UNIVERZITA KARLOVA V PRAZE,
LÉKAŘSKÁ FAKULTA V HRADCI KRÁLOVÉ
A
FAKULTNÍ NEMOCNICE V HRADCI KRÁLOVÉ

XVII. VĚDECKÁ KONFERENCE

P R O G R A M

23. ledna 2013

Velká posluchárna teoretických ústavů Lékařské fakulty UK,
Šimkova 870, Hradec Králové

XVII. vědecká konference Lékařské fakulty Univerzity Karlovy v Hradci Králové a Fakultní nemocnice Hradec Králové 23. ledna 2013

09.00 – 09.15 Z a h á j e n í k o n f e r e n c e
prof. MUDr. Radek Pudil, Ph.D.
prof. MUDr. RNDr. Miroslav Červinka, CSc. děkan lékařské fakulty
prof. MUDr. Roman Prymula, CSc., Ph.D. ředitel fakultní nemocnice

Sekce I Předsedající: **prof. MUDr. Radek Pudil, Ph.D.**

09.15 - 09.30 Analýza vybraných prognostických a prediktivních markerů u karcinomů orofaryngu a hrtanu
MUDr. David Kalfeřt
GA UK 444311 (LF)

09.30 - 09.45 Mutace genu K-ras v karcinogenezi endometriálního karcinomu
MUDr. Eva Křepinská (Dvořáková)
GA UK 157310 (LF)

09.45 - 10.00 Hodnocení vztahu leptinu a markerů kostního metabolismu u předčasně narozených dětí
MUDr. Petra Kanioková Veselá
GA UK 432411 (LF)

10.00 - 10.15 Poškození srdce vyvolané protinádorovými léčivy a ischemií-reperfuzí: nové možnosti farmakologické kardioprotekce.
prof. MUDr. Vladimír Geršl, CSc.
GA ČR 305/09/0416 (LF)

10.15 – 10.30 Proteomická identifikace biomarkerů intraamniálního zánětu v plodové vodě pacientek se spontánním předčasným porodem
MUDr. Marian Kacerovský, Ph.D.
MŠMT ME10025 (FN)

10.30 – 11.00 *Přestávka – občerstvení*

Sekce II Předsedající: **prof. MUDr. Zuzana Červinková, CSc.**

11.00 - 11.20 POSTDOK I. - Podpora vytváření, rozvoje a mobility kvalitních výzkumně-vývojových týmů na Univerzitě Karlově
prof. MUDr. Radek Pudil, Ph.D.
MŠMT OP VK CZ.1.07/2.3.00/30.0022 (LF)

11.20 - 11.35 HEPIN - Příprava personálního zabezpečení VaV v Hepatologickém institutu v Hradci Králové
prof. MUDr. Petr Hůlek, CSc.
MŠMT OP VK CZ.1.07/2.3.00/09.0082 (LF)

11.35 - 11.50 IT MEDIK - Inovace a rozvoj studijního programu Všeobecné lékařství na Lékařské fakultě UK v Hradci Králové pomocí uplatnění informačních technologií
prof. MUDr. Aleš Ryška, Ph.D.; doc. Ing. Josef Hanuš, CSc.
MŠMT OP VK CZ.1.07/2.2.00/15. 0164 (LF)

11.50 - 12.05 BBMRI
prof. MUDr. Aleš Ryška, Ph.D.
(odp. řešitel: prof. MUDr. Dalibor Valík, Ph.D. – MOÚ Brno)
MŠMT BBMRI_CZ (LF)

12.05 - 12.20 OPtimization of Treatment and Management of Schizophrenia in Europe
prof. MUDr. Jan Libiger, CSc.
(odp. řešitel: prof. dr. René S. Kahn - University Medical Center Utrecht)
FP7 OpTiMiSE (LF)

12.20 - 14.00 *Přestávka na oběd*

Sekce III Předsedající: **prof. MUDr. Aleš Ryška, Ph.D.**

14.00 - 14.15 Regionální centrum II - Centrum obrazových dat
MUDr. Vratislav Sedlák
(odp. řešitel: doc. Ing. Otto Dostál, CSc. – MU Brno)
MŠMT OP VK CZ 1.07/2.2.00/07.0022 (LF)

14.15 - 14.30 Physi-Sci-Net síť pro zkvalitnění personálního zabezpečení výzkumu a vývoje prostřednictvím dalšího odborného vzdělávání pracovníků a zkvalitnění technického zabezpečení
prof. MUDr. Zuzana Červinková, CSc.
(odp. řešitel: prof. MUDr. Otomar Kittnar, MBA, CSc. – 1. LF UK)
MŠMT OP VK CZ 1.07/2.3.00/09.0129 (LF)

14.30 - 14.45 Standardizace a sdílení vzdělávací platformy mezi lékařskými fakultami v rámci projektu MEFANET
doc. Ing. Josef Hanuš, CSc.
(odp. řešitel: Ing. Daniel Schwarz, Ph.D. – MU Brno)
MŠMT OP VK CZ.1.07/2.4.00/12.0050 (LF)

14.45 - 15.00 IMPACT - Inovace, metodika a kvalita jazykového vzdělávání a odborného vzdělávání v cizích jazycích v terciární sféře v ČR
PhDr. Jan Comorek, Ph.D.
(odp. řešitel: PaedDr. Marta Rybičková, Ph.D. – MU Brno)
MŠMT OP VK CZ.1.07/2.2.00/28.0233 (LF)

15.00 - 15.15 Neurovědy - Lidské zdroje pro neurovědní výzkum v Královéhradeckém a Ústeckém kraji
prof. MUDr. Stanislav Filip, Ph.D., DSc.
(odp. řešitel: prof. Eva Syková, DrSc., FCMA – ÚEM Praha)
MŠMT OP VK CZ.1.07/2.3.00/20.0274 (LF)

15.15 – 15.30 Neuropsychiatrické aspekty neurodegenerativních onemocnění
doc. MUDr. Petr Smolík, CSc.
(odp. řešitel: prof. MUDr. Evžen Růžička, DrSc. - 1. LF UK)
MSM 0021620849 (LF)

15.30 – 15.45 U k o n č e n í k o n f e r e n c e
prof. MUDr. Roman Prymula, CSc., Ph.D. ředitel fakultní nemocnice
prof. MUDr. RNDr. Miroslav Červinka, CSc. děkan lékařské fakulty
prof. MUDr. Radek Pudil, Ph.D.

SOUHRNY VÝZKUMNÝCH ÚKOLŮ

ŘEŠENÝCH NA LF UK A VE FN V HRADCI KRÁLOVÉ

(ABECEDNĚ)

Title of the project: Diffuse large B cell lymphoma and follicular lymphoma - analysis of prognostic factors and treatment guideliness to patient´s outcome; lymphoma project of Czech Republic

Grant Agency: Ministry of Health ***Project Number:*** NT/12193-5

Principal Investigator: M. Trněný

Co-investigators: D. Belada, L. Boudová, A. Janíková, M. Jankovská, T. Papajik, K. Kubáčková, M. Matuska, M. Lysý

Starting date: 1.6.2011 ***Duration (years):*** 5

Total funds allocated for project - Kč (thousands): 7026

Summary of 2012 results

Title of the presentation: Diffuse large B cell lymphoma and follicular lymphoma - analysis of prognostic factors and treatment guidelines to patient´s outcome; lymphoma project of Czech Republic

Authors: D.Belada, L.Boudova, A.Janíková, M.Jankovská, T.Papajik, K.Kubáčková, M.Matuska, M.Lysý

Czech Lymphoma Study Group (CLSG) consist of the majority of University Hospitals in Czech Republic (CR) which are focused on lymphoma diagnosis and management as well as of the number of regional hematology and oncology centers. The proposed multicentric project is based on the current level of collaboration in this field in Czech Republic and is focused on analysis of selected subgroups of Non-Hodgkin´s lymphomas (Diffuse large B cell lymphoma and follicular lymphoma) registered in CLSG registry and to describe the situation in Czech republic - clinical features, therapy, outcome. The number of patients in our databasis is estimated about 6500. The importance of proposed project is seen in the addressing of unanswered question of description of "real-life" situation in lymphoma field in Czech Republic and the analysis of different lymphoma subgroups and the description of clinical features, therapeutic approaches and the outcome of patients in Czech Republic. During 2011 we analysed cohort of patients with relapsed follicular lymphoma - retrospective analysis on subgroup of patients has been performed. In our clinic about 60 newly diagnosed patients with diffuse large B cell lymphoma has been diagnosed, and about 15 newly diagnosed patients with follicular lymphoma. All these patients were included into analysis. Results has been presented and discussed on local meetings in Czech Republic as well as on international meeting of American Society of Haematology in December 2012.

Project was supported by Internal Grant Agency of Ministry of Health NT/12193-5.

Address for correspondence: Czech Lymphoma Study Group -David Belada, 4th Clinic of Internal Medicine - Haematology, Sokolska street 581, Hradec Kralove 5, 50005, Czech Republic; e-mail: david.belada@fnhk.cz.

Title of the project: Observational study for the newly diagnosed patients with mantle cell lymphoma unfit for high dose therapy with stem cell support based on the treatment with R-CHOP chemotherapy alternating with R-Ara-C (3+3 cycles)

Grant Agency: Ministry of Health ***Project Number:*** NT/13072-4

Principal Investigator: M. Trněný

Co-investigators: P. Klener, J. Trka, D. Belada, M. Šimkovič, D. Šálek, A. Janíková, V. Procházka, Z. Kapitánová

Starting date: 1.6.2012 ***Duration (years):*** 4

Total funds allocated for project - Kč (thousands): 8686

Summary of 2012 results

Title of the presentation: Observational study for the newly diagnosed patients with mantle cell lymphoma unfit for high dose therapy with stem cell support based on the treatment with R-CHOP chemotherapy alternating with R-Ara-C (3+3 cycles)

Authors: D.Belada, M.Trněný, P. Klener, J. Trka, M.Šimkovič, D.Šálek, A.Janíková, V.Procházka, Z.Kapitánová

The aim of this observational study for the newly diagnosed patients with mantle cell lymphoma unfit for high dose therapy with stem cell support based on the treatment with R-CHOP chemotherapy alternating with R-Ara-C (3+3 cycles) is to assess efficacy and treatment outcomes of this therapy to the cohort of older patients with unfavourable type of non-Hodgkin´s lymphoma. During first 6 months about 25 newly diagnosed patients with mantle cell lymfoma has been included and treated within this protocol. In our centre, altogether 9 patients has been included and treated (one of them was excluded for another diagnosis than MCL). Based on our hypothesis, treatment with R-CHOP chemotherapy alternating with R-Ara-C, more clinical responses are expected comparing with historical controls (R-CHOP chemotherapy alone). PET scan is used for the clinical assessment of treatment response. Another aim of this study is to examine minimal residual disease in this cohort of patients and compare it with historical controls and results from European Mantle Cell Network. To this date, we have no reliable data of MRD assessment from this treatment protocol. Clinically, in our centre seven patients finished treatment within this protocol, and five of them achieved complete remission based on data from PET scan. Treatment is well tolerated and this preliminary result are encouraging for future.

Address for correspondence: Czech Lymphoma Study Group -David Belada, 4th Clinic of Internal Medicine - Haematology, Sokolska street 581, Hradec Kralove 5, 50005, Czech Republic; e-mail: david.belada@fnhk.cz.

Title of the project: Ischaemia reperfusion injury in accute myocardial infarction

Grant Agency: Ministry of Health ***Project Number:*** NT/13709-3

Principal Investigator: J. Bis

Co-investigators: Z. Zadák, R. Štětina, P. Fikrová, J. Šťásek, J. Dušek, J. Vojáček

Starting date: 1.4.2012 ***Duration (years):*** 3

Total funds allocated for project - Kč (thousands): 2856

Summary of 2012 results

Title of the presentation: Ischaemia reperfusion injury in accute myocardial infarction

Authors: J. Bis

Up to 50% of myocardial damage is caused by reperfusion injury and excessive release of free oxygen radicals. The aim of the study is evaluation of ischemia reperfusion injury of cardiomyocytes in acute myocardial infarction by measurement of DNA damage with comet assay, comparing group with stable coronary artery disease. Oxidative damage of DNA is caused by free oxygen radicals excessively released at reperfusion. This year we started recruitment of patients with STEMI and stable coronary artery disease and laboratory analysis of commet assay and myocardial damage has been performed. Proof of reperfusion injury and its possible quantification could improve and allow testing of new therapies to reduce reperfusion injury.

Address for correspondence: josef.bis@fnhk.cz

Title of the project: The role of insulin resistance in the pathogenesis of cardiometabolic risk in diabetes mellitus

Grant Agency: Ministry of Health ***Project Number:*** NT/12287-5

Principal Investigator: V. Bláha

Co-investigators: L. Sobotka, J. Lesná, F. Musil, A. Šmahelová, R. Hyšpler, M. Bláha, J. Víšek

Starting date: 1.7.2011 ***Duration (years):*** 5

Total funds allocated for project - Kč (thousands): 6907

Summary of 2012 results

Title of the presentation: Effect of low calorie diet and controlled fasting on insulin sensitivity and glucose metabolism in obese patients with type 1 diabetes mellitus

Authors: F. Musil, A. Šmahelová, V. Bláha, R. Hyšple1, A. Tichá, J. Lesná, Z. Zadák, L. Sobotka. Fac. Med., Charles Univ., Hr.Králové, IIIrd Dept Metabolism and Gerontology, University Hospital, Hradec Králové; Charles University, Prague, Czech Republic

Obesity in T1DM patients is associated with the components of metabolic syndrome. The influence of controlled fasting and low calorie diet (LCD) on insulin sensitivity and glucose metabolism was studied in 14 obese patients with type 1 diabetes mellitus (T1DM) (42.6±9.4 years, BMI 32.4±2.1 kg m^{-2}). Insulin sensitivity in obese T1DM patients was measured using a hyperinsulinemic-euglycemic clamp before fasting, immediately after 7 days of fasting, and after 21 days of LCD. Glucose oxidation and non-oxidative glucose disposal were measured before and during the clamp by indirect calorimetry. In the control group of 13 of non-obese T1DM patients (36.9±13.9 years, BMI 22.6±2.1 kg m^{-2}), only one hyperinsulinemic-euglycemic clamp was performed. Obese T1DM patients lost 6.1±1.1 kg after fasting and maintained reduction in body weight after 21 days of LCD. Fasting transiently reduced insulin-mediated glucose disposal in the clamp (from 9.69±1.48 to 6.78±1.21 mg min^{-1} kg^{-1}, $P<0.001$). This was caused by reduced glucose oxidation after the fasting period (from 2.81±0.52 to 0.88±0.98 mg min^{-1} kg^{-1}, $P<0.001$). We conclude that one week of fasting transiently decreased insulin-mediated glucose disposal in T1DM patients. This was caused by reduced glucose oxidation.

Address for correspondence: V. Bláha, IIIrd Department of Metabolic Care and Gerontology, University Hospital Hradec Králové, Sokolská 581, 50005 Hradec Králové, Czech Republic.

Title of the project: Design and enzyme targeting of antibacterial active compounds against multidrug resistant strains

Grant Agency: Ministry of Health ***Project Number:*** NT/13346-4

Principal Investigator: J. Vinšová

Co-investigator: V. Buchta, P. Paterová, M. Vejsová

Starting date: 1.4.2012 ***Duration (years):*** 4

Total funds allocated for project - Kč (thousands): 6624

Summary of 2012 results

Title of the presentation: *In vitro* antimycobacterial and antimicrobial activity of new synthetic substances.

Authors: V. Buchta (1), P. Paterová (1), M. Vejsová (1)
Fac. Med., Charles Univ., Hr. Králové: Dept. of Clinical Microbiology (1)

Text:

Tuberculosis represents a leading cause of mortality and morbidity over the world population. In particular, infections caused by MDR and XDR strains of *Mycobacterium tuberculosis* (TB) are difficult to treat. Hence there is a need of novel antituberculotic drugs with specific mechanism of action.

Susceptibility tests of the project were focused on pyrazine derivatives and their *in vitro* efficacy against human pathogenic mycobacteria, and selected bacteria and fungi using broth microdilution CSLI standards. Minimal inhibitory concentration (MIC) and its relationship to *in vitro* antimicrobial effect were evaluated.

A series of 19 new pyrazinamide derivatives were synthesized and tested against *Mycobacterium* strains. Antituberculotic activity (MIC = 6.25–12.5 mg/L) of nine of the compounds was similar or better compared to pyrazinamide. 3-(benzylamino)pyrazine-2,5-dicarbonitrile inhibited all of the tested mycobacterial strains with MIC within the range 12.5–25 mg/L. Parallel testing of *in vitro* antifungal and antibacterial activity of the same and other (n=90) compounds related to pyrazine showed no significant results with exception of one pyrazine-2-carboxyamide derivative with broad-spectrum antifungal effect.

Literature:

J. Zitko; P. Paterová; V. Kubíček et al. *Bioorg. Med. Chem. Lett*. 23, 476–479, 2013.
B. Servusová; D. Eibinová; M. Doležal et al. *Molecules*. 17, 13183–13198, 2012
M. Krátký, J. Vinšová, V. Buchta, J. Stolaříková. *Chem. Listy*. 106, 565, 2012

Project was supported by the Internal Grant Agency of Ministry of Health, No NT/13346-4

Address for correspondence: Vladimír Buchta, Dept. of Clinical Microbiology, Charles University in Prague, Faculty of Medicine in Hradec Králové, Sokolska tr. 581, 500 05 Hradec Králové, Czech Republic; vladimir.buchta@fnhk.cz

Title of the project: Targeted screening of colorectal cancer in patients with type 2 diabetes mellitus and in subjects with high cardiovascular risk: a prospective multicentre study

Grant Agency: Ministry of Health ***Project Number:*** NT/13673-4

Principal Investigator: Š. Suchánek

Co-investigators: J. Bureš, J. Cyrany, D. Kohoutová, A. Šmahelová, M. Kubíčková, A. Homola, J. Vinšová, M. Středová, L. Pázlerová, P. Hlúbik

Starting date: 1.4.2012 ***Duration (years):*** 4

Total funds allocated for project - Kč (thousands): 15143

Summary of 2012 results

Title of the presentation: Targeted screening of colorectal cancer in type 2 diabetes mellitus and in subjects with high cardiovascular risk: a prospective multicentre study

Authors: J. Bureš (for and on behalf of co-investigators)

Colorectal cancer occurs more frequently in patients with type 2 diabetes mellitus and in subjects with metabolic syndrome. The hyperinsulinaemia-hypothesis suggests that elevated levels of insulin and free IGF-1 promote proliferation of colon cells and lead to a survival benefit of transformed cells, ultimately resulting in colorectal cancer. In patients with type 2 diabetes mellitus, epidemiological studies show an increased risk for colorectal cancer and an even higher risk if patients are treated with sulphonylureas or insulin. Moreover, tumour progression at hyperinsulinaemia is more rapid and tumour-associated mortality is increased. Colorectal cancer can be avoided by screening. The aim of this prospective multicentre study is to set the incidence of colorectal cancer in the Czech Republic in type 2 diabetes mellitus and in subjects with high cardiovascular risk according to the Systematic Coronary Risk Evaluation (SCORE) function (SCORE >10%). The second objective of the Project is to assess feasibility and efficacy of the targeted one-step screening programme by means of primary screening colonoscopy. Seven Czech centres entered the study in the cooperation with general practitioners and the Institute of Biostatistics and Analyses.

Address for correspondence: J. Bureš, 2nd Department of Internal Medicine – Gastroenterology, Charles Univ. Faculty of Medicine and University Hospital Hradec Králové, Sokolská 581, 500 05 Hradec Králové. E-mail: bures@lfhk.cuni.cz; jan.bures@fnhk.cz

Title of the project: Management of diagnostics and therapy of swallowing disorders

Grant Agency: Ministry of Health ***Project Number:*** NT/13725-4

Principal Investigator: M. Černý

Co-investigators: P. Mandysová, K. Zeleník

Starting date: 1.4.2012 ***Duration (years):*** 4

Total funds allocated for project - Kč (thousands): 4005

Summary of 2012 results

Title of the presentation: Establishing of dysphagia team in University Hospital Hradec Králové

Authors: M. Černý, V. Chrobok, J. Šatanková, D. Stránská, J. Hofmanová (1), J. Dědková, P. Dvořák (2), D. Zimandlová (3), J. Víšek (4), L. Strmisková, M. Vališ (5), E. Vaňásková (6)
University Hospital Hradec Králové: Dpt. of Otolaryngology (1), Dpt. of Radiology (2), 2nd Dpt. of Internal Medicine Gastroenterology (3), 3rd Dpt. of Internal Medicine Metabolic Care and Gerontology (4), Dpt. of Neurology (5), Dpt. of Rehabilitation (6)

The swallowing disorder (dysphagia) is a serious medical and socio-economical problem occurring in variety of diagnosis and medical conditions. Long lasting or severe forms of dysphagia may lead to critical complications, and any dysphagia significantly worsens the quality of life of the patient. The guideline for complex care and managing of dysphagia patients in Czech Republic had so far not been established.
Diagnostics and treatment belong to interdisciplinary teams including otolaryngology, speech and language pathologist, neurology, radiology, gastroenterology, clinical nutrition physiotherapy/ergotherapy. For treatment effect evaluation some assessment tools are necessary.
In 2012 in University Hospital Hradec Králové the dysphagia team was formed and the basic rules for handling patients were set up. Special Flexible Endoscopic Evaluation of Swallowing (FEES), Modified Barium Swallowing (MBS) and Oesophageal Impedance examination were introduced to the diagnostic scheme. By the FEES 110 patients, 73 male and 37 female, were examined. Quality of Life Questionnaires SWAL-QOL and SWAL-CARE were translated to Czech and the process for validation has been started and will be finished in first half of 2013. Further data are expected by the end of 2013.

Address for correspondence: M. Černý, Department of Otolaryngology, University Hospital Hradec Králové, Sokolská 581, 500 05 Hradec Králové, Czech Republic

Title of the project: New procedures in diagnostics and therapy of lifestyle diseases and diseases connected with ageing of population.

Grant Agency: Charles University ***Project Number:*** P 37

Principal Investigator: M. Červinka

Co-investigators: Z. Červinková, Z. Fiala, M. Kaška, J. Krejsek, M. Kuba, J. Malý, S. Mičuda, J. Mokrý, A. Ryška, E. Rudolf, R. Pudil, L. Sobotka

Starting date: 1.7.2012 ***Duration (years):*** 5

Total funds allocated for the project - Kč (thousands): 39000

Summary of 2012 results

Title of the presentation: New procedures in diagnostics and therapy of lifestyle diseases and diseases connected with ageing of population.

Authors: M. Červinka, Z. Červinková, Z. Fiala, M. Kaška, J. Krejsek, M. Kuba, J. Malý, S. Mičuda, J. Mokrý, A. Ryška, E. Rudolf, R. Pudil, L. Sobotka

The PRVOUK project is focused on the most current problems of Czech as well as world medicine. The starting point of the project is the fact that population ageing and associated health problems, increasing number of people suffering from lifestyle diseases and the necessity to use rationally the finance sources to cover the needs of general population health care are interconnected. These reasons have originated the need to realise intensive, effective and complex research in this area.

In tune with the above mentioned facts the project is focused on three basic areas in which the Faculty of Medicine of Charles University in Hradec Králové has had a long and successful tradition:

1. Research in the sphere of lifestyle diseases affecting cardiovascular system is focused on problems of ischemic heart disease, sudden heart death and specification of risks, but also on a non-pharmacological and pharmacological prevention of such events. Another sphere of the research are the conditions for regeneration of myocardium in experiment and in clinical practice and diseases affecting gastrointestinal system (functional disorders, precarcinoses, usage of the latest diagnostic methods, possibilities for prevention and so on.
2. The sphere of oncology and haemato-oncology: The study of prediction of the impact and toxicity of the treatment, importance of individual dosage regulation of medicaments and prediction of the response to these medical procedures. A significant attention is paid to oncological problems of digestive tract. The reason is occurrence of tumours, namely tumours of the large intestine and also probable impact of today´s diet and other lifestyle factors.
3. The problem of ageing and related health problems including the study of regeneration on all levels. The research will be aimed at basic metabolic and molecular manifestation of ageing and on reparation and regeneration processes. An accompanying sphere of interest is the study of damage and reparation on the level of DNA, cell and organ level, including possibilities to influence such processes.

The research tasks to be solved within the PRVOUK project draw upon existing successful research activities (research plan of the faculty, cooperation on other research plans, projects from grants, projects financed from EU funds) and will enable to strengthen existing research teams and quality research results (namely publications in impacted journals or monographs); it will further enable presentation of the results at various professional encounters. Monitoring indicators that are used when evaluating these projects are most of all publications in reviewed journals with an impact factor and monographs and other articles in reviewed professional periodicals.

The research work in the three mentioned interconnected spheres has been realising by 12 working groups. The result of the first year of the project are 100 original research papers and publications with total impact factor of more than 300. The main achievements are:

- Studies in biological response of colon cancer cells to selected cytostatic agents, evaluation of cytotoxicity of new perspective anticancer agents as well as collagenolytic potential of rat liver myofibroblasts.
- Steatotic rat hepatocytes in primary culture are more susceptible to the acute toxic effect of model hepatotoxic substances; During neonatal period mitochondrial permeability transition pore of heart mitochondria is better protected against damaging effect of calcium load and oxidative stress in comparison with liver mitochondria.
- New approaches in diagnostics and therapy of cardiovascular diseases.
- Optimization of surgical therapy in adult patients.
- New information about anthracycline cardiotoxicity, mechanisms of cardioprotective effect of dexratoxane, mechanism of hepatotoxicity of epigallokatechin-gallate.
- Studies of transplantation of bone marrow cells or GFP+lin-Sca-1+ cells into myeloablated mice demonstrate that the induced cell chimerism is not transient in the gastrointestinal tract and could thus be used for long-term treatment of various disorders.
- Electrophysiological differentiation of aging and pathological CNS processes.
- Biomarkers in medicine and evaluation of clinical results in haematology, endocrinology, gastroenterology, cardiology, oncology, psychiatry.
- New markers of toxic effects of polycyclic aromatic hydrocarbons on immune system. Post traumatic development of man
- The immunopathogenesis of foetal inflammatory response syndrome, and dynamics of inflammation induced by either cardiac surgery or talc particles during pleurodesis were investigated.
- Two new tumour entities of salivary glands - cribriform adenocarcinoma and mammary analogue secretory carcinoma have been recently described and characterized.
- We described positive effect of rheophaeresis on nonvascular age-related macular degeneration. In obese type I diabetic patients we found favourable influence of fat reduction on plasma adipocyte fatty acid-binding protein concentration.

- ***Address for correspondence:*** M. Červinka, Charles University in Prague, Faculty of Medicine in Hradec Králové, Šimkova 870, 50038 Hradec Králové, Czech Republic

Title of the project: 9th International Medical Postgraduate Conference

Grant Agency: Ministry of Education ***Project Number:*** 264905

Principal Investigator: M. Červinka

Co-investigators:

Starting date: 1.1.2012 ***Duration (years):*** 1

Total funds allocated for project - Kč (thousands): 1000

Summary of 2012 results

Title of the presentation: New Frontiers in the research of PhD Students

Authors: M. Červinka

The 9th International Medical Postgraduate Conference took place in Hradec Kralove on November 22-23, 2012 under the auspices of Rector of the Charles University in Prague. Medical schools across the Europe nominated 30 students of medical doctoral study programmes from 9 European countries (Great Britain, the Netherlands, Austria, Poland, Hungary Croatia, Georgia, Slovak and Czech Republics). The members of International Evaluation Committee were the experts from 8 countries inclusive the President of ORPHEUS (Organization of PhD Education in Biomedicine and Health Sciences in European System) and the President of Association of Medical Schools in Europe.

All presentations were published in the conference proceedings.

We consider this particular meeting of postgraduate students in biomedicine very important from the point of international harmonisation of PhD studies in Europe and for its multidisciplinary focus. The participants often find that other fields of medicine are interesting and benefical for them and how knowledge of other areas of medicine may be valuable.

The other conference aims were also fulfilled, namely comparing achieved results and levels of PhD programmes at medical schools, presentation of the scientific works, meeting the students and experts from European countries and the opportunity to discuss common problems.

The best three participants received a financial award.

Address for correspondence: M. Červinka, Dept. of Medical Biology and Genetics, Charles University in Prague, Faculty of Medicine in Hradec Králové, Šimkova 870, 500 38 Hradec Králové, Czech Republic

Title of the project: Physi-Sci-Net network for the improvement of human resources in research and development through further training of personnel and improvement of technical support.

Grant Agency: Ministry of Education ***Project Number:*** CZ 1.07/2.3.00/09.0129

Principal Investigator: O. Kittnar

Co-investigators: Z. Červinková, M. Holeček, M. Adamcová, H. Lotková, P. Staňková

Starting date: 1.9.2009 ***Duration (years):*** 3

Total funds allocated for project - Kč (thousands): 3504105

Summary of 2012 results

Title of the presentation: Physi-Sci-Net - activities organized by the Department of Physiology, Faculty of Medicine in Hradec Kralove in the period 2009 - 2012

Authors: Z. Červinková, M. Holeček, M. Adamcová, H. Lotková

The project aimed to support further education of following target groups: postgraduate students, young tutors and undergraduate students interested in the research field of human physiology and pathophysiology. The additional aim of the project was to establish the optimal conditions for cooperation among young researchers.

Our Dept. of Physiology organized three seminars every year, namely: (1) Evaluation of drug-induced cardiotoxicity and possibilities of its pharmacological cardioprotection; (2) Selected methods to study protein and amino acids metabolism in rat under in vivo and in vitro conditions (3) Hepatocytes as a tool for the evaluation of hepatotoxic and hepatoprotective mechanisms, and one practical course: Evaluation of energy metabolism using high-resolution respirometry. Number of supported persons is given in the table.

Year	**Number of supported persons**				**altogether**
	Seminar 1	Seminar 2	Seminar 3	Practical course	
2010	12	12	16	6	**46**
2011	7	13	6	7	**33**
2012	26	15	15	19	**75**
Sum	**45**	**40**	**37**	**32**	**154**

All participants of the seminars passed the multiple-choice questionnaire and obtained certificate of course attendance. The goal of our activities was clearly achieved. The course contributed to the deepening of theoretical and practical knowledge of participants, exchange of experience and establishment of contacts and cooperation among young people. The seminars and course were highly appreciated by the students. In addition, the study materials prepared under the project PhysiSciNet can be repeatedly used in the study of both undergraduate and postgraduate students.

Address for correspondence: Zuzana Červinková, Dept. of Physiology, Charles University in Prague, Faculty of Medicine in Hradec Králové, Šimkova 870, 500 38 Hradec Králové, Czech Republic. wolff@lfhk.cuni.cz

Title of the project: IMPACT –Innovation, Methodology and Quality of Language Teaching and Language for Specific Purposes Teaching in Tertiary Sphere in the Czech Republic

Grant Agency: Ministry of Education ***Project Number:*** CZ.1.07/2.2.00/28.0233

Principal Investigator: M. Rybičková

Co-investigators: J. Comorek, L. Koláčková, Z. Kůs

Starting date: 1.5.2012 ***Duration (years):*** 3

Total funds allocated for project - Kč (thousands): 3200

Summary of 2012 results

Title of the presentation: Innovation, Methodology and Quality of Language Teaching and Language for Specific Purposes Teaching in Tertiary Sphere in the Czech Republic

Authors: PhDr. Jan Comorek, Ph.D.

The project is focused on two main spheres of teaching foreign languages at tertiary education to students who do not have languages as their major subject. The two spheres are language curricula and language testing. Within the first one the main goal is the innovation of existing curricula so that they fit the requirements of today´s technology and science and within the second the goal is to set up a working general system for testing LSP in all partners of the project and other similar tertiary educators. The project has two other goals – to improve methodology and didactics of foreign language teaching through individual improvement and passing good practice and to introduce collaborative teaching in university type of education.

Concerned languages in the case of the Faculty of Medicine, Hradec Králové, Charles University Prague are Latin and English. (The main Investigator is dealing also with other languages: German, French, Russian, Spanish)

A basis for all evaluations is CEFR (Common European Framework of Reference). General language evaluations are relatively well prepared, structured and objective; on the other hand to evaluate (or to test the level of) language for specific purposes is extremely difficult because of the need to standardise language levels in individual branches. There has been done a little in the area of finance and business but not much in such areas like medicine, law and others. The need to standardise levels and requirements for evaluation bands within CEFR and for individual language skills is very urgent. Its importance has been highlited by students´ need and wish to travel, study and work abroad not only in today´s Europe but overseas.

The project has been planned for three years, the first year (2012) materials for testing and new curricula were gathered and structured test and new curricula were created and moderated. Second year (2013) the investigators will be piloting new tests and new or altered curricula and in the last year (2014) the new system will be implemented in practice.

Address for correspondence: PhDr. Jan Comorek, Ph.D., Dept. of Languages, Charles University in Prague, Faculty of Medicine in Hradec Králové, Czech Republic, comorekj@lfhk.cuni.cz

Title of the project: Molecular biology investigation of somatostatin and estrogen receptors in clinically non-functioning pituitary tumors

Grant Agency: Charles University ***Project Number:*** 723912

Principal Investigator: M. Drastíková

Co-investigators: M. Beránek, F. Gabalec, J. Čáp

Starting date: 3.4.2012 ***Duration (years):*** 3

Total funds allocated for project - Kč (thousands): 243

Summary of 2012 results

Title of the presentation: Molecular biology investigation of somatostatin and estrogen receptors in clinically non-functioning pituitary tumors

Authors: M. Drastíková (1), M. Beránek (1), F. Gabalec (2), J. Čáp (2)
Charles University in Prague-Faculty of Medicine and University Hospital Hradec Kralove, Department of Clinical Biochemistry and Diagnostic (1) and 4th Department of Internal Medicine (2)

Non-functioning pituitary adenomas (NFAs) comprise about 20 % of all pituitary adenomas. Because of supra- or parasellar extension of the tumor, transsphenoidal neurosurgery is often not completely successful and frequently leaves tumor remnants which can regrow. Therefore now therapeutical strategies have been developed, such as medical treatment (somatostatine analogues-SAs, dopamine agonists-DAs and estrogen receptor modulators). The effect of these drugs is mediated by receptors on the cell surface. Our aim is to determine the somatostatin (SSTR1 and 4) and estrogen receptor 1 (ER1) profile in NFAs. Adenoma tissue samples were obtained from 69 patients during transsphenoidal surgery. The group of patients was made up of 41 men (37-87 years old; median 65.5) and 28 women (36-83 years old; median 65.5). Operated tissue samples were immediately submerged in RNA later Tissue Protect and transported to the laboratory. The RNA was isolated by Trizol Reagent and transcribed to cDNA. The expression of the receptors was determined by quantitative real time PCR on RotorGene 6000. Diluted plasmid DNA was used to construct the six-point calibration curve (10^1 – 10^6 copies/µl). Results were normalized to the beta-glucoronidase housekeeping gene.All receptors were expressed in the 69 examined tumor samples. The median relative quantification values were: 63.8 % for SSTR1, 26.1 % for SSTR4, and 75.4 % for ER1.

Address for correspondence: Monika Drastíková, Department of Clinical Biochemistry Faculty of Medicine and University Hospital Hradec Kralove, Sokolská 581, 500 05 Hradec Králové, e-mail: monika.drastikova@fnhk.cz

Title of the project: Treatment of sudden sensorineural hearing loss with rheohaemapheresis

Grant Agency: Ministry of Health ***Project Number:*** NT/13475-4

Principal Investigator: J. Dršata

Co-investigators: V. Chrobok, V. Bláha, M. Bláha, M. Lánská

Starting date: 1.4.2012 ***Duration (years):*** 4

Total funds allocated for project - Kč (thousands): 6374

Summary of 2012 results

Title of the presentation: Treatment of sensorineural hearing loss with rheohaemapheresis.

Sudden idiopathic sensorineural hearing loss (SISHL) is a serious medical, social and economic problem. The disease appears to be a uniform manifestation of heterogeneous causes, which cannot be distinguished in practice. The project is targeted to SSIHL, at which there is no satisfactory, and meta-analyses based effective therapy. The project is based on the promising results of previous studies with nine patients (accepted to publication). Our further study wants to improve hearing by separation of defined spectrum of unfavorable plasmatic substances (mainly protein macromolecules). Patients, refractory to the standard treatment of SSIHL, undergo a series of rheohaemaphereses (1 – 3 procedures) by means of our original modification of cascade plasma filtration. The therapeutic goal is to improve the hearing loss according to exactly elected criteria and also to improve the incidental tinnitus. The treatment effect is controlled by audiometry (pure tone audiometry, tinnitometry, impedance audiometry, brainstem evoked potentials, speech audiometry, otoacoustic emissions, handicap test) and hematological tests (substantial decrease both of fibrinogen level and some other macromolecules level). The whole complex of laboratory and clinical tests was introduced in the first year of the study (2012), first 4 patients have been recruited and successfully treated.

Authors: J. Dršata (1), M. Bláha (2), V. Chrobok (1), M. Lánská (2), E. Rencová (3). Dpt. of ORL HNS (1), 2nd Dpt. of Internal Medicine (2), Dpt. of Ophthalmology (3); University Hospital Hradec Kralove, Charles University in Prague, Faculty of Medicine in Hradec Kralove.

Address for correspondence: Jakub Dršata, MD, Ph.D., Dpt. of ORL-HNS, University Hospital Hradec Kralove, Sokolska 581, 500 05 Hradec Králové, Czech Republic

Title of the project: Evaluation of multimodal therapy in colorectal cancer liver metastases patients treated by multimodal approach in Czech Republic complex oncologic centers

Grant Agency: Ministry of Health ***Project Number:*** NT/13660-4

Principal Investigator: M. Ryska

Co-investigators: A. Ferko

Starting date: 1.4.2012 ***Duration (years):*** 4

Total funds allocated for project - Kč (thousands): 794

Summary of 2012 results

Title of the presentation: Evaluation of multimodal therapy in colorectal cancer liver metastases patients treated by multimodal approach in Czech Republic complex oncologic centers

Authors: Ferko A.(1), Šubrt Z.(1), Kubala E.(2)
(1) Dept. of Surgery, (2) Dept. of Oncology

The aim is to verify the benefits of a multidisciplinary team approach to comprehensive treatment and evaluation of results for groups of patients defined by selected parameters, compare nationwide data with those of selected comprehensive cancer centers, while respecting the customized approach, to evaluate the cost / benefit and quality of life in patients treated for colorectal cancer liver metastases.

Project started in 9/2012. 10 patients operated for colorectal cancer metastatses were prospectively enrolled. All patients treated for colorectal cancer liver metastases in hospital Hradec Králové will be retrospectively included to the on-line database till February 2013.

Address for correspondence: prof. MUDr. A. Ferko, CSc., Dept. of Surgery, University Hospital and Faculty of Medicine in Hradec Králové, Sokolska 581, 500 05, Hradec Králové, Czech Republic

Title of the project: Human Resources for Neurosciences in the Hradec Kralove and Usti Regions

Grant Agency: Ministry of Education ***Project Number:*** CZ.1.07/2.3.00/20.0274

Principal Investigator: E. Syková

Co-investigators: S. Filip, J. Mokrý, J. Petera, S. Řehák, Y. Mazurová, E. Rudolf, G. Dayanithi, J. Syka, P. Jendelová, M. Anděrová

Starting date: 1.11.2012 ***Duration (years):*** 3

Total funds allocated for project - Kč (thousands): 18 728

Summary of 2012 results

Title of the presentation: Human Resources for Neurosciences

Authors: S. Filip (1), E.Syková (2); (1) Oncology and Radiotherapy, Medical Faculty and Teaching Hospital, Hradec Králové; (2) Institute of Experimental Medicine AS CZ, Prague.

At present, the global issues of biotechnology addressed the introduction of new technologies and procedures in the diagnosis and treatment of disease. Request of an interdisciplinary approach leads to a demand for closer cooperation of clinical and research centers. IEM AS CZ in Prague (Institute of Experimental Medicine, Academy of Science), expanded considerably issues of neuroscience, cell therapy and regenerative medicine, and its activity excels in the scientific field and the training of young scientists. Medical Faculty of Charles University in Hradec Kralove has priority status in the education of future physicians in the Czech Republic as well as in clinical medicine, both in diagnosis and therapy. Linking these complementary activities enable to establish new research teams that communicate with each other to create new information and methodological approaches in the diagnosis and treatment of serious diseases. The former cooperation between Medical Faculty in Hradec Kralove and IEM has previously been created by one working group of experts aimed at the regeneration of supporting tissues (cell biology, genetics, orthopedics, neurosurgery, oncology and tissue banks) and developed a new treatment method focused on the treatment of degenerative and traumatic damage to the musculoskeletal system using cellular therapy. The main purpose of the project is to tranfer the theoretical and methodological experience of experiemental scientific teams of IEM to the training of future doctors at the Medical Faculty in particular in the field of neuroscience, and additional current neurooncology directions with high research and social potential.

Address for correspondence: S.Filip, Oncology and Radiotherapy, Medical Faculty and Teaching Hospital in Hradec Králové, Sokolská street 548, 500 05 Hradec Králové, Czech Republic., tel. +420 495 834 618, filip@fnhk.cz

Title of the project: Quantitative analysis of somatostatin receptors in pituitary adenomas.

Grant Agency: Ministry of Health ***Project Number:*** NT/11344-4

Principal Investigator: F. Gabalec

Co-investigators: M. Beránek, J. Čáp, J. Marek

Starting date: 1.9.2010 ***Duration (years):*** 4

Total funds allocated for project - Kč (thousands): 2932

Summary of 2012 results

Title of the presentation: Quantitative analysis of somatostatin receptors in pituitary adenomas – continuous report for Faculty of Medicine

Authors: F. Gabalec[1], M. Drastíková[2], M. Beránek[2], D. Netuka[3], V. Masopust[3], T. Česák[4], J. Machač[5], J. Marek[6], J. Čáp[1]

[1]Fac. Med., Charles Univ. and University Hospital, 4th Department of Internal Medicine, Hradec Králové; [2] Fac. Med., Charles Univ., and University Hospital, Department of Clinical Biochemistry and Diagnostics , Hradec Králové, [3]Dep. of Neurosurgery, Central Military Hospital, Prague, [4]Dep. Of Neurosurgery, Charles Univ. Hospital in Hradec Králové,[5]University Hospital in Olomouc, Dept. of Neurosurgery, [6] 3rd Dept. of Internal Medicine, 1st Faculty of Medicine, Charles Univ. in Prague

The aim of the study is quantitative analysis of somatostatin receptors (sst) in pituitary tumors using real-time RT-PCR and correlation with immunohistochemical profile. This method could help to choose patients profiting from expensive medical treatment with somatostatin analogues and chimeric compounds and preventing residuum tumor growth. Up to now we collected more than 300 hundred specimens of pituitary tumors from 3 departments of neurosurgery in Czech Republic.We finished optimalization for sst_1 and sst_4 and quantitative analysis was performed for all five somatostatine receptors in 78 clinically non-functioning pituitary adenomas. All adenomas expressed $sst_{1,2,3}$ and $_4$. Sst_5 was expressed in 42 % of adenomas. High variability of expression for particular type was present. Sst1 mRNA was expressed from 909.98 to 240069, sst_2 1174.8–146 680.8, sst_3 62.9–46 914.3, sst_4 567-99 226 and sst_5 mRNA 0–43 776.6 (all in copies/5µl cDNA). Sst2 and sst3 expression was not statistically different in regard to histological type of adenoma. Sst5 was highly expressed in silent corticotroph adenomas. A very heterogeneous level of SSTR expression may be the reason why experimental use of dopamine and somatostatine analogs and „dopastatins“ is not clinically effective in the majority of CNFAs.

Project is supported by Ministry of Health Project No. NT/11344-4/2010

Address for correspondence: Filip Gabalec, University Hospital, 4th Department of Internal Medicine, Sokolská 581, 500 05 Hradec Králové, Czech Republic, filip.gabalec@fnhk.cz

Title of the project: Myocardial damage induced by anticancer drugs and ischemia-reperfusion: new possibilities of pharmacological cardioprotection.

Grant Agency: Czech Republic ***Project Number:*** 305/09/0416

Principal Investigator: V. Geršl

Co-investigators: M. Štěrba, O. Lenčová-Popelová, E. Jirkovský, Y. Mazurová, M. Adamcová, T. Šimůnek, A. Vávrová, K. Vávrová, J. Stulík, J. Neckář, F. Kolář, O. Szárszoi

Starting date: 1.1.2009 ***Duration (years):*** 4

Total funds allocated for project - Kč (thousands): 6276

Summary of 2012 results

Title of the presentation: Cardioprotective effects of dexrazoxane and its novel derivatives against anthracycline cardiotoxicity.

Authors: E. Jirkovský (1), J. Roh (2), O. Lenčová-Popelová (1), A. Vávrová (3), Y. Mazurová (4), M. Adamcová (5), T. Šimůnek (3), K. Vávrová (2), M. Štěrba (1), V. Geršl (1)

Fac. Med., Charles Univ., Hr. Králové: Dept. of Pharmacology (1), Dept. of Histol. Embryol. (4), Dept. of Physiol. (5), Fac. Pharm., Charles Univ., Hr. Králové: Dept. of Biochem. Sci. (3), Dept. of Inorg. Organic Chemistry (2)

Cardioprotective effects of dexrazoxane (DEX) were studied on a rabbit model of chronic anthracycline cardiotoxicity (DAU 3 mg/kg, weekly for 10 weeks). DEX (60 mg/kg) was administered either with each DAU dose (early intervention) or since DAU cumulative dose of 300 mg/m^2 (delayed intervention recommended by current guidelines). Both schedules of DEX administration prevented incidence of premature deaths and development of end-stage heart failure. While the early administration of DEX nearly completely prevented systolic dysfunction, histological and molecular alterations in the myocardium, the delayed one was markedly less effective. Furthermore, the cardioprotection did not correspond well with protection from oxidative stress. In addition, four novel DEX derivatives were synthesized - two derivatives of putative active metabolite of DEX (ADR-925) with enhanced lipophilicity (KH-TA4 and JR-1) and two derivatives of DEX (MK-15 and ES-5). Potential protective effects of these compounds were studied both in vitro using isolated cardiomyocytes exposed to DAU and H_2O_2 and in vivo using the rabbit model. While derivatives of the ADR-925 showed a potential to protect the cells from H_2O_2-induced toxicity, they were unable to protect the cells and the rabbit hearts from DAU-induced toxicity. MK-15, a close DEX derivative, which is hydrolyzed to the metabolite with lower chelating capacity, did not show distinct protection against DAU cardiotoxicity in vitro and in vivo. Similar outcomes were found also with ES-5 which is hydrolyzed analogically to DTPA, a well-known metal chelator. These data suggest that early cardioprotection with DEX shows better outcomes and other mechanism than iron chelation and protection from oxidative stress may be important for effective cardioprotection. Supported by the Grant GA CR No. 305/09/0416.

Address for correspondence: V. Geršl, Dept. of Pharmacology, Charles University in Prague, Faculty of Medicine in Hradec Králové, Šimkova 870, 500 38 Hradec Králové, Czech Republic.

Title of the project: Research Center for the Study of Toxic and Protective Effects of Drugs on Cardiovascular System.

Grant Agency: Ministry of Education ***Project Number:*** UNCE 204019/304019

Principal Investigator: T. Šimůnek

Co-investigators: V. Geršl, M. Štěrba, O. Lenčová-Popelová, K. Vávrová, P. Nachtigal, P. Zimčík, P. Kovaříková, R. Kučera, J. Lenčo, I. Němečková, J. Roh, P. Mladěnka, V. Nováková, K. Kopecký, P. Hašková

Starting date: 1.1.2012 ***Duration (years):*** 6

Total funds allocated for project - Kč (thousands): 18152

Summary of 2012 results

Title of the presentation: Study of toxic effects of sunitinib towards cardiovascular system in spontaneously hypertensive and normotensive rats

Authors: M. Štěrba (1), O. Lenčová-Popelová (1), I. Němečková (2), E. Jirkovský (1), M. Hroch (1), M. Adamcová (3), P. Nachtigal (2), T. Šimůnek (4), V. Geršl (1)

Fac. Med., Charles Univ., Hr. Králové: Dept. of Pharmacology (1), Dept. of Physiol. (3), Fac. Pharm., Charles Univ., Hr. Králové: Dept. of Biol. Med. Sci. (2), Dept. of Biochem. Sci. (4)

Sunitinib is a modern targeted anticancer drug belonging into the class of multikinase inhibitors. Although its chronic toxicity has been characterized preclinically, the toxicity towards cardiovascular system has not been documented well. Importantly, recent clinical trials have reported significant cardiotoxicity and heart failure to be associated with this drug as well as frequent incidence of hypertension. Furthermore, mechanisms responsible for the cardiovascular toxicity of this drug are uncertain. Hence, in this study we have administered sunitinib (10 mg/kg, p.o.) daily to WKY and SH rats for 8 weeks and after the 5-days of wash out, the treatment followed for 2 or 8 weeks, respectively. Surprisingly, sunitinib treatment appeared to be better tolerable by SH than WKY rats as judged by body weight gain profile and general toxicity parameters. Hemodynamic parameters were evaluated and currently are being analyzed. The treatment induced slight significant rise of myocardial lipoperoxidation in both treatment groups. Nevertheless, we found no elevation of the cardiac troponin T in plasma, no changes in heart/body weight ratio over the corresponding controls as well as no gross signs of blood congestion, heart failure or cardiomyopathy. However, analysis of the vascular tissue suggested presence of endothelial dysfunction and vascular toxicity. Using immunohistochemistry followed by stereorological analysis we found significant induction of expression of the adhesion molecules (ICAM-1, PECAM-1) and HO-1 in both treatment groups, but induction of expression of endothelin-1, eNOS and iNOS was found only in the SHR. These results will be corroborated by Western Blot and qPCR analyses and compared to functional and morphological changes in heart and vessels to obtain deeper insight into the cardiovascular safety of this drug. Supported by the Research project UNCE 204019/304019/2012.

Address for correspondence: V. Geršl, Dept. of Pharmacology, Charles University in Prague, Faculty of Medicine in Hradec Králové, Šimkova 870, 500 38 Hradec Králové, Czech Republic.

Title of the project: Intensification of Scientific Cooperation and Interconnection of Medical Biophysics Institutes of Medical Faculties in the Czech Republic

Grant Agency: Ministry of Education ***Project Number:*** CZ.1.07/2.4.00/17.0058

Principal Investigator: H. Kolářová

Co-investigators L. Bolek, J. Hanuš, V. Mornstein, J. Rosina

Starting date: 1.6.2011 ***Duration (years):*** 3

Total funds allocated for project - Kč (thousands): 17239

Summary of 2012 results

Title of the presentation: Scientific Cooperation of Medical Biophysics Institutes of Medical Faculties in the Czech Republic in the year 2012

Authors: J. Hanuš, P. Stránský, V. Mašín, A. Bezrouk, J. Záhora, J. Bukač
Fac. Med., Charles Univ., Hr. Králové: Dept. of Medical Biophysics

The main goal of the project is the support of cooperation among departments of medical biophysics of all medical faculties in Czech Republic. The support of educational and scientific activities is realized by organization of local seminars and annual scientific conference (35th Days of Medical Biophysics – in current year). The Czech society of medical physics (one of the 107 professional societies of Czech Medical Association of J.E. Purkyně) guarantees professional quality of these seminars. Six local seminars and traditional 35th scientific conference were realized in the year 2012. The following seminars were prepared and organized by Department of Medical Biophysics of Faculty of Medicine in Hradec Králové: What could physician know about the substitutive material used for tissue implants (20.3.2012), IT support of education and teaching – our experiences with application of LMS Moodle in the course of Medical Biophysics and Biostatistics (30.5.2012). Radiation protection during medical irradiation – what could know the physician indicating medical treatment by using irradiation (25.9.2012). More details about all topics of seminars are presented on the webpage of Czech society of medical physics (http://ww.cslf.cz).

Project was supported by the Operational Programme Education for Competitiveness of Ministry of Education

Address for correspondence: J. Hanuš, Dept. of Medical Biophysics, Charles University in Prague, Faculty of Medicine in Hradec Králové, Šimkova 870, 500 38 Hradec Králové, Czech Republic

Title of the project: Standardization and sharing of educational platform among medical faculties in the MEFANET project

Grant Agency: Ministry of Education ***Project Number:*** CZ.1.07/2.4.00/12.0050

Principal Investigator: D. Schwarz

Co-investigators: L. Bolek, J. Hanuš, V. Mihál

Starting date: 1.10.2009 ***Duration (years):*** 3

Total funds allocated for project - Kč (thousands): 27323

Summary of 2012 results

Title of the presentation: Connection of Faculty of Medicine in Hradec Králové to educational platform Mefanet

Authors: J. Hanuš (1), A. Ryška (2), V. Mašín (1), A. Bezrouk (1), J. Záhora (1) - Fac. Med., Charles Univ., Hr. Králové: Dept. of Medical Biophysics (1), The Fingerland department of Pathology (2)

The main goals of the MEFANET project is to advance medical teaching and learning with the use of modern information and communication technologies. As an instrument for that, MEFANET developed an original and uniform solution for educational web portals which are used, together with a central gate, to offer and share digital educational content. The educational web portal is an official publication platform of the MEFANET network, which serves for publication of electronic versions of all types of educational and teaching materials. Its main task is accessibility to all types of electronic didactic materials developed accross the whole MEFANET network, curently including all medical faculties in Czech and Slovak Republic. There are currently eleven portal platforms developed within the MEFANET project covered by a central gate that allows for effective searching within the whole content available. The publication and education portal of Medical Faculty in Hradec Králové (URL http://mefanet.lfhk.cuni.cz) currently contains 53 educational works from seventeen departments.

Project was supported by the Operational Programme Education for Competitiveness of Ministry of Education

Address for correspondence: J. Hanuš, Dept. of Medical Biophysics, Charles University in Prague, Faculty of Medicine in Hradec Králové, Šimkova 870, 500 38 Hradec Králové, Czech Republic

Title of the project: The relationship between thyroid hormones and haemostasis/haemocoagulation in thyroid cancer patients

Grant Agency: Ministry of Health ***Project Number:*** NT/13535-3

Principal Investigator: J. Horáček

Co-investigators: J. Malý, I. Svilias, J. Vižďa, L. Smolej, J. Čepková

Starting date: 2.4.2012 ***Duration (years):*** 3

Total funds allocated for project - Kč (thousands): 1378

Summary of 2012 results

Title of the presentation: The relationship between thyroid hormones and haemostasis in thyroid cancer patients

Authors: J. Horáček, J. Malý, I. Svilias, J. Vižďa, L. Smolej, J. Čepková

While increasing levels of thyroxine may be a risk factor for venous thromboembolism (1), there is a relative lack of detailed data on the effect of thyroid hormones on haemostatic system. In 2012, we started to analyze multiple markers of haemostasis in a unique cohort of patients shifting from severe hypothyroidism to mild hyperthyroidism during their differentiated thyroid cancer treatment. Following total thyroidectomy for cancer, selected tests are being performed on two occasions: (a) in severe hypothyroidism before radioiodine remnant ablation (TSH around 90 mIU/L), and (b) 6 to 8 weeks later on levothyroxine treatment, with low-normal to suppressed TSH (around 0.3 mIU/L). The changes in the variables are being assessed using Wilcoxon test for paired data. The preliminary results reveal a significant increase in fibrinogen, plasminogen activator inhibitor 1, von Willebrand factor and factor VIII, suggesting a shift towards pro-coagulation activities in the haemostatic balance. In the following course of the project (till 2014), we suppose to recruit more patients (total expected number ca. 90) and to include further tests related to primary haemostasis (i.e. platelet adhesion and aggregation). Our preliminary data give support to the hypothesis of haemostatic system activation (prothrombotic state) in hyperthyroidism (2).

1. van Zaane B, Squizzato A, Huijgen R, van Zanten AP, Fliers E, Cannegieter SC, Büller HR, Gerdes VE, Brandjes DP. Increasing levels of thyroxine as a risk factor for a first venous thrombosis: A case-control study. Blood 2010; 115: 4344-4349

2. Stuijver DJF, van Zaane B, Romualdi E, Brandjes DPM, Gerdes VEA, Squizzato A. The effect of hyperthyroidism on procoagulant, anticoagulant and fibrinolytic factors. Thrombosis and Haemostasis 2012; 108: 1077-1088.

Address for correspondence: Prof. MUDr. Jiří Horáček, CSc., IV. interní klinika, Fakultní nemocnice, Sokolská 581, 50005 Hradec Králové; jiri.horacek@fnhk.cz

Title of the project: Formation of human resources for the Hepatology Institute in Hradec Králové

Grant Agency: Ministry of Education ***Project Number:*** CZ.1.07/2.3.00/09.0082

Principal Investigator: P. Hůlek

Co-investigators: V. Šafka, V. Jirkovský, T. Fejfar, Z. Červinková, S. Rejchrt, A. Krajina

Starting date: 1.8.2009 ***Duration (years):*** 3

Total funds allocated for project - Kč (thousands): 12000

Summary of 2012 results

Title of the presentation: Formation of human resources for the Hepatology Institute in Hradec Králové

Authors: P. Hůlek (1), V. Šafka (2), V. Jirkovský (3)

Fac. Med., Charles Univ. Hr. Králové: 2nd Dept. of Internal Med. (1), Dept. of Physiology (2); Univ. Hospital Hr. Králové, 2nd Dept. of Internal Med. (3)

The aim of the project was to form and build a team of multidisciplinary specialist focused on hepatological research. The method was to increase the specialized knowledge and experience of the academic and other specialized personnel of Medical Faculty and University Hospital in Hradec Králové using different kinds of specialized courses and seminars. Every year, Seminar of experimental hepatology in vitro and Seminal of experimental hepatology in vivo, Course of endoscopy in diagnosis and treatment of hepatological diseases, Course of TIPS, Course of medical statistics, Seminar of good laboratory practice, Seminar of good clinical practice, Seminar on protection, evaluation and administration of intellectual property, Seminar on use of new materials in health care, Seminar on transfer of research and development results into practice, Course on management of human resources in research and development and Course on management of quality and environment took place. All these seminars and courses took place once every year of the project so every course and seminar was organized three times during the project.

Another activity to increase the knowledge of the educated group and its engagement in the national hepatological research was supporting its participation on national liver congress being held every May in Karlovy Vary and enabling all its members short visits at other research centers of the Czech Republic.

Finally, there was a meeting of the whole educated group every year enabling sharing new experience and knowledge within the group. All the activities of the project were announced and shared on the portal www.Hepin.cz which was founded and ran due to the support and for the purpose of this project.

The aims of the project were fulfilled, a group of 44 specialists from different experimental and clinical departments was supported creating condition for another level of cooperation, for the international cooperation in the hepatological research.

Project was supported by the Ministry of Education project OPVK CZ.1.07/2.3.00/09.0082

Address for correspondence: Petr Hůlek, 2nd Dept. of internal medicine, University Hospital Hradec Králové, Sokolská 581, 50005 Hradec Králové

Title of the project: The development of a diagnostic panel for the monitoring of perioperative small bowel injury.

Grant Agency: Ministry of Health ***Project Number:*** NT/13536-4

Principal Investigator: R. Hyšpler

Co-investigators: Z. Zadák, A. Tichá, M. Kaška, I. Svobodová, A. Ferko, E. Havel, J. Cerman, M. Blažek, M. Vašatová, L. Plíšková

Starting date: 1.4.2012 ***Duration (years):*** 4

Total funds allocated for project - Kč (thousands): 5412

Summary of 2012 results

Title of the presentation: Potential markers in small bowel damage

Authors: R. Hyšpler[1], Z. Zadák[1], A. Tichá[1], M. Kaška[2], I. Svobodová[1], A. Ferko[2], E. Havel[2], J. Cerman[2], M. Blažek[2], M. Vašatová[3], L. Plíšková[3]

[1]Dept. of Research and Development, [2]Dept. of Surgery, [3]Dept. of Clinical Biochemistry and Diagnostic, University Hospital Hradec Králové

Gastrointestinal dysfunction in critically ill or postoperative patients is associated with a worse prognosis. The prevalence of gastrointestinal symptoms on the first day in ICU was found to be predictive of patient mortality. The aim of the project is to develop and validate suitable and easily available markers for testing of the severity of perioperative or other damage of the small bowel tissue and the functional reserve of the intestinal mucosa. There is no one universal biochemical marker of small bowel damage available at present. Potential markers of small bowel damage are: intestinal fatty acid binding protein (i-FABP), citrulline, D-lactate, expired hydrogen and bacterial DNA of *Escherichia coli*.

Patients undergoing resection of the large intestine for operable colorectal carcinoma are included in this study. Blood samples are drawn before and 2 hours after surgery and during the following four days. Currently, plasma samples of 15 patients have been analyzed. Intestinal-FABP was analyzed by ELIZA kit (Hycult Biotech, Netherlands), D-lactate by kit Megazyme (Co.Wicklow, Ireland), citrulline was analyzed by HPLC method, bacterial DNA of *Escherichia coli* by real time PCR, and expired hydrogen was analyzed by Gastrolyzer (Bellefonte, USA). Data are presented as mean ± standard deviation. Statistically significant differences ($p < 0,01$) were found in D-lactate (the highest values on the second day after surgery 113,9 ± 40 umol/l vs. before surgery 51,3 ± 11,6 umol/l) and in citrulline (before 35,6 ± 8,8 umol/l followed by significant decrease after surgery). The cohort of patients will consist of 100 probands and data will be analyzed and validated.

The project was supported by Ministry of Health, No NT13536-4/12.

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Title of the project: Comparison of the effect of autologous serum-eye drops and umbilical blood serum-eye drops in patients with ocular surface defects

Grant Agency: Ministry of Health ***Project Number:*** NT/12376-4

Principal Investigator: I. Fales

Co-investigators: N. Jirasková

Starting date: 1.11.2011 ***Duration (years):*** 3

Total funds allocated for project - Kč (thousands): 215

Summary of 2012 results

Title of the presentation: Comparison of the effect of autologous serum and umbilical blood serum in patients with ocular surface defects

Authors: N. Jiraskova

We are the co-investigators of the project NT 12376 on the comparison of efficiency of the autologous serum – eye drops and the umbilical blood serum – eye drops in the patients with severe dry eyes that have no improvement after treatment with artificial tears or lubricants. This project has started in November 2011. Up to now we have solved the technical matters on eye drops production and we have started treatment in carefully selected patients with severe dry eyes and ocular surface defects. First results are very promising.

Address for correspondence: N. Jiraskova, Dept. of Ophthalmology, University Hospital, Hradec Kralove, Sokolska 581, 500 05 Hradec Kralove, Czech republic

Title of the project: Proteomic identification of biomarkers of intraamniotic inflammation in amniotic fluid in preterm birth patients

Grant Agency: Ministry of Education ***Project Number:*** ME10025

Principal Investigator: M. Kacerovský

Co-investigators: J. Lenčo, J. Tošner, M. Link, V. Tambor, H. Hornychová

Starting date: 1.1.2010 ***Duration (years):*** 3

Total funds allocated for project - Kč (thousands): 2763

Summary of 2012 results

Title of the presentation: Proteomic identification of biomarkers of intraamniotic inflammation in amniotic fluid in preterm birth patients

Authors: M. Kacerovský (1), J. Lenčo (2), V. Tambor (3)

University Hospital Hradec Králové, Dept. Obstetrics and Gynaecology (1), Univ. Defence, Fac. Military Health Sci. Inst. Molecular Pathology (2), University Hospital Hradec Králové, Biomedical Research Center (3)

Advanced proteomic methods have been used to identify novel potential biomarkers of intraamniotic infection in amniotic fluid from preterm birth patients with intact membranes. All samples were collected during active labor by transvaginal amniocentesis at the Perinatal Research Center, Nashville, TN, USA. The amniotic fluid samples from caucasian women were classified into two groups with respect to the presence (n=31) and absence (n=26) of both microbial invasion of the amniotic cavity and histological chorioamnionitis. The exploratory proteomic analysis of pooled amniotic fluid samples, involving removal of ballast proteins, peptide fractionation based on the presence of cysteine, initial separation on reversed phase at basic pH, and eventually, reversed-phase HPLC-MALDI-TOF/TOF analysis of a total 32 fractions, led to the recording of 26.230 MS/MS spectra, identifying 13.259 distinct peptides at a maximum 5% FDR. Based on these peptides, 1091 amniotic fluid proteins were identified at a maximum 5% FDR. The quantitative information obtained owing to the iTRAQ labeling revealed 25 significantly differed proteins ($p \leq 0.05$) between the group with and without both microbial invasion of the amniotic cavity and histological chorioamnionitis. A prioritized candidate list for subsequent verification was compiled. Based on the statistical and proteomics criteria, 16 proteins (ubiquitin, cystatin-SA, lipocalin-1, antileukoproteinase, neutrophil defensin 3, glycodelin, carbonic anhydrase 1, complement component 8 beta chain, collagen alpha -1 (I) chain, triosephosphatase isomerase, actin cytoplasmic 1, nicotinamide phosphoribosyltransferase, mucin-5B, matrix-remodelling associated protein 8, filaggrin, and carboxyl peptidase M) were selected for further validation using LC-SRM (Selected Reaction Monitoring) proteomic technology. The LC-SRM results indicate that glycodelin, nicotinamide phosphoribosyltransferase, neutrophil defensin 3 and ubiquitin merit further attention as putative peripartum markers of microbial invasion of the amniotic cavity and histological chorioamnionitis.

Address for correspondence: Marian Kacerovský, Department of Obstetrics and Gynecology, University Hospital Hradec Kralove, Sokolska 581, 50005 Hradec Kralove.

Title of the project: Characterization of the diagnostic potential of native polypeptides in amniotic fluid

Grant Agency: Ministry of Health ***Project Number:*** NT/13599-4

Principal Investigator: J. Lenčo

Co-investigators: M. Kacerovský

Starting date: 1.4.2012 ***Duration (years):*** 4

Total funds allocated for project - Kč (thousands): 3913

Summary of 2012 results

Title of the presentation: Characterization of the diagnostic potential of native polypeptides in amniotic fluid

Authors: M. Kacerovský (1), J. Lenčo (2), M. Vajrychová (2)
University Hospital Hradec Králové, Dept. Obstetrics and Gynaecology (1), Univ. Defence, Fac. Military Health Sci., Inst. Molecular Pathology (2)

To characterize diagnostic potential of amniotic fluid native polypeptides in regard to presence or absence of both microbial invasion of the amniotic cavity (MIAC) and histological chorioamnionitis (HCA) we have been collecting amniotic fluid samples by transabdominal amniocentesis from women with preterm premature rupture of the membranes. Totally, 42 samples were retrieved in 2012, aliquots of which are available for the project.

Independently on sample collection, we performed first series of tests for native peptides isolation. The most straightforward protocol involved protein reduction, protein denaturation with chaotropic agents, ultrafiltration and solid-phase extraction. Using simple fractionation coupled to mass spectrometry we identified native peptides cleaved from several parent proteins (collagen alpha-1(III) chain, collagen alpha-5(IV) chain, collagen alpha-1(I) chain, collagen alpha-1(XI) chain, alpha-2-HS-glycoprotein). Different composition of this segment of amniotic fluid proteome can be expected in MIAC and HCA positive samples.

In addition, using commercially available ELISA kits we assessed concentration of dermcidin and neutrophil gelatinase-associated lipocalin (NGAL) in MIAC and HCA positive (n=17) and negative amniotic fluid samples (n=17). Dermcidin levels in amniotic fluid is not affected by the presence of both MIAC and HCA (p=0.58), whereas NGAL showed significant increase in concentration in positive samples (p<0.0001).

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Title of the project: The relationship between bacterial load in amniotic fluid and the intensity of intraamniotic inflammatory response in women with preterm prelabor rupture of membranes

Grant Agency: Ministry of Health ***Project Number:*** NT/13461-4

Principal Investigator: M. Kacerovský

Co-investigators: C. Andrýs, R. Sleha

Starting date: 1.4.2012 ***Duration (years):*** 4

Total funds allocated for project - Kč (thousands): 3968

Summary of 2012 results

Title of the presentation: Amniotic fluid protein profiles of intraamniotic inflammatory response to *Ureaplasma* spp. and other bacteria

Authors: Marian Kacerovsky(1), Peter Celec (2), Barbora Vlkova (2), Ctirad Andrys (3)
(1) Dept. of OB/GYN, Charles University in Prague, Faculty of Medicine Hradec Kralove.
(2) Institute of Molecular Biomedicine, Comenius University in Bratislava, Slovak Republic.
(3) Dept. of Clinical Immunology and Allergy, University Hospital Hradec Kralove.

This study aimed to evaluate the amniotic fluid protein profiles and the intensity of intraamniotic inflammatory response to *Ureaplasma* spp. and other bacteria, using the multiplex xMAP technology. A total of 145 pregnant women with preterm prelabor rupture of membranes between gestational age 24+0 and 36+6 weeks were included in the study. Amniocenteses were performed. The presence of *Ureaplasma* spp. and other bacteria was evaluated using 16S rRNA gene sequencing. The levels of specific proteins were determined using multiplex xMAP technology. The presence of *Ureaplasma* spp. and other bacteria in the amniotic fluid was associated with increased levels of interleukin (IL)-6, IL-8, IL-10, brain-derived neurotropic factor, granulocyte macrophage colony stimulating factor, monocyte chemotactic protein-1, macrophage inflammatory protein-1, and matrix metalloproteinasis-9. *Ureaplasma* spp. were also associated with increased levels of neurotropin-3 and triggering receptor expressed on myeloid cells-1.
The presence of *Ureaplasma* spp. in the amniotic fluid is associated with a slightly different protein profile of inflammatory response, but the intensity of inflammatory response to *Ureaplasma* spp. is comparable with the inflammatory response to other bacteria.

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Title of the project: Analysis of selected prognostic and predictive markers of oropharyngeal and laryngeal tumours

Grant Agency: Charles University ***Project Number:*** 444311

Principal Investigator: D. Kalfeřt

Co-investigators: J. Vokurka

Starting date: 29.3.2011 ***Duration (years):*** 2

Total funds allocated for project - Kč (thousands): 427

Summary of 2012 results

Title of the presentation: Expression p16INK4a (p16) and galectin-3 in glottic laryngeal cancer

Authors: Kalfeřt D.[1], Laco J.[2], Čelakovský P.[1], Ludvíková M. [3]

Dept. of Otorhinolaryngology and Head and Neck Surgery, University Hospital, Faculty of Medicine in Hradec Kralove, Charles University in Prague (1), The Fingerland Dept. of Pathology, University Hospital, Faculty of Medicine in Hradec Kralove, Charles University in Prague (2), Institute of Biology, Faculty of Medicine in Pilsen, Charles University in Prague (3)

Laryngeal squamous cell carcinoma (LSCC) is one the most common type of the head and neck cancer. LSCCs are often located in the glottic area. Není pravda glottis a supraglotis jsou řadě studií zastoupeny stejně The aim of our study is to assess the significance of p16 and galectin-3 (gal-3) expression in glottic LSCC. Fifty eight patients after surgical treatment of the glottic LSCC were enrolled in the retrospective study. The p16 and gal-3 expression was immunohistochemically detected in tumor tissue. The results were statistically correlated with clinical and pathological parameters.

Protein p16 was expressed in glottic LSCC of 15 patients (25.9%). Statistically significant higher p16 expression was proven in nonsmokers in comparison with smokers (75% versus 18%; p=0.003). Recurrent cancer was diagnosed in 8 patients (13.8%), and all these tumors were p16 negative. Gal-3 was expressed in glottic LSCC of 54 patients (93.1%). The gal-3 expression did not statistically correlate with clinical and pathological parameters.

Our study shows, that p16 expression in glottic LSCC especially in subgroup of nonsmokers suggests that may be the potential association of HPV infection with glottic LSCC. The preliminary results suggest that p16 expression in glottic LSCC may identify patients at low risk of disease recurrence. However, the pathobiology of this tumor as well as predictive role of p16 and gal-3 expression in laryngeal cancer still remains to be better elucidated.
This work was supported by Charles University Grant Agency (Grant No. 444311)

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Title of the project: Leptin and it's relation to grow and bone density of eutrophic and hypotrophic pre-term newborns

Grant Agency: Charles University ***Project Number:*** 432411

Principal Investigator: P. Kanioková Veselá

Co-investigators: M. Bayer

Starting date: 1.1.2011 ***Duration (years):*** 2

Total funds allocated for project - Kč (thousands): 555

Summary of 2012 results

Title of the presentation: Leptin and bone metabolism

Authors: P. Kanioková Veselá, Department of Pediatrics

The peak bone mass volume is result of bone increasing from intrauterine life to early adult life. The growing and developing of bone structure from newborn life and early infancy have a predictive informative value for a quality of bone structure and fracture risk in adult age.
Leptin, a cytokine-like hormone secreted by adipocytes, is known to regulate food intake but has also emerged as a significant factor in the regulation of bone mass. In humans, states of energy deprivation with low serum leptin have been associated with low bone mass.
The aim of this study was to analyse leptin, 25 OH D, osteocalcin, Ca, P in cord blood of pre-term hypothopic and eutrophic newborns and than their blood level during early infancy (first two years of life). In two years of live was analyzed bone mineral density. There was investigated 63 patients. There was not foud significant correlation between bone mineral density and serum leptin level.

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Title of the project: Development of preoperative preparation for a more effective surgical therapy

Grant Agency: Ministry of Education ***Project Number:*** 264904

Principal Investigator: M. Kaška

Co-investigators: A. Ferko, J. Harrer, M. Broďák, P. Šponer, S. Řehák, J. Tošner, P. Rozsíval, V. Chrobok, R. Slezák, V. Černý, D. Šimkovič, J. Manďák, J. Vojáček, P. Žáček, M. Kanta, P. Dostál, J. Špaček, H. Langrová, N. Jirásková, A. Šimůnek, R. Ivančaková, and postgradual students

Starting date: 1.1.2012 ***Duration (years):*** 1

Total funds allocated for project - Kč (thousands): 1042

Summary of 2012 results

Title of the presentation: Advance in surgical patient preoperative preparation.

Authors: Kaška M. et al. (above-mentioned)

Introduction. Up to date methods in preparation of surgical patients for operation are based on very intensive evaluation of all possible risk factors with negative impact on perioperative and postoperative period.

Methods. Clinical trials according to individual groups of patients in the fields of surgery, ophthalmology, gynecology, dentistry, anesthesiology, and otorhinolaryngology dealing with application and evaluation of above mentioned methods.

Clinical results. Surgical group was concentrated on a better outcomes in a field of healing digestive tract anastomoses and number decreasing of anastomotic leakes during postoperative period with the better control of intestinal functions and preoperative nutritive care. Ophthamologic group was focused on an perioperative care in patients with advanced retinal dysfunctions, macular edema, and surgery of eye injuries. Orthopaedists performed next studies in perioperative care for patients with endoprostheses hip and knee joints. Neurosurgeons performed some trials dealing with neurocranial injuries and risk factors prediction in these conditions. Urologists performed clinical trials in patients with prostate gland cancer and tranplantation of kidneys. Cardiosurgeons are continuing in a clinical research of mini-invasive surgery of cordial ischaemic disease and in surgical reparation of heart valvular dysfunctions. Gynecologist were publishing some information about new findings in gynecological organ infections and in predictive process in risk pregnancy and birth injuries and next complications. Anesthesists and intesivists published some new dates about vital important organs tissue microcirculation and emergency methods for management of life threating conditions. Dentists were concentrated on new methods in implantology and conservative management of intrabony defects anf oral inflammations.

Conclusions. Application of results in all surgical investigative groups has very good impact on effective development of medical management in particular specializations.

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Title of the project: Factors affecting apoptosis in the colonic mucosa

Grant Agency: Ministry of Health ***Project Number:*** NT/13413-4

Principal Investigator: D. Kohoutová

Co-investigators: J. Cyrany, I. Tachecí, J. Bureš, P. Morávková, V. Buchta, M. Morávková, M. Drahošová, J. Vávrová, J. Pejchal, D. Šmajs

Starting date: 1.4.2012 ***Duration (years):*** 4

Total funds allocated for project - Kč (thousands): 5789

Summary of 2012 results

Title of the presentation: Apoptosis in the colonic mucosa

Authors: D. Kohoutová

The aim of our project is to determine the degree of apoptosis in the colonic epithelial cells. Apoptosis (programmed cell death) plays undoubtedly an important role how to keep homeostasis of colonocytes and is thought to be altered in the majority of colonic diseases. Factors, which might influence apoptosis, have not been clarified yet in a satisfactory way. We suppose that not only primary disease itself, but also alteration of mucosal prostaglandins and S100 proteins, microbial population and their products (especially bacteriocins) play a role in apoptosis. Painless biopsies from different locations (ascending colon, transverse colon, rectum) are taken during the diagnostic colonoscopy and degree of apoptosis is determined in these biopsies by available methods (counting of apoptotic and mitotic indices in the hematoxylin eosin stained slides by light microscopy, determination of apoptosis by monoclonal antibodies M30). Intestinal microbiota and bacteriocin production are investigated. We have got the very first results from the examinations performed during the year 2012. They provided promising data (apoptotic and mitotic indices differ in patients with large bowel pathology from controls), however the data are not robust enough to carry out final statistical evaluation. We suppose that our project will help to clarify the pathogenesis of serious diseases, to which colorectal carcinoma with its high incidence in the Czech Republic belongs.

Literature:

Farkas-Himsley H, Zhang YS, Yuan M, Musclow CE. Partially purified bacteriocin kills malignant cells by apoptosis: programmed cell death. Cell Mol Biol 1992; 38: 643-651.

West NJ, Courtney ED, Poullis AP, Leicester RJ. Apoptosis in the colonic crypt, colorectal adenomata, and manipulation by chemoprevention. Cancer Epidemiol Biomarkers Prev 2009; 18(6): 1680-1687.

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Title of the project: Risk factors of acute pancreatitis as a complication of double balloon enteroscopy

Grant Agency: Ministry of Health ***Project Number:*** NT/13414-4

Principal Investigator: M. Kopáčová

Co-investigators: J. Bureš, I. Tachecí, S. Rejchrt, J. Vávrová, V. Palička

Starting date: 1.4.2012 ***Duration (years):*** 4

Total funds allocated for project - Kč (thousands): 8467

Summary of 2012 results

Title of the presentation: Risk factors of acute pancreatitis as a complication of double balloon enteroscopy

Authors: M. Kopáčová, J. Bureš, I. Tachecí, S. Rejchrt, J. Vávrová, V. Palička

The introduction of double balloon enteroscopy (DBE) represents a basic technological progress in the investigation of the small bowel. DBE allows endoscopic investigation and treatment of the whole small intestine. The complications of DBE are rare, acute pancreatitis is one of the most redoubtable ones. There is lot of hypotheses explaining this fact: direct trauma of the pancreas caused by pressure of the endoscope against the vertebral column, the disorders in microcirculation during the procedure, increase in intraluminal duodenal pressure during the endoscopic procedure caused by inflation of the two balloons, reflux of duodenal fluids into the pancreatic duct, the timing of the procedure, etc. Our group as the first in the world published a prospective study concerning this risk (1). This current project plans priority investigation of known or supposed protective and risk factors (rehydration, oral DBE, time of procedure, number of cycles, the depth of intubation, CO2 insufflation) in correlation with predicted plasmatic high-risk markers of acute pancreatitis (procalcitonin, hs-CRP, S100 proteins, cathepsin B, PSTI – pancreatic secretory trypsin inhibitor, lactoferrin, E-selectin). The project assumes the outcome of possibility of identifying the high risk patients for DBE pancreatitis. This project is priority and socially weighty.

Reference:

(1) Kopáčová et al. Gastrointest Endosc 2007; 66(6): 1133-1138.

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Title of the project: Pre-attentional processing of visual information in man: electrophysiological study

Grant Agency: Czech Republic ***Project Number:*** 309/09/0869

Principal Investigator: J. Kremláček

Co-investigators: M. Kuba, Z. Kubová, J. Szanyi, J. Langrová, F. Vít

Starting date: 1.1.2009 ***Duration (years):*** 5

Total funds allocated for project - Kč (thousands): 1849

Summary of 2012 results

Title of the presentation: The visual "mismatch negativity" diminished by visual attention load

Authors: J. Kremláček, M. Kuba, Z. Kubová, J. Szanyi, J. Langrová, F. Vít
Fac. Med., Charles Univ., Hradec Králové: Dept. of Pathological Physiology

Mismatch negativity (MMN), a component of the event-related potentials, is evoked when of temporal regularity in the acoustic modality is violated and it is recommended for clinical use (International Federation of Clinical Neurophysiology, 2009). MMN has also been described in the visual modality (vMMN), where its clinical use is still unclear because of high demands on patients' attention.

In our work we used the so-called "roving" paradigm to shorten the time required for vMMN registration. Temporal regularity was built up by repetition of two successive radial movements of opposite directions on the periphery of the visual field. Violation of the regularity was formed by using the opposite direction sequence. To minimize the influence of attention on the vMMN the subjects had to resolve two continuous parallel tasks (detection of semantic and color information) during recording.

We examined a group of 11 subjects (5 women 6 men, age 19 to 25; median 23). While the motion-onset VEP in response to peripheral radial movement and P3 wave in response to target stimuli were clearly defined, we failed to detect statistically significant vMMN.
The results indicate that the suppression of visual attention toward the vMMN stimuli is accompanied by the vMMN elimination (like in the auditory MMN).

Supported by Grant Agency of the Czech Republic 309/09/0869.

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Title of the project: Longitudinal study of visual perception of sight-recovery patients after a long-term sensory deprivation

Grant Agency: Czech Republic ***Project Number:*** P407/12/2528

Principal Investigator: J. Kremláček

Co-investigators: M. Kuba, Z. Kubová, J. Szanyi, J. Langrová, F. Vít

Starting date: 1.1.2012 ***Duration (years):*** 3

Total funds allocated for project - Kč (thousands): 1458

Summary of 2012 results

Title of the presentation: Visual and cognitive evoked potentials in patient with partial recovery of visual functions after 53 years of blindness

Authors: J. Kremláček (1), R. Šikl (2), M. Kuba (1), J. Szanyi (1), Z. Kubová (1), J. Langrová (1), F. Vít (1), M. Šimeček (2), P. Stodůlka (3)
Fac. Med., Charles Univ., Hradec Králové: Dept. of Pathological Physiology (1), Institute of Psychology, Academy of Sciences of the Czech Republic (2), Gemini Eye Clinic, Zlín, Czech Republic (3)

72-year-old subject, KP, who recovered his sight after 53 years of visual deprivation, was examined by visual evoked potentials (VEPs) to pattern-reversal and motion-onset stimuli and by cognitive event related potentials (ERPs) in the oddball paradigm to evaluate the effect of long-term deprivation on a mature visual system. KP lost his sight at the age of 17 years due to a severe corneal involvement and light projection onto his right retina was restored at 71 years by a corneal implant.

Nine months after sight recovery we recorded reproducible responses to all reported stimuli. The response to a pattern reversal contained a P100-like dominant peak that was significantly delayed (260 ms) in comparison to the pattern reversal VEPs of two age matched control subjects examined by stimuli adjusted in size and contrast to match the KP's vision. The motion onset VEPs peaks were also significantly delayed (262 and 272 ms) for KP compared to control responses. The P3b/P300 component of the ERP to target stimuli in the oddball paradigm was not further prolonged in addition to already delayed sensory processing.
KP's degraded vision and extensive sensory deprivation prolonged electrophysiological responses related to contrast reversal and motion detection, whereas his subsequent cognitive processing of visual information was not compromised.

Supported by Grant Agency of the Czech Republic 407/12/2528.

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Title of the project: Mutation of K-ras gene in carcinogenesis of endometrial carcinoma

Grant Agency: Charles University ***Project Number:*** 157310

Principal Investigator: E. Křepinská (Dvořáková)

Co-investigators: M. Chmelařová, V. Palička, J. Špaček

Starting date: 1.5.2010 ***Duration (years):*** 3

Total funds allocated for project - Kč (thousands): 890

Summary of 2012 results

Title of the presentation: Methylation analysis of tumor suppressor genes in endometroid carcinoma of endometrium using Methylation-specific Multiplex Ligation-dependent Probe Amplification (MS-MLPA)

Authors: E. Dvořáková (1), M. Chmelařová (2), V. Palička (2), J. Špaček (1)
Medical Faculty of Charles University and Faculty Hospital Hradec Králové: (1) Department of Obstetrics and Gynecology, (2) Institute for Clinical Biochemistry and Diagnostics.

Epigenetic changes are considered to be a frequent event during tumor development. Hypermethylation of promoter CpG islands represents an alternative mechanism for inactivation of tumor suppressor genes, DNA repair genes, cell cycle regulators and transcription factors. The aim of this study was to investigate promoter methylation of specific genes in endometrial cancer by comparison with normal endometrial tissue.

We used MS–MLPA (Methylation-specific Multiplex ligation-dependent probe amplification) to compare the methylation status of 59 tissue samples of endometroid type of endometrial carcinoma with 20 control samples of non-neoplastic endometrium.

Using a 15% cut-off for methylation, we observed significantly higher methylation in the *CDH13* gene ($p<0,001$) in endometrial cancer group compared to control group. We observed a significantly higher methylation in both *WT1* ($p=0,002$) and *GATA5* ($p=0,05$) genes in IB stage compared with stage IA of endometroid cancer samples. We also observed a significantly higher methylation in *GATA5* gene ($p=0,05$) in the group of poorly differentiated endometroid carcinoma compared with the group of grade 1 and grade 2 tumors. The findings suggest the importance of hypermethylation of *CDH13*, *WT1* and *GATA5* genes in endometrial carcinogenesis and could have implications for future diagnostic and therapeutic strategies of endometrial cancer based on epigenetic changes.

The study was supported by grant GAUK No. 157310.

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Title of the project: The activity of selected platelet and coagulation markers after LDL-apheresis and rheopheresis

Grant Agency: Charles University ***Project Number:*** 373611

Principal Investigator: M. Lánská

Co-investigators: M. Bláha, I. Fátorová, M. Košťál, V. Mašín

Starting date: 1.1.2011 ***Duration (years):*** 3

Total funds allocated for project - Kč (thousands): 860

Summary of 2012 results

Title of the presentation: Dynamics of blood count after rheohemapheresis in age-related macular degeneration - possible association with clinical changes ?

Authors: M. Kostal (1), M. Blaha (1), E. Rencova (2), H.Langrova (2), M. Lanska (1), P. Rozsival (2)

Fac. Med., Charles Univ., Hr. Králové: 4th Dpt. of Internal Medicine, Haematology (1), Dpt. of Ophthalmology (2)

46 patients with age-related macular degeneration were treated with a serie of 8 rheohemapheretic (RHF) procedures.. RHF caused decrease of hemoglobin ($p<0,001$), leukocytes ($p<0,034$) and an increase of platelets ($p=0,005$). We found negative correlation between amount of platelets and their volume. Platelet/MPV ratio was positivly associated with changes in DPED area ($p=0,0286$, Pearson Correlation Coefficient 0,360). Patients with this ratio (before the last rheopheresis) under 23 have significantly worse outcome ($p= 0,007$, mean regression in DPED area 0,809mm2 (±2,79) vs. 3,55 mm2 (±2,89). Conclusion: Basic blood count parameters are changed after RHF and some changes correlate with clinical results (with DPED reduction).

Supported by the Charles University Grant Agency, No 373611.

Address for correspondence: M. Lánská, MD, 4th Dpt. of Medicine, Haematology, Charles University, Faculty of Medicine in Hradec Králové, Sokolskastreet 481, 500 09 Hradec Králové, Czech Republic.

Title of the project: EUFEST and OPTIMISE

Grant Agency: EGRIS , 7 FP EU ***Project Number:*** EUFEST, OptiMise

Principal Investigator: R. Kahn

Co-investigators: J. Masopust, J. Hons, A. Urban, R. Přikryl, T. Kašpárek, P. Mohr, F. Španiel, M. Kopeček, I. Tůma, E. Češková, D. Seifertová

Starting date: 2002 and 2011 ***Duration (years):*** 6 and 6

Total funds allocated for project - Kč (thousands): 572

Summary of 2012 results

Title of the presentation: **EUFEST and OPTIMISE : multinational pragmatic studies in search for optimal antipsychotic treatment in patients with schizophrenia**

Authors: **Libiger J, Masopust J, Tuma I for the Czech EUFEST and Optimise teams**

Optimise is an international multisite trial supported by 7th FP of the EU. Its main objective is to identify the optimal sequence of antipsychotic treatment in first episode schizophrenia. This is of the paramount practical importance, because first episodes are the most sensitive period in the course of the disorder and the treatment success at this stage is significant for the future responsivity of schizophrenia and functional status of patients.The study is based on the results of the preceding EUFEST study, conducted by an international group that included Czech centres. The results led so far to approximately 23 publications with huge impact. Together with the American trial CATIE, the EUFEST project was an indpendent, large scale, prospective and randomized study, that used discontinuation because of any reason as the main outcome measure. This presentation sums up the main results of the EUFEST, that in fact were the first major argument to reconfirm the position of second generation antipsychotics as the more effective treatment than low doses (that do not induce confounding adverse effects) of the standard first generation drug haloperidol. The primary EUFEST outcome separated second generation antipsychotics and haloperidol in Kaplan- Meyer´s survival analysis. Also, the predefined response (PANSS TS>50%) and remission (symptomatic remission over 6 months) criteria supported the superior efficacy of amisulpiride and olanzapine, well in accordance with the results of major recent metaanalyses. Interpretation of results will be discussed as well as additional results based on the EUFEST data: the importance of negative symptoms and the questions on the nature of treatment continuation in a naturalistic study. The distribution of adverse effects and concomitant medication in EUFEST provided data corresponding with the defensive approach to the choice of an antipsychotic. The results of this project, focused on first episode psychosis, provided background for the Optimise protocol.There were more than 100 patient recrutied into this EU supported study so far.

Address for correspondence: Prof. Jan Libiger, Dept. of Psychiatry, Charles University Faculty of Medicine and Faculty Hospital Hradec Králové, Czech Republic, CZ- 500 11

Title of the project: Racionalisation of therapy of multiple myeloma

Grant Agency: Ministry of Health ***Project Number:*** NT/12215-4

Principal Investigator: J. Bačovský

Co-investigators: V. Maisnar, I. Špička, E. Gregora, M. Krejčí

Starting date: 1.9.2011 ***Duration (years):*** 4

Total funds allocated for project - Kč (thousands): 6479

Summary of 2012 results

Title of the presentation: **RMG – Registry of Monoclonal Gammopathies**

Authors: V. Maisnar (1), J. Bačovský (2), I. Špička (3), E. Gregora (4), M. Krejčí (5)

2nd Dept. of Medicine - Div. of Clin. Haematology, Faculty Hospital Hradec Králové (1), 3rd Dept. of Medicine, Faculty Hospital Olomouc (2), 1st Dept. of Medicine, General Faculty Hospital Prague (3), Dept. of Hematology, Faculty Hospital Královské Vinohrady Prague (4), Hemato-oncological Department., University Hospital Brno - Bohunice (5)

Registry of monoclonal gammopathies is one of the main Czech Myeloma Group projects. The purpose of this project is the prospective data analysis of monoclonal gammopathies patients in the region of the middle and also the east Europe including incidence of diseases, therapeutical modalities used, the treatment results and the most frequent adverse events of therapy.

Co-investigators and his datamanagers are responsible for data collection in their Faculty Hospitals, validation and digitalisation of data, which is necessary for planned analysis within different topics of the project. They will participate on statistical analysis, evaluation of different statistical analysis and their presentation at domestic and international scientific meetings according to the agreement with principal investigator.

Registry of monoclonal gammopathies represent the main project of the Czech Myeloma Group. Currently it is registered almost 5.000 patients with monoclonal gammopathies, of them 2984 patients with multiple myeloma and 1811 patients with monoclonal gammopathies of undetermined significance. It is ambitious project ranks among the top 5 similar registers in the world which help us to improve the care about patients with monoclonal gammopathies in Czech republic.

Address for correspondence: V. Maisnar, 2nd Department of Medicine - Division of Clinical Haematology, Charles University in Prague, Faculty Hospital in Hradec Králové, Sokolská 581, 500 05 Hradec Králové, Czech Republic

Title of the project: Influence of epigalocatechingallate (EGCG) on liver regeneration after partial hepatectomy in rats

Grant Agency: Charles University ***Project Number:*** 668512

Principal Investigator: V. Mezera

Co-investigators: Z. Červinková, O. Kučera, A. Moravcová

Starting date: 1.6.2012 ***Duration (years):*** 3

Total funds allocated for project - Kč (thousands): 262

Summary of 2012 results

Title of the presentation: Influence of epigalocatechingallate (EGCG) on early phase of liver regeneration after partial hepatectomy

Authors: V. Mezera, Z. Červinková, O. Kučera, A. Moravcová
Department of Physiology, Faculty of Medicine in Hradec Králové, Charles University in Prague

Liver resection is performed for a variety of malignant and benign focal liver lesions. Protection against the oxidative stress may hypothetically enhance liver regeneration after resection. Partial hepatectomy (PHx) is a well-established model for studying of liver regeneration. In our study, we tested the effect of epigallocatechin gallate (EGCG), an antioxidant from green tea, on early phases of liver regeneration after PHx in rats.

Experimental animals (male Wistar rats, 200-300 g of body weight) were divided into 4 groups: 1) Laparotomy + EGCG at a dose of 50 mg / kg; 2) PHx + Vehiculum; 3) PHx + EGCG at a dose of 20 mg / kg; 4) PHx + EGCG at a dose of 50 mg / kg. We measured body weight and resection alive, biochemical serum testing (blood glucose, total and conjugated bilirubin, ALT, AST, ALP, MDA) and further analysis of regenerating liver after death. All animals survived. Weight of rats did not differ significantly between groups. The rate of liver regeneration did not differ in either of the formulas used. Content of malondialdehyde, glutathione content, amount of the cytokine TNF-alpha, and gene expression of Nqo-1 and HO-1 did not differ significantly among hepatectomized groups.

After hematoxylin-eosine staining, there was an accumulation of lipids in hepatocytes in all hepatectomized groups, none of the rats demonstrated histopathological signs of inflammatory infiltration. In bromdeoxyuridine (BrdU) stained slides, we observed lower incorporation of BrdU (and thus lower DNA synthesis) in group IV when compared to group II and III ($p<0.001$); groups II and III did not differ significantly from each other. Interestingly, activity of executive caspases 3/7 was lower in group IV whe compared to groups II and III ($p<0,01$).

Address for correspondence: Vojtěch Mezera, Department of Physiology, Faculty of Medicine in Hradec Králové, Charles University in Prague, Šimkova 870, 500 38 Hradec Králové, Czech Republic

Title of the project: Breast cancer tumor pathophysiology and its modulation by two plant-derived anticancer agents, boldine and alpha-tomatine

Grant Agency: Ministry of Health ***Project Number:*** NT/13473-3

Principal Investigator: S. Mičuda

Co-investigators: P. Tomšík, L. Suchá, J. Grim, I. Slánská, J. Cermanová, M. Zagórová, M. Řezáčová

Starting date: 1.4.2012 ***Duration (years):*** 3

Total funds allocated for project - Kč (thousands): 3467

Summary of 2012 results

Title of the presentation: Anticancer activity of boldine

Authors: P. Tomšík (1), L. Suchá (1), J. Grim (3), I. Slánská (3), J. Ćmielová (1), J. Cermanová (2), M. Zagórová (2), M. Řezáčová (1), S. Mičuda (2). Fac. Med., Charles Univ., Hr. Králové: Dept. of Medical Biochemistry (1), Dept. of Pharmacology (2), Dept. of Oncology (3)

The aim of the present project is to study breast cancer tumor biology using molecular diagnostics of serum regulatory chemokines during neoadjuvant chemotherapy in patients with breast cancer as well as in mice with a corresponding tumor type. Using this mice model, we are also studying the anti-breast cancer activity, mechanism of action, serum tumor chemokine response, pharmacokinetics, and possible adverse effects and interaction potential of two promising anticancer plant derived agents, boldine and alpha-tomatine. During the first year, we have focused on the serum sample collections from patients undergoing neoadjuvant chemotherapy of breast cancer for cytokine analysis and especially on the preclinical evaluation of anticancer activity of orally administered boldine. We have detected significant anticancer effect of the compound at non-toxic concentrations against solid Ehrlich mammary adenocarcinoma raised in mice. The effect was comparable with that of doxorubicin, the agent commonly used in this indication in humans. Co-administration of both agents showed synergism in cancer mass reduction and the life-span prolongation. The mechanism of boldine action will deserve closer evaluation in the next year of project. Moreover, we have detected significant choleretic activity of boldine in rats after either acute or long-term administration without any sigh of toxic effect. The possible implication of this finding will be further studied.

The project is supported by the grant from Ministry of Education No. NT/13473-3/2012.

Address for correspondence: S. Mičuda, Dept. of Pharmacology, Charles University in Prague, Faculty of Medicine in Hradec Králové, Šimkova 870, 500 38 Hradec Králové, Czech Republi

Title of the project: Pathophysiological mechanisms of diseases – possibilities of prevention, new diagnostic and therapeutic approaches

Grant Agency: Ministry of Education ***Project Number:*** 264901

Principal Investigator: S. Mičuda

Co-investigators: M. Červinka, V. Geršl, Z. Červinková, J. Hanuš, M. Řezáčová, J. Mokrý, Z. Fiala

Starting date: 1.1.2012 ***Duration (years):*** 1

Total funds allocated for project - Kč (thousands): 1694

Summary of 2012 results

Title of the presentation: Pathophysiological mechanisms of diseases – possibilities of prevention, new diagnostic and therapeutic approaches

Authors: S. Mičuda (1), M. Červinka (2), V. Geršl (1), Z. Červinková (3), J. Hanuš (4), M. Řezáčová (5), J. Mokrý (6), Z. Fiala (7). Fac. Med., Charles Univ., Hr. Králové: Dept. of Pharmacology (1), Dept. of Medical Biology and Genetics (2), Dept. of Physiology (3), Dept. of Medical Biophysics (4), Dept. of Medical Biochemistry (5), Dept. of Histology and Embryology (6), Dept. of Hygiene and Preventive Medicine (7)

The present project was focused on the support of postgraduate students' research at the theoretical departments of Faculty of Medicine in Hradec Králové. The scientific background originated from the continuous research of participating groups and the joint aim was to study mechanisms involved in the pathophysiology of diseases and various organ impairments, and consequently to derive and evaluate suitable prophylactic, diagnostic and therapeutic interventions. Thus, the project consisted of both preclinical and clinical parts. The preclinical part was targeted especially at in vitro and in vivo evaluation of various cytostatics with respect to their mechanism of action, capability of different cancer suppression, pharmacokinetics and toxicological events. Special attention was paid to liver mechanisms involved in the protection, impairment and regeneration of the organ after partial hepatectomy or after application of various noxious stimuli such as high fat or sucrose diet or estrogen administration. Importantly, tissue regeneration was also studied with respect to stem cells isolation, cultivation, characterization and transplantation. The clinical research in the project was focused on the identification and quantification of risk factors involved in the origin and development of diseases in population. Biochemical, cytogenetic, immunological or even socioeconomic responses/status of evaluated volunteers were studied after their exposure to chemical (polycyclic aromatic hydrocarbons), physical (noise) or psychological (teaching) insults – usually as a part of their employment. In addition, new diagnostic approaches were studied in neurodegenerative disorders and during the therapy of prostatic cancer. Supported by project No SVV-2012-264901.

Address for correspondence: S. Mičuda, Dept. of Pharmacology, Charles University in Prague, Faculty of Medicine in Hradec Králové, Šimkova 870, 500 38 Hradec Králové, Czech Republi

Title of the project: Centre for innovation in biomedical sciences (CEPIN)

Grant Agency: Ministry of Education ***Project Number:*** CZ.1.07/2.4.00/17.0115

Principal Investigator: J. Špelda

Co-investigators: R. Pudil, Z. Fiala, L. Radoňová, E. Tůmová

Starting date: 1.6.2011 ***Duration (years):*** 3

Total funds allocated for project - Kč (thousands): 19886

Summary of 2012 results

Title of the presentation: CEPIN: Centre for innovation in biomedical sciences

Authors: J. Špelda (1), R. Pudil (2), Z. Fiala (3), L. Radoňová (4), E. Tůmová (5)
Faculty of Medicine, Charles University in Hradec Králové: Grants and International Division (1,4,5), Dept. of Internal Medicine (2,3),

The project is realized within The Operational programme „Education for competitiveness“, the field of support 2.4 Partnership and network.

The main objective of the project is to create a functional network of partners from the area of biomedicine, in particular, and to facilitate their mutual cooperation and transfer of information. The goal is to increase foreknowledge about the activities the main project partners are involved in and to raise awareness about activities of home and foreign companies in biomedicine. The project aims to benefit from the cooperation of the partners and others involved in the project for transfer of research results into practice and, vice versa, for transfer of needs from practice to scientific research.

Main project activities are:

- short term stays of employees and Ph.D. students in European universities and research facilities,
- short term stays of Ph.D. students in Czech research institutions,
- educational activities focused on mutual cooperation of private research companies, and universities, specialized seminars, excursions and annual conferences.

The beneficiary of the project and the main project promoter is Charles University in Prague, Faculty of Medicine in Hradec Králové. The project is realized in cooperation with partners:

- University of Defence, Faculty of Military Health Sciences Hradec Králové,
- Charles University in Prague, Pharmaceutical Faculty in Hradec Králové,
- University Hospital Hradec Králové,
- TECHNOLOGICAL CENTRE Hradec Králové p.s.c,
- University of Hradec Králové, Faculty of Informatics and Management

Detailed information about the project are available on project web pages www.cepin.eu.

Address for correspondence: Jan Špelda, Charles University in Prague, Faculty of Medicine in Hradec Králové, Šimkova 870, 500 38 Hradec Králové, Czech Republic

Title of the project: Genetic prediction of late toxicity of radiotherapy for cervical cancer

Grant Agency: Ministry of Health ***Project Number:*** NT/11334-4

Principal Investigator: J. Petera

Co-investigators: M. Beránek, S. Brokešová, I. Sirák, V. Palička, M. Vošmik, M. Chmelařová

Starting date: 1.9.2010 ***Duration (years):*** 4

Total funds allocated for project - Kč (thousands): 5971

Summary of 2012 results

Title of the presentation: **The significance of polymorphisms in ATM and TGFB1 genes in the prediction of late complications of curative radiotherapy in patients with advanced cervical cancer**

Authors: Simona Paulikova M.D.[1], prof. M.D. Jiri Petera Ph.D.[1], M.D. Igor Sirak Ph.D.[1], M.D. Milan Vosmik Ph.D.[1], Mgr. Monika Drastikova[2], doc. RNDr. Ladislav Dusek[3], Mgr. Michaela Cvanova[3], assoc. Prof.. M.D. Renata Soumarova Ph.D.[4], Martin Beranek, Assoc. Prof., Pharm.D., Ph.D.[2], Spaček Jiri doc.MUDr. Ph.D.,IFEPAG[5]

[1] Department of Oncology and Radiotherapy, University Hospital Hradec Kralove, Czech Republic

[2] Institute of Clinical Biochemistry and Diagnostics, University Hospital Hradec Kralove, Czech Republic

[3] Institute of Biostatistics and Analyses, Masaryk University Brno

[4] Cancer Centre Novy Jicin, Czech Republic

[5] Department of Obstetrics and Gynecology, University Hospital Hradec Kralove, Czech Republic

Abstract

Purpose: The main aim of our study was to establish whether there is a statistically significant association between the occurrence of late toxicity after radiotherapy and the presence of polymorphisms in *ATM* and *TGFB1* in patient treated for cervical cancer.

Methods and Materials: In 55 patients treated with chemoradiotherapy and 102 healthy volunteers, we conducted an analysis of genetic polymorphisms in the *ATM* and *TGFB1* genes using molecular biological methods. Late toxicity was assessed by EORTC/RTOG criteria.

Results: We did not find an association between polymorphism 5557G>A in the ATM gene and late toxicity. A combination of polymorphisms of TGFB1gene, the heterozygous genotype TRIPLE (combination of SNPs -509C>T and L10P with polymorphism del-1552AGG) and DOUBLE1 (combination of SNPs -509C>T and L10P), was statistically significant as a protective factor in the prediction of late toxicity grades III–IV (p = 0.021, results by multi-dimensional logistical regression).

Conclusions: Our study confirmed the postulated association between late toxicity after radiotherapy and two polymorphic genotypes of the gene TGFB1, the TRIPLE and DOUBLE1 heterozygotes. We also established a significant association between the radiation dose to the parametrium 14Gy and grade III–IV complications of late toxicity (p = 0.006).

Address for correspondence: Paulikova Simona, M.D., Department of Oncology and Radiotherapy, University Hospital Hradec Kralove, Sokolska 581, Hradec Kralove 5, 50005, Czech Republic. Fax: : + 420 495 832 081; Phone: +420 495 834 617; E-mail: simonabrokesova@seznam.cz

Title of the project: The influence of fibroblast growth factor FGF-1 on gene expression in liver myofibroblasts

Grant Agency: Charles University ***Project Number:*** 699912

Principal Investigator: E. Peterová

Co-investigators: J. Kanta, K, Foltánová, M. Hajzlerová, A. Mrkvicová, L. Suchá

Starting date: 25.4.2012 ***Duration (years):*** 3

Total funds allocated for project - Kč (thousands): 283

Summary of 2012 results

Title of the presentation: The influence of fibroblast growth factor FGF-1 on gene expression in liver myofibroblasts

Authors: J. Kanta, K, Foltánová, M. Hajzlerová, A. Mrkvicová, L. Suchá

Hepatic myofibroblasts (MFB) contribute to the development of hepatic fibrosis, where connective tissue, mainly type I collagen, replaces the damaged tissue. FGF1 and FGF2 were suggested as agonists in carbon tetrachloride-induced hepatic injury. FGF-1 has an antifibrotic effect in human lungs and keloids - it stimulates the expression of collagenase and decreases the expression of type I collagen. We have used MFB to study the effect of FGF-1 on the expression of genes involved in the formation of liver scar tissue – type I collagen, matrix metalloproteinases (MMPs), their inhibitor TIMP-1 and osteopontin. Collagenase MMP-13 is responsible for cleaving native type I collagen, gelatinase MMP-9 cleaves denatured collagen. Gene expression was studied on mRNA level. MFB were cultured on plastic substrate or on collagen gel. Culture medium was supplemented with FGF-1 or heparin or with a combination of both. Collagen gel mimics cell environment in liver fibrotic tissue. Heparin was added to stabilize the binding of FGF-1 to its receptor and to enhance its biological effect. We found that FGF-1 affected gene expression in MFB. The working concentration depends on the substrate. We found the concentration 25 ng/ml to be effective on plastic, in collagen gel 10ng/ml was used. In combination FGF-1 and heparin we used 10 ng/ml and effective concentration of heparin was 10 µg/ml on plastic and 0.1 µg/ml in gel. The more effective concentration of heparin alone was 10 ug/ml. FGF-1 significantly increased the expression of TIMP-1 and osteopontin in MFB cultured on plastic substrate. When added to the MFB on collagen gel FGF-1 increased the expression of MMP-13 and decreased the expression of type I collagen. When heparin was added to FGF-1, it significantly increased the expression of MMP-13 on both surfaces. Heparin alone didn´t affect the expression of all genes in MFB on plastic, but the gene expression in MFB cultured on the gel was significantly decreased. Collagen is one of components of extracellular matrix. Its quantity increases in liver fibrosis. Another component of extracellular matrix is heparan sulfate that was substituted with heparin in our experiments. The cultivation of MFBs in three-dimensional collagen gel significantly changes their phenotype. Our experiments with MFB on collagen gel show that FGF-1 may have similar effect in these cells as in human lungs and keloids. The expression of MMP-13 was twice as high in MFB cultured with FGF-1 and heparin as the expression of MMP-13 in MFB cultured only with FGF-1. We think that heparin alone may stabilize products of translation measured genes. This theory needs to be confirmed on protein level.

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Title of the project: Targeted proteomic analysis in hypertrophic cardiomyopathy

Grant Agency: Ministry of Health ***Project Number:*** NT/13721-4

Principal Investigator: R. Pudil

Co-investigators: J. Stulík, L. Horáková

Starting date: 1.4.2012 ***Duration (years):*** 4

Total funds allocated for project - Kč (thousands): 5893

Summary of 2012 results

Title of the presentation: Targeted proteomic analysis in hypertrophic cardiomyopathy

Authors: R. Pudil (1), J. Stulík, (2), A. Fučíková (3), L. Horáková (3), J. Lenčo (3)
1- Faculty of Medicine in Hradec Králové, 2 - Institute of Molecular Pathology, Faculty of Military Health Sciences, Hradec Králové, 3 - University Hospital Hradec Králové

The main objective of the proposed project is to verify the analytical potential of selected biomarkers of peripheral blood for diagnostics of hypertrophic cardiomyopathy. The project is focused on verification and validation of the concentration of these proteins in peripheral blood of patients with hypertrophic cardiomyopathy; the comparison of the results with the healthy population and other diseases that are accompanied by structural changes in the myocardium (dilated cardiomyopathy, ischemic heart disease, arterial hypertension and aortic stenosis).
The summary of the 2012 results:
1st: Study population: enrollment of the patients with hypertrophic cardiomyopathy (HCM) into the study, evaluation of the clinical and laboratory data. Preparation of the control groups (healthy blood donors, patients with dilated cardiomyopathy, arterial hypertension, coronary artery disease and aortic valve stenosis).
2nd: The experimental studies focused on the optimal preparation of the blood sample for measurement of mass spectrometry were finished (the effect of urea and quinidine chloride on peptide cleavage was tested) . The results showed that the best result was achieved with urea.
3rd: The evaluation of the selective reaction monitoring (SRM) technique. We focused on the plasma protein fibronectin.
All supportive work was finished. The first plasma samples of the patients will be analyzed in January.

Address for correspondence: prof. MUDr. R.Pudil, Ph.D., Charles University in Prague, Faculty of Medicine in Hradec Králové, Šimkova 870, 50038 Hradec Králové, Czech Republic

Title of the project: Increasing of the R&D capacity at Charles University through new positions for graduates of doctoral studies

Grant Agency: Ministry of Education ***Project Number:*** CZ.1.07/2.3.00/30.0061

Principal Investigator: M. Moravová

Co-investigators: J. Mokrý, S. Mičuda, R. Pudil

Starting date: 1.7.2012 ***Duration (years):*** 3

Total funds allocated for project - Kč (thousands): 9231

Summary of 2012 results

Title of the presentation: POSTDOC II: Increasing of the R&D capacity at Charles University through new positions for graduates of doctoral studies

Authors: R. Pudil, M. Moravová, Grants and International Division, Dean's Office, Faculty of Medicine in Hradec Králové

The project is the second phase of the project POSTDOC I.
The aim of the project is to support the establishment, development and mobility of the research teams of the Faculty of Medicine in Hradec Králové. The project is organized by Charles University and is supported from the European Structural Founds and Ministry of Education, Youth and Sports. The project allows establish seven new research positions for recent PhD graduates (post doc positions) in our medical faculty.
The main activities of the postdocs are focused on three fields. The main field is the research. The students are joining the research teams at our faculty, they also participate in the teaching of the pre- and postgraduate students, and have a possibility to stay in foreign scientific institutions with the aim to learn new research methods and to transfer them in our faculty.
Compared to project POSTDOC I, the project POSTDOC II started later, the research positions are now opened for candidates.

Research characteristics of the postdoc positions:

Postdoc 01: The research will be focused on the development and research application of the new methods for the study of nuclear receptors regulating gene transcription. This research is focused on genes important for liver hemostasis of endo- and xenobiotics and the interaction with medication.

Postdoc 02:

The research will be focused on the stem cell biology: new methods in cultivation of the mezenchymal and pluripotent stem cells and its differentiation. The special attention will be paid to characterization of the biological properties of the stem cells in vitro, evaluation of the cellular kinetics, their potential for differentiation.

Address for correspondence: Ing. Markéta Moravová, Grants and International Division, Dean's Office, Faculty of Medicine in Hradec Králové, Šimkova 870, 50038 Hradec Králové, Czech Republic

Title of the project: Support of establishment, development, and mobility of quality research teams at the Charles University (POSTDOC I)

Grant Agency: Ministry of Education ***Project Number:*** CZ.1.07/2.3.00/30.0022

Principal Investigator: M. Moravová

Co-investigators: R. Pudil, J. Stulík, V. Geršl, J. Mokrý, M. Řezáčová, J. Chládek, H. Řehulková, L. Zídková, M. Hroch, J. Ćmielová, O. Popelová, D. Diaz

Starting date: 1.1.2012 ***Duration (years):*** 3

Total funds allocated for project - Kč (thousands): 26364

Summary of 2012 results

Title of the presentation: POSTDOC I: Support of establishment, development, and mobility of quality research teams at the Charles University

Authors: R. Pudil (1), J. Stulík, (2), Vl. Geršl (3), J.Mokrý (4), M. Rezáčová (5), J. Chládek (6), Faculty of Medicine, Charles University in Hradec Králové: Dept. of Internal Medicine (1,2), Dept. of Pharmacology (3,6), Dept. of Histology (4), Dept. of Medical Biochemistry (5).

The aim of the project is to support the establishment, development and mobility of the research teams of the medical faculty in Hradec Králové. The project is organized by Charles University and is supported from the European Structural Founds and Ministry of Education, Youth and Sports. The project allows establish seven new research positions for recent PhD graduates (post doc positions) in our medical faculty.

The main activities of the postdocs are focused on three fields. The main field is the research. The students are joining the research teams at our faculty, they also participate in the teaching of the pre- and postgraduate students, and have a possibility to stay in foreign scientific institutions with the aim to learn new research methods and to transfer them in our faculty.

Research characteristics of the postdoc positions:

Postdoc 01: Cultivation of stem cells and their characterization incl. proof of their multipotency or pluripotency. Interaction of stem cells with other cells and components of extracellular matrix will be tested using cell transplantation and recellularisation.

Postdoc 02: The introduction of molecular biological methods to help the stem cell research, tuition and training of students in above mentioned methods. Another aim is focused on regulation of activity of stem and tumor cells.

Postdoc 03: Identification of new plasma markers of hypertrophic cardiomyopathy (HCM) using the proteomic methods. Secondary aim is to confirm the uniqueness of new biomarkers that could be potentially useful in clinical practice in the diagnostics of HCM.

Postdoc 04: Identification of new plasma markers of dilated cardiomyopathy using the proteomic approach. Secondary aim is to confirm the uniqueness of these biomarkers. Also, project is based on the use of the methods of targeted proteomic analysis.

Postdoc 05: Research in the field of the antitumor activity of the selected compounds of the natural origin, including natural steroid and apomorphine alcaloids, etc. The research will be focused on pharmacokinetics in mammals.

Postdoc 06: Research in also focused into the field of the antitumor activity of the selected compounds of the natural origin, including natural steroid and apomorphin alcaloids, etc. The main aim of the research will be to study the molecular mechanisms of the cytostatic effects.

Postdoc 07: The study of the molecular mechanisms of anthracycline cardiotoxicity and possibilities of effective pharmacological cardioprotection (the study of the molecular remodeling of the left and right ventricle in response to chronic anthracycline cardiotoxicity, expression of myofibrillar proteins and remodeling).

Address for correspondence: prof. MUDr. R.Pudil, Ph.D., Charles University in Prague, Faculty of Medicine in Hradec Králové, Šimkova 870, 50038 Hradec Králové, Czech Republic

Title of the project: Biobanking and Biomolecular Resources Research Infrastructure (BBMRI)

Grant Agency: Ministry of Education ***Project Number:*** BBMRI_CZ

Principal Investigator: D. Valík

Co-investigators: A. Ryška, V. Palička, J. Laco, R. Kutová

Starting date: 1.1.2011 ***Duration (years):*** 4

Total funds allocated for project - Kč (thousands): 4500

Summary of 2012 results

Title of the presentation: The Benefits of Cryopreservation

Authors: Laco, J., Ryška, A., Kutová, R., Palička, V.

Cryopreservation is a process where cells or whole tissues are preserved by cooling to sub-zero temperatures, thereby stopping any biological activity, including cell death. This keeps DNA, RNA and proteins intact for further biological and medical research. In this context, the preservation of malignant tumor samples is of particular importance and interest.

During the year 2012, both main solving institutes, i.e. The Fingerland Department of Pathology and Institute of Clinical Biochemistry and Diagnostics, were completely equipped with necessary devices and instruments for cryopreservation. Detailed operating procedures were developed for collection, transport and storage of both patients´ blood samples and fresh tumor tissue samples. Close cooperation with other clinics was initiated and the routine collection of samples will start at the very beginning of the year 2013.

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Title of the project: IT Medik - Innovation and development of General medicine study programme at the Charles University Medical Faculty in Hradec Králové using implementation of information technologies

Grant Agency: Ministry of Education ***Project Number:*** CZ.1.07/2.2.00/15.0164

Principal Investigator: A. Ryška

Co-investigators: J. Hanuš

Starting date: 1.1.2011 ***Duration (years):*** 3

Total funds allocated for project - Kč (thousands): 13031

Summary of 2012 results

Title of the presentation: IT medik - implementation of IT supported teaching in routine curriculum

Authors: A. Ryška, J. Hanuš, M. Mirošová

Modern tution methods include more and more implementation of information technologies. Students, who are fully familiar with use of computers, tablets, smartphones etc. are open to use these means and thus the teachers have to reflect this paradigm shift. There are basically two different options, how to use IT in teaching of medical students: 1) support of classical teaching (e.g. presentations available in advance, pre-prepared laboratory protocol forms, etc.) or 2) e-learning courses, which can - to certain extent - replace some parts of traditional teaching. This regards namely to classical lectures (student is a passive recipient of information from the teacher) by interactive e-learning courses, which require much deeper engagement of students and enable control of effectivity of the tution.

During first two years of the project, 140 authors from 28 different departments have prepared 1350 hours of presentations and 95 hours of e-learning courses.

Address for correspondence: Prof. Aleš Ryška, MD, Ph.D.; The Fingerland Department of Pathology; Charles University Medical Faculty Hospital; CZ-500 05 Hradec Králové; CZECH REPUBLIC; ryskaale@fnhk.cz

Title of the project: New methods and approaches in diagnostics and search for predictive and prognostic markers in neoplastic disorders

Grant Agency: Ministry of Education ***Project Number:*** 264902

Principal Investigator: A. Ryška

Co-investigators: V. Buchta, A. Krajina, J. Krejsek, P. Živný

Starting date: 1.1.2012 ***Duration (years):*** 1

Total funds allocated for project - Kč (thousands): 1402

Summary of 2012 results

Title of the presentation: New methods and approaches in diagnostics and search for predictive and prognostic markers in neoplastic disorders

Authors: Ryška A (1), Buchta V (2), Krajina A (3), Krejsek J (4), Živný P (5)

(1) The Fingerland Department of Pathology , (2) Institute of Clinical Microbiology, (3) Department of Radiology, (4) Institute of Clinical Immunology and Alergology, (5) Institute of Clinical Biochemistry and Diagnostics

Malignant neoplasms are one of the major groups of diseases with significant impact on healthcare costs, morbidity and mortality in general population. Increasing knowledge of heterogeneity of tumors results in individualization of treatment for each patient (tailored therapy). Therefore, extremely precise classification of neoplasms (grading, staging, typing, molecular profiling, genetic analysis) is essential. In our project we have focused on search for predictive and prognostic markers from different points of view (imaging, biochemical markers, histologic features, immunologic data, etc.). Individual sub-projects included: evaluation of changes in DNA methylation in ovarian cancer (analysis of GATA4 by MS-MLPA and MSP, CDH13 by MS-HRM) and in hepatocellular cancer (methylation of specific promotor regions in 28 tumor supressor genes. In vitro analysis of antimicrobial activity of 15 ftalocyanins on selected bacterial and fungal pathogenes by real-time PCR and DNA sequencing. Study of invasive fungal infections in critically ill patients, focused on Aspergillus and Fusarium sp. Study of effectiveness of high pressure port catheters in 200 patients with malignant tumors. They enable administration of contrast media during CT controls. Series of 12 hypervascularized hepatic tumors (mostly HCC) chemoembolized by microparticles containing cytostatic drugs. Study of 64 inoperable malignant renal tumors (mostly in patients with a solitary kidney) treated by radiofrequency ablation. Study of detection of fusion gene EML4/ALK in lung adenocarcinomas was focused on analysis of sensitivity and specificity of available imunohistochemical and FISH methods to prepare an optimal algorithm for routine testing. Analysis of series of highly aggressive triple-negative breast carcinomas.Altogether, 19 fulltext papers were published, 2 doctoral theses were succesfully defended.

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Title of the project: Optimising extracorporeal elimination strategy with regard to the calcium and phosphate metabolism disturbances (CKD-MBD) in patients with chronic kidney failure

Grant Agency: Ministry of Health ***Project Number:*** NT/11355-4

Principal Investigator: R. Šafránek

Co-investigators: S. Dusilová Sulková, M. Kubišová, E. Mistrík, L. Sobotka

Starting date: 1.9.2010 ***Duration (years):*** 4

Total funds allocated for project - Kč (thousands): 2836

Summary of 2012 results

Title of the presentation: SERUM CONCENTRATIONS OF VITAMIN D-BINDING PROTEIN IN HEMODIALYSIS PATIENTS - NO INFLUENCE OF MEMBRANE FLUX OR DIALYSIS CALCIUM CONCENTRATION

Authors: R. Safranek (1), S. Dusilova Sulkova (1), M. Kalousova (2)

1) Hemodialysis center, Medical Faculty and University Hospital, Hradec Kralove; 2) Institute for Clinical Biochemistry, 1st Medical Faculty, Charles University, Prague; Czech Republic

Clinical significance of vitamin D levels and its supplementation is still debated in dialysis patients. Recent research shows that free and bioavailable vitamin D levels might be more tightly linked to clinical effects of vitamin D than its total levels. Serum concentration of vitamin D-binding protein (DBP) is used for calculations of free and bioavailable fraction of vitamin D. The aim of our work was to investigate effects of renal failure and dialysis treatment on DBP.

Serum DBP was measured in Caucasians - 60 healthy controls and 72 chronic hemodialysis patients using ELISA method. In dialysis patients we repeatedly measured DBP levels before and after dialysis procedure (HD or HDF) to be able to assess effects of different settings of dialysis treatment on DBP concentrations. Postdialysis DBP concentrations were corrected for hemoconcentration using change in total protein concentration. Data are given as median and interquartile range, statistical significance at p 0.05.

We found no significant difference in serum DBP concentrations between healthy controls 216 (162; 248) mcg/ml and dialysis patients 205 (153; 238) mcg/ml, there was no significant effect of age and sex on DBP concentrations. There is no loss of DBP during hemodialysis procedure, on the other hand, we observed slight significant 11% increase in DBP concentration even after correction for hemoconcentration. Results are similar for low-flux hemodialysis and high-flux hemodiafiltration. Serum CRP, parathormone, FGF-23, fetuin-A levels, as well as calcium concentration in dialysis solution has also no association with serum DBP concentrations. During 36 months of follow-up, vitamin D-binding protein was not marker of prognosis.

Availability of vitamin D is not modified by DBP in dialysis patients. DBP concentration may be used in hemodialysis patients for calculations of vitamin D availability regardless of type of treatment and parathormone concentrations.

Supported by the Internal Grant Agency of the Ministry of Health, No. NT/11355-4.

Address for correspondence: R.Šafránek, Hemodialysis Center, University Hospital Hradec Králové, Sokolská 581, 500 05 Hradec Králové, Czech Republic

Title of the project: Regional center II – Center of image data, Operational Programme Europen Structural Fundes, Education for improving competition

Grant Agency: Ministry of Education ***Project Number:*** CZ 1.07/2.2.00/07.0022

Principal Investigator: O. Dostál

Co-investigators: F. Salajka, V. Sedlák, V. Koblížek, V. Bartoš, J. Ruta

Starting date: 1.8.2009 ***Duration (years):*** 3

Total funds allocated for project - Kč (thousands): 2624

Summary of 2012 results

Title of the presentation: Center for digital image processing for medical case reports and education

Authors: **Sedlák, V., Salajka, F., Koblížek, V., Bartoš, V., Ruta, J.**

Aim of the project: creation of new educational materials and innovation of education utilizing new methods of processing of medical image information

Methods: Bronchoscopic unit of Dept. of Respiratory Medicine and the team of medical doctors performing diagnostic and therapeutic bronchoscopic examination was engaged in the study as the co-operating site of principal investigator. The project consisted of instalationof viewing technology and educational materials preparation. 3 PC workstations with DICOM wiever and large LCD panels for educational purposes were installed at different places at the Dept. of Respiratory Medicine. Co-investigator started to harvest interesting and educational medical case reports using images from bronchoscopic examination and CT and CXR scans. The case report were presented as presentations. Education was targeted on medical students of 3rd, 4th and 5th year of general medicine, for medical doctors as a part of postgraduate medication, and postgraduate nurse education.

Results: During run of the project were 580 case reports and presentation created and stored in presenting PC workstations. We have arraged lectures with presentations of case reports for 225 medical students, 28 medical doctors and 42 nurses. Database of case reports is being used for pregradual and postgradual education after the end of the project. Part of the case reports were offered to share with the other engaged sites in the project.

Conslusion: The project improved the quality of pregraduate and postgraduate medical education in our Department.

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Title of the project: Complex assessment of microenvironment and its impact on clinical course of chronic lymphocytic leukemia.

Grant Agency: Ministry of Health ***Project Number:*** NT/13412-4

Principal Investigator: L. Smolej

Co-investigators: C. Andrýs, V. Řezáčová, D. Vokurková, M. Šimkovič, F. Vrbacký

Starting date: 1.3.2012 ***Duration (years):*** 4

Total funds allocated for project - Kč (thousands): 2451

Summary of 2012 results

Title of the presentation: Complex assessment of microenvironment and its impact on clinical course of chronic lymphocytic leukemia.

Authors: Smolej L[1], Andrýs C[2], Řezáčová V[2], Vokurková D[2], Šimkovič M[1], Vrbacký F[1]
1 - 4th Department of Internal Medicine - Hematology, 2 - Institute of Clinical Immunology and Allergology, University Hospital and Faculty of Medicine, Hradec Králové

Chronic lymphocytic leukemia (CLL) is extremely heterogeneous in terms of prognosis. Nowadays, there is a search for prognostic factors capable of identification of high-risk patients in order to optimize the therapeutic approach. Microenvironment of bone marrow and lymph nodes plays a fundamental role in CLL biology. This project aims to assess prognostic and predictive significance of markers of interaction of CLL cells with the microenvironment and their relationship with clinical course. Assessment of membrane antigens (CD49d, CD31, CD105, CD54), circulating plasma proteins (sCD105, angiopoietin-2, endostatin, thrombospondin-1, TGF-beta1), genes affecting angiogenesis (FGF-2, CD105), and circulating endothelial cells will be performed. The expected benefit of the project lies in improvement of care of CLL patients by identification of independent factors which could be used to refine individual patient´s prognosis and thereby create conditions for the development of novel diagnostic and therapeutic approaches. In 2012, collection of specimens for all of the abovementioned methods started. A pilot study on the surface expression of CD223 (LAG-3), CD49d, and CD31 revealed a very heterogeneous CD49d expression (mean ± standard deviation: 25.3 ± 36.6 %). CD31 was uniformly expressed in very high levels (96.7 ± 6.5 %). On the other hand, expression of CD223 was very low in most patients (2.2 ± 5.6 %). Furthemore, CD31 and CD223 expression was higher in patients with clinically stable disease ($p=0.056$ and $p=0.033$). With regard to gene expression analysis, higher expression of CD105 was associated with shorter time to first treatment and overall survival ($p=0.0003$ and $p=0.066$).These results indicate that the markers we selected may indeed have an important role in the biology and progression of CLL; further results are pending.

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Assoc. Prof. Lukáš Smolej, M.D., Ph.D., 4th Department of Internal Medicine - Hematology, University Hospital and Faculty of Medicine, Sokolská 581, 50005 Hradec Králové, Czech Republic. E-mail: lukas.smolej@fnhk.cz

Title of the project: Neuropsychiatrical Aspects of Neurodegenerative Diseases

Grant Agency: Ministry of Education ***Project Number:*** 0021620849

Principal Investigator: E. Růžička

Co-investigators: S. Nevšímalová, P. Smolík, J. Bušková, D. Kemlink, E. Havrdová, J. Roth, R. Jech, H. Kovářů, Z. Fišar, R. Jirák, K. Kupka, T. Zima, O. Slanař, J. Pláteník, A. Baxová, Z. Seidl, J. Vymětal, M. Hrdlička, J. Vymazal, I. Štětkářová, D. Urgošík

Starting date: 1.1.2007 ***Duration (years):*** 7

Total funds allocated for project - Kč (thousands): 19030

Summary of 2012 results

Title of the presentation: Scoring Sleep in Patients with neurodegenerative disesases.

Authors: P. Smolík

The 2007 edition of the American Association of Sleep Medicine (AASM) Manual for the Scoring of Sleep and Associated Events was a major effort to establish scoring rules for sleep with the best available evidence in the medicine and science of sleep. Their recommendations have been highly influential and are followed by many sleep laboratories throughout the world, including our sleep laboratory. According to the authors, the manual is not intended to remain immutable and should be reviewed on a periodic basis with additions, modifications, and deletions made based on new scientific data accumulated over interim periods. The emphasis on the continual refinement of methodological issues in polysomnography has been considered as the unsubstitutable presumption of valid results in sleep research. We have followed studies targeted in the scoring of sleep in patients with neurological and psychiatric disorders, particularly in those with neurodegenerative disorders. According to Santamaria et al. "each one of the three parameters used to score sleep—the EEG, the EOG and the mental EMG—may be altered as a result of the neurodegenerative process"(1). Thus, sleep scoring in neurodegenerative diseases needs to follow some different rules than those reported in the Manual. We have collected studies contributed to the recent AASM manual corrections and prepared the set of subsidiary criteria for our own research purpose.

(1) Santamaria J et al: Scoring Sleep in Neurological Patients: The Need for Specific Considerations. Sleep. 2011; 34:1283-4

Address for correspondence: P. Smolík, Dpt. of Psychiatry, Charles University Prague, Faculty of Medicine Hradec Králové, Sokolovská 581, 500 05 Hradec Králové, Czech Republic

Title of the project: Predictive factors of pathologic response to neoadjuvant chemotherapy in patients with HER-2 positive or triple negative breast carcinoma

Grant Agency: Ministry of Health ***Project Number:*** NT/13564-4

Principal Investigator: B. Melichar

Co-investigators: H. Študentová, T. Adam, Z. Kolář, N. Zlámalová, K. Cwiertka, E. Hlídková, J. Ehrmann, D. Solichová, L. Krčmová, A. Ryška, H. Hornychová, J. Dvořák

Starting date: 1.4.2012 ***Duration (years):*** 4

Total funds allocated for project – Kč (thousands): 9900

Summary of 2012 results

Title of the presentation: Prevalence of perfusion defects detected by stress technetium-99m sestamibi myocardial perfusion single-photon emission computed tomography in asymptomatic patients with breast cancer

Authors: B. Melichar, J. Doležal, H. Kalábová, L. Krčmová, M. Kašparová, R. Hyšpler, H. Procházková-Študentová, V. Šrámek, M. Vošmik, M. Pecka, A. Svobodník, D. Solichová

With improved survival of many types of cancer, long-term sequels of the disease or therapy have become an important issue. An increased incidence of complications of atherosclerosis has been noted in cancer survivors. The aim of the present study was to investigate relation between myocardial perfusion assessed during stress with single-photon emission computed tomography (SPECT) and laboratory parameters of atherosclerosis risk in asymptomatic patients with breast carcinoma. One-hundred and eighty-one female patients with histologically verified breast carcinoma and no cardiac disorder were included in the present study. SPECT was performed using technetium-99m sestamibi under rest and stress. Hemoglobin, peripheral blood cell count, D-dimers, fibrinogen, glycosylated hemoglobin, serum C-reactive protein (CRP), lipoprotein (a), cholesterol, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, triglycerides, homocysteine, glucose, magnesium, creatinine, uric acid, albumin, retinol, alpha-tocopherol and urinary neopterin, albumin and N-acetyl-beta-D-glucosaminidase (NAG) were measured. Differences between groups of patients were analyzed by the Mann-Whitney U test. Categorical data were analyzed with Fisher exact test. Multivariate analysis was performed using logistic regression. Perfusion defects were detected with SPECT in only 12 patients (7%). Higher body-mass index, increased concentrations of D-dimers, CRP, fibrinogen, glucose, triglycerides, urinary albumin, and the history of hypertension or radiotherapy to the left chest wall were associated with increased risk of perfusion defects In conclusion, perfusion defects suggestive of myocardial ischemia are rare in asymptomatic patients with breast cancer. These perfusion defects may be increased in patients with the history of the irradiation of the left chest wall.

The project was supported by Ministry of Health Internal Grant Agency, No. NT13564-4/2012

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Title of the project: Tissue trauma and postoperative stress in patients with surgically treated early endometrial cancer stages

Grant Agency: Ministry of Health ***Project Number:*** NT/13566-4

Principal Investigator: R. Pilka

Co-investigators: B. Melichar, M. Kudela, D. Ondrová, T. Adam, D. Friedecký, D. Solichová, L. Krčmová

Starting date: 1.4.2012 ***Duration (years):*** 4

Total funds allocated for project – Kč (thousands): 6986

Summary of 2012 results

Title of the presentation: Prognostic significance of CD3+ tumor-infiltrating lymphocytes in patients with endometrial carcinoma

Authors: P. Čermáková (1), B. Melichar (2,4), M. Tomšová (1), Z. Zoul (2), H. Kalábová (4), J. Špaček (3)

(1) Fingerland Institute of Pathology, (2) Dept. of Oncology and Radiotherapy and (3) Dept. of Gynecology and Obstetrics, Charles University Medical School and Teaching Hospital, Hradec Králové, and (4) Dept. of Oncology, Palacký University Medical School and Teaching Hospital, Olomouc

Objective: Endometrial carcinoma is the most common gynecological cancer in developed countries. The presence of tumor-infiltrating leukocytes was shown to correlate with improved prognosis in tumors of different primary location, including endometrial carcinoma. The aim of the present study was to investigate tumor-infiltrating leukocytes in patients with endometrial carcinoma. **Methods:** We evaluated retrospectively by immunohistochemistry tumor-infiltrating lymphocytes, including $CD3^+$, $CD8^+$ and $C20^+$ tumor-infiltrating lymphocytes (TIL) and $CD68^+$ tumor-associated macrophages (TAM), in tumor specimens of 124 patients with endometrial carcinoma. **Results:** A significant decrease of $CD3^+$ TIL and an increase of $CD68^+$ TAM counts was observed with increasing stage. In patients with early-stage, high-risk tumors, low intraepithelial $CD3^+$ TIL counts were associated with significantly inferior survival. In multivariate analysis in all patients with early-stage tumors as well as in the subgroup of patients with early-stage, high-risk tumor intraepithelial $CD3^+$ TIL counts were an independent predictor of survival. **Conclusion:** Present data demonstrate that in patients with endometrial carcinoma a decrease of intraepithelial $CD3^+$ TIL counts is associated with advanced stage and risk group. Intraepithelial $CD3^+$ TIL counts are also an independent predictor of survival in patients with early tumors.

The project was supported by Ministry of Health Internal Grant Agency, No. NT13566-4/2012

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Title of the project: The use of the synthetic biomaterials in the treatment of the extensive skeletal defects in revision total hip arthroplasty

Grant Agency: Ministry of Health ***Project Number:*** NT/13477-4

Principal Investigator: P. Šponer

Co-investigators: E. Syková, K. Urban

Starting date: 1.4.2012 ***Duration (years):*** 4

Total funds allocated for project - Kč (thousands): 7557

Summary of 2012 results

Title of the presentation: Application of mesenchymal stem cells in bone repair

IGA MH CR NT13477

Authors: P.Šponer (1), E.Syková (2), K.Urban (3), S.Filip (1), V.Palička (1), P.Lesný (2), T.Kučera (3)

1 - Faculty of Medicine in Hradec Kralove

2 - Institute of Experimental Medicine AS CR in Prague

3 - University Hospital Hradec Kralove The aim of the project is preclinical and clinical research of possible improvement of the quality and quantity of the extensive femoral defect´s healing (identified and present during revision total hip arthroplasty) using the application of suitable biomaterial on the base of higly porous osteoconductive scaffold combined with autologous mesenchymal stem cells.

The suitable synthetic biomaterial was identified as a carrier of cultivated mesenchymal stem cells. Vitoss bone graft substitute (tricalcium phosphate biomaterial) will be mixed immediately before orthopaedic application with the mesenchymal cell expanded aseptically under a good manufacturing practice conditions. The algorythm of the exact surgical technique was created. The clinical study to SÚKL was prepared.

According to the literature, the apllication of stem cells looks promising and our future clinical study will explore the use of mesenchymal stem cells as a first-line therapy for bone defects in patients with large femoral defects identified during revision total hip arthroplasty.

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Title of the project: Anthracycline cardiotoxicity – new possibilities of pharmacological cardioprotection and risks of combination with biological targeted anticancer treatment

Grant Agency: Ministry of Health ***Project Number:*** NT/13457-4

Principal Investigator: M. Štěrba

Co-investigators: O. Lenčová-Popelová, E. Jirkovský, V. Geršl, Y. Mazurová, M. Adamcová, T. Šimůnek, A. Vávrová

Starting date: 1.4.2012 ***Duration (years):*** 4

Total funds allocated for project - Kč (thousands): 6372

Summary of 2012 results

Title of the presentation: Study of potential cardioprotective effects of dietary nitrate against chronic anthracycline cardiotoxicity

Authors: O. Lenčová-Popelová (1), E. Jirkovský (1), A. Vávrová (2), Y. Mazurová (3), M. Adamcová (4), T. Šimůnek (2), V. Geršl (1), M. Štěrba (1)

Fac. Med., Charles Univ., Hr. Králové: Dept. of Pharmacology (1), Dept. of Histol. Embryol. (3), Dept. of Physiol. (4), Fac. Pharm., Charles Univ., Hr. Králové: Dept. of Biochem. Sci. (2)

Inorganic nitrites have been found cardioprotective in animal models of myocardial ischemia-reperfusion injury and similar effects were also associated with dietary nitrates, as they are reduced to nitrites in the GIT. Although molecular mechanisms of nitrate/nitrite-induced cardioprotection are not fully understood, it has been connected with modulation of function of complex I and other important proteins through reversible S-nitrosylation. In addition, involvement of several preconditioning pathways has been implicated. Importantly, a recent study by Zhu SG et al. (2011) has suggested that cardioprotective effects of dietary sodium nitrate may be translatable to anthracycline (ANT) cardiotoxicity settings which raised great interest among cardiologists. However, the study tested protective effects of the dietary nitrate against acute ANT cardiotoxicity only. Thus, potential protective effects of this intervention against clinically more relevant chronic ANT cardiotoxicity remain unknown. Furthermore, the safety of this approach may be unsure as released NO may interact with superoxide produced by ANT redox cycling to produce very dangerous peroxynitrite. Moreover, NO releasing compounds have reported to possibly interfere with the antiproliferative effects of anticancer drugs. Hence, in this project we have initiated the study of cardioprotective effects of the dietary sodium nitrate (administered in the same schedule as reported previously) on a well-established rabbit model of chronic ANT cardiotoxicity (daunorubicin 3 mg/kg, weekly for 10 weeks). The first results show that dietary nitrate does not protect animals from daunorubicin-induced premature deaths and collected samples and records will be analyzed further. Supported by the Grant IGA MZ No. NT13457-4/2012.

Literature: Zhu SG et al. J Am Coll Cardiol. 2011;57(21):2181-9.

Address for correspondence: M. Štěrba, Dept. of Pharmacology, Charles University in Prague, Faculty of Medicine in Hradec Králové, Šimkova 870, 500 38 Hradec Králové, Czech Republic.

Title of the project: MEFANET – clinical reasoning

Grant Agency: Ministry of Education ***Project Number:*** CZ.1.07/2.2.00/28.0038

Principal Investigator: D. Schwarz

Co-investigators: I. Tachecí

Starting date: 1.4.2012 ***Duration (years):*** 4

Total funds allocated for project - Kč (thousands): 33982

Summary of 2012 results

Title of the presentation: Virtual patients in undergraduate medicine education

Authors: Ilja Tachecí, Aleš Ryška
Second Dpt. of Internal Medicine, University Hospital, Hradec Králové

Virtual patients (virtual cases) based learning is proven and promising complement of conventional problem-cased learning on medical faculties. One of the important tasks which should be gained during this form of education is adoption of basic diagnostic and therapeutic algorithms. The aim of our project is to develop dynamic database of virtual patients in an outpatient clinic based on educational portal e-kazuistiky.cz. The system will simulate the real clinical practice as much as possible by means of randomly generated set of unique, individual virtual patients (clinical cases). The spectrum of diagnoses, number of patients and criteria for completion of the course will be defined in advance by the tutor. The system is designed as much flexible, as possible, without any limitation regarding type of disease, clinical specialisation, type of diagnostic procedure, etc. The main advantages are comprehensiveness and diversity of presented cases, possibility to compare students' knowledge, possibility to present optimal, suboptimal and incorrect diagnostic algorithm, to demonstrate less frequent or even very rare symptoms, syndromes and diseases. In addition, each student can prepare assigned case individually at home and later on discuss it with the tutor and colleagues during the classes.

During the first year of the project the complete implementation team was formed. We started to contact potential authors and reviewers and developed completely new web interface for authors. The first series of the gastroenterology cases was currently prepared and tested by teachers and students during elective courses: Gastroenterology - virtual cases and digestive endoscopy with positive outcomes. Our portal was also presented during workshop on 6th international conference of Czech and Slovak faculties of medicine (November 27-28, 2012, Brno, Czech Republic). We started to collect the multi-medial databases of findings and diagnosis to improve the spectrum of cases.

Address for correspondence: MUDr.Ilja Tachecí, Ph.D. 2nd. Dpt. of Internal Medicine - Gastroenterology, University Hospital, Hradec Králové

Title of the project: The efficiency of colonic capsule endoscopy in detection of colorectal polyps and cancers comparing to colonoscopy: multicenter, prospective crosses over study

Grant Agency: Ministry of Health ***Project Number:*** NT/11524-5

Principal Investigator: Š. Suchánek

Co-investigators: I. Tachecí, M. Beneš, P. Drastich

Starting date: 1.10.2010 ***Duration (years):*** 5

Total funds allocated for project - Kč (thousands): 7339

Summary of 2012 results

Title of the presentation: The efficiency of colonic capsule endoscopy in detection of colorectal polyps and cancers comparing to colonoscopy: multicenter, prospective crosses over study

Authors: I. Tachecí, T. Douda
Second Dpt. of Internal Medicine, University Hospital, Hradec Králové

The colorectal cancer incidence and mortality in the Czech Republic belongs to the highest in the world. Screening of the precancerous lesions represented by adenomas and early cancers is an important part of secondary prevention. Our multicenter, prospective study is focused on comparing efficiency of colonic capsule endoscopy and colonoscopy in detection of colorectal polyps and cancers. In years 2010 – 2014, 232 healthy people (asymptomatic individuals aged ≥ 50) will be examined in all 4 centres participating in our study (first by colonic capsule and afterwards by conventional colonoscopy). The total number of detected lesions (polyps and cancers) , the sensitivity and specificity will be observed and the bowel preparation and acceptability of the examinations will be evaluated. One of the goals of the study is to verify whether capsule colonoscopy could be useful in colorectal cancer screening.

Our project started in October 2010. We developed new methodology and protocol of the capsule colonoscopy and evaluated 35 patients. We observed no clinical complications during capsule endoscopy or colonoscopy. The capsule investigation failed due to the extremely fast peristalsis and capsule excretion in one patient. We identified 34 polyps (up to the 6 mm) and 2 polyps (8 and 10 mm) by means of capsule endoscopy and 34 polyps (up to the 6 mm) and 2 polyps (8 and 11 mm) during the colonoscopy at all. The histology confirmed all polyps as hyperplastic or low grade adenomas, we did not identify any advanced adenomas or carcinoma in our subgroup yet. The polyps missed by capsule endoscopy were localised mostly in right hemicolon and were tiny (from 2 to 5 mm).

Address for correspondence: MUDr.Ilja Tachecí, Ph.D. 2nd. Dpt. of Internal Medicine - Gastroenterology, University Hospital, Hradec Králové

Title of the project: Wireless capsule endoscopy in diagnostics of enteropathy induced by non-steroidal anti-inflammatory drugs

Grant Agency: Ministry of Health ***Project Number:*** NT/13532-4

Principal Investigator: I. Tachecí

Co-investigators: J. Bureš, M. Kopáčová, T. Douda, P. Bradna, S. Rejchrt

Starting date: 1.4.2012 ***Duration (years):*** 4

Total funds allocated for project - Kč (thousands): 4967

Summary of 2012 results

Title of the presentation: The efficiency of capsule endoscopy in detection of non-steroidal anti-inflammatory drugs induced enteropathy

Authors: I. Tachecí, T. Douda
Second Dpt. of Internal Medicine - Gastroenterology, University Hospital, Hradec Králové

The small bowel damage by NSAIDs represents important problem due to the probable high prevalence especially in the elderly polymorbid population. Capsule endoscopy is minimally invasive diagnostic tool enabling accurate investigation of the small intestine. The main goal of our study is to evaluate the clinical, endoscopic, and laboratory characteristics of NSAID-induced enteropathy. We expect statistically significantly higher prevalence of enteropathy in the long-term NSAIDs users in comparison with the control group of healthy volunteers. We also focused on laboratory and/or clinical predictors for NSAIDs induced enteropathy by comparison the endoscopy findings and clinical/laboratory data. We are planning to include 110 individuals divided into the three groups (rheumatoid arthritis patients, osteoarthritis patients and healthy volunteers).

Our project started in April 2012. We developed methodology and protocol of the study and created the databases of potential healthy volunteers and patients with rheumatoid arthritis and osteoarthritis fulfilling inclusion criteria of our study. After addressing them, we put together a schedule and undertake an investigation according to the study protocol. We included first 29 healthy volunteers and 6 patients with osteoarthritis yet.

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Title of the project: Development of production technology and application forms of glutathione with high bioavailability for the suppression of oxidative stress (radiation, chemotherapy)

Grant Agency: Ministry of Commerce ***Project Number:*** FR-TI3/496

Principal Investigator: Z. Zadák

Co-investigators: R. Hyšpler, A. Tichá, I. Svobodová, J. Krejcarová, M. Vacková, S. Janáčková

Starting date: 1.3.2011 ***Duration (years):*** 4

Total funds allocated for project - Kč (thousands): 19700

Summary of 2012 results

Title of the presentation: Glutathione, its bioavailability and possible chemical modifications

Authors: Z. Zadák, R. Hyšpler, A. Tichá, I. Svobodová, J. Krejcarová, M. Vacková, S. Janáčková
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Glutathione (GSH) is a ubiquitous tripeptide important in cellular redox equilibrium stability and antioxidative protection. Its supply in various clinical conditions may be beneficial.
During this year, chemical modifications of the GSH molecule were performed with the aim of increasing biological availability. The target of modification was cysteine sulfur as a key part of the GSH molecule. Sulfur reactive, low toxicity compounds may be found in plants of the genus Allium (*Allium cepa*, *Allium sativum*) and these compounds (propanethial *S*-oxide, allicin, allylsulfides,…) were found as efficient modifiers of GSH sulfur. The chemical structure of new compounds was analysed by HPLC-MS. Their biological efficiency and possible toxicity will be tested using in vivo experiments during the following year.

Literature:
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4. FRATERNALE, A., PAOLETTI, M. F., CASABIANCA, A. et al. Antiviral and immunomodulatory properties of new pro-glutathione (GSH) molecules. *Curr Med Chem,* 2006, 13(15), p. 1749-1755.
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Project is supported by Ministry of Commerce, No FR-TI3/496.

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Title of the project: The Use of Tomatine, a Tomato Alkaloid, in the Therapy of Cancer

Grant Agency: Czech Republic ***Project Number:*** P303/12/P536

Principal Investigator: P. Tomšík

Co-investigators: D. Muthná

Starting date: 1.1.2012 ***Duration (years):*** 3

Total funds allocated for project - Kč (thousands): 1.436

Summary of 2012 results

Title of the presentation: The effect of alpha-tomatine on solid tumors in vivo and in vitro

Authors: P. Tomšík (1), S. Mičuda (2), L. Suchá (1), J. Knížek (3), D. Muthná (1), J. Ćmielová (1), Y. Mazurová (4), P. Šuba (1), M. Niang (1), P. Živný (6), E. Čermáková (5), M. Řezáčová (1)

Fac. Med., Charles Univ., Hr. Králové: Dept. of Medical Biochemistry (1), Dept. of Pharmacology (2), Dept. of Medical Biophysics (3), Dept. of of Histology and Embryology (4), Computer Technology Center (5), Univers. Hospital Hr. Králové: Inst. for Clinical Biochem. and Diagnostics (6)

During the first year, we evaluated the effect of alpha-tomatine, a glycoalkaloid from tomatoes, on solid Ehrlich tumor in mice as well as on different cancer cell lines, including MCF-7 (human breast cancer) in vitro. Alpha-tomatine inhibited dose-dependently both the tumor growth and the proliferation activity of tumor cells in vivo. Its combination with doxorubicin showed a synergistic effect and significantly prolonged the survival of the mice. On the other hand, neither alpha-tomatine nor doxorubicin influenced the infiltration of tumors with CD3+ lymphocytes. We also could not find an in vivo modulation of iNOS and phosphorylated ERK2, formerly reported in vitro as the principal anti-cancer mechanism of alpha-tomatine.

Alpha-tomatine however inhibited DNA and protein synthesis in Ehrlich tumor cells in a short-term culture in vitro. In MCF-7 cells, alpha-tomatine reduced viability and proliferation. Nevertheless, it induced neither single- nor double-strand DNA breaks, nor it induced apoptosis.

Some experimental data were used for the development of new biostatistical methods which we described in three studies; they include the optimization of the point and interval estimates of IC50.

The project is supported by the grant GACR P303/12/P536.

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Title of the project: Risk factors for development of CMV virostatic resistance in the patients after allogeneic stem cell transplantation

Grant Agency: Ministry of Health ***Project Number:*** NT/13691-4

Principal Investigator: P. Hubáček

Co-investigators: P. Sedláček, P. Žák, L. Plíšková, E. Vejražková, R. Kutová, M. Lengerová, P. Cetkovský

Starting date: 1.4.2012 ***Duration (years):*** 3

Total funds allocated for project - Kč (thousands): 9827

Summary of 2012 results

Title of the presentation: Incidence and characterization of Cytomegalovirus resistance to antivirals

Authors: P. Žák

Aim of our project is clarify the risk factors involved in the development of virostatic resistance of human cytomegalovirus (CMV)among the patients after allogeneic haematopoietic stem cell transplantation and find potential impact of CMV genetic types on course of the CMV infection and resistance development in these patients. In the project, we plan to use both retrospective and prospective approach which enables us to increase the cohort of patients for statistical analysis. Retrospectively, the stored samples of DNA from CMV positive and treated patients will be tested, while in the cohort of prospectively tested patients, we plan to test CMV DNA and also peripheral blood levels of ganciclovir and valganciclovir to clarify possible influence of different levels on development of CMV drug resistance.

Preliminary results:

Incidence and characterization of Cytomegalovirus resistance to antivirals in children and adult hematopoietic stem cell transplant recipients from the Czech Republic was analyzed between I/2002 – VI/2012. First-line antiviral treatment, usually ganciclovir, was initiated when CMV load exceeded 1,000 normalized viral copies (NVCs), and switched to foscarnet or cidofovir in case of none Clinical resistance was suspected after 2 weeks of unsuccessful well-conducted treatment response.

Mutation of UL97 and UL54 will be analyzed in 70 patients. The samples of peripheral blood were collected from different department of Czech Republic. We examined 16 patients with CMV infection, who were drug resistance. Mutation of UL97 and UL54 weren´t detected. Frozen samples for gancyclovir level analysis are ready for processing.

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