECTS ON MORPHOLOGY, MARKER EXPRESSION AND CELL PROLIFERATION OF RAT DENTAL PULP STEM CELLS DURING NEURODIFFERENTIATION
Karola Kálló, Bernadett Gánti, Gábor Varga
Program: Dental research

E/VII-8 GENETIC DETERMINANTS AND HERPES VIRUSES IN THE BACKGROUND OF PERIODONTITIS IN THE HUNGARIAN POPULATION
Péter Stiedl[1,2], Csilla Páska[1], Gabriella Jobbágy-Óvári[1], Xénia Kelemen[1], Borbála Soós[3], Bálint Molnár[2], Gábor Nagy[4], Gábor Hullám[5], Péter Antal[5], Gábor Varga[1], István Gera[2]
Program: Dental research

E/VII-9 MODELLIG THE PH REGULATION OF AMELOBLASTS BY NOVEL TWO DIMENSIONAL CELLULAR SYSTEM
Erzsébet Bori[1], Antonius LJJ Bronckers[2], Pamela Den Besten[3], Hidemitsu Harada[4], Gábor Varga[1]
Program: Dental research

E/VII-10 NEW NON-INVASIVE APPROACH TO EVALUATE IMPLANT STABILITY
Sándor Farkasdi[1]; Katalin Perczel-Kovách[1]; Márta Fülöp Papp[1]; Beáta Kerémi[1]; Bence Szabó[2]; Róbert Rácz[1]; Csaba Dobó-Nagy[2]; József Blazsek[1]; Gábor Varga[1]
Program: Dental research

E/VII-11 SMALL BOWEL ISCHEMIA – A COMPARATIVE EXPERIMENTAL STUDY
Zsolt Turóczi, Zoltán Czigány, Olivér Rosero, András Fülöp, Tibor Kovács, Péter Ónody, Dávid Garbaisz, László Harsányi, Attila Szijártó
Program: Clinical and experimental research in Angiology

E/VII-12 LEVOSIMENDAN PROTECTS AGAINST LIVER ISCHEMIC-REPERFUSION INJURY
András Fülöp[1], Rita Stangl[1], Péter Ónody[1], Zsolt Turóczi[1], Olivér Rosero[1], Dávid Garbaisz[1], Zoltán Rakonczay[2], László Harsányi[1], Attila Szijártó[1]
Program: Gastroenterology

P/I-5 THREE DIMENSIONAL HISTOLOGICAL EXAMINATION OF DENTAL ROOT CEMENT: A METHODICAL INNOVATION APPROACH
Milán Gyurkovics[1], István Stuber[2], Anna Zurányi[3], Noémi Szathmári[3], Csaba Korom[4], Zsolt Lohinai[1]
Program: Dental research

P/I-6 THE EFFECT OF METFORMIN ON GLYCOTOXIC INTERMEDIATES IN PATIENTS WITH TYPE 2 DIABETES.
Zoltán Kender[1], Péter Reismann[1], Thomas Fleming[2], Károly Rácz[1], Peter Nawroth[2]
Program: Hormonal regulations

P/I-7 INVESTIGATION OF METHYLATED CFDNA FRACTION CHANGES IN PATIENTS WITH COLORECTAL CANCERCOMPARED TO IBD, ADENOMA AND HEALTHY CONTROLS
Andrea Schöller[1], Sándor Spisák[2], Katalin Leiszter[1], Kinga Tóth[1], Árpád V. Patai[1], Alexandra Kalmár[1], Barnabás Wichmann[2], Barbara K. Barták [1], Zsófia B. Nagy[1], Zsolt Tulassay[2], Béla Molnár[2]
Program: Gastroenterology

P/I-8 CHARACTERISTIC MIRNA EXPRESSION ALTERATIONS IN COLORECTAL CANCER
Zsófia Brigitta Nagy[1], Barbara Kinga Barták[1], Árpád V. Patai[1], Barnabás Wichmann[1,2], Alexandra Kalmár[1], Gábor Valcz[2], Andrea Schöller[1], István Fűri[1], Zsolt Tulassay[1,2], Béla Molnár[1,2] , Sándor Spisák[2]
Program: Gastroenterology

P/I-9 ALTERATION OF DNA METHYLATION PATTERN IN COLORECTAL ADENOMA-CARCINOMA SEQUENCE
Barbara Kinga Barták[1], Árpád V. Patai[1], Sándor Spisák[1,2], Zsófia Brigitta Nagy[1], Alexandra Kalmár[1], Barnabás Wichmann[1,2], Gábor Valcz[1,2], Andrea Schöller[1], István Fűri[1], Zsolt Tulassay[1,2], Béla Molnár[1,2]
Program: Gastroenterology

P/I- 10 MONITORING OF THE ADHESION OF CREVICULAR FLUID CELLS AND ITS MODIFICATION BY OLIGOTUFTSIN DERIVATIVES
Sára Slezák[1], Eszter Lajkó[1], Éva Pállinger[1], Katalin B. Bai[3], Gábor Mező[3], István Gera[2], László Kőhidai[1]
Program: Dental research

P/I-11 THE METHYLATION STATUS OF HUMAN DNA DETERMINES THE AUTOLOGACTIVATION OF TLR9 PATHWAY ON HT29 COLORECTAL CANCER CELLS

István Fűri[1], Sándor Spisák[2], Árpád V. Patai[1], Ferenc Sipos[1], Györgyi Műzes[1], Alexandra Kalmár[1], Gergő Kiszner[3], Gábor Valcz[1], Barnabás Wichmann[2], Béla Molnár[1,2], Zsolt Tulassay[1,2]

Program: Gastroenterology

P/IV-16 PROSTAGLANDIN D2 RECEPTOR (PTGDR) GENE HYPERMETHYLATIONIN COLORECTAL ADENOMA-CARCINOMA SEQUENCE

Alexandra Kalmár [1], Bálint Péterfia[1,2,3]; Péter Hollósi[2]; Sándor Spisák[1,3]; Wichmann Barnabás[1,3]; Vivien Kubák[2]; Katalin Kiss[2]; Zsolt Horváth[2], Gábor Valcz[1]; Zsolt Tulassay[1,3]; Béla Molnár[1, 3]

Program: Gastroenterology

PHARMACEUTICAL SCIENCES DOCTORAL SCHOOL

E/VI-1 IN VITRO AND CELLULAR STUDY OF BENZOTHIOPHENE-3-CARBOXAMIDES AS INHIBITORS OF AURORA KINASE FAMILY

Pál Gyulavári[1], Kinga Pénzes[1], Zoltán Greff[2], Bálint Szokol[2], László Orfi[3], György Keri[1,2], Tibor Vantus[1]

Program: Modern trends in pharmaceutical scientific research

E/VI-2 DAPOXETIN AND ITS METABOLITES: SYNTHESIS AND ENANTIOSEPARATION BY CYCLODEXTRIN-MODIFIED CAPILLARY ELECTROPHORESIS

András Darcsi[1], Ida Fejős[1], Gergő Tóth[1], Tamás Sohajda[2], Lajos Szente[2], Szabolcs Béni[1]

Program: Modern trends in pharmaceutical scientific research

E/VI-3 THE LONG TERM EFFECT OF HORMONAL IMPRINTING INDUCED BY INSULIN AND SEROTONIN ON CELL PHYSIOLOGICAL PARAMETERS OF TETRAHYMENA

Eszter Lajkó[1], Éva Pállinger[1], György Csaba[1], László Kőhidai[1]

Program: Modern trends in pharmaceutical scientific research

E/VI-4 SYNTHESIS OF 6B-ACYLAMINO AND HYDROXYLAMINE DERIVATIVES OF MORPHINANS

Ákos Urai, András Váradi, Péter Horváth, Sándor Hosztafi, Béla Noszál

Program: Modern trends in pharmaceutical scientific research

E/VI-5 RADIOLABELED MONOCLONAL ANTIBODIES AND PEPTIDE ANALOGS FOR CANCER IMAGING IN SPONTANEOUS DISEASED ANIMAL MODELS

Zita Pöstényi[1,2], András Polyák[2], Alberto Signore[3], Filippo Galli[3], Gabriella Dabasi[4], Péter Róbert Jóba[4], László Seres[5], Lajos Balogh[2]

Program: Experimental and clinical Pharmacology

E/VI-6 ENANTIOSEPARATION OF ALOGLIPTIN BY CYCLODEXTRIN-MODIFIED CAPILLARY ELECTROPHORESIS

Ida Fejős[1], Zsuzsanna Urbancsok[1], Wei Zhou[2], Tamás Sohajda[3], Wen Hui Hu[2], Lajos Szente[3], Szabolcs Béni[1]

Program: Modern trends in pharmaceutical scientific research

E/VI-7 THE COMPLETE MICROSPECIATION OF OVOTHIOL, THE SMALLEST TETRAFUNCTIONAL BIOMOLECULE

Arash Mirzahosseini, Sándor Hosztafi, Gábor Orgován, Béla Noszál

Program: Modern trends in pharmaceutical scientific research

E/VI-8 PREPARATION AND CHARACTERIZATION OF ELECTROSPUN POLYMER FIBERS CONTAINING AMORPHOUS FAMOTIDINE

Attila Marosi[1], Olivér Ács[2], Dénes Janke[3], Lászlóné Tóth[3], Gergő Tóth[1], Balázs Németh[3], Zoltán Kazsu[3], Béla Noszál[1],György Marosi[2], Ádám Demeter[3], Zsombor Kristóf Nagy[2]

Program: Modern trends in pharmaceutical scientific research

E/VI-9 PRECLINICAL FORMULATION DEVELOPMENT OF A CARRIER SYSTEM FOR NANOPARTICLE ALBUMIN BOUND VORICONAZOLE

Petra Füredi, Kristóf Kovács, Krisztina Ludányi, István Antal, Imre Klebovich

Program: Experimental and clinical pharmacology

E/VI-10 SITE-SPECIFIC GLYCOSYLATION ANALYSIS OF PLASMA PROTEINS

Eszter Tóth, Oliver Ozohanics, László Drahos, Károly Vékey

Program: Modern trends in pharmaceutical scientific research

E/VI-11 PREDICTION OF THE ORAL DISINTEGRATION TIME OF FAST DISINTEGRATING TABLETS AFTER OPTIMIZATION

Gergely Szakonyi

Program: Modern trends in pharmaceutical scientific research

P/III-1 ANTHRAQUINONE COMPONENTS OF *RUBIA TINCTORUM* AS CANDIDATE ANTICANCER AGENTS FOR DRUG TARGETING

Eszter Lajkó[1], Péter Bányai[2], Éva Szőke[2], László Kőhidai[1]

Program: Modern trends in pharmaceutical scientific research

P/III-2 SOLUBILITY IMPROVEMENT OF APIGENIN

Zsófia Edit Pápay, Zita Sebestyén, Nikolett Kállai, Krisztina Ludányi, Emese Balogh, István Antal

Program: Modern trends in pharmaceutical sciences

P/III-3 SOMATIC ONCOGENE MUTATIONS IN FINE-NEEDLE ASPIRATION BIOPSY FROM THYROID COLD NODULES

Bálint Tobiás[1], Bernadett Balla[1], János P. Kósa[1], János Horányi[2], István Takács[1], Zsolt Nagy[1], Péter Horváth[1], Balázs Járay[3], Eszter Székely[3], Roland Istók[3], Tamás Székely[3], Péter Lakatos[1]

Program: Experimental and clinical pharmacology

P/III-4 RHEOLOGICAL CHARACTERIZATION OF HYDROCOLLOID GELS IN FORMULATION DEVELOPMENT

Enikő Szabadi, Lívia Budai, Mária Hajdú, Imre Klebovich, István Antal

Program: Modern trends in the pharmaceutical sciences

P/III-5 THE EFFECTS OF ANGIOTENSIN II ON THE NMDA-TYPE GLUTAMATE RECEPTORS OF THE PYRAMIDAL CELLS IN THE PREFRONTAL CORTEX (PFC)

Adrienn Hanuska

Program: Experimental and clinical pharmacology

P/III-6 THE DEVELOPMENT AND CHARACTERIZATION OF NOVEL KINASE INHIBITORS DESIGNED FOR TARGETED DELIVERY

Zoltán Nemes[1], Nóra Breza[2], Csaba-Kis Szántai[2], Eszter Illyés[2], Zoltán Horváth[2], Dániel Erős[2], Ed E Moret[3], Péter Horváth[1], György Kéri[2,4], László Őrfi[1,2]

Program: Modern trends in the pharmaceutical sciences

P/III-7 ENANTIOSEPARATION OF ASPARTATE AND GLUTAMATE BY CE-LIF IN BRAIN TISSUE SAMPLES

Tamás Jakó[1], Zsolt Wagner[1], Tamás Tábi[1], Gergely Zachar[2], András Csillag[2], Éva Szökő[1]

Program: Experimental and clinical pharmacology

P/III-8 EFFECT OF VACUUM-ULTRAVIOLET (V-UV) PHOTOLYSIS TRANSFORMATION PRODUCTS OF DICLOFENAC ON THE PROLIFERATION AND MIGRATORY RESPONSES OF *TETRAHYMENA PYRIFORMIS*

Júlia Láng[1], Eszter Arany[2], Dávid Somogyvári[2], Krisztina Gajda-Schrantz[2,3,4], Láng Orsolya[1], András Dombi[2], László Kőhidai[2]

Program: Modern trends in pharmaceutical sciences

P/III-9 PREPARATION AND CHARACTERIZATION OF FORCESPUN POLYVINYLPYRROLIDONE-IODINE FIBER MAT FOR WOUND DRESSING

István Sebe

Program: Modern trends in pharmaceutical sciences

MENTAL HEALTH SCIENCES DOCTORAL SCHOOL

E/II-1 GENETICS OF SUICIDAL BEHAVIOR: ROLE OF THE MICRORNA SYSTEM
Attila József Pulay, János Réthelyi
Program: Psychiatry

E/II-2 THE ATTITUDE OF DRUG USERS ABOUT DEATH
Pap Ágota
Program: Mental health sciences

E/II-3 PERSONALITY TRAITS AND TOBACCO USE: AFFECTIVE TEMPERAMENTS AND THEIR RELATIONSHIP WITH SMOKING PATTERNS. A CROSS-SECTIONAL STUDY
Ajándék Előry, Péter Torzsa, Zoltán Rihmer
Program: Psychiatry

E/II-4 ERROR-RELATED BEHAVIORAL INDICATORS IN PATIENTS SUFFERING FROM ADULT ATTENTION DEFICIT/HYPERACTIVITY DISORDER (ADHD)
Program: Mental health sciences

E/II-5 HEALTH CONDITION OF GYPSIES
Gellért Gyetvai
Program: Sociological and mental health approaches to resources for individuals and communities

E/II-6 DIFFERENCES AND SIMILARITIES BETWEEN THE FAMILY THERAPY OF MALE AND FEMALE PATIENTS WITH ANOREXIA NERVOSA
Ágnes Mezei, István Karácsony, Ferenc Túry
Program: Mental health sciences

E/II-7 BEHAVIORAL TREATMENT OF OBESITY
Ildikó Papp, Ágnes Udvardy – Mészáros, Edit Czeglédi, Gabriella Vizin,
Dóra Perczel Forintos[1]
Program: Mental health sciences

E/II-8 SOCIOCULTURAL AND ETHNICAL DIFFERENCES IN THE RISK FACTORS OF SERIOUS SUICIDE ATTEMPTS IN HUNGARY
Mónika Ditta Tóth, Szilvia Ádám, Tamás Zonda, Éva Susánszky, György Purebl
Program: Mental health sciences

E/II-9 EFFECTS OF ORGAN DONATION ATTITUDE AND FAMILY APPROACH ON ORGAN DONATION ACTIVITY
Sándor Mihály
Program: Mental health sciences

E/II-10 PSYICHOSOCIAL AND FAMILY DYNAMICS STUDY OF EPILEPTIC PATIENTS AND PATIENTS LIVING WITH CHRONIC SPINAL PAIN
Daniella Kováts, Viola Sallay, Noémi Császár, Judit Békés, Vera Juhos, Tamás Kurimay
Program: Clinical Psychology and Psychiatry,

P/II-1 STRESS AT WORK: PSYCHOSOCIAL RISK AND PROTECTIVE FACTORS AMONG EDUCATION AND HEALTHCARE PROFESSIONALS
Katalin Nistor[1], Szilvia Ádám[1], Anita Szabó[2], Tünde Zakor[3], Adrienne Stauder[1]
Program: Mental health sciences

P/II-2 THE SURVEY OF PROTECTIVE ELEMENTS OF COMMUNITIES, THE ATTITUDE OF HUNGARIAN AND ITALIAN ADOLESCENTS TO RELIGION, RELIGIOUS COMMUNITIES
Eszter Sabadel
Program: Sociological and mental health approaches to resources for individuals and communities

P/II-3 EMPATHIC RESPONSE TO OTHERS' PAIN IN BORDERLINE PERSONALITY DISORDER: STRESSING THE IMPORTANCE OF MULTICOMPONENTIAL ANALYSIS
Dóra Fogd[1], Katalin Egyed[2], Vera Konok [3], Levente Juhász[4], Szilvia Somogyi[1], Zsolt Unoka[1]
Program: Clinical Psychology and Psychiatry

P/II-4 FACILITATING THE IMPLEMENTATION OF MEDICATION RECONCILIATION
Ádám Freisinger, Judit Lám, Lilla Barki, Márton Király, Éva Belicza
Program: Mental health sciences

P/II-5 SOCIOCULTURAL ASPECTS OF EATING DISORDERS WITH SPECIAL FOCUS ON MEDIA USE TV – INTERNET – MAGAZINES
Kornélia Szabó, Irena Szumska, Ferenc Túry
Program: Mental health sciences

P/II-6 MIDWIVES'ROLE IN CHANGING SMOKING PATTERNS AMONG WOMEN WHO SMOKE IN PREGNANCY
Ágnes Szélvári
Program: Mental health sciences

P/II-7 THE SITUATION OF CHILDREN RETURNED FROM THEIR ADOPTIVE FAMILY TO THE CHILDCARE SYSTEM
Júlia Andrási
Program: Sociological and mental health approaches to resources for individuals and communities

P/II-8 EXAMINING DYSKINESIA IN CHILDREN WITH ADHD
Ágnes Keresztény[1,2], Judit Balázs[2,3]
Program: Clinical Psychology and Psychiatry

P/II-9 OBSTRUCTIVE SLEEP APNEA WITHOUT EXCESSIVE DAYTIME SLEEPINESS IN KIDNEY TRANSPLANT RECIPIENTS

Katalin Zsuzsanna Rónai[1], Enikö Mózes[1], Sándor Alpár Lázár[1,2], András Szentkirályi[1,3], Rezsö Zoller [1,4], Anett Lindner[1,5], Csilla Turányi[1], Júlia Szöcs[1], Katalin Fornádi[1,5], Miklós Zsolt Molnár[1,6,7], István Mucsi[1,6,8], Márta Novák[1,9]

Program: Mental health sciences

P/II-10 SOCIO- DEMOGRAPHIC CHARACTERISTICS OF RELIGIOUS COMMUNITIES

Csaba Bálity

Program: Sociological and mental health approaches to resources for individuals and communities

P/II-11 GENDER DIFFERENCES IN SLEEP EEG CORRELATES OF SUPERIOR IQ

Péter Przemyslaw Ujma, Róbert Bódizs

Program: Mental health sciences

P/II-12 THE ROLE OF SOCIAL SUPPORT IN PATIENTS WITH MALIGNANT MELANOMA TREATED WITH ADJUVANT LOW-DOSE INTERFERON – 1 YEAR FOLLOW-UP

Péter Kovács[1,2], Gitta Pánczél[1], Kinga Borbola[1], Gabriella Juhász [2], Gabriella Liszkay[1]

Program: Clinical Psychology and Psychiatry

SPORT SCIENCES DOCTORAL SCHOOL

E/III-4 MEASURING FUNCTIONAL CHARACTERITICS OF THE ATHLETE'S HEART WITH TDI

Eszter Csajági, Zsuzsanna Major, Zsuzsanna Kneffel, Gábor Pavlik

Program: Training and adaption

„JÁNOS SZENTÁGOTHAI" NEUROSCIENCES DOCTORAL SCHOOL

E/III-1 VGLUT3-CONTAINING RAPHE NEURONS REPRESENT A NEW MODULATORY POSSIBILITY

Andor Domonkos

Program: Functional neurosciences

E/III-2 METABOLIC CHANGES DURING DIFFERENTIATION OF NEURAL STEM CELLS

Attila Jády; Tünde Kovács; Susan Van-Weert; László Tretter; Emília Madarász

Program: Neuromorphology and cell biology

E/III-3 EFFECT OF UNILATERAL AND BILATERAL STN STIMULATION AND LEVODOPA ON DISTAL AND PROXIMAL ALTERNATING MOVEMENT OF THE UPPER LIMB IN PARKINSON'S DISEASE

Péter Radics , Loránd Erőss, Annamária Takáts, Dustin. Heldman, Joseph.Giuffrida, László Entz, Dániel Fabó, Gertrúd Tamás

Program: Clinical neurological research

P/IV-10 ASIAN-SPECIFIC MITOCHONDRIAL GENOM POLYMORPHISM (9 BP DELETION) IN THE HUNGARIAN POPULATION

Klára Pentelenyi[1], Viktória Reményi[1], Gyöngyvér Tömöry[2], Bernadett Csányi[2], Anikó Gál[1], István Raskó[2], Mária Judit Molnár[1]

Program: Clinical neurosciences

MOLECULAR MEDICINE DOCTORAL SCHOOL

E/III-15 CORRELATION OF CLINICAL FINDINGS AND CLOT ULTRASTRUCTURE IN ARTERIAL THROMBI

András Kovács

Program: Pathobiochemistry

E/IV-1 IN VITRO DIFFERENTIATION OF TH17 CELLS

Eszter Baricza, Barbara Molnár-Érsek, Edit Buzás, György Nagy

Program: Basis of human molecular genetics and gene diagnostics

E/IV-2 GENETIC VARIATIONS IN THE PROMOTER REGION OF THE WFS1 GENE ARE RISK FACTORS OF TYPE 2 DIABETES MELLITUS

Nóra Németh, Zsuzsanna Elek, Suzanne Prokop, Anikó Somogyi, Mária Sasvári-Székely, Zsolt Rónai

Program: Pathobiochemistry

E/IV-3 THE PHOSPHOINOSITIDE 3-KINASE B AND Δ REGULATE OSTEOCLAST DEVELOPMENT AND FUNCTION

Dániel Csete

Program: Cellular and molecular physiology

P/IV-1 THE ROLE OF GLUT10 IN THE ARTERIAL TORTUOSITY SYNDROME

Csilla Németh[1], Éva Margittai[1], Marcolongo Paola[2], Benedetti Angiolo[2], Gábor Bánhegyi[1]

Program: Pathobiochemistry

P/IV-2 DEVELOPMENT OF NEW MOLECULAR TOOLS TO MONITOR VARIOUS INOSITOL COMPOUNDS IN STIMULATED HUMAN HEK-293T FIBROBLASTS

József T. Tóth, Gergő Gulyás, Dániel J. Tóth, László Hunyady, Péter Várnai

Program: Cellular and molecular Physiology

P/IV-3 7H3 IS A NOVEL BURSAL STEM CELL ANTIGEN

Nóra Fejszák, Imre Oláh, Nándor Nagy

Program: Embryology, theoretical, experimental and clinical developmental Biology

P/IV-4 GENETIC RISK FACTORS OF ANTHRACYCLINE CARDIOTOXICITY – RELEVANT POLYMORPHISMS IDENTIFIED IN ENZYMES AND TRANSPORTERS OF ANTHRACYCLINE PHARMACOKINETICS

Nóra Kutszegi[1], Ágnes F. Semsei[1], Orsolya Lautner-Csorba[1], Márta Hegyi[2], Csaba Szalai[1,3], Gábor T. Kovács[2], Dániel J. Erdélyi[2]

Program: Basis of human molecular genetics and gene diagnostics

P/IV-5 *YAP1* IN THE HIPPO PATHWAY INFLUENCES THE RISK OF ASTHMA

Lili Erika Fodor[1], Ildikó Ungvári[1], Orsolya Lautner-Csorba[1], Csaba Szalai[1,2]

Program: The basis of human molecular genetics and gene diagnostics

P/IV-6 DEVELOPMENTAL MAPPING OF CD45+ CELLS IN EARLY AVIAN EMBRYO

Dávid Dóra, Imre Oláh, Nándor Nagy

Program: Embryology, theoretical, experimental and clinical developmental Biology

PATHOLOGICAL SCIENCES DOCTORAL SCHOOL

E/IV-4 MODELING THE TEMPERATURE-RELATED AVERAGED ANNUAL RUN OF RELATIVE LB INCIDENCE IN THE PERIOD OF 1998-2012 IN HUNGARY

Attila. Trájer, Ákos. Bede-Fazekas, János. Bobvos, Anna. Páldy

Program: Public health sciences

E/IV-5 CLINICOPATHOLOGICAL FEATURES OF HEAD AND NECK CANCERS AND THEIR RELATION TO BIOMARKER-EXPRESSION

Kornél Dános, Diána Brauswetter

Program: Oncology

E/IV-6 EXPLORING CONNEXIN EXPRESSION AND FUNCTIONS IN MELANOCYTIC TUMORS

Gergő Kiszner, Ivett Teleki, Péter Balla, Nóra Meggyesházi, Zsófia Buday

Program: Oncology

E/IV-7 MODULATED ELECTRO-HYPERTHERMIA CAUSES PROGRAMMED CELL DEATH IN HT29 COLORECTAL CARCINOMA XENOGRAFT

Nóra Meggyesházi[1], Gábor Andócs[2], Sándor Spisák[3]

Program: Oncology

E/IV-8 DIFFERENTIAL CONNEXIN EXPRESSION IN GIANT CELL TUMOUR OF BONE (GCTB)

Péter Balla, Ivett Teleki, Nóra Meggyesházi, Gergő Kiszner, Tibor Krenács

Program: Oncology

E/IV-9 IN SITU ANALYSIS OF MAMMALIAN TARGET OF RAPAMYCIN (MTOR) COMPLEXES
Noémi Nagy, Ágnes Márk, Sándor Paku, László Kopper, Anna Sebestyén
Program: Experimental Oncology

E/IV-10 THE ROLE OF ALTERED CYTOKINE PRODUCTION IN HHV-7 INFECTIONS
Balázs Stercz
Program: Study of the immunobiological effects of microorganisms and of their components at molecular and cellular level and in the organisms

E/IV-11 COMPARATIVE ANALYSIS OF PATIENT DERIVED AND *IN VITRO* SELECTED VEMURAFENIB RESISTANT MELANOMA CELL MODELS
Tamás Garay, Eszter Molnár, Walter Berger, József Tímár, Balázs Hegedűs
Program: Oncology

E/IV-12 THE ROLE OF HYPERGLYCAEMIA IN PANCREATIC FIBROSIS
Katalin Kiss, Gábor Firneisz, Ilona Kovalszky
Program: Oncology

P/IV-11 META-ANALYSIS OF BIOMARKER CANDIDATES PREDICTING SURVIVAL AFTER TAMOXIFEN TREATMENT
Zsuzsanna Mihály[1], Máté Kormos[2], András Lánczky[2], Balázs Győrffy[1]
Program: Oncology

P/IV-12 IONIZING RADIATION INDUCED EFFECT OF GDF-15 AND TGFB1IN MAMMARY CARCINOMA CELLS
Boglárka Schilling-Tóth[1], Nikolett Sándor[1], Enikő Kis[1], Géza Sáfrány[1], Hargita Hegyesi[1]
Program: Oncology

P/IV-13 BIOMARKERS OF PLATINUM RESISTANCE IN OVARIAN CANCER
Zsófia Pénzváltó, András Lánczky
Program: Oncology

P/IV-14 INHIBITION OF AUTOPHAGIC CELL DEATH AND RADIOSENSITISATION WITH SILENCING OF TP53INP1 IN HUMAN FIBROBLAST CELLS
Nikolett Sándor, Boglárka Schilling-Tóth, Enikő Kis, Géza Sáfrány, Hargita Hegyesi
Program: Oncology

DOCTORAL SCHOOL – SZEGED

E/V-1 COMPARISON OF RAT AND HUMAN ORTHOLOGS OF ORGANIC CATION/CARNITINE TRANSPORTER (OCTN2)
Kitti Szabó[1,2], Péter Krajcsi[1], Zoltán Nagy[1], Viktória Juhász[1]
Doctoral School: Oláh György Doctoral School
Program: Examination of renal transporters

E/V-2 THE UL54 GENE OF PSEUDORABIES VIRUS MAY BE PART OF THE TRANSCRIPTIONAL INTERFERENCE NETWORK AND MAY SPECIFICALLY REGULATE LATE GENES

Nándor Póka, Péter Oláh
Doctoral School: Multidisciplinary
Program: B Biochemisrty, Biophysics, Molecular-and Cell Biology

E/V-3 MODERATE INHIBITION OF GELATINOLYTIC ACTIVITY BY ILOMASTAT REDUCES INFARCT SIZE IN BOTH ISCHEMIC AND REPERFUSION INJURY IN VIVO

Krisztina Kiss[1], Péter Bencsik[1,2], János Pálóczi[1], Gabriella F. Kocsis[1], Anikó Görbe[1], Judit Pipis[1], Csaba Csonka[1,2], Tamás Csont[1,2], Péter Ferdinandy[2,3]
Doctoral School: Multidisciplinary
Program: Biochemisrty, Biophysics, molecular-and cell Biology

E/V-4 ISOLATION AND ANALYSIS OF LARGE BACTEROIDES PLASMIDS

Viktor Sándor Fenyvesi
Doctoral School: Clinical Medicine
Program: Oral and Clinical Microbiology

P/IV-7 GRAFTED NEUROCTODERMAL STEM CELLS RESCUE DAMAGED RAT RETINAL GALNGLION CELLS OTHERWISE DESTINATED TO DIE

Péter Balázs Kocsis[1], Zoltán Fekécs[2], Antal Nógrádi[1]
Program: Clinical and experimental research for reconstructive and organ-sparing surgery

P/IV-8 GLYCOGEN DISTRIBUTION IN A HYPERMUSCULAR MOUSE MODEL

Tamás Kocsis, Júlia Baán, Luca Mendler, Anikó Keller-Pintér, László Dux.
Doctoral School: Multidisciplinary, University of Szeged.
Program: Biochemistry, Biophysics, molecular- and cell Biology

P/IV-9 THE *COMPACT* MUTATION OF MYOSTATIN CAUSES A GLYCOLYTIC CHANGE IN THE PHENOTYPE OF SKELETAL MUSCLES

Júlia Baán, Tamás Kocsis, Anikó Keller-Pintér, Luca Mendler, László Dux
Doctoral School: Multidisciplinary, University of Szeged.
Program: Biochemistry, Biophysics, molecular-and cell Biology

P/IV-15 METABOLIC SYNDROME INFLUENCES CARDIAC GENE EXPRESSION PATTERN AT THE TRANSCRIPT LEVEL IN MALE ZDF RATS

Márta Sárközy[1], Ágnes Zvara[2], Nóra Gyémánt[1], Veronika Fekete[1], Judit Pipis[1], Gergő Szűcs[1], Csaba Csonka[1], László G Puskás[2], Péter Ferdinandy[3], Tamás Csont[1]
Doctoral School: Multidisciplinary Medicine
Program: Biochemistry, Biophysics, molecular and cell Biology

DOCTORAL SCHOOL- PÉCS

P/I-4 THE EFFECT OF KIDNEY TRANSPLANT PATIENTS' BODY IMAGE CHARACTERISTICS ON THEIR RECOVERY

Melinda Látos[1], Katalin Barabás[2], György Lázár[3], Márta Csabai[4]
Doctoral School: Psychology Doctoral School, Faculty of Humanities, University of Pécs,
Program: Theoretical Psychoanalysis Program

STUDENTS' SCIENTIFIC ASSOCIATION, SEMMELWEIS UNIVERSITY

E/I-5 PREDICTORS OF MORTALITY IN MECHANICALLY VENTILATED PATIENTS OUT OF THE ICU IN THE INTERNAL MEDICAL WARDS

Shimon Izhakian[1], Andreas Buchs[2], Lidia Sreter[3]
Shimon Izhakian is a graduate student

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