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October 19-21, 2017 | Rome, Italy

Posters

World Cancer 2017

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A specific neuronal calcium sensor protein as potential predictive biomarker for ovarian cancer therapy

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Sporadic ovarian cancer has the highest relative mortality among gynecological cancers as approximately 75% of patients are diagnosed at an advanced stage, resulting in poor overall survival. To improve patient's outcome targeted therapy strategies are required urgently. In search of new biomarkers for personalized therapies, we recently identified a gene encoding a specific neuronal calcium sensor (NCS). The NCS-family is known to be involved in calcium-signaling on membranes and functions as a calcium dependent molecular switch. We demonstrated that its expression, analyzed on mRNA as well as on protein level, was significantly associated with patient survival. Moreover, the putative biomarker persisted also as a significant factor for OS ($p=0.008$) and RFS ($p=0.014$) in multivariable analyses. As little is known about the involvement of the protein in cancer, we established stable knock-downs in ovarian cancer cell lines to explore the effect of its expression on cancer cell viability and migration. Most strikingly, the knock-down cells reacted significantly less sensitive to cisplatin treatment as compared to the control cells. This effect was further investigated using different cisplatin concentrations and treatment durations. The differences were reproducible and remained significant. Since platinum-based therapy represents the "gold-standard" in ovarian cancer treatment, we postulate a predictive potential of our candidate to select patients that most probably benefit from platinum-based treatment from patients which will likely not have a benefit.

Biography

Sarah Konrad has completed her MSc in Chemistry from the Technical University of Munich (TUM) in 2014. She is now a PhD student of the German Cancer Research Center (Deutsches Krebsforschungszentrum, DKFZ) and is conducting her PhD in the Department of Gynecological Tumor Genetics (Prof. Alfons Meindl / Dr. Juliane Ramser) at the Technische Universität München (TUM). Her project focuses on identifying and functionally characterizing new prognostic and therapy-relevant biomarkers for personalized ovarian cancer therapy.

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Regulation of TP63 α /sonic hedgehog axis in n-dimethylnitrosamine-induced liver cancer stem cells

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Nitroso-compounds are critical dietary risk factor of liver cancer. Cancer stem cells (CSCs) play a significant role in the formation and development of cancer. To date, the action of nitroso-compounds on the induction of liver CSCs as well as the underlying mechanisms has not been defined. In the present study, we revealed that chronic N-nitroso dimethylamine (NDMA) exposure induced malignant transformation of human normal liver cells. We further showed that NDMA-induced malignant transformed liver cells exhibited CSCs properties, as evidenced by increased sphere formation capacity in serum-free-medium culture, dramatically elevated expression of liver CSCs markers and increased number of CD133+ cells, along with upregulation of TAp63 α , downregulation of Δ Np63 α , and activation of Sonic Hedgehog pathway. Moreover, we illustrated that suppression of Sonic Hedgehog activity inhibited NDMA-induced liver CSCs properties; over expression of TAp63 α activated Sonic Hedgehog pathway and promoted liver CSCs activity, whereas down expression of TAp63 α inhibited Sonic Hedgehog and suppressed liver CSCs; an opposite action of Δ Np63 α on Sonic Hedgehog pathway and liver CSCs was demonstrated. Taken together, our data suggested for the first time the vital role of TP63 α /Sonic Hedgehog axis in regulating NDMA-induced liver CSCs, and thus could provide new insights into the molecular mechanisms of liver carcinogenesis as well as its target intervention.

Biography

Hongyu Han has completed her PhD from Sun Yat-sen University Cancer Center in 2010. She was a research scientist in University of Pennsylvania and Fox Chase Cancer Center during 2014-2016. Currently, she is a Scientist in the Department of Nutrition in Sun Yat-sen University Cancer Center. Her research interests focus on the effects and mechanisms of dietary factors and cancer development. She has published more than 10 papers in reputed journals.

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Phenethyl isothiocyanate inhibits colorectal cancer stem cells by suppressing Wnt/ β -catenin pathway

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Cancer stem cells (CSCs) play a crucial role in the process of cancer development. Targeting CSCs may be an effective way for adjuvant therapy to prevent the progression of cancer and prolong life. Phenethyl isothiocyanate (PEITC), the major active component from cruciferous vegetables, exhibits inspiring interventional effects in various human cancers. However, the effects of PEITC on colorectal CSCs and the underlying mechanisms remain unclear. The present study examined the inhibitory effects of PEITC on CSC-like properties in colorectal cancer spheroids. We revealed that PEITC inhibited the spheroid formation capacity of colorectal cancer cells as well as the expression of colorectal CSCs markers, along with suppression of cell proliferation and induction of apoptosis. Moreover, we illustrated that PEITC down-regulated the activation of Wnt/ β -catenin pathway, whereas up-regulation of Wnt/ β -catenin diminished the inhibitory effects of PEITC on colorectal CSCs. Taken together, this study suggests that PEITC can be an effective natural compound targeting colorectal CSCs through suppression of Wnt/ β -catenin pathway, and thus may be a promising agent for colorectal cancer intervention.

Biography

Caiyun Zhong has completed his PhD from University of California, Davis, USA in 2005 and received Diplomate of the American Board of Toxicology (DABT) in 2010. He is the Director and Professor of the Department of Nutrition and Food Safety, School of Public Health, Nanjing Medical University. He has published more than 40 papers in reputed journals and has been serving as an Editorial Board Member of journals.

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HuAL1 peptide from complementarity-determining region 1 (CDR-1) of mAb HuA induces necroptosis in B16F10-Nex2 cells

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Treatment of melanoma, mainly on the metastatic stage, is a great clinical challenge because conventional chemotherapy is rather ineffective. Other strategies, including immunotherapy, have been introduced and are very encouraging. We have previously shown that peptides derived from complementarity determining regions of immunoglobulins (CDRs) display antimicrobial and antitumor activities regardless of the specificity of the antibodies they were derived from. In the present study, we show that CDR 1 from the light chain (L1) of a human IgM, mAb (HuA), specific for difucosyl human blood group A (HuA) induces necroptotic cell death in the murine melanoma cell line B16F10-Nex2 and in other murine and human tumor cell lines. HuAL1 did not exert cytotoxic effects in non-tumorigenic cell lines. Melanoma cells treated with HuAL1 showed DNA degradation, propidium iodide incorporation and abundant superoxide anion production. Moreover, peptide treatment induced mitochondrial swelling and disruption of mitochondrial cristae. All these effects were caspase-independent and RIPK1- and MLKL-dependent, since cell death was abolished when cells were co-incubated with necrostatin or necrosulfonamide. Confocal microscopy showed that HuAL1 peptide localizes to the cell nucleus, and ELISA assay showed that it probably binds to H3 histone. We propose that necroptosis is induced after chromatin disorganization upon peptide binding to histone. Our results show, for the first time, that a peptide derived from an Ig-CDR can induce necroptotic cell death on tumor cells.

Biography

Denise C Arruda is graduated in Pharmacy from the Federal University of Santa Catarina in 2000. She pursued PhD in Biology Sciences from University of São Paulo (ICB-USP) with postdoctoral degree at the Experimental Oncology Unit - Discipline of Cell Biology, Federal University of São Paulo from 2008-2014. Currently, she is a professor and researcher at the Integrated Nucleus of Biotechnology at University of Mogi das Cruzes. She has published 17 papers in reputed journals, some of them in collaboration with international research groups, and received awards for poster presentation in five international meetings.

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Genetic variations of interleukin 28B (IL28B) in meningioma

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Meningioma is the most common tumor of the central nervous system and despite of their benign characteristic and slow growth, they frequently recur after surgical removal. Interleukin 28B seems to be involved in antiviral and antitumor immune response. Recently, IL28B rs12979860 C/T polymorphism was associated with outcome of treatment with IFN α and ribavirin in patients with Hepatitis C virus. Also, patients with CC genotype have higher chances of viral depuration than those with other genotypes. However, there are few data on this polymorphism in tumors, especially in meningioma. Thus, the aim of this study was to analyze allele and genotype frequencies of this polymorphism in patients affected by meningioma and healthy individuals (control) and to sequencing IL28b gene, searching for novel genetic variations. Sixty patients treated by UNESP Neurosurgery Service were included in this study. The Research Ethics Committee approved this study and each subject signed an informed consent form before tissue was obtained. Analysis of rs12979860 C/T polymorphism was performed by PCR-RFLP (PCR - Restriction Fragment Length Polymorphism) and the complete sequencing of the IL28B gene was performed by Sanger Sequencing Capillary Electrophoresis (Applied Biosystems™). The present study showed unpublished results that evidenced a greater frequency of TT genotype in the meningioma patients when compared to healthy individuals. Novel genetic variations (missense and silent) were detected in IL28B gene and only three have been reported in the scientific literature, but not in tumor samples. Amino acids exchanged as consequence of the missense variations are located mainly in the binding domains of IL28B protein to its receptor, reinforcing the probable importance of these alterations in protein function. These results suggest that IL28B protein and its genetic variations may participate in the molecular mechanisms of meningioma.

Biography

Adriana Camargo Ferrasi has completed her PhD from São Paulo State University - Institute of Biosciences and Post-doctoral studies from São Paulo State University - Botucatu Medical School. She is a Permanent Professor of the Post-Graduation Program (Stricto sensu) in Medical Biotechnology of São Paulo State University (UNESP) and Titular Professor in Paulista University (UNIP). She works in the area of molecular biology applied to cancer studies.

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The effect of sex in the storage capacity of red blood cell concentrates in CPD/SAGM

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Statement of the Problem: Red blood cells (RBCs) are the most frequently transfused blood labile product. The "Donor variation effect", which refers to donor-to-donor differences observed in both blood storage quality and 24h recovery, is probably a key factor in the efficiency of transfusion therapy. Donor variation effect may be associated with genetically determined features of RBCs and plasma. The aim of this study was to examine whether the donor's sex may independently affect the storage capacity of donated RBCs.

Methodology & Theoretical Orientation: For this purpose, 14 leukoreduced units of RBC concentrates in CPD/SAGM (7 male-7 female) were stored for 42 days at 4-6°C. Several parameters of storage quality (including hemolysis, redox status etc) were examined before and throughout the storage period. SPSS was used for statistical analysis of the results.

Findings: In-bag hemolysis, as well as osmotic and mechanical hemolysis, and intracellular calcium indexes were equally low in both groups during the whole period of storage. On the contrary, redox status markers such as total and uric acid-dependent antioxidant capacity of the supernatant were significantly higher in male donors' units ($p < 0.01$). In the same group of donors, intracellular ROS accumulation was higher during the first two weeks of storage ($p < 0.05$), while exogenously stimulated ROS production was higher after the middle of the storage period (797 ± 220 vs 504 ± 48 RFU, $p < 0.05$).

Conclusion & Significance: Donor's sex does not seem to affect the hemolytic parameters of the leukoreduced RBC units under storage in CPD/SAGM. Male sex is rather associated with better extracellular antioxidant activity, but worse intracellular redox status and increased susceptibility to exogenous oxidative stimuli. Sex may represent a genetic variant that affects some aspects of the RBC storage lesion. This study was supported by "IKY FELLOWSHIPS OF EXCELLENCE FOR POSTGRADUATE STUDIES IN GREECE - SIEMENS PROGRAM" to Vasileios Tzounakas.

Biography

Vasileios L. Tzounakas is a Post-doctoral researcher at the Department of Biology (Section of Cell Biology & Biophysics) of the National and Kapodistrian University of Athens (NKUA). He has obtained Ph.D. in Cell Biology. He has served as reviewer in international journals while his main research interests include blood transfusion biology (mainly, red blood cell storage lesion in blood products used for transfusion), erythrocyte biology in health and disease and the study of extracellular vesicles. He has expertise in evaluating the key parameters that affect storage lesion and post-transfusion performance of red blood cells and in the management of blood supplies in a way that will lead to the individualization of transfusion therapy. In this context, he has focused on the elucidation of storage lesion's features that may serve as a donor's signature, namely 'the donor variation effect'.

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Shuttle system for hyperthermia tumor treatment

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Nowadays cancer is one of the leading causes of death in Europe. Major challenges in the management of the disease are due to the lack of agents used for early diagnosis and associated with severe and often therapy-limiting side effects. Although chemotherapeutics can kill neoplastic cells, they also will induce toxicity in non-neoplastic tissues. Therefore, new approaches are necessary with the purpose of optimizing anticancer therapy. Among new experimental approaches, the magnetic particle hyperthermia has been suggested. Hyperthermia, as anticancer therapy, has been proposed since the 1970s, but it has still not established in clinical routine owing to the inability in focusing the heat only to the intended region without damaging the surrounding healthy tissue. By contrast, the so-called magnetic particle hyperthermia has the potential to address this shortcoming. Magnetic nanoparticles (NPs) may be made to accumulate exclusively in tumor tissue. Nevertheless, the only use of NPs is not enough for reducing side effects, they could in fact distribute randomly in the body, causing several adverse effects to non-neoplastic tissues. To develop directed particles, the NP have been coated with peptides, known to deliver the NP to cancer cells selectively. These magnetic NPs, when exposed to Alternating Magnetic Fields (AMF), can generate heat due to hysteresis loss. This behavior may be exploited for treating cancer, revolutionizing the existing hyperthermia procedures. Cancer cells when exposed to elevated temperatures are more sensible to chemotherapeutics and radiations, therefore, hyperthermia can also be associated to chemotherapy and radiotherapy boosting their effect.

Biography

Chiara Ruggirello has completed her Master's Degree in Medical Veterinary and Pharmaceutical Biotechnologies from Parma University. She did her Master's thesis at the Technical University of Denmark (DTU) of Copenhagen, in Nanotechnologies. She started her PhD last October at Leipzig University at the Department of Biochemistry.

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Relationship with colorectal cancer and microbiota

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Colorectal cancer (CRC) is one of the most common types of cancer and the fourth leading cancer deaths all around the world. Many risk factors such as tobacco and alcohol consumption, over consumption of red and processed meat, age, physical activity, body weight, diet, inflammatory bowel disease, obesity and diabetes are associated with colorectal cancer. Another factor in the development of colorectal cancer is microbiota. Microbiota consist of bacteria, viruses, fungi and parasites that colonize the gastrointestinal tract from the mouth to the colon. Microbiota influences physiological functions from the maintenance of barrier homeostasis locally to metabolism, haematopoiesis, inflammation, immunity and other functions systemically. The composition of microbiota is related to various diseases such as cancer, non alcoholic fatty liver disease, obesity. Studies show that microbiota plays a role in the etiology of various types of cancer by affecting inflammation, DNA damage and apoptosis. Microbiota has a great influence on immune responses and chronic inflammation is a known risk factor for colorectal cancer. Colon mucosa is constantly exposed to intestinal microbiota and its metabolites, it has the potential of continuous low-grade inflammation with bacterial stimulation of immune responses. Gut dysbiosis is largely associated with direct hostility to colonic cancer or metabolic change. Studies show that various bacterial species include the pathogenesis of CRC. Functional different bacterial species are involved in tumor microbiology during tumorigenesis. For example, some potential pro-oncogenic pathogens such as enterotoxigenic *B. Fragilis* and *Escherichia-Shigella* may induce tumor formation. The tumor cells are located in the nucleus of the immune cells, which serve both the pro- and antitumor immunity and can be shaped by the resident microbiota even after progression to the CRC. Microbiota, immune system, and CRC are multifactorial associations that should deeply consider.

Biography

Esma Oguz has completed his/her Bachelor of Nutrition and Dietetic from Yeditepe University and is currently enrolled in the master's programme at the Department of Nutrition and Dietetic, Marmara University. He/She is also Research Assistant at the same university.

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Peptide R18H from Brn-2 transcription factor POU domain displays anti-melanoma activity *in vitro* and *in vivo*

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The Brn-2 transcription factor is related to the development of malignant melanoma, inducing cell proliferation and invasion and, consequently, the formation of metastases. The Brn-2 protein is expressed in melanocytes and overexpressed in melanoma cells. Peptides derived from the Brn-2 transcription factor could compete with the DNA binding sites, thus interfering with the development of melanoma, as well as activating the mechanisms of cell death. In the present work, the cytotoxic activities of peptides derived from the Brn-2 transcription factor were determined against murine melanoma B16F10-Nex2. Cells were treated for 24h with the peptides E12F, R18H, L13S and C9K, derived from the POU domain of the Brn-2 transcription factor. Among the peptides tested, only the R18H peptide was cytotoxic in B16F10-Nex2 cells. Moreover, a time curve was taken to evaluate the antitumor activity of R18H for 30 minutes, 1, 2, 4, 6, 12 and 24 hours. It was observed that the peptide displays antitumor activity early in the first hours of treatment, however, the cytotoxic effect increases only after 24 hours. The R18H peptide induced DNA degradation, chromatin condensation, increase of superoxide anions, phosphatidylserine translocation, activation of caspase 3 and 8, and release of extracellular cytochrome c in B16F10-Nex2 cells. These effects characterize death by apoptosis and because caspase 8 was activated we suggest that the extrinsic pathway is followed. R18H also induced membrane permeabilization in cells treated for 24 h, however, the same effect was not observed after treatment for 2 h. To determine if the membrane permeabilization effect could be due to late apoptosis or if in addition to apoptosis the R18H peptide also induced necrosis or necroptosis, we tested the peptide in the presence of necroptosis inhibitors and verified the release of LDH in the extracellular environment of treated cells. The peptide kept its cytotoxic effect in the presence of inhibitors of necroptosis and treated cells did not present LDH release in the extracellular medium. These data indicate that membrane permeability is a late apoptosis event. It was also observed that peptide R18H showed antitumor activity *in vivo*. It was observed in the metastatic model that C57Bl/6 mice treated with the R18H peptide showed lower numbers of pulmonary nodules than untreated mice. The peptide was not toxic in mice at high doses, as observed in histopathological analysis of the lung, liver, kidney, heart and spleen. These results suggest that the R18H peptide has potential to be developed as a new drug for the treatment of melanoma.

Biography

Denise C Arruda is graduated in Pharmacy from the Federal University of Santa Catarina in 2000. She pursued PhD in Biology Sciences from University of São Paulo (ICB-USP) with postdoctoral degree at the Experimental Oncology Unit - Discipline of Cell Biology, Federal University of São Paulo from 2008-2014. Currently, she is a professor and researcher at the Integrated Nucleus of Biotechnology at University of Mogi das Cruzes. She has published 17 papers in reputed journals, some of them in collaboration with international research groups, and received awards for poster presentation in five international meetings.

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Identify specific gene associated with carcinogenesis by *Clonorchis sinensis* and N-nitroso-dimethylamine on host cell using transcriptome sequencing

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Clonorchis sinensis, the most prevalent parasite in Korea, has been reclassified as Group I bio-carcinogen for cholangiocarcinoma (CCA) in humans by IARC in 2009, *C. sinensis* associated cholangiocarcinoma (CCA) is still unknown. The aim of this study was to identify distinct gene expression associated with carcinogenesis of *C. sinensis*. In human cholangiocyte line, H69 cells were continuously exposed to N-nitroso dimethylamine (NDMA) and excretory-secretory product of *C. sinensis* (ESP) over one year. H69 cells that were continuously exposed to ESP of *C. sinensis* and NDMA showed cancer-like characteristics including cell proliferation was more than 5.7 times and the proportion of cells in the G2/M phase increased up to 42% compare to non-treated H69 cells. Moreover, the expression of the cell cycle protein E2F1 and the cell proliferation related proteins, ki67, and cytokeratin 19 were more than 30-fold increased when NDMA and ESP were added together. Based on these results, whole-transcriptome sequencing was performed to compare the genome-wide gene expression patterns of H69 stimulation with NDMA and/or *C. sinensis* ESP with non-treated H69. A total of 1301 differentially expressed genes (DEGs) were identified, 521 of which were up-regulated and 780 were down-regulated. Gene ontology and Kyoto Encyclopedia of Genes and Genomes enrichments revealed that numerous DEGs belong to cancer-relevant genes, involved in cell cycles, cell proliferation, and cell adherent-relevant pathways. Among them, we focused on the P53 K-ras signaling genes and found that two genes increased and eight genes decreased from a number of their genes. This result was also confirmed by real-time PCR. In conclusion, these data suggest that the P53 and K-ras signal plays a key role in regulation of cell proliferation, which may cause cholangiocarcinoma under stimulation by ESP of *C. sinensis* and NDMA.

Biography

Eun-Min Kim has completed his PhD from Seoul National University College of Medicine and had worked as a Research Professor in Busan National University College of Medicine. Currently, he is studying the mechanism of cholangiocarcinoma at Yonsei University in South Korea.

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c-Met overexpression of fibroblasts increases angiogenic signal in breast cancer

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We found that c-Met overexpression was induced in normal breast fibroblast (NBF) by the conditioned medium (CM) of cancer cells regardless of subtypes, which made us to hypothesize that c-Met overexpression is a property of cancer-associated fibroblast (CAF). Therefore, we investigated whether c-Met overexpressing NBFs contribute to tumor progression. To this end, extracellular matrix (ECM) gene expression alteration was analyzed from the NBFs transfected with c-Met overexpression plasmid using cDNA microarray since CAF constructs tumor microenvironment by ECM remodeling. In our microarray data, matrix metalloproteinase 1 (MMP1) was most up-regulated in c-Met overexpressing NBF (approximately 10-fold) compared to the control NBF. According to previous studies, MMP1 induces VEGFR2 (Vascular endothelial growth factor receptor 2) expression in endothelial cells (ECs). So, it was assumed that c-Met overexpressing NBF contributes to breast cancer angiogenesis. In our study, the CM of c-Met overexpressing NBF induced a better tube formation of endothelial cells (Hy926) than that of control. On the other hand, tube formation by c-Met overexpressing NBF CM was reduced in the presence of c-Met inhibitor. Similar results were also observed in the co-culture of NBF and breast cancer cell lines (luminal A, B, Her2, and TNBC). The expression of c-Met and MMP1 was increased by the co-culture, whereas was decreased in the presence of c-Met inhibitor. Tube formation of EC was increased by the CM of the co-culture, whereas decreased by c-Met inhibitor-treated co-culture CM. Based on our results, c-Met inhibitor may be able to suppress angiogenesis in breast cancer by decreasing c-Met-induced MMP1 expression of CAFs.

Biography

Seong Gyeong Mun has completed her Bachelor's degree in Molecular Biology from Dankook University. She is currently pursuing Master's degree in Yonsei University School of Medicine. She had studied about breast tumor microenvironment in her graduate school days.

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Potential transcription factor involves NFE2L1 in hepatoma cell invasiveness through ROS induction

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Mitochondrial dysfunction is an important metabolic feature in human cancer. However, underlying mechanisms how mitochondrial dysfunction affects tumorigenesis remain unclear. To address the role of transcriptomic regulation by mitochondrial defects in liver cancer cells, we performed gene expression profiling for three different cell models of mitochondrial defects: cells with chemical respiratory inhibition, cells with mitochondrial DNA depletion, and liver cancer cells harboring mitochondrial defects. By comparing gene expression in the three models, we identified 10 common mitochondrial defect (CMD)-related genes that may be responsible for retrograde signaling from cancer cell mitochondria to the intracellular transcriptome. Among the CMD genes, we found that NFE2L1 is a key regulator to regulate hepatoma invasiveness. This study aims to elucidate how mitochondrial defect regulates NFE2L1 transcription. Interestingly, SNU354 and SNU423 cells showed high intracellular reactive oxygen species (ROS) levels. Exogenous treatment of H₂O₂ increased intracellular ROS and NFE2L1 expression in SNU387 cell harboring active mitochondria. We further selected 11 transcription factors (TFs) that could bind to promoter region of NFE2L1 by using TRANSFAC program. By monitoring NFE2L1 mRNA levels after knocking-down of the TFs, 4 TFs (USF2, STAT3, JUN and SREBP1) were identified to regulate NFE2L1 transcription. Further detailed molecular mechanisms of how mitochondrial ROS regulates NFE2L1 transcription are currently under investigation.

Biography

Eun-Beom Lee is pursuing Master's Degree from Ajou University School of Medicine. Her major Research Interest is in mitonuclear communication in tumorigenesis and retrograde signaling in hepatoma cells.

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Decrease in expression of the mitoribosomal subunit, MRPL13, enhances hepatoma cell invasiveness via elevated claudin-1

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Impaired mitochondrial oxidative phosphorylation (OXPHOS) capacity, accompanied by enhanced glycolysis, is a key metabolic feature of cancer cells, but its underlying mechanism remains unclear. Previously, we reported that human hepatoma cells that harbor OXPHOS defects exhibit high tumor cell invasiveness via elevated claudin-1 (CLN1). In the present study, we show that OXPHOS-defective hepatoma cells (SNU354 and SNU423 cell lines) exhibit reduced expression of mitochondrial ribosomal protein L13 (MRPL13), a mitochondrial ribosome (mitoribosome) subunit, suggesting a ribosomal defect. Specific mitoribosomal translation inhibition with doxycycline and chloramphenicol, or siRNA-mediated MRPL13 knockdown decreased mitochondrial protein expression, reduced the oxygen consumption rate (OCR), and increased CLN1-mediated tumor cell invasiveness in SNU387 cells, which have active mitochondria. Interestingly, we also found that exogenous lactate treatment suppressed MRPL13 expression and OCR, and induced CLN1 expression. A bioinformatics analysis of the open RNA-Seq database from The Cancer Genome Atlas Liver Hepatocellular carcinoma (TCGA-LIHC) cohort disclosed a significant negative correlation between MRPL13 and CLN1 expression. Moreover, in LIHC patients with low MRPL13 expression, two oxidative metabolic indicators, pyruvate dehydrogenase B expression and the ratio of lactate dehydrogenase (LDH) type B to LDH type A, significantly and negatively correlated with CLN1 expression. This observation implied that the combination of elevated glycolysis and deficient MRPL13 activity is negatively linked to CLN1-mediated tumor activity in LIHC. These results suggest that OXPHOS defects may be initiated and propagated by lactate-mediated mitoribosomal deficiencies and that these deficiencies are critically involved in LIHC development.

Biography

Young-Kyoung Lee received her PhD in Biochemistry from Ajou University School of Medicine, Suwon, Korea. She is working as a Post-Doctoral Research Fellow at Ajou University School of Medicine. For about last ten years, her research has been focused on elucidation of molecular mechanisms of mitochondrial respiratory defects which are often observed in cancer, the retrograde signaling triggered by the respiratory defect and its relevance to cancer activities.

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Place of functional beverages in preventive treatment for cancer

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Functional beverages help us to maintain healthy conditions and to provide comfort just for general nutrition. For this reason, functional beverages play a significant role in our daily lives. It has been found that functional beverages have benefits in many areas of health such as cancer prevention, healthy digestive system, immunity defenses, body weight reduction, energy and hydration, improve overall health, show antioxidant activity, improve cardiovascular health. The positive effects of functional beverages on health are explained by different mechanisms. Reduce oxidative stress and help to prevent many chronic diseases, as well as strengthen the immune system of the individual. Besides water, the best known and most commonly used functional beverages are tea, coffee and fruit juices. Functional beverages contain antioxidant bioactive compounds and different nutrient including alkaloids, anthocyanins, carotenoids, flavonoids, glucosinolates, isoflavones, phenolic acids, tannins and terpenes, vitamins (vitamin C, folate and provitamin A), minerals (potassium, calcium, magnesium) and fibers that have been associated with reduced cancer risk. Reactive oxygen species damages many tissues such as lipids, proteins, especially DNA in living organisms. Free radicals mediate oxidative damage in cancer. The biological damage that occurs in this way is called oxidative stress, and the phenolic components involved in functional beverages have a vital role in removing oxidative stress. DNA is highly susceptible to free radical damage. Modification of DNA is the most important consequence of oxidative stress, and it can become permanent via the formation of mutations and other types of genomic instability. Excessive production of reactive oxygen species and lack of adequate antioxidant components (alkaloids, anthocyanins, carotenoids, flavonoids, glucosinolates, isoflavones, phenolic acids, tannins and terpenes) in the body trigger to formation of cancer. It is thought that phytochemicals in beverages and balanced diet can be a natural treatment method to improve the individual's health condition and to prevent the development of the cancer cell with the minimal toxicity. It has been found that functional components taken with beverages contribute approximately 30% to the prevention of cancer formation in industrial countries. Functional beverages (fruit juices, vegetable juices, caffeinated beverages, dairy and soy beverages, some fermented beverages) provide sufficient quantities of antioxidant component that reduces cancer formation by preventing DNA damage and reducing oxidative stress in the body.

Biography

Gül Ögren has completed her Bachelor of Nutrition and Dietetic from Erciyes University and is currently enrolled in the Master programme in Department of Nutrition and Dietetic, Marmara University. She is also a Research Assistant at the same university.

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25th WORLD CANCER CONFERENCE

October 19-21, 2017 | Rome, Italy

The importance of exercise in patients with breast cancer

Veysel Akduman, Emel Mete, Abdurrahman Tanhan, İkşan Demirbüken and Zübeyir Sarı
Marmara University, Turkey

Breast cancer leads to physical and mental distress which is linked with increased prevalence of malignancy-related mortality among females worldwide. Survival rates for breast cancer have been improving for more than 20 years and this appears likely to continue. Therapeutic exercises as well as adjuvant treatments are important improving the quality of life and increasing survival rates in cancer patients. Exercise is recommended to minimize the side effects of chemotherapy and radiotherapy, to maximize cardio pulmonary status especially early diagnosis. Aerobic and resistance exercise are mostly performed exercises types in this population, either separately or in combination, have been shown to improve physical functioning and manage some side effects in breast cancer patients receiving chemotherapy. It has been showed that exercise program can help manage symptoms and improve physical functioning during radiation therapy. Some studies in the literature have shown that aerobic exercise in cancer patients reduces fatigue as well as increases quality of life. For many cancer patients, fatigue is a severe and limiting problem. The impairment of physical and mental performance prevents from working or carrying out regular daily activities and hence results in a substantial reduction of the quality of life. In response to fatigue, patients are usually advised to rest and down-regulate their level of daily activities. However, since inactivity induces muscular catabolism and cardio-pulmonary endurance, extended rest can help perpetuate fatigue. Moreover, exercise has been proposed as a nonpharmacologic intervention for the treatment of cancer-related fatigue. An isometric exercise is one of the resistance training. One study found that three-week isometric-strength exercise program improved physical performance and reduced fatigue. In another study pointed that the effects of all forms of performed aerobic or resistance exercise, or both, with programme duration of at least six weeks should be considered. Although the exercise training is one of the necessary approach in the non-pharmacological treatment of breast cancer to reduce fatigue, there are still not enough studies in the literature. It is necessary to perform more randomized controlled studies investigating the proper exercises type and procedure to improve quality of life in breast cancer survivors.

Biography

Veysel Akduman has completed his Bachelor of Physical Therapy and Rehabilitation from Afyon Kocatepe University and then graduated his Master's Degree in Department of Physiotherapy and Rehabilitation, Sifa University. He is currently enrolled in the PhD programme in Department of Physical Therapy and Rehabilitation, Marmara University, in which he is also a Research Assistant.

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October 19-21, 2017 | Rome, Italy

Efficiency of acupuncture in cancer patients

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Cancer is defined as a class of diseases in which abnormal cells divide without control and can invade other tissues. It is a leading cause of death worldwide and accounted for 7.6 million deaths (around 13% of all deaths) in 2008. Acupuncture is one of the major treatment methods in Chinese medicine (CM). The value and safety of acupuncture are documented in the growing body of literature on acupuncture treatment for chronic pain, osteoarthritis, migraine, and the relief of procedural anxiety. In addition, acupuncture has been used to treat a range of problems associated with cancer and cancer treatments, such as hot flashes, chronic fatigue, neuropathy, nausea and vomiting, xerostomia, and dysphagia. Needle stimulation causing a typical needle sensation has been claimed to be important for reaching maximum effects on pain. Acupuncture points in the cutaneous nerve can be used to reduce pain, vomiting and nausea and to treat depression. Cancer treatment can also be used to reduce other effects such as xerostomia and sensory impairment. According to a study, acupuncture treatment was found to be effective in pain control in cancer, acupuncture alone was not better than standard drug treatment, but acupuncture and drug therapy combination was significantly more effective than drug treatment alone. In another study, standard pain treatment with hand-foot acupuncture was compared in terms of side effects and analgesic efficacy in patients with liver cancer. Acupuncture has resulted in a longer analgesic effect without any side effects. Literature reviews indicate that acupuncture is effective in pain management and it has no side effects. On the other hand, inadequate number of randomized controlled trials and the fact that studies are performed on fewer patients and the short follow-up time lead to an inaccurate explanation of the effectiveness of acupuncture. We think that there is not enough research about acupuncture on cancer and that more randomized controlled trials are needed.

Biography

Emel Mete graduated from Istanbul University Physiotherapy and Rehabilitation Department in 2007. She is pursuing her Master Program in Physiotherapy and Rehabilitation Department at Marmara University. She is also a research assistant at the same department.

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October 19-21, 2017 | Rome, Italy

Inhibitory effect of *Lactobacillus helveticus* SBT2171 on the growth of colon carcinoma cells and the novel action mechanism

Kazunobu Baba

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Lactobacillus helveticus SBT2171 (LH2171; provided by Megmilk Snow Brand Co., Ltd.) is a lactic acid bacterium that inhibits excessive immune responses. We have revealed that LH2171 shows inhibitory effects on the proliferation of BJAB, a B lymphoma cell line, through reduction of phosphorylation level of c-Jun, a critical regulator of cell proliferation. c-Jun is phosphorylated by activation of MAPKs (Mitogen-activated protein kinases) - (JNK and ERK) signaling pathway. JNK (Jun N-terminal kinases) and ERK are activated by MEK4/7 or MEK1/2 pathway, respectively. In this study, we investigated the effect of LH2171 on the proliferation of MC38, a mouse colon carcinoma cell line and HT-29, a human colorectal adenocarcinoma cell line. LH2171 inhibited the proliferation of both MC38 cells and HT-29 cells. As a result of assay for the phosphorylation of factors regulating cell growth, LH2171 inhibited phosphorylation of JNK, but not of ERK and MEK4 in MC38 cells. In addition, LH2171 induced the expression of JNK-inactivating phosphatase, MKP1 and MKP1 siRNA treatment could suppress the effect of LH2171 to inhibit cell proliferation. These results indicate that the inhibitory effect of LH2171 on the proliferation of MC38 cells depends on the induction of MKP1 to inhibit JNK activity.

Biography

Kazunobu Baba has completed her PhD from Kwansei Gakuin University. She is a Postdoctoral Fellow of Institute for Genetic Medicine in Hokkaido University. She has been studying the function and roles of probiotics to apply the study in prevention and treatment of cancer. She has once received Paper of the Week on *Journal of Biological Chemistry*.

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October 19-21, 2017 | Rome, Italy

Anti-cancer effects of less polar Curcumin analogues on gastric adenocarcinoma and esophageal squamous cell carcinoma cells

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Curcumin and its chalcone derivatives inhibit the growth of human cancer cells. It is reported that replacement of two OH groups in curcumin with less polar groups like methoxy increases its antiproliferative activity. In this study, we explored benzylidene cyclohexanone derivatives with non-polar groups, to see if they possess increased anti-cancer activity. Novel 2,6-bis benzylidene cyclohexanone analogues of curcumin were synthesized, and their inhibitory effects on gastric adenocarcinoma (AGS) and esophageal squamous cell carcinoma (KYSE30) cancer cells were studied using an MTT assay. Cell apoptosis was detected by EB/AO staining, and cell cycle was analyzed by flow cytometry. Real-time PCR was performed for gene expression analysis. All synthesized analogues were cytotoxic toward gastric and esophageal cancer cells and showed lower IC₅₀ values than curcumin. Treatment with 2,6-Bis-(3-methoxy-4-propoxy-benzylidene)-cyclohexanone (BM2) was 17 times more toxic than curcumin after 48 h incubation. All novel compounds were more effective than curcumin in apoptosis induction and cell cycle arrest at G1 phase. These results suggest that less polar analogues of curcumin have potent cytotoxicity *in vitro*. However, they need to be investigated further, especially with animal tumor models, to confirm their chemotherapeutic activity *in vivo*.

Biography

Fatemeh Alibeiki has been studying at Ardabil University of Medical Sciences, Iran. Currently, she is in her final year of education as a medical student. So far, she has published two papers in high-profile journals. Participating in numerous conferences and workshops is one of her interests and has done so, on a regular basis throughout the years as a student which brought her experience, extensive knowledge and so many scientific certificates. She has also associated with different groups in her university that resulted in holding several conferences and meetings.

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October 19-21, 2017 | Rome, Italy

Effect of *WNT7B* in macrophage-stimulated mesothelial cells on ovarian cancer cell adhesion

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Kyung Hee University, South Korea

Ovarian cancer is a remarkably metastatic disease that is often characterized by widespread peritoneal dissemination. Recently, several studies have suggested that tumor microenvironment plays a significant role in ovarian cancer metastasis. However, the interaction between macrophages and mesothelial cells for ovarian cancer metastasis is unclear. We first investigated the effect of macrophages on gene expression pattern in mesothelial cells. Following treatment of mesothelial cells with conditioned medium (CM) of macrophages, we conducted a comparative analysis of global expression changes in mesothelial cells using mRNA sequencing. When compared to that in unstimulated-macrophages, 945 genes were up-regulated and 777 genes were down-regulated more than 2-fold in macrophage-stimulated mesothelial cells (MSM). Among the total 1722 genes, 94 genes including *WNT7B* were known to be associated with the regulation of cell adhesion. Interestingly, knockdown of *WNT7B* using siRNA attenuated the adhesion of ovarian cancer cells to mesothelial cells. These results indicate that the enhanced levels of *WNT7B* in MSM may play a role in the peritoneal dissemination of ovarian cancer.

Biography

Seung-Kye Cho is pursuing his Master's degree in Life and Nano-pharmaceutical Sciences at Kyung Hee University. He graduated in Oriental Pharmaceutical Science from the Kyung Hee University. He has interests in providing evidence supporting the importance of the interplay between ovarian cancer cells and mesothelial cells, and discovering novel factors of peritoneal dissemination of ovarian cancer.

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October 19-21, 2017 | Rome, Italy

Hexokinase 2 is a molecular bridge linking telomerase and autophagy

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Autophagy is systematically regulated by upstream factors and nutrients. Recent studies report that telomerase and Hexokinase 2 (HK2) regulate autophagy through mTOR and that telomerase has the capacity to bind to the HK2 promoter. Here, we show that HK2 is a molecular bridge linking telomerase to autophagy. TERT-induced autophagy activation and its further enhancement by glucose deprivation were suppressed by HK2 inhibition in HepG2 cells. The HK2 downstream factor mTOR was responsible for TERT-induced autophagy activation under glucose deprivation, implying that TERT promotes autophagy through a HK2-mTOR pathway. TERC played a similar role as TERT, and simultaneous expression of TERT and TERC synergistically enhanced HK2 expression and autophagy. At the gene level, TERT bound to the HK2 promoter at a specific region harboring the telomerase-responsive sequence TTGGG. Mutagenesis of TERC and the TERT-responsive element on the HK2 promoter revealed that TERC is required for the binding of TERT to the HK2 promoter. We demonstrate the existence of a telomerase-HK2-mTOR-autophagy axis and suggest that inhibition of the interaction between telomerase and the HK2 promoter sensitizes cells to metabolic stress, and this pathway could be targeted for anti-cancer therapies.

Biography

Jae-il Roh has completed his PhD from Yonsei University and continuing his research at the same laboratory. He is working in Prof. Han-Woong Lee's lab and interested in mouse genetics, generation of mouse models, and cancer.

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October 19-21, 2017 | Rome, Italy

Senescent tumor cells lead the collective invasion in thyroid cancer

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Cellular senescence has been perceived as a barrier against carcinogenesis. However, the senescence-associated secretory phenotype (SASP) of senescent cells can promote tumorigenesis. Here, we show senescent tumour cells are frequently present in the front region of collective invasion of papillary thyroid carcinoma (PTC), as well as lymphatic channels and metastatic foci of lymph nodes. In in vitro invasion analysis, senescent tumour cells exhibit high invasion ability as compared with non-senescent tumour cells through SASP expression. Collective invasion in PTC is led by senescent tumour cells characterized by generation of a C-X-C-motif ligand (CXCL)12 chemokine gradient in the front region. Furthermore, senescent cells increase the survival of cancer cells via CXCL12/CXCR4 signalling. An orthotopic xenograft in vivo model also shows higher lymphatic vessels involvement in the group co-transplanted with senescent cells and cancer cells. These findings suggest that senescent cells are actively involved in the collective invasion and metastasis of PTC.

Biography

Young Hwa Kim has completed all the requirements for the Doctoral Degree in Biomedical Science and expect to obtain the Ph.D. Degree Certificate at the end of February 2016, officially. She has published 8 papers, out of which she is the first author of 4 papers.

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e-Poster

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October 19-21, 2017 | Rome, Italy

The impact of rerouting cancer diagnoses from emergency presentations to GP referrals: Evidence from population-based patient-level data

Mauro Laudicella¹, Brendan Walsh², Elaine Burns³, Paolo Li Donni⁴ and Peter C Smith⁵

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Background: Studies on alternative routes to diagnosis stimulated successful policy interventions reducing the number of emergency diagnoses. A dearth of evidence on costs might prevent new policies from achieving more ambitious targets.

Methods: Retrospective cohort study on colorectal (88,051), breast (90,387), prostate (96,219), and lung (97,696) cancer patients diagnosed after a GP referral or an emergency presentation (EP) in the English Cancer Registry. Costs of care and survival were compared one year before and five years after diagnosis, including non-conversion costs. Basu-Manning estimator was used to calculate the effect of rerouting patients after risk-adjusting.

Results: The cost per year of life saved is £6,456 in colorectal, £1,057 in breast, -£662 in prostate (savings), and £819 in lung cancer (three years only). Reducing the overall proportion of EP to those achieved by the 20% of CCGs with the lowest EP percentage would result in £11,481,948 against 1,863 years of life saved for Colorectal, £847,750 against 889 years for breast, -£943,434 (cost savings) against 1,195 years for prostate, and £609,938 against 1,011 years for lung cancer.

Conclusion: Rerouting diagnoses from EP to GP/TWW referral appears an achievable target that can produce large benefits to patients against modest additional costs to the NHS.

Biography

Mauro Laudicella is a Senior Lecturer in Health Economics in the School of Health Sciences at City University London and an Honorary Research Fellow in the Business School at Imperial College London. He is currently leading a three-year research programme investigating the costs of cancer in England sponsored by Macmillan Cancer Support. He has actively contributed to several funded research grants investigating various topics in health economics, including: value for money in health care, patient choice and competition, equity, and diffusion of new technologies for the treatment of cancer. His research has been published in *the Journal of Health Economics*, *Social Science & Medicine*, *Health Services Research* and *Health Affairs*.

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October 19-21, 2017 | Rome, Italy

Serum uric acid is effectively correlated with the quality of donated red blood cells under blood bank conditions

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Statement of the Problem: During their preservation at blood banks, red blood cells (RBCs) undergo several physiological alterations/deteriorations collectively known as “RBC storage lesion”. A significant part of the storage lesion is driven by oxidative stress, while some of its critical aspects are considered donor-related. Having in mind that serum uric acid (UA) represents almost 60% of the total antioxidant capacity of the donor’s plasma, the aim of this study was to provide evidence regarding the potential usefulness of UA as a donor-specific marker of storage quality.

Methodology & Theoretical Orientation: For this purpose, 47 non-leukoreduced units of RBC concentrates in CPDA-1 produced from male regular blood donors were stored for 35 days. Several storage quality parameters (cell shape, redox homeostasis, extracellular vesicles/EVs etc.) were examined at the beginning (day 2), the middle (day 18) and the end (day 35) of the storage period. SPSS was used for statistical analysis. Findings: Antioxidant capacity of the blood bags’ supernatant was correlated with the UA levels *in vivo* ($R=0.718$, $p<10^{-7}$) throughout the storage period. A posteriori splitting of the donors in high- and low-UA groups, revealed statistically lower intracellular ROS and calcium accumulation after the middle of storage ($p<0.05$) in the high UA group. Finally, units from high UA donors demonstrated lower levels of irreversibly modified RBCs ($22.5\pm2.9\%$ vs $27.1\pm1.6\%$) and different size distribution of EVs on day 35 of storage ($p<0.05$).

Conclusion & Significance: Variability in UA levels *in vivo* is maintained during storage and of note, it seems to be associated with the redox status and morphology of stored RBCs. Uric acid as a donor’s signature in blood components may be a very promising candidate biomarker of RBC storage lesion. This study was supported by “IKY FELLOWSHIPS OF EXCELLENCE FOR POSTGRADUATE STUDIES IN GREECE – SIEMENS PROGRAM” to Vasileios Tzounakas.

Biography

Vasileios L Tzounakas is a Post-doctoral researcher at the Department of Biology (Section of Cell Biology & Biophysics) of the National and Kapodistrian University of Athens (NKUA). He has obtained Ph.D. in Cell Biology. He has served as reviewer in international journals while his main research interests include blood transfusion biology (mainly, red blood cell storage lesion in blood products used for transfusion), erythrocyte biology in health and disease and the study of extracellular vesicles. He has expertise in evaluating the key parameters that affect storage lesion and posttransfusion performance of red blood cells and in the management of blood supplies in a way that will lead to the individualization of transfusion therapy. In this context, he has focused on the elucidation of storage lesion’s features that may serve as a donor’s signature, namely “the donor variation effect.”

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October 19-21, 2017 | Rome, Italy

Decision-making of cancer patients about end-of-life: The live experience

Angela Katrina G Fonte

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Understanding the perception of an end-stage cancer patient about end-of-life decision making can help the patient's relatives, healthcare providers, and the person himself or herself in attaining the best quality of life in their exit event. The aim of this study is to deeply gain an understanding of the voice and feelings of stage 4 cancer patients in making decisions for end-of-life. The study was conducted using a qualitative phenomenological approach. Five participants who are of sound mind and able to make rational decisions shared their preferences. The participants were selected using a non-probability, criterion, purposive sampling. Data were gathered through the use of a semi-structured interview. Four major themes emerged from the analysis of the data. The themes were leaving protracted misery, divesting the burden, feeling of complacency and living in a former time. These themes encircle mainly on the issue of cycle of suffering and prolonging one's agony with the use of life-saving measures which can reduce the quality of life. Findings of the study revealed that end-of-life decision making is encapsulated with different factors which include physical discomfort and exhaustion, emotional distress, spiritual dilemma and financial burden. Recommendations include educational training for nurses about end-of-life care and discussion of ethical issues, culturally competent care, and management of patients who are facing end-of-life decision making. It is also recommended that physicians should take the lead and explore the end of-life preferences of patients and their families.

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October 19-21, 2017 | Rome, Italy

Spectrum of non-AIDS defining cancers, Indian study

A Alahari Dhir

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Introduction & Aim: With the availability of combined antiretroviral therapy and treatment of opportunistic infections there is an increased life expectancy of HIV positive patients and hence an increase in chronic diseases inclusive of cancers is expected. Malignancies account for more than one-third of the causes of death among HIV infected patients. We studied the spectrum of Non AIDS defining cancers among HIV positive cancer cases at a tertiary referral cancer in India.

Material & Methods: We used the gender and age-specific proportions of each cancer site of the year 2002 that was recorded in the Hospital Cancer Registry at Tata Memorial Hospital, to estimate an expected number of various cancer sites among HIV positive cancer patients during the period 2007-2015. The observed number of site specific cancer cases was divided by the expected number to obtain proportional incidence ratio (PIR). An increased PIR means that proportion of cancer for a particular cancer site is more in HIV positive cancer cases compared to that expected from the data of hospital based cancer registry. The standard error of the PIR was estimated to compute 95% CI.

Results: There were 758 patients with HIV related cancers in the study period. Males were predominant (53.8%). 43.66% cases were non AIDS defining cancers (NADC). 51.66% patients were in the age group of 41-60 years. 45.7% patients were known HIV positive at the time of diagnosis of cancer. In males PIR was increased for anal cancer (PIR=4.21, 95%CI 2.21-8.17), penile cancer (PIR=2.66, 95%CI 1.47-4.8) and conjunctival cancer (PIR=4.75, 95%CI 1.19-19.01). Among females the PIR for anal cancer (PIR=3.37, 95% CI 1.27-8.99), Hodgkin's disease (PIR=2.76, 95%CI, 1.32-5.79), conjunctival cancer (PIR=14.27, 95%CI 3.57-57.08) and vulval cancers (PIR=4.58, 95%CI 1.72-12.2) was increased.

Conclusions: Most patients were detected to have HIV at the time of diagnosis of cancer. There were more AIDS defining cancers than Non AIDS defining cancers. The non-AIDS defining cancers seen with a higher proportional incidence ratio among HIV infected patients with cancer are inclusive of anal cancer, penile cancers, conjunctival cancers, Hodgkins disease and vulval cancer. All non AIDS defining cancers which were increased in proportion among the HIV infected patients are infection related cancers.

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October 19-21, 2017 | Rome, Italy

Effectiveness of progressive muscle relaxation training in managing chemotherapy-induced nausea and vomiting in Chinese lung cancer patientsDan Luo¹ and Huaping Liu²¹University of Sydney, Australia²Peking Union Medical College, China

Background: Behavioral techniques such as progressive muscle relaxation training are becoming increasingly important in dealing with chemotherapy-induced nausea and vomiting.

Objective: This study was designed to assess the effectiveness of progressive muscle relaxation training (PMRT) in reducing the nausea and vomiting by highly emetogenic chemotherapy in lung cancer patients.

Methods: 72 chemotherapy-naïve lung cancer patients participated and were divided into two groups. 36 patients in the experimental group received PMRT 1 h before and after chemotherapy with cisplatin for 3 days, and daily thereafter for another 4 days (totally 7 days). Patients received PMRT twice per day and each session lasted for 25 minutes. The instruments used for data collection was MASCC Antiemesis Tool (MAT) which was used daily for the 7 post-chemotherapy days.

Results: The use of PMRT considerably decreased the vomiting episodes and nausea intensity in the experimental group compared with the control group in the delayed phase ($P < 0.01$), whereas there were no differences in acute phase. Neither nausea nor vomiting differed in incidents between the two groups in the acute and delayed phases.

Conclusion: Such findings suggest that PMRT is a useful technique in the delayed phase to reduce nausea and vomiting by highly emetogenic chemotherapy. Incorporating the interventions into the care plan can improve symptom management of cancer patients who experience gastrointestinal side effects of chemotherapy.

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October 19-21, 2017 | Rome, Italy

Identification of anti-apoptotic AREL1 E3 ubiquitin ligase as a novel oncogene that promotes tumor angiogenesis via HIF-1

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We previously reported the anti-apoptosis functions of a novel anti-apoptotic E3 ubiquitin ligase, AREL1, which ubiquitinates and promotes the proteasome-dependent degradation of cytosolic forms of IAP antagonists. In the present study, we identified AREL1 as an oncogene that targets PHD2. Elevated expression of AREL1 was detected in 65% of randomly selected human lung and colon cancer cell lines and also found in 42% of 424 human tumor tissues. Furthermore, AREL1-transgenic mice enhanced chemical-induced carcinogenesis as compared to wild-type ones. The oncogenic function of AREL1 led us to screen AREL1 target proteins involving in oncogenesis. PHD2, which regulates angiogenesis and tumor development, was identified as an AREL1-interacting protein from a yeast two-hybrid screen. PHD2 was down-regulated by AREL1. This down-regulation was blocked by either a potent proteasome inhibitor, MG132 or expression of an E3 activity-deficient mutant form of AREL1, AREL1-A790A. Taken together with that ubiquitination of endogenous PHD2 was enhanced by AREL1, these results indicate that AREL1 ubiquitinates and promotes a proteasome-dependent degradation of PHD2. Tumor angiogenesis of xenograft of AREL1-expressing cells was enhanced in association with down-regulation of PHD2 and up-regulation of HIF-1. Furthermore, endothelial cell tube formation assay revealed enhanced release of pro-angiogenic factors from AREL1-expressing cells. Therefore, these results suggest that elevated expression of AREL1 contributes to tumorigenesis through targeting PHD2 as well as IAP antagonists, thus blocking apoptosis and enhancing angiogenesis.

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October 19-21, 2017 | Rome, Italy

Value of non-contrast MR imaging with diffusion-weighted imaging for detection of primary small (≤ 20 mm) solid pancreatic tumors and prediction of pancreatic ductal adenocarcinoma

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Aim of this study is to determine the diagnostic performance of noncontrast MRI with diffusion-weighted imaging (DWI) (NonMRI) for detection of primary small (<20 mm) pancreatic solid tumor and prediction of pancreas ductal adenocarcinoma (PDAC) in comparison with pancreas CT (PanCT) and pancreas MRI with MR cholangiopancreatography (PanMRI). The institutional review board approved this retrospective study and waived the requirement for informed consent. A total of 126 patients who underwent PanCT and PanMRI, including 94 small (<20 mm) pancreatic tumors (51 PDACs, 34 neuroendocrine tumors [NETs], 9 solid pseudopapillary tumors [SPTs]), and 32 patients with normal pancreas, comprised study population. Two observers assessed three sets of images: PanCT, PanMRI and NonMRI (T1- and T2-weighted images and DWI). ROC curve analysis, diagnostic accuracy (area under the receiver operating characteristic curve [Az]) were used for statistical analysis. On NonMRI and PanMRI, all of tumors except one NET were detected, but eight tumors (6 NETs, 1 PDAC, 1 SPT) were not detected on PanCT ($P < 0.01$). For prediction of PDAC, the Az value of the NonMRI (0.884 for observer 1; 0.930 for observer 2) was comparable with PanCT (0.922; 0.924) ($P > 0.05$), and inferior to PanMRI (0.930; 0.977) ($P < 0.05$), but all of 51 PDACs were considered as probable or definite PDAC on NonMRI by both observers. In conclusions, NonMRI showed better performance than PanCT, and competitive performance to PanMRI for detection of primary small solid pancreatic tumors, and showed reasonable sensitivity for prediction of PDACs compared with PanCT and PanMRI.

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October 19-21, 2017 | Rome, Italy

Does low volume high-intensity interval training elicit superior benefits to continuous low to moderate-intensity training in cancer survivors?

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It is generally recommended that exercise form part of the standard of care for all cancer survivors, however, the optimal evidence-based clinical exercise guidelines for cancer survivors are currently not clear. The aim of this study was to determine the effectiveness of low volume high-intensity interval training (LVHIIT) and continuous low to moderate-intensity exercise training (CLMIT) on health outcomes in cancer survivors. Sedentary cancer survivors (n=75) within 24 months of diagnosis, aged 51±12 y were randomised into three groups for 12 weeks of LVHIIT (n=25), CLMIT (n=25) or control group (n=25). The LVHIIT group performed 7 x 30s intervals (≥85% predicted maximal heart rate), the CLMIT group performed continuous aerobic training for 20 min (≤55% predicted maximal heart rate) on a stationary cycle, 3 times per week. An interaction effect (p=0.01) for waist circumference in the LVHIIT group was found. The LVHIIT group had larger improvements in emotional well-being compared to the other groups (p<0.01). Participants in the CLMIT and LVHIIT group demonstrated improvements in physical and functional well-being (p< 0.01). LVHIIT elicited greater benefits in improving waist circumference and emotional well-being compared to the other groups in this study. Exercise positively impacted body composition, white blood cell count (WBC) and haemodynamic variables, without any adverse effects. Future research should explore the mechanisms involved in the changes reported in this study, so that clinicians can provide clinically relevant evidenced-based exercise prescription for cancer survivors.

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October 19-21, 2017 | Rome, Italy

Systematical administration of *Clostridium ghonii* spores results in significant tumour regression and strong antitumour Th1 responses in TC-1 tumour bearing mice

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Up to 85% of solid cancers, once diagnosed, lost the opportunity to be operable. These cancers have anoxia regions that limit the effectiveness of conventional therapies, which however, provide a haven for anaerobic bacteria. Our laboratory has adapted the spores of an extracellular *Clostridium ghonii* strain that caused targeted oncolysis by selectively germinating, multiplying and digesting away of the solid cancer extramatrix, cellular structure, and cancer cells, resulting in significant enhanced tumour regression. Other anaerobic bacteria also showed a Toll-like receptor 4-mediated antitumor host response together with significant increases of intra-tumour IFN γ , CXCL9 and CXCL10 levels as well as more infiltration of macrophages, neutrophils, CD4⁺ and CD8⁺ T cells in C3H/HeN mice. In this report, we employed a HPV E7 transformed TC-1 cell tumour bearing mice as a model and demonstrated that intratumoural and/or intravenous administration of a strain of a devirative of *Clostridium ghonii* (DCG) spore leads to a significant tumour regression and a tumour local pro-inflammatory response characterized with increased levels of IL-6, IL-17 and IFN γ . IFN γ secreting T cells are also attracted to the tumour site. Low numbers of antigen specific T cells were elicited after DCG treatment are elicited by intravenous DCG treatment. The results suggested that both oncolytic effects and the anticancer immune responses are contributing to cancer regression. Furthermore, strategies for optimum combined oncolytic, i.e.: oncolytic therapy, if combined with a therapeutic vaccine, more antigen specific T cells may be attracted to the tumour site and therefore, may achieve better outcome for cancer treatment.

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25th WORLD CANCER CONFERENCE

October 19-21, 2017 | Rome, Italy

Studies on anti-neoplastic enzyme: enhanced L-asparaginase activity by filamentous fungus from the Brazilian Savanna using Plackett-Burman Design for screening of culture medium variables

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L-asparaginase is an enzyme used for treatment of Acute Lymphoblastic Leukemia (ALL) in children. Neoplastic cells cannot synthesize L-asparagine unlike normal cells due the absence of L-asparagine synthetase; therefore they obtain the required asparagine from circulating pools. It is important to find new sources of Lasparaginase producing microorganisms that can avoid adverse effects obtained from bacterial L-asparaginase, such as anaphylactoid reactions. Screening and selection of the fungi and optimum concentration of the medium component are very important to determine the overall economic feasibility of the production process. Therefore, the purpose of this study was to evaluate the important variables that influence Lasparaginase activity by a filamentous fungus isolated from the Brazilian Savanna soil. Eleven independent variables were considered to evaluate their effect on Lasparaginase activity by a filamentous fungus (DCFS10) in submerged fermentation. The different variables were prepared in two concentration levels, (-1) low level and (+1) high level. L-asparaginase activity was assayed by measuring the amount of aspartate hydroxamate produced from asparagine and hydroxylamine according to Drainas et al. (1977). The results obtained from PBD showed a wide range of Lasparaginase activity, from $0.5 \text{ U/g} \pm 0.018$ to $6.5 \text{ U/g} \pm 0.284$. Studies are being conducted in order to purify L-asparaginase produced in this culture medium. This study showed that the screening of culture medium variables using Plackett-Burman increased L-asparaginase activity of a filamentous fungus isolated from the Brazilian Savanna soil as a potential novel anti-leukemic source from eukaryote cell.

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October 19-21, 2017 | Rome, Italy

Why extracts of five Indian plants cure cancer: Enhanced protection of DNA but destruction of nucleotides through the endogenous fenton reaction, and inhibition of human topoisomerases**Rajagopal Chattopadhyaya and Indrani Kar**
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The influence of substoichiometric amounts of seven plant extracts in the Fenton reaction-mediated damage to deoxynucleosides, dNMPs, dNTPs and supercoiled plasmid DNA were studied to rationalize anticancer properties reported in the extracts of *Acacia catechu*, *Embllica officinalis*, *Spondias dulcis*, *Terminalia belerica*, *Terminalia chebula*. Extracts from these five plants, as well as four pure compounds contained, enhance the extent of damage in Fenton reactions with all monomeric substrates but protect supercoiled plasmid DNA, compared to standard Fenton reactions. However, *Dolichos biflorus* and *Hemidesmus indicus* extracts generally do not show this enhancement for the monomeric substrates though they protect plasmid DNA. A catalytic mechanism involving the presence of a ternary complex of the nucleoside / nucleotide substrate, a plant compound and the hydroxyl radical was proposed [J. Biomol. Struct. Dyn. 2016; doi:10.1080/07391102.2016.1244493]. Such a mechanism cannot operate for plasmid DNA. These plant extracts will slow down DNA replication in rapidly dividing cancer cells. In another set of experiments, extracts of the same five plants completely inhibit human topoisomerase I at 40 µg/ml concentration while *Hemidesmus indicus* and *Dolichos biflorus* extracts inhibit partially. All seven plant extracts partially inhibit human topoisomerase II at 120 µg/ml concentration. Chebulagic and chebulinic acids purified from *Terminalia chebula* extract inhibited human topoisomerase I at around 2 µM and 3 µM respectively [Molecular Enzymology and Drug Targets 2017. Vol. 2. No. 2. <http://www.imedpub.com>]. The nuclear fragmentation leading to apoptosis observed earlier in cancerous cell lines with such plant extracts may thus be explained by the inhibition of topoisomerases.

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October 19-21, 2017 | Rome, Italy

Second hand smoking is positively associated with breast cancer risk but not with N-acetyltransferase 2 genetic variants among Arab women in Israel—a case-control studyAvraham Z¹, Baron-Epel O¹, Hemmond SK² and Keinan-Boker L^{1,3}¹University of Haifa, Haifa, Israel²University of California, USA³Israel Ministry of Health, Israel⁴Ziv Medical Center, Israel

Background & Aim: The effect of second-hand smoking (SHS) on breast cancer etiology is controversial. Genetic variants of the enzyme N-Acetyl-transferase 2 (NAT2) which is involved in the metabolism of tobacco carcinogens, may modify the association between SHS and breast cancer. The aim of the current study was to evaluate the relationship between SHS and breast cancer risk by NAT2 variants in Arab women in Israel, a unique population with high exposure to SHS and low active smoking and alcohol consumption rates.

Methods: This is a population-based case-control study consisting of never-smoking Arab women aged 30-70 from Northern Israel: 137 prevalent (diagnosed in 2008-2013) breast cancer patients and 274 population-based controls. All participants were interviewed using a detailed questionnaire relating to past and current exposure to SHS and to socio-demographic, gynecological and obstetric characteristics. Each participant provided a buccal smear for NAT2 genotype analyses. Logistic regression models adjusted for potential confounders and stratified by NAT2 variants were used to assess the association between SHS and breast cancer.

Results: SHS was associated with breast cancer risk with an adjusted odds ratio (OR) of 2.14 (95% confidence interval, CI 1.21-3.78). Higher exposure to SHS was associated with higher risk of breast cancer compared to never exposed women, those exposed to SHS during childhood, adolescence and currently had an OR of 3.60 (95% CI 1.85-7.21) while those exposed during adolescence and currently but not during childhood had an OR of 1.73 (95%CI 1.05-2.86). NAT2 variants did not modify these associations.

Conclusions: SHS exposure in Arab women that never smoked is associated with increased risk for breast cancer. NAT2 genetic variation does not seem to play a role in the association. Additional studies are needed in order to support these findings.

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October 19-21, 2017 | Rome, Italy

Successful anesthetic management for a medialization thyroplasty in a case of vagus nerve damage from breast cancer recurrence

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Introduction: Medialization thyroplasty is a procedure for voice palliation secondary to vagus nerve damage. An intraoperative voice assessment may be necessary to evaluate the success of the procedure, and anesthetic management should not impair the ability of the patient to follow instructions. We present the case of a patient with unilateral vocal cord paralysis presenting for thyroplasty where the use of local anesthesia provided significant benefits.

Case Report: A 58-year-old female with left unilateral vocal cord paralysis presented for a medialization left thyroplasty with Gore-Tex graft. Two milligrams of midazolam were administered in the preoperative holding area. In the operating room, a propofol infusion was initiated at 75 mcg/kg/min and discontinued after a local anesthetic injection of the surgical site (1% lidocaine with 1:100,000 epinephrine) had been performed by the surgeon. Phenylephrine and oxymetazoline were also administered intranasally. A left thyroid cartilage window was created to enter the periosteum, perichondrium, and the inner perichondrium. A speech pathologist used a nasal fiberoptic scope to inspect the larynx. Under direct visualization, the Gore-Tex was placed behind the vocalis muscle, pushing it medially. Intraoperative voice assessment verified correct placement of the graft. The patient maintained spontaneous ventilation and the procedure was completed without complications.

Discussion: The use of local anesthesia with minimal sedation proved to be successful for many reasons in this case. This modality allowed for real time intraoperative voice assessment and proper placement of the Gore-Tex graft, potentially leading to improved surgical outcomes. Additionally, the use of local anesthesia avoided possible complications of laryngeal mask airway (LMA) insertion. While some studies have performed thyroplasty using an LMA, this modality increases the pharyngeal space and decreases exposure to the surgical field, potentially interfering with vocal cord medialization. Sedatives such as dexmedetomidine may also be administered with local anesthesia to inhibit laryngeal motion and reflexes without impairing respiration, thus allowing for a quiet surgical field and safe intraoperative voice assessment. Performing a thyroplasty while the patient is awake can potentially lead to better surgical outcomes, decreased surgical/anesthesia complications, a more cost and time effective treatment and better tolerated treatment for patients with significant sensitivity to anesthetics.

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