Abstracts

Plenary Session

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New approaches and expertise in technology transfer to fund translational research

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The funding of translational research, particularly in the life sciences, is currently faced with significant challenges. This is especially true for the stages of research that reside between basic academic research, on the one hand, and later stage commercial research and development, on the other. Basic academic research is often funded through government or philanthropic support. Much later, once it has already been demonstrated that an innovation is likely to achieve commercial success, and thus, the risk of failure has been substantially reduced, large companies, venture capital investors or other funding partners are likely to support the research. In between, however, it can be very difficult to find funding support. The challenge, therefore, is how to bridge the co-called "valley of death" in research funding between the academic laboratory and the commercial sector. Doing so requires new approaches and different types of expertise for academic institutions to bring their technologies from the laboratory to the marketplace. There is a need for new, creative sources of funding, which at times requires investment by the academic institution itself. Coordinating the process of identifying innovations that are worthy of funding and then managing the investments once they are made are often not within the skill set of academic technology transfer office personnel. Even if the personnel possess these skills, utilizing those skills might consume so much time and effort that it would be unreasonable for the office to undertake those tasks on a regular basis for what could become a significant portfolio of projects and investments. This session will describe several new programs that Cedars-Sinai Medical Center has established to meet these challenges – bridging the research funding valley of death and deploying a staffing model, including specific outside expertise that supports these activities without overburdening the technology transfer office. The session will also include a case study featuring a technology developed in South America that Cedars-Sinai is bringing to the global marketplace through use of this enhanced, modern approach to technology transfer.

Update of research and perspectives of collaboration of Institute of Cell Biology (ICB) within RECOOP association

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There are several basic research approaches which are presently developed in the Department of Regulation of Cell Proliferation and Apoptosis at the ICB (NAS of Ukraine) and are perspective for conducting closer collaboration within the RECOOP Association:
1) NanoBioTech. Project: Development of novel magnetic and polymeric nanoscale materials for medical treatment and diagnostics (ex. bio-imaging of apoptotic cells and macrophages). RECOOP partners: Institute of Macromolecular Chemistry (Prague, Czech Republic), Wroclaw Technical University (Wroclaw, Poland), Institute of Biochemistry (Kyiv, Ukraine). None-RECOOP partner: Lviv National Polytechnic University (Lviv, Ukraine).
2) Cancer. Project: Pre-clinical study (*in vitro* and *in vivo*) of novel anticancer drugs of natural (Landomycins) and synthetic (4-thiazolidone derivatives) origin. RECOOP partners: Lviv National Medical University (actual partner), Pecz University (potential partner under the Visegrad fellowship support). None-RECOOP partner: Institute for Cancer Research at Vienna Medical University, Austria). See posters of Panchuk et al. and Chumak et al.
3) Stress (Immunity and Autoimmunity). Project: Immunoglobulin glycosylation as a diagnostic instrument at autoimmune diseases. RECOOP partner: University of Osijek, Croatia (planned). None-RECOOP partner: Medical University in Erlangen, Germany. See poster of Bilyy et al.
5) Cardiovascular Diseases. Project: Identification of novel genes capable of protecting against massive cell death (via apoptosis and necroptosis) after ischaemia-reperfusion, as well as after tumor-induced cachexia and neurodegenerative processes. Potential RECOOP partners: Institute of Cardiology, Debrecen, Hungary, Clinic for Internal Medicine, Osijek, Croatia. None-RECOOP partner: Percuros BV & Leiden University Medical Center, The Netherlands). See poster of Korchynskyi et al.
5) Preterm Birth. Project: Identification of novel auto-antigens and specific gene polymorphism involved in pathogenesis of the recurrent pregnancy loss (RPL). Potential RECOOP partner: Department of Obstetrics and Gynaecology, Charles University in Prague, Faculty of Medicine Hradec Kralove, University Hospital Hradec Kralove, Czech Republic, School of Medicine, Osijek, Croatia. None-RECOOP Partner: Institute of the Hereditary Pathology, Lviv, Ukraine). See poster of Zastavna & Kit et al.
6) Infection in Reproductive Biology. Project: Targeting glycocalyx for identification and isolation of specific (ex. apoptotic) cells at infection by the uropathogenic strains of E. coli in women. Interested RECOOP partners are welcome to joint the project. None-RECOOP partner: University of Lille, France. See poster of Dumych et al.

Infantile hemangiomas and retinopathy of prematurity: common mechanisms of pathogenesis?

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Aims: Retinopathy of prematurity (ROP) is an eye disease that affects the retina of the preterm infant and can cause impairment of vision. Infantile hemangiomas (IHs) are benign vascular tumors that develop in infancy. Studying IH and ROP may further increase our understanding of the mechanisms of normal or abnormal vasculogenesis.
Methods: We undertook the present study to examine the concordance between IH and ROP in populations of preterm infants in the U.S. and Hungary. Clinically collected data from infants with gestational ages less than 32 weeks born between May 1, 2007 and December 31, 2010 were analyzed. A total of 897 infants with gestational ages less than 32 weeks were admitted to the NICUs at Iowa and Pécs, 684 subjects were eligible for the study (236 from Pécs and 448 from Iowa). Their data were entered into a study database and were analyzed by center and then combined through meta-analysis.
Results: There were no significant demographic differences between populations. After univariate analysis of potential covariates in Iowa and Pécs populations, hyperglycemia, transfusion, infection, breast feeding, postnatal corticosteroids, gestational age, birth weight, highest bilirubin, and days on oxygen were all related significantly to IH or ROP and entered into a logistic regression model. After stepwise regression, hemangioma remained in the logistic regression model in each population but showed only a trend toward significant relation to ROP. When the corrected associations from the two populations were combined through random effects meta-analysis, a significant relationship between IH and ROP was detected (OR=1.84, 95 % CI 1.08-3.12).
Conclusions: These combined results suggest that IH and ROP do not occur independently in preterm infants. Further study of these conditions and their association may shed new light on the role of abnormal vasculogenesis in these disorders and on common mechanisms of pathogenesis in IH and ROP.
Key Words: Angiogenesis · Hemangioma · Preterm infants · Retinopathy of prematurity

Markers to diagnose infection in PPROM

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Spontaneous preterm birth is an enduring and principal cause of perinatal morbidity and mortality worldwide. Approximately 30 % of all preterm births are preceded by preterm prelabor rupture of membranes (PPROM). Besides requiring acute intensive care, the newborns are often threatened by lifelong adverse sequelae (e.g. cerebral palsy).

One of the most common complications of PPROM is microbial invasion of the amniotic cavity (MIAC), which complicates PPROM in approximately 30 % of cases. Specific motifs on the microbial surface, as well as endogenous molecules released from damaged tissue and cells, are recognized by pattern recognition receptors.

Activation of these specific receptors lead to the development of intraamniotic inflammation (elevated levels of inflammatory mediators in the amniotic fluid) followed by the recruitment of neutrophils and other immune cells from the uterine wall to the placenta and fetal membranes. The neutrophil infiltration of the placenta and fetal membranes is then called histological chorioamnionitis (HCA). The presence of MIAC leading to HCA, determining an infectious phenotype of PPROM, is responsible for serious neonatal morbidity, including chronic pulmonary diseases and adverse neurodevelopmental outcome, both of which have long-term consequences on quality of life and health care costs.

This suggests that the identification of MIAC and HCA is crucial for improving neonatal outcome and parental counselling of women at risk. Regrettably, there is no robust diagnostic tool currently available for identifying these conditions. Nevertheless, proteomic analyses of amniotic fluid and ultrasound evaluation of the fetus offer alternative view on the protein composition and functional changes associated with these pathological conditions.

Luminescent carbon materials in medicine

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The strong request for fluorescence materials for sensing, imaging, cell targeting, physical destruction and drug delivery lead to nanoscale structures of carbon. They include graphene G-dots, graphene oxide GO-dots, modified carbon nanotubes, nanodiamonds and, essentially, the C-dots that combine simplicity of production and absence of toxicity with high brightness. The properties of these new materials will be analyzed with the focus on their presently realized and prospective applications as scaffolds for constructing multifunctional nanocomposites.

In these applications, carbon nanomaterials feature essential advantages over semiconductor Quantum Dots. Their production is easy, inexpensive and 'green'. They can be made of different sizes, and high surface areas and simple co-synthetic incorporation of reactive groups allows assembling the structures of different functionalities. The absence of toxicity and high drug-carrying ability offer additional advantages. In contrast to organic dyes they do not bleach under strong visible or UV light.

The *in vitro* and *in vivo* applications of these materials are on initial stage and their success will be illustrated on several examples.

Pneumococcal conjugate vaccines

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Pneumococcal disease is a major cause of morbidity and mortality throughout the world and Invasive pneumococcal disease (IPD) represents a significant burden to individuals and to society. A highly effective pneumococcal conjugate vaccine (PCV), offering protection against disease caused by seven virulent serotypes, was first licensed in the USA in 2000 and has since been incorporated into the immunization programs of an increasing number of developed countries for children up to 5 years of age. New vaccine formulations containing more conjugated serotypes have been developed and licensed afterwards. The incidence and mortality of IPD, including bacteremic pneumococcal pneumonia, is especially elevated in older adults and risk of pneumococcal diseases development is multiplied in chronic ill adults. This is the reason why originally pediatric formulation of PCV13 was licensed for adults recently.

However still some questions remains: immunogenicity of pneumococcal vaccines particularly in elderly and patients with chronic diseases impairing immunity, immunosenescence, serotype coverage, hyporesponsiveness, herd effect, effect of paracetamol on immunogenicity of vaccines, etc.

Existing pneumococcal conjugate vaccines (PCVs) have significantly decreased the incidence of pneumococcal disease, although a high disease burden still remains. Widespread use of PCVs has also contributed to a shift in serotype epidemiology. Therefore, there is still a need for new pneumococcal vaccines that offer broader serotype coverage.

To meet this need, pneumococcal proteins that are highly conserved amongst Streptococcus pneumoniae strains, which may then induce protection against all pneumococcal serotypes are tested. The *S. pneumoniae* proteins, histidine triad protein D (PhtD) and detoxified pneumolysin (dPly), either alone, or in combination with PCVs, are potential candidates for such vaccines.

KEYWORDS: Immunization, *S. pneumoniae*, conjugate vaccines, Invasive pneumococcal disease

Gender-related differences in coronary artery disease risk factors in three Central European countries

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Aims: The clinical characteristics of coronary artery disease (CAD) vary between populations depending on various risk factors, and CAD has a different pattern in male and female patients. To explore these differences, we analyzed clinical data from patients from three Central European countries (Croatia, Czech Republic and Hungary) presenting with CAD, with a special focus on gender-related differences. Since Split is a Mediterranean city, we expected to see differences compared to the other three centers which are continental. Methods: Data was obtained from patients hospitalized for CAD in 2007 in two centers in Croatia (Osijek and Split) and one center in both Czech Republic (Prague) and Hungary (Debrecen) . This comparison focuses on differences in traditional CAD risk factors– age and gender, body mass index (BMI), cholesterol and HDL, LDL and triglyceride levels. The sample included 295 patients from Osijek, 195 from Split, 247 from Debrecen and 400 from Prague. Results: Patients from Split were the oldest on admission (68.8 ± 11.5 years; $p < 0.001$), followed by patients from Osijek, Debrecen and Prague. The difference in age on admission is mostly due to the age of male patients in Split. Also, female patients in Croatia were older than females in Debrecen and Prague ($p = 0.002$). Patients from Split also had the lowest BMI ($p < 0.001$), with similar results in other centers. Hypertension was most prevalent in Split (71.4 %), followed by Debrecen, Osijek and Prague. The chi-square test for prevalence of diabetes was not significant in male patients, but was significant in females, with Debrecen having the largest prevalence (38.1 %). Cholesterol values were similarly high in Split, Osijek and Prague, with Debrecen having the lowest values ($p < 0.001$). HDL was highest in Split and Debrecen, but the difference is again due to values male patients' values, in females the four-way comparison was not significant. LDL was highest in Split and Prague, followed by Osijek and Debrecen. Triglycerides were highest in Split and Osijek, followed by Debrecen and Prague. Again, Split had the highest values due to male patients' results, and Prague had the lowest due to female patients' results. Conclusions: We observed significant differences between the samples. Patients from Split were the oldest, had the lowest BMI and highest HDL, but also had the highest cholesterol, LDL and triglyceride values, which was surprising. This result is most likely due to the advanced age of patients in Split and is mostly caused by high values in male patients, with females having values similar to their counterparts in other Central European centers. Overall, the pattern between the continental centers (Osijek, Debrecen, and Prague) was different to the one in Split which is a Mediterranean city. We observed gender-related differences in every center were involved in Central Europe. Delete: and in general the male patients' values contributed the most to the overall results of the comparisons.

Central and Eastern Europe demography for risk factors in preterm birth

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BACKGROUND: Retrospective studies, which look backward over a period of time and normally attempt to compare the frequency of occurrence of a determinant in groups of diseased and non- diseased individuals.

AIMS: To assess and compare demography risk factors leading to preterm birth in CEE. The main advantage of retrospective studies is that they make use of data that have already been collected like the RECOOP M&CH Research Network did.

METHODS: The demographic data on health indicators (birth and death rate, deliveries, abortion, incidence of offspring), distribution of the population, food consumption, employment and abuses by sex and countries (Romania, Czech Republic, Hungary, Slovakia, Croatia) were collected retrospectively from statistical offices from years 2007 to 2010 by the RECOOP M&CH Research Network.

RESULTS: On the population we have data only from Czech Republic and Slovakia and in both countries are more women than men. Marriages is in average 5 in Slovakia and divorces 2.3 per 1000 inhabitants, in Czech Republic 3. We found live births around 58 000 in Slovakia, 22 000 in Czech Republic and 42 000 in Croatia from years 2007 to 2009. Stillborns were around 200 in Slovakia and Croatia also. The highest birth rate was in Czech Republic 11.5, the next is Slovakia with 10.6 and with 9.9 Croatia in year 2008. The death rate is closed to birth rate, 11.9 was in Romania and 9.5 in Slovakia also in year 2008. The most preterm births were in Czech Republic 13 %, in Croatia 4% and around 7% in Slovakia. Singleton pregnancy predominates in all observed countries but the most deliveries were in Czech Republic (115 000). Twins are also common but triplets and quadruplets occur not often. We gained data also on food consumption in each country. From meat the biggest consumption was of pork in Czech Republic (10 kg), than Slovakia (32 kg) and Croatia (14 kg). After poultry the next often consumed meat was beef. Sugar, cereal and soft drink consumption is big in all countries. In alcohol usage is the winner Slovakia. Narcotics abuse is bigger at men than women in all CEE countries. Some of the parameters were not available in all the countries.

CONCLUSIONS: There is no way of knowing the extent of the similarity between the two different populations therefore it is necessary compare the available population statistical data to the term and preterm birth retrospective data.

KEY WORDS: risk factors, term and preterm birth, CEE

Enteroviruses: a common cause of neonatal sepsis

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Non-polio enteroviruses are the most common viral threats of neonates. Most infections cause only fever but meningo-encephalitis and other -even more serious- afflictions may occur. Neonatal enterovirus sepsis occurs 5–10x more often than Herpes of the neonate and has equally bad consequences. The latter is not always appreciated.

Fever shortly before term leads frequently to a decision to treat the mother with antibiotics and terminate the pregnancy. In case of a bacterial infection this decision is justified, in case of a viral cause it is not: It may even worsen the condition for the child.

Neonatal enterovirus sepsis will be discussed in terms of incidence, diagnosis, prevention and treatment.

Key Words: Enteroviruses, Neonatal sepsis syndrome, maternal infection, treatment, prevention.

RECOOP HST Association's Life Sciences Research (LFSR) Platform

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In 2006 Cedars–Sinai Medical Center (CSMC), Los Angeles, CA, USA with eleven CEE universities and academic organizations from six countries formed the Regional Cooperation for Health, Science and Technology (RECOOP HST) Consortium. The Consortium is continuously growing and beside the 12 Founding Members additional 8 Associate Members are participating in the research and support networks from Croatia, Czech Republic, Denmark, Hungary, Poland, Romania, Slovakia, Ukraine and USA.

In 2012 CSMC converted the Consortium into the Association for Regional Cooperation in the Fields of Health, Science and Technology is registered by the Court of Debrecen in Hungary under the registry number 4160 on May 10, 2012, TAX ID: 18299140-1-09. Members of the Association from 9 countries (Croatia, Czech Republic, Denmark, Hungary, Romania, Slovak Republic, Ukraine and USA) and 16 higher education or research organizations are continuously implementing new research projects.

The RECOOP HST Association's main goal is to enhance research collaboration and provide platforms for scientific networking in life sciences within Europe and Cross – Atlantic. The research priorities of the Association is the major public health problems including women's and children's health, cardiovascular, metabolic, neurologic disorders and cancer in the Visegrad Four European Macro-Region (Czech Republic, Hungary, Poland and Slovakia) and the neighboring countries (Croatia, Romania, Ukraine). The Association with the Mother and Child Health (M&CH) and the Women's Health and Cardiovascular Diseases (WH&CVD) and NanoBioTechnology Research Networks paves the way toward GLOBAL Research Programs and supports the National Institutes of Health, the World Health Organization and private funds (Gates, Clinton) goals to improve the health of public Worldwide.

In the RECOOP Research Networks 147 scientists are working in 17 research projects – basic, translational and clinical research studies. RECOOP scientists and clinicians are investigating biological pathways leading to gender differences in cardiovascular diseases, preterm birth, ovarian, breast and prostate cancer. The M&CH and the WH&CVD Research Networks' retro and prospective clinical research studies are using web based electronic data entry forms (EDEF http://www.flexiform.hu/).

The Association's activities compliment the U.S. Government's commitment to the Global Health Initiative – "is the next chapter in the way U.S. Government agencies conduct global health activities, building on successful bipartisan leadership in global health and expanding their impact for sustainable results around the world." In the Global Health Initiative the U.S. Department of Sate is already building public – private

partnership could be the frame for the regional network development and scientific competitiveness.

All over the World the Health Research Consortiums and Networks should be founded on local qualities and create a critical mass at the regional level in well defined geographical regions have lingual, cultural, historical, economic and/or political common ground like Central and Eastern Europe, Scandinavia, the Benelux Countries, the Mediterranean Countries Arab League, Central and South America, South East Asia and the Anglophone and Francophone Africa. After formation of regional research networks they could compete at the global level as the RECOOP HST Association is doing.

Health Research Consortiums and Networks could provide platform also for the re-entry grants for students and scholars from less developed or developing countries spent years in the USA and in Europe. The G20 countries or the top 28 economies should provide co-funding for re-entry grants.

A strong public – private partnership would be the fundament for the research networks and for the regional young scientists' life sciences conferences. Organizations should solicit support from industry (Pharmaceuticals, Biotechnology & Life Sciences, Health Care Equipment & Services; Food and Beverage, Information Technology, and Energy) and from private founds (Bill & Melinda Gates Foundation, Warren Edward Buffett, the William J. Clinton Foundation).