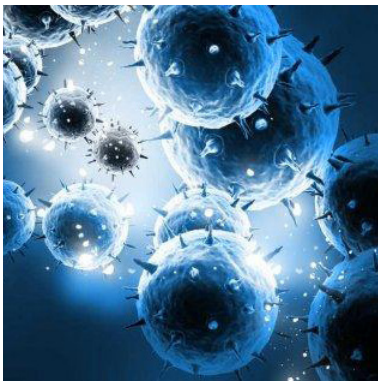
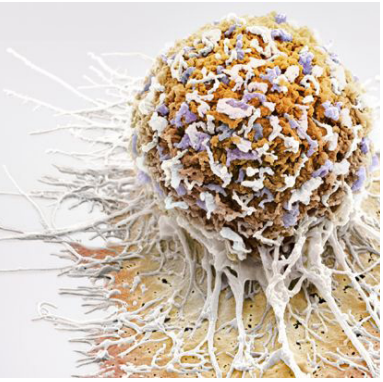
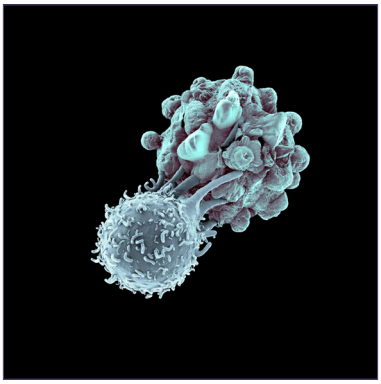
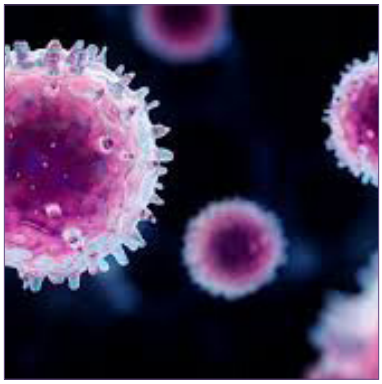
Poster Presentation

Cancer 2018



12th World Cancer Congress

July 23-25, 2018 | Moscow, Russia

Liver-specific gene delivery using engineered virus-like particles of Hepatitis E Virus

Seung Kew Yoon, Eun Byul Lee, Jung-Hee Kim and **Wonhee Hur**
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Virus-like particles (VLPs) possess the potential for organ-specific transport of therapeutic agents owing to their empty space surrounded by viral capsid proteins and a tropism similar to those of with the original viruses. However, there have been few reports on suitable VLPs for target-specific delivery. Hepatitis E virus (HEV) is one of the hepatotropic viruses showing remarkable liver tropism. N-terminal truncated ORF2 (Nt-ORF2) of HEV can form VLPs via self-assembly. In this study, we investigated whether HEV-LPs could specifically deliver foreign genes through tropism to the liver. HEV-LPs were obtained by Nt-ORF2 expression in Huh7 cells transduced with recombinant baculovirus and were then purified by continuous density gradient centrifugation. The purified HEV-LPs efficiently penetrated liver-derived cell lines such as Huh7 cells and SK-Hep-1 cells. Next, to verify the utilization of HEV-LPs as gene delivery tools, GFP-encoding plasmids were encapsulated into HEV-LPs in a disassembly/reassembly procedure. After encapsulation, EGFP was expressed in only liver-derived cells. HEV-LPs produced in mammalian cells by transduction with recombinant baculovirus can encapsulate foreign genes into the central cavity of HEV-LPs. Moreover, encapsulated foreign genes can specifically transport and express to liver-derived cells by property of HEV-LPs. This study may provide valuable information for the development of novel gene therapy tools for liver disease.

Speaker Biography

Seung Kew Yoon is now a professor of the division of Hepatology and Gastroenterology, Department of Internal Medicine, College of Medicine, The Catholic University of Korea, Seoul, Korea. He earned his MD at the Catholic University of Korea in 1985. He trained in Hepatology & Gastroenterology at Seoul St.Mary's Hospital, The Catholic University of Korea from 1992 to 1994. He then subsequently trained as research fellow in Molecular Hepatology Laboratory, MGH, Harvard Medical School, Boston, USA from 1996 to 1998. He has been principal investigator in several International Multicenter Researches on antiviral therapy against hepatitis virus B & C, and target therapy for HCC. He holds scientific membership in numerous professional associations in Korea and is a member of the American Association for the Study of Liver Diseases (AASLD), EASL and APASL. He served as a secretary general of Korean Association for the Study of the Liver (KASL) from 2013 to 2015. Also, he served as a secretary general of APASL STC 2016 in Busan. Now he is a vice president of Korean Association of Internal Medicine. He works as a Director of Liver Cancer Center in Seoul St,Mary's Hospital and Catholic University Liver Research Center. He has published more than 300 authored and co-authored original articles on the viral hepatitis B and C, NASH, and HCC. He had also written chapter on molecular diagnostics of HCC in the textbook "Principles of Molecular diagnostics and personalized cancer medicine".

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Features of HPV infection in squamous cell cervical carcinomas of Immunocompromised patients

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Persistence of high carcinogenic risk (HR) HPVs in immunocompetent patients is limited by effective anti-viral immune response, while immune suppression leads to persistence of HR-HPV types, eventual transformation, and development of squamous cell cervical carcinomas (SCCC) with alterations in expression of check-point inhibitor genes including *PD-1* and *PD-L1*. We analyzed distribution of HR-HPV types, and *PD-1* and *PD-L1* gene expression in SCCC tissues of patients immunocompromised by HIV-1, mycobacterial/TB infections, and HIV/TB-coinfection. Study included 10 HIV(-)TB(-), 8 HIV(-)TB(+), 9 HIV(+)TB(-) and 13 HIV(+)TB(+) patho-morphologically verified SCCC cases. Total DNA and RNA was extracted from FFPE samples using All Prep DNA/RNA FFPE kit (Quiagen). Presence of 12 HR-HPV types was determined by quadruplex real-time PCR (AmpliSense HPV HOR genotype FL). *PD1* and *PD-L1* expression was assessed by real-time PCR after reverse transcription. HPV16, 18 and 33 were found in all; HPV39 in HIV(+)TB(-); HPV31, 35, 39, 52 in HIV(-)TB(+); and HPV33, 35, 39, 45, 52, 56, 59 in tumors of HIV(+)TB(+)-patients. HIV(+) samples were characterized by relatively decreased expression of *PD-1* (76%) and increased expression of *PD-L1* (151%). Expression of *PD-L1* tended to correlate with HPV18 load (R=0,69; p=0.08). In conclusion, immunosuppression due to HIV-infection results in increased abundance in SCCC tissues of HR-HPV of types other than 16, 18 and 33, and immunosuppression due to HIV/TB-coinfection, to additional increase in the number of circulating HR-HPV types. HR-HPVs modulate the level of PD-L1 expression. Significance of PD-1/PD-L1 findings would be verified after complementation of the cohort with additional samples.

Speaker Biography

Elizaveta Starodubova has completed her PhD in the Engelhardt Institute of Molecular Biology, Russian Academy of Sciences, and continued her postdoctoral studies there and at the Department of Microbiology, Tumor and Cell Biology (MTC), Karolinska Institutet, Stockholm. She performs her studies in the field of antigen processing and design of prototype DNA-vaccines against viral infections and cancer.

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Distribution of high-risk HPV genotypes in HIV-infected women of the Moscow region

Daria Podcufarova [1], Lebedeva NN[1,2], Enaeva MV[3], Isaguliants MG[1] and **Pronin AYu[2]**

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HIV-infection increases the incidence of squamous intraepithelial lesions ultimately leading to cervical cancer. This study characterized the incidence of SIL and prevalence of high carcinogenic risk types (HR-HPV) types in HIV-positive women in relation to their immune status. Cervical smears of HIV-infected (n=618) and HIV-negative (n=100) women aged 19-62 were subjected to cytological screening (BD SurePath™) and HPV16/18-specific PCR (Abbott RealTime High-Risk HPV). Of HIV(+)- women, 31% had cervical pathology: HSIL (3%), LSIL (14%), ASC-H (2%), ASC-US (12%). None had cervical cancer. Pathology was not related to immune status: women with CD4-nadir >500 and <500 cells/ul had similar frequencies of ASC-US/ASC-H/LSIL/HSIL. Positivity for HR-HPV types was high among women aged<30, and decreased with age as described. The decrease was dramatic in HIV-negative (21% in aged <30 vs 2% in aged >40 years), and milder in HIV-infected (31% in aged <30 vs 17% in aged >40) (p<0,05). Prevalence of HR-HPV types was higher among HIV(+) than HIV(-)-women, specifically aged >30. HIV(+)-women with lesions were infected with at least one HR-HPV: HPV16 (HSIL, ASC-H) or non-HPV16 (LSIL, ASC-US). Women with CD4-nadir <500 cells/ul had highprevalence of HR-HPVs other than HPV16/18. Prevalence of lesions and positivity for HPV16/18 was equal in ART-treated and untreated. We confirm higher prevalence of HR-HPV, specifically HPV16, in HIV-infected compared to healthy women, not directly related to immunosuppression. In HIV-infected women, grieve neoplasia were strongly associated with detection of HPV16, advocating creation of therapeutic HPV16-based vaccines for HIV-infected.

Speaker Biography

Daria Podcufarova has graduated Russian State Medical University, has a specialty in medical biochemistry and is currently working at N. F. Gamaleya Federal Research Center for Epidemiology & Microbiology. She is studying the diversity of HPV types in human mucosa in norm and pathology.

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Genomic analysis of racial differences in triple negative Breast Cancer

Lesleyann Hawthorn
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Triple negative breast cancer (TNBC) is more prevalent in African Americans (AAs), has a more aggressive clinical course including a higher mortality rate and increased occurences of metastases. This study was designed to determine if racial differences at the molecular level might explain the more aggressive phenotype in AAs. Mutation profiling, was performed on 51 AA and 77 CA tumor/ normal pairs. Transcript expression analysis was performed on 35AA and 37CA. Genes with high frequency mutation rates such as MUC4 and TP53 were common to both racial populations, however genes that were less frequently mutated differed between the races suggesting that those cause the more aggressive nature of TNBC in AA women. Overall, AA patients had a higher freaquency of mutations in a wider array of genes suggesting increased levels of genomic instability. JAK-Stat and HER2 signaling were unique to the AA and PTEN and mTOR were unique to the CA profiles. Many pathways identified by the mutational profiles were predicted to be down-regulated by the transcript expression profiles.

Speaker Biography

Lesleyann Hawthorn recieved her Ph.D. from the University of London, UK. She completed a postdoc at the Cleveland Clinic, OH, USA. Subsequently she obtained an Assistant Professorship at Rosewell Park Cancer Institute, NY, USA. She was awarded an Associate Professorship at Georgia Health Sciences University, GA, USA and is currently a Professor at the Georgia Cancer Institute at Augusta University, GA, USA. Her research interests include genomic analysis of solid and hematological cancers using mutational and transcript expression analyses and she has published over 60 peer reviewed manuscripts and book chapters in the field.

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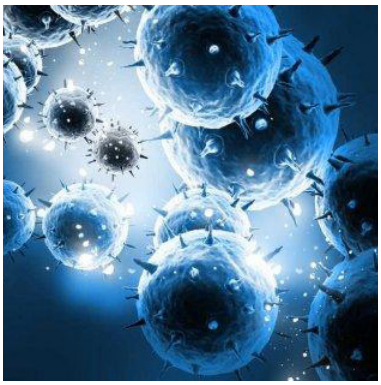

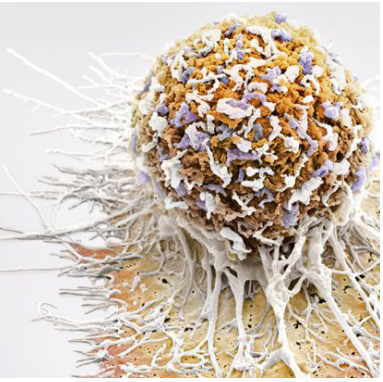
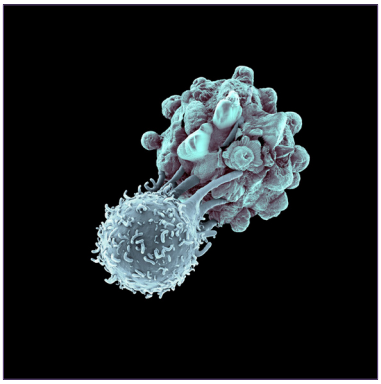
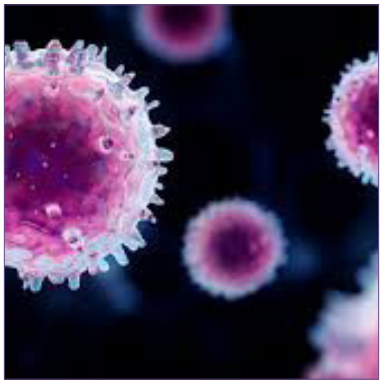

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Synthesis of metallacarboranes-based delocalized lipophilic cations for diagnostics and Cancer treatment

Dugin Sergey, P Belov, E Gurkova, V Pasko and **P Storozhenko**

JSC RSC GNIIChTEOS, Russian Federation

Metallacarboranes represent the wide class of polyhedral boron compounds with low toxicity, high boron content and catabolic stability. Applied in boron neutron capture therapy metalcarboranes derivatives are of interest. All of that sets apart metallacarboranes in the separate broad group of perspective pharmacophores. Carboranes containing the Delocalized Lipophilic Cations (DLCs) arouse big interest. DLCs are perspective compounds for diagnostics and cancer treatment. Eight compounds based on fluorescent dyes Rodamine 6G, B, were synthetized and characterized in our laboratory. Developing this direction, the optimal methods of bis (dicarbollide) cobalt-based DLCs syntheses were invented.

Speaker Biography

Dugin Sergey has completed his PhD at the age of 25 years from RSC GNIIChTEOS, Russian Federation. He is the leading scientist in GNIIChTEOS. He has over 200 publications that have been cited over 200 times, and his publication H-index is 20 and has been serving as an editorial board member of reputed Journals.

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Accepted Abstracts

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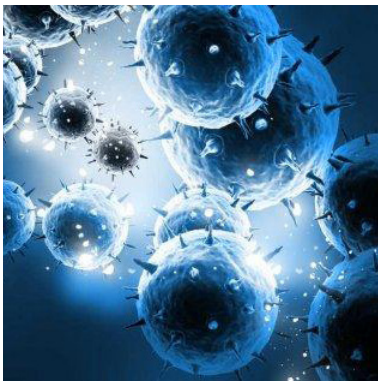

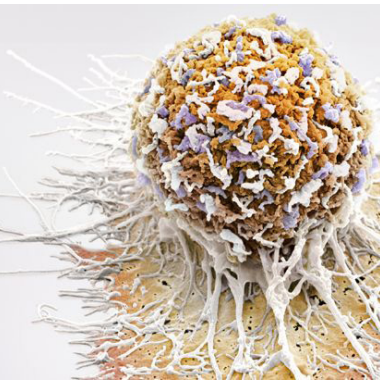
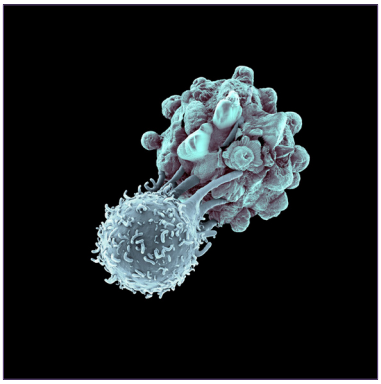
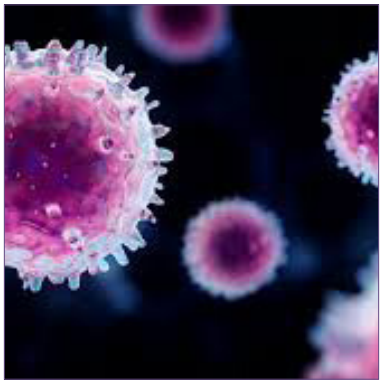

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Biomedical significance and ameliorative potentials of inducible nitric oxide synthase (iNOS) inhibitors in the development, progression and Metastasis of Prostate Cancer: A review

Lawrence Okonkwo Aka
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Nitric oxide (NO) is synthesized in a variety of tissues and organs in a reaction where the amino acid L-arginine is converted into L-citruline. The enzyme catalyzing this reaction is designated as nitric oxide synthase (NOS). Inducible nitric oxide synthase (iNOS) is one of the three different isoforms of nitric oxide synthase. Aside the desirable effects of enhanced neurotransmission and vasodilation produced by the constitutive isoforms (nNOS and eNOS), the inducible isoform (iNOS) is associated with cytotoxicity of macrophages and tumor-induced immunosuppression. Expression of (iNOS) in various human tumors has been classically demonstrated in which case it promotes the progression of such tumors. The selective expression of iNOS has been reported in human prostrate carcinoma and thus nitric oxide consequently produced may have many roles in the development, progression and metastasis of prostate cancer. Prostatic intraepithelial neoplasia (PIN) significantly characterizes the development and progression of prostatic adenocarcinoma and has been associated with high levels of iNOS. Interestingly debates over PIN distribution and expression of (iNOS) is gaining momentum and points to the potentials of inducible nitric oxide synthase inhibitors in the amelioration of this development and progression. The immunohistochemical examination of the activity of iNOS in prostatic carcinoma has been significantly demonstrated in both basal epithelial cells and secretory cells of the glandular epithelium. Though nitric oxide produced by iNOS can have cytotoxic and cytostatic effects on tumor cells, and may act as tumor growth suppressors, its identified role in promoting angiogenesis in tumor suggests that it may stimulate tumor growth rather than inhibit it. There are conflicting information on the specific role of NO in cancer growth. While some hold the opinion of NO acting as a tumor suppressor others suggest that it actually promotes cancer growth hence a dual role. Recent findings suggest that NO may be relevant for tumor progression through at least two mechanisms: the stimulation of angiogenesis and increased mutagenesis through the direct action of free radicals on the DNA. In addition, NO released from tumor cells is suggested to participate in the tumor-induced immunosuppression via the anti-proliferative effect of NO on tumor-infiltrating lymphocytes. Many evidences abound regarding the strong association between iNOS expression and rapid prostate cancer cell proliferation rate, depicting a good predictor of poor survival in univariate analysis, but was inferior to established prognostic factors in multivariate analysis. From the various experimental observations, all three isoforms of NOS can be involved in promoting or inhibiting the etiology of cancer including prostate cancer in humans. NOS activity has been detected in tumor cells of various histogenetic origins and has been associated with tumor grade, proliferation rate, and expression of important signaling components associated with cancer development such as the estrogen receptor. Increased NO generation in a cell may select mutant P53 cells and contribute to tumor angiogenesis by upregulating vascular endothelial growth factor (VEGF). Due to the importance of NO in various pathological processes including prostatic carcinoma, NOSes are regarded as an important pharmacological target and a great deal of effort has been made to design specific NOS inhibitors. However, the high degree of similarity among NOS isoforms poses an obstacle when attempting to find a specific inhibitor of a particular isoform. From the upcoming experimental observations on the expression of NOS IN prostate carcinoma, it becomes very apt to suggest that inhibiting the production of NO synthesis by iNOS inhibitors would provide great opportunities and potentials for the management and amelioration of prostatic carcinoma. Therefore, an understanding of the molecular dynamics of NO in prostatic carcinoma would be very valuable in the development of drugs that potentially can be helpful in adult male prostate cancer patients.

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Oral Cancer in Odisha "An epidemiological study"

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Introduction: Oral Cancer is the commonest cancer in India, approximately 90% occurring in developing countries. Tobacco chewing is the most important cause. The site, side of lesion and chewing habits, vary with geographical areas. In Western India the base of tongue is the commonest site and in South / East, buccal mucosa is common. In Odisha the lower gingivo buccal (Quid Bed) is the commonest site.

Material & Method: This study was conducted in the Department of Head and Neck Oncology of Regional Cancer Centre, Cuttack. A total number of 3705 patients were studied in a period of 10 years. Data regarding age, sex, site and side of lesion, relation to various chewing habits and associated dental pathology and premalignant lesions were observed.

Results: Out of the total numbers of 3705 cases, 66.9% were males. Majority were 41- 60 years. Periodontitis (32%) ,gingivitis (29%), leukoplakia (82.6%) and sub mucous fibrosis (9.6%) were detected .Buccal Mucosa was a common site (51.5%). Left sided was common (62.5%). Incidence was 62.8% in heavy chewers and 13.4% in light chewers . The quality of betel quid was responsible in 60.8% and contact period was important (62.8% with >14 hrs).

Conclusion: Our study proves the carcinogenic effect of tobacco use. The incidence of oral cancer depended on early-age chewers, heavy chewers, keeping betel-quid intraoral overnight, frequent/continuous chewers, smoking and chewing, chewing with lime and tobacco, poor oral hygiene and malnutrition.

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Cancer in nonagenarian: A hospital-based survival study

Manigreeva Krishnatreya, Jagannath Dev Sharma, Amal Chandra Kataki, Nizara Baishya, Mouchumee Bhattacharyya and **Manoj Kalita**

Dr Bhubaneswar Borooah Cancer Institute, India

Cancers in a nonagenarian patient is rarely seen and there is always a moral dilemma for the family members and patient of whether to opt for the treatment or not. The main objective of this study was to identify the survival differences between treated and not treated nonagenarian cancer patients. This was a retrospective study of Hospital-based Cancer Registry data from 2010 to 2016. The data of all nonagenarian cancer patients were analyzed for gender distribution, leading sites of cancer, stage distribution, types of treatment received, and survival. The survival was calculated from the date of first diagnosis. Kaplan-Meier analysis was done to present the survival. Of 60,087 patients, 146 (0.2%) patients were of 90 years and above. Hypopharynx in males (20.5%) and tongue (20.5%) in females were the top cancer sites, 60% patient data were in stages III and IV, 37 (25.3%) patients received treatment and 86% patients were treated by radiotherapy. The overall survival (OS) was 14.3%. OS in the treatment group was 21.3% versus 7.7% (P=0.001) in the no treatment group. The unadjusted HR for no treatment group was 3.8 (P=0.003, CI=1.5-9.7). Selected nonagenarian cancer patients from our population with a good performance status should receive curative treatments in all possible ways.

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Radiation induced oxidative stress mediated toxicity and possible protective measures

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An increasing rate of cancer is likewise confronted with an array of environmental, health and lifestyle factors. Cigarette smoke, consumption of alcohol, heavy use of cellphone are a part of lifestyle factors and equally responsible for the cancer. Cancer is likely to be affected by the intense exposure to heat and extreme exposure to pesticides, radiations, radioactivity and other hazardous substances. The present evidence on cell phone or other electronic gadgets are based on scientific research and public policy initiative to give an overview of what is known of biological effects that occur at radiofrequency (RF)/ electromagnetic fields (EMFs) exposure. Several types of ionizing and non-ionizing radiations surround us and both have recognized causative effects on biological system. The reviews of last few decades on health endpoints reported to be associated with RF include childhood leukemia, brain tumors, genotoxic effects, neurological effects and neurodegenerative diseases, immune system deregulation, allergic and inflammatory responses, infertility and some cardiovascular effects. Most of the reports conclude a reasonable suspicion of cell phone risk based on clear evidence of bio-effects. In the present scenario, limited studies found a solution against protection to these radiations. There are many known compounds which can act as antioxidants, anti-cancerous leads; mainly green tea, melatonin, hydroxyl apatite nanoparticle etc. These antioxidants play an important role against RF-EMF radiations. The study will explore the possible mechanism of RF-EMF radiation interaction and protection against these radiations

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The p52 isoform of *Shc1* is a key driver of Breast Cancer initiation

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Family of Shc adaptor proteins (encoded by Shc1 gene) consists of three functionally distinct isoforms (p46Shc, p52Shc, and p66Shc) that serve as intracellular adaptors for several key signaling pathways in breast cancer. Despite the broad evidence implicating Shc1 as a central mediator of breast cancer, testing the isoform-specific roles of Shc1 have been inaccessible due to the lack of isoform-specific inhibitors or gene knockout models. Here, we addressed this issue by generating the first isoform-specific gene knockout models for p52Shc and p66Shc, using germline gene-editing in the SS rat strain. Compared with the wild type (WT) rats, we found that genetic ablation of the p52Shc isoform significantly attenuated mammary tumor formation, whereas the p66Shc knockout had no effect. These data, combined with p52Shc being the predominant isoform that is upregulated in human and rat tumors, provide the first evidence that p52Shc is the oncogenic isoform of Shc1 in breast cancer. Compared with WT tumors, 893 differentially expressed genes were detected in p52Shc KO tumors compared with only 18 differentially expressed genes in the p66Shc KO tumors, further highlighting that p52Shc is the relevant Shc1 isoform in breast cancer. Finally, gene network analysis revealed that p52Shc KO disrupted multiple key pathways that have been previously implicated in breast cancer initiation and progression, including ESR1, mTORC2/RICTOR, and STAT5. Collectively, these data demonstrate the p52Shc isoform is the key driver of DMBA-induced breast cancer while the expression of p66Shc and p46Shc are not enough to compensate.

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Circulating tumor cells: Clinical utility, challenges and future prospects

Qing He Meng
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The detection of CTCs has been used as useful biomarkers in prognosis and monitoring therapeutic response of patients with metastatic cancer. However, during the course of cancer therapy, CTCs have undergone epithelial-mesenchymal transition (EMT) (i.e., EMT CTCs) and the current FDA-approved technology is unable to detect such EMT CTCs. Using new technologies such as antibody against cell-surface vimentin (CSV) exclusively expressed on EMT CTCs, we are able to detect EMT CTCs from breast, colon, and prostate tumor types and monitor disease progression and predict the prognosis. This presentation will briefly review the current status of CTC detection, the detection technology and clinical utility of CTC. The challenges of the current technology and new technology in determination of CTC will be addressed. The detection of EMT CTCs especially CTC with molecular profiling for cancer diagnosis, monitoring therapeutic responses, predicting prognosis, and guiding personalized therapy will be discussed. Detection of CTCs and molecular characterization as one of the liquid biopsy approach may serve as an instrumental role for noninvasive approach in personalized cancer medicine

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Solution proposed to a 2000 year old problem in Oncology

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University College London, UK

A bimodal pattern of hazard of relapse among early stage breast cancer patients has been identified in multiple databases from US, Europe and Asia. We are studying these data to determine if this can lead to new ideas on how to prevent relapse in breast cancer. Using computer simulation and access to a very high quality database from Milan for patients treated with mastectomy only, we proposed that relapses within 3 years of surgery are stimulated somehow by the surgical procedure. Most relapses in breast cancer are in this early category. Retrospective data from a Brussels anesthesiology group suggests a plausible mechanism. Use of ketorolac, a common NSAID analgesic used in surgery was associated with far superior disease-free survival in the first 5 years after surgery. The expected prominent early relapse events in months 9-18 are reduced 5-fold. Transient systemic inflammation accompanying surgery (identified by IL-6 in serum) could facilitate angiogenesis of dormant micrometastases, proliferation of dormant single cells, and seeding of circulating cancer stem cells (perhaps in part released from bone marrow) resulting in early relapse and could have been effectively blocked by the perioperative anti-inflammatory agent. If this observation holds up to further scrutiny, it could mean that the simple use of this safe, inexpensive and effective anti-inflammatory agent at surgery might eliminate early relapses. Similar bimodal patterns have been identified in other cancers suggesting a general effect. Based on the writings of Galen and Celsus, such an effect was known to them 2000 years ago.

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Clinico-economic analysis of PD-1 inhibitor and iBRAF+iMEK combination for treating Metastatic Melanoma with BRAF V600 mutation

Alexey Cheberda
Center for Pharmacoeconomics Research, Russia

Skin melanoma is an important, severe condition and one of the most aggressive oncological diseases, characterized by high lethality. Relatively high costs of novel innovative treatments for this condition necessitate analysis of clinico-economical properties of such treatments in Russian healthcare setting. The pharmacoeconomic analysis included cost-effectiveness analysis and budget impact analysis performed using a model constructed based on a network meta-analysis of fist-line treatments of melanoma with BRAF mutation including target therapy and immunotherapy. The alternatives compared were PD-1 inhibitor pembrolizumab compared to nivolumab and BRAF inhibitor combined with MEK inhibitor. Model assessed total survival, average progression-free survival and direct costs. Obtained results indicate that year of pembrolizumab treatment was 29% less expensive than dabrafenib+trametinib combination, and 60% less expensive than vemurafenib+cobimetinib, while also 1,7% less expensive than nivolumab treatment. Cost-effectiveness ration for pembrolizumab was the lowest of all alternatives compared, indicating highest cost-effectiveness. Budget impact analysis has shown that expansion of pembrolizumab use to 50% (at the expense of other alternatives) would result in budgetary savings totalling 1 507,5 million rubles accounted for Russian patient population size.

Use of pembrolizumab as first-line treatment in patients with BRAF V600 positive melanoma is thus associated with highest cost-effectiveness and budgetary savings and is pharmacoeconomically expedient.

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Pharmacoeconomic evaluation of regorafenib as metastatic Colorectal Cancer treatment within Russian healthcare context

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By prevalence, colorectal cancer occupies third place among the malignant oncological conditions in men, and second in women. Regorafenib presents significant clinical interests due to having demonstrated efficacy in both patients with wild-type and mutant-type KRAS gene, especially in patients demonstrating progression despite chemotherapy, use of anti-VEGF and anti-EGFR treatments. This pharmacoeconomic research was carried out to evaluate use of regorafenib in wild-type KRAS patients with metastic colorectal cancer patients who have shown progression on anti-VEGF or had counter-indications to anti-VEGF therapy and who have not received but could receive anti-EGFR treatment. A model was constructed to carry out budget impact analysis of regorafenib compared to cetuximab and panitumumab. Sensitivity analysis and lost opportunity analysis were also performed. Treatment length was accounted for, and relevant randomized clinical trials were used as sources of data in this regards. It was found that 1 month of therapy on regorafenib is associated with lower spending than any of the alternatives, with full course of regorafenib amounting to 292 thousand rubles per patient, which is 481 thousand roubles (62%) lower than full course of cetuximab and 676 thousand roubles (70%) lower than treatment with panitumumab. Budget impact analysis demonstrated that inclusion of regorafenib in ONLP system would allow to reduce budget spending by 261,98 million rubles during first year, 255 million roubles on second year and 248 million roubles on the third year. Sensitivity analysis confirms the stability of the results.

These results indicate that expansion of regorafenib's use in colorectal patients in the Russian federation would be associated with reduction in spending, and its inclusion in ONLP woulr result in reduction of budget burden associated with government guarantees of free medical help. It should also be noted that unlike all other alternatives regorafenib would also be able to adequately address the needs of patients with mutant KRAS that currently have limited therapeutic options in ONLP context.

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Effects of folic acid on progesterone-enhanced Breast Cancer cell proliferation and migration

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Previously, we have demonstrated that female sex hormone receptors and folic acid receptor form a complex and female sex hormone can abolish the folic acid-inhibited proliferation and migration in endothelial cells. The findings of interaction between female sex hormone and folic acid led us to propose that folic acid might interfere with the progesterone-enhanced breast cancer cell proliferation and migration. In the present study, we demonstrate that treatment with progesterone enhanced proliferation and migration of breast cancer cell lines (T47D, MCF-7 and BT474), while co-treatment with folic acid abolished the progesterone-induced enhancement of proliferation and migration in these breast cancer cell lines. Since we previously showed that progesterone enhanced breast cancer cell proliferation and migration through activating the cSrc-mediated signaling pathway, we investigated the molecular mechanism underlying folic acid-prevented the progesterone-enhanced breast cancer cell proliferation and migration by examining the effect of co-treatment with progesterone and folic acid on the cSrc activity. Our data showed that co-treatment with folic acid and progesterone increased the formation of p140Cap-cSrc complex, subsequently activating Csk, which in turn phosphorylated cSrc at Tyrosin-527, thereby causing cSrc inactivation. The findings of this study might provide a new strategy for preventing the progesterone-enhanced breast cancer progress

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Polyurethane implants in reconstructive breast surgery

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The goal of reconstructive breast surgery following mastectomy is to restore the maximally symmetrical shape with the contralateral breast. Majority of patients has some degree of breast ptosis, which is a physiological phenomenon, tending to worsen over time. Therefore, to achieve complete symmetry with a healthy breast, it is necessary to preserve or to restore the inframammary fold (IMF), to have an excess of the skin cover and to use anatomical shape implants, which allows to simulate the ptosis of the reconstructed breast. It should be noted that around the expander, installed on the first stage of breast reconstruction, a fibrous capsule is formed and the front sheet of which must be completely removed in order to increase the area of the skin cover, which in turn leads to increase a seroma formation. However, the creation of all these conditions for the restoration of breast ptosis leads to a risk the anatomical implant rotation. In turn, the movement of the implant inside the "free" pocket creates the risk of destruction the reconstructed IMF and the fold becomes smoothed, that we observed in 6% of cases used textured implants. The lack of sufficient cover tissues after mastectomy increases the risk of capsular contracture, which occurs in 14.5% of cases using implants with a textured surface. To reduce of the above-mentioned complications, we suggest to reconstruct the ptotic breast using polyurethane coated anatomical implants, which have a manufacturer's warranty of rotation and malposition, which was confirmed by us. Due to its spongy shell, the implant rapidly coalesces with surrounding tissues, which not only reduces seroma formation, but also the risk of capsular contracture to 5.5%, which is significantly lower than that of textured ones. In summary, we consider polyurethane coated prostheses as implants of choice in the two-stage breast reconstruction.

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Cancer Prevalence and its associated factors in India: A study based on NFHS 2015-16

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Introduction: According to National Institute of Cancer prevention and research (NICPR), average estimated prevalence of Cancer in India is 25 lakhs in 2010 and incidence is about 7 lakhs in the same year, there were 5.56 lakh deaths due to Cancer.

Objective: To investigate the factors associated with Cancer prevalence among both men and women in India.

Data and Methods: The study is based on data from National Family Health Survey, round IV (2015-16) conducted by International Institute for Population Sciences, Mumbai. Bivariate analysis using Pearson's Chi-square tests and all the socio-economic, behavioural and biological predictors were further analysed using Poisson regression models to establish association between all independent predictors and the outcome variable.

Results: Cancer Prevalence among women and men in India is 170 and 280 cases per lakh respectively. Among both women and men Asthma and Diabetes emerged as the main determinants for Cancer prevalence. Among women who smokes tobacco are 1.76 times significantly more likely to get Cancer (IRR = 1.76, P<0.05) where as in case of men who smokes cigerrate 11 and above per day are 2.65 times significantly more likely to get Cancer (IRR = 2.65, P<0.05). Among both women and men Non-vegetarian diet emerged to be important determinants for Cancer prevalence i.e. (IRR = 1.58, P<0.05) for women and (IRR = 3.17, P<0.05) for men. Among women who are exposed to Arsenic through Ground water are 1.81 times significantly more likely to get Cancer (IRR = 1.81, P<0.05).

Conclusion: From the study it has been found that Asthma and Diabetes among Biological factors and Tobacco and Alcohol consumption, consumption of Non-vegetarian food and Arsenic exposure (only among women) among behavioural factors are the main determinants of Cancer prevalence among both men and women in India

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Anti-Cancer immune response as instrument for early diagnostic and treatment of malignant tumors

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The low efficiency of targeted therapy in oncology, which became a surprise for molecular pharmacologists, is not result of miscalculations in the choice of molecular targets for monoclonal antibodies, but rather in the wrong initial paradigm. Attempts to defeat cancer by targeted antibodies can be likened to fruitless attempts to destroy a holographic image with the break of the hologram fragments (main feature of the hologram is the fundamental indivisibility of the image). The systemic phenomenon of malignancy scarcely be sensitive to targeted "breaks". Hardly we will be able to solve the problem, if do not realize the words Dr. Zalmanoff: "Attempts to find an antidote to cancer are fruitless, because the key is not a cancer cell, but a person affected by cancer." Cancer is a disease of the whole organism, not the genomes of individual cells. Accordingly, the most effective approaches rather be restoration the organismal supervision and control over the tissues growth and differentiation, but not attempts of destroying the malignancy by external agents (chemical or physical). Key may be related to the ability of the immune system of tumor-bearing patient "to see" the malignant cells. This is proved by the presence of autoantibodies to tumor-associated antigens in such patients. Why the immune system usually does not destroy malignant cells? How to activate internal anti-tumoral mechanisms? Can antibodies to tumor-associated antigens be used for early serological diagnosis of malignant tumors? These issues will be discussed.

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Tumor-on-a-chip in an integrated microfluidic platform

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Organoid and organ-on-a-chip technologies are rapidly advancing towards deployment for drug and toxicology screening applications. The organoids replicate native tissue structure and function and thus are superior to traditional 2D cultures in order to study organ development, function and drug toxicity. We developed an assortment of bioengineered tissue organoids and tissue constructs that are integrated in a closed circulatory perfusion system, facilitating inter-organ responses. We observe drug responses that depend on inter-tissue interaction, illustrating the value of multiple tissue integration for in vitro study of both the efficacy of and side effects associated with candidate drugs. Other applications focus on diseases such as tissue fibrosis and cancer. Specifically, to study tumor growth and drug response for future use in personalized/precision medicine

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Proposal of a Nutritional Screening for Malnutrition in GI tract Cancer patients under surgery

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Introduction: Limited resources force hospitals from relying on nutrition screening tools to identify malnutrition patients. The Nutritional Control Index (CONUT) increased attention in the nutritional screening and assessment is due to its simple and automatized method of three parameters: lymphocytes, cholesterol and albumin. There is an ongoing debate regarding the value of albumin as a clinical marker of malnutrition, because it's affected by systemic inflammation, common in gastrointestinal cancer patients. The objective of this study is to propose a nutritional screening tool for detecting malnutrition in these patients.

Methods: This is a randomized, single-blinded, case control study done in the Mexican Institute for Social Security. An established number of 50 patients with GI cancer, an output of <500mL/d and surgery candidates undergo prospective random assignment to CONUT (n=25, control group) or IMSS Score (n=25, study group). Weight, cholesterol and lymphocytes were measured in both groups, with only difference of albumin for control, and total proteins for study group, pre and post-surgery (4 days after). Outcome variables include preoperative and postoperative nutritional status.

Results: CONUT and IMSS score effectively detected malnutrition. The pre-operative study group score showed less cases of moderate malnutrition proved by mean reduction (mean: 5.2 ± 0.1959) than the control group (mean: 7.52 ± 0.2917) and statistical significance ($p<0.0062$, r: 0.9629). The post-operative study group got only moderate malnutrition cases (mean: 6.8 ±0.1512), while the control group got mixed several and moderate malnutrition (mean: 9.96± 0.2813), having the most statistical difference ($p<0.0001$, r: 0.8886).

Conclusion: IMSS score was able to significantly provide a nutritional status in GI cancer patients, this study could be a first step for a novel nutritional screening. However, further studies should be done in more heterogeneous populations and larger samples

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