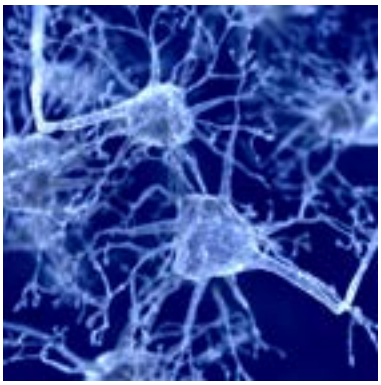
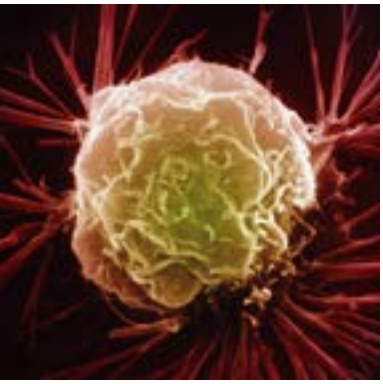
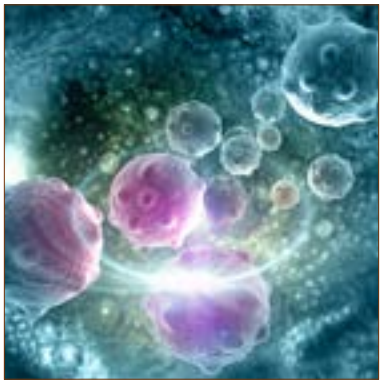
Keynote Forum
November 27, 2017

Oncology and Biomarkers Summit 2017







Annual Congress on

ONCOLOGY AND BIOMARKERS SUMMIT

November 27-28, 2017 | Atlanta, USA

Bakhos A Tannous

Harvard Medical School, USA

Tumor-educated platelets: A blood-based platform for biomonitoring and molecular cancer diagnostics

Tumor-educated blood platelets (TEPs) are implicated as central players in the systemic and local responses to tumor growth, thereby altering their RNA profile. In this presentation, we will discuss the potential use of TEPs for pan-cancer multiclass cancer and companion diagnostics, enabling clinical advances in blood-based “liquid biopsies”.

Speaker Biography

Bakhos A Tannous is an Associate Professor of Neurology at Harvard Medical School and Director for the Interdepartmental Neuroscience Center at the Massachusetts General Hospital. He is a Member of the Dana Farber/Harvard Cancer Center and also acts as Co-Director of the Molecular Neurogenetics Unit-East and Director of the MGH Viral Vector Production Facility. His research interest includes novel imaging and high throughput discovery of gene/cell/drug therapies for brain tumors, as well as blood-based platforms for cancer molecular diagnostics. He has published >100 papers in peer-review journals and serves as an Editorial Board Member of several journals.

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Marsha Rich Rosner

University of Chicago, USA

Rewiring metabolic and redox networks in cancer as a novel diagnostic and therapeutic strategy

One of the most exciting strategies that has recently gained traction for treatment of cancer is to target metabolic processes. Although metabolic drugs that work in theory have been identified, the glycolytic status of the tumors often makes these approaches ineffective. Recent work from the Rosner laboratory has identified a transcription factor that controls the respiration status of triple-negative breast cancer (TNBC), the most aggressive subtype of breast cancer. Therapeutic removal of this protein promotes sensitivity to agents that target oxidative phosphorylation such as metformin. Bioinformatic analyses of patient data also suggests that use of this transcription factor in conjunction with genes involved in oxidative phosphorylation can serve as biomarkers to predict therapeutic response to such treatments in not only breast cancer but across multiple cancer types. These findings provide a conceptual framework for cancer therapy development and can be leveraged in conjunction with other complementary treatments for both patient selection and long-term treatment.

Speaker Biography

Marsha Rich Rosner has earned her BA in Biochemistry from Harvard University and her PhD in Biochemistry from MIT. In 1982, she became an Assistant Professor in the Dept. of Applied Biological Sciences at MIT. She has joined the University of Chicago faculty as an Associate Professor in 1987 and was promoted to Full Professor in 1994. She was the Founder and First Chair of the Committee on Cancer Biology, a degree-granting graduate program leading to the PhD in Cancer Biology. She was appointed the Charles B Huggins Professor and later became the Chair of the Ben May Department for Cancer Research for 13 years. She is currently a Fellow of the Institute for Molecular Engineering and the Institute for Genomics and Systems Biology. She has received several honors including election as a Fellow of the American Association for the Advancement of Science (AAAS) in 2011.

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George Vasmatzis

Mayo Clinic, USA

Molecular karyotypes: SVA tools for junction detection and copy number variation of genome-wide chromosomal rearrangements by mate-pair sequencing (MPseq)

We have developed MPseq all long-insert next-generation sequencing approach for the detection of genomic structural variants. SVA tools is a set of algorithms to detect both chromosomal rearrangements and large (>10kb) copy number variants (CNVs) in genome-wide MPseq data. SVA tools can also predict disrupted genes and gene fusions and characterize the genomic architecture of complex rearrangements. SVA tools with MPseq provides comprehensive and accurate whole-genome junction detection with improved breakpoint resolution, compared to karyotype FISH and CMA combined. Copy number variation (CNV) is a common form of structural variation detected in aberrant human genomes, such as those observed in cancer. Cytogenetic techniques like chromosomal microarray (CMA) are widely used in analyzing these structural variations. An algorithm will also be presented, capable of performing copy number analysis from mate-pair sequencing (MPseq) data. The algorithm uses a step-wise procedure involving normalization, segmentation and classification of the sequencing data. The segmentation technique is novel in that it is the first technique to combine both read depth and discordant mate-pair reads to increase the sensitivity and resolution of CNV calls. This allows for the classification step to accurately calculate copy number.

Speaker Biography

George Vasmatzis is an Associate Professor in the Department of Molecular Medicine and a Member of the Mayo Clinic Cancer Center, as well as the Co-Director of the Biomarker Discovery Program, within the Center for Individualized Medicine. He is also the Founder of a software company called WholeGenome. His research program consists of bioinformatics specialists, molecular biologists, epidemiologists and pathologists. This team has demonstrated success in discovery and translation of several biomarkers as well as developing evidence-based models that should help clinicians stratify (cancer) patients in order to provide each individual with the appropriate care. With the recent advances in Next Generation Sequencing (NGS) technologies, his laboratory has been engaging in massive sequencing to scan the genome of cancer cells for abnormalities that can be used for clinical purposes such as diagnosis and stratification of patients for optimal treatment. He has published papers in Journal of Clinical Oncology, Cancer Research and BLOOD, further demonstrate our discovery, validation and translation capabilities. Recently, Mayo Clinic has launched a whole genome mate-pair sequencing test that was primarily developed by his program.

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George G Chen

The Chinese University of Hong Kong, China

ZBP-89 and hypoxia-inducible factor 1a in hepatocellular carcinoma

The level of hypoxia-inducible factor 1a (HIF-1a) plays an important role not only in the development of in hepatocellular carcinoma (HCC), but also in its metastasis, recurrence and resistance to anti-tumor chemotherapy. ZBP-89 is a transcription factor that binds to gene promoter GC-rich sequence to activate or suppress the transcription of genes that are associated with cell growth and cell death. However, the relationship between HIF-1a and ZBP-89 is unknown in HCC. In this study, we examined the levels of HIF-1a and ZBP-89 in HCC cells and HCC tissue samples. We found that the expression of HIF-1a was significantly in all HCC tumor samples, compared with non-tumor liver tissues. The levels of ZBP-89 was slightly increased in the well-differential HCC tumor samples but obviously decreased in moderately or poorly differential tumor samples, compared with non-tumor liver tissue samples. Overall, the expression of ZBP-89 was inversely correlated with the stage of the tumor differentiation and the level of HIF-1a in HCC samples, indicating that the higher HIF-1a, the lower ZBP-89. In conclusion, there is a negative relationship between the level of HIF-1a and the expression of ZBP-89 in HCC. The data suggest that the low level of ZBP-89 may contribute to the upregulation of HIF-1a. Considering the fact that ZBP-89 can induce apoptosis in HCC cells, whether upregulation of ZBP-89 will negatively impact the expression of HIF-1a remains an interesting question.

Speaker Biography

George G Chen is a Professor in the Department of Surgery, Director of Surgical Research Laboratories and Faculty of Medicine of Chinese University of Hong Kong, China. He has extensive experience in cancer research, particularly in the area of liver and lung cancers. He has authored or co-authored more than 200 papers and has written a number of books or book chapters.

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November 28, 2017

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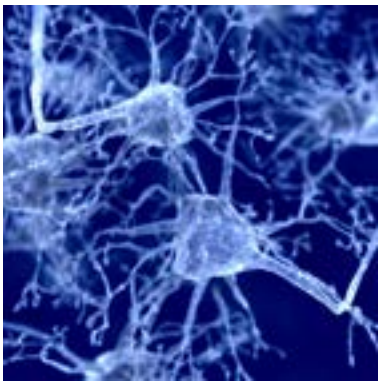

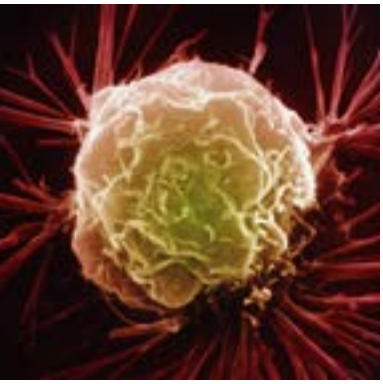

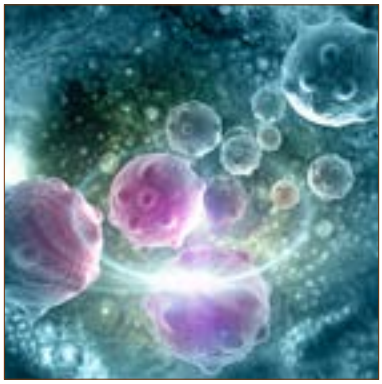

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Jennifer Wu

Northwestern University, USA

Novel antibody for cancer immunotherapy: Beyond and synergistic with immune checkpoint blockade therapy

During tumorigenesis, human cells were induced to express a family of MHC I-chain related molecules A and B (MICA and MICB, generally termed MIC) on the surface which serve as the ligands for the activating immune receptor NKG2D expressed by all human NK, CD8 T, NKT and subsets of γδ T cells. Theoretically, engagement of NKG2D by tumor cell surface MIC deemed to signal and provoke the immune system to eliminate transformed cells. Clinically, almost all advanced tumors in cancer patients produce soluble MIC through proteolytic shedding mediated by metalloproteases, or by release in exosomes derived from the cell membrane. Tumor-derived sMIC is known to be highly immune suppressive and profoundly insults the immune system by downregulating receptor NKG2D expression on effector NK and T cells, driving the expansion of tumor-favoring myeloid suppression cells, skewing macrophages into alternatively activated phenotypes and perturbing NK cell peripheral maintenance. High levels of serum sMIC significantly correlate with advanced diseases of many types of cancer. These observations clearly endorse sMIC to be a cancer immune therapeutic target. However, due to mice lack homologues to human MIC, this concept was not proven until our recent studies. Using a "humanized" MIC-transgenic spontaneous mouse model which recapitulates the NKG2D-mediated onco-immune dynamics of human cancer patients, we show that neutralizing circulating sMIC with a first-in-field monoclonal antibody B10G5 alleviates the immune suppressive effect of sMIC and revamps endogenous anti-tumor immune responses. Therapy with B10G5 results in effective debulking of primary tumor and elimination of metastasis, with no observed toxicity. Furthermore, we show that clearing sMIC with B10G5 also enhanced the efficacy of other cancer immunotherapeutic modalities, such as immune checkpoint blockade or adoptive cell-based therapy pre-clinically. Our study has launched a new avenue of cancer immunotherapy which can be readily translated into clinical trials.

Speaker Biography

Jennifer Wu joined Northwestern University in August 2017 as a tenured Professor in Urology. Dr. Wu previously served as a Professor of Microbiology and Immunology at the Medical University of South Carolina and the University of Washington. Dr. Wu obtained her PhD from the University of British Columbia in Canada followed by post-doctoral training in Fred Hutchinson Cancer Research Center (FHCRC) and faculty position at the University of Washington. Dr. Jennifer Wu's research focuses on understanding how cancer cells edit the immune system with the ultimate goal to develop effective immune therapy to control cancers.

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Vagharsh Khachikyan

Life Sciences International Postgraduate Educational Center, Armenia

The dysfunction of cGMP-activated Na^+/Ca^{2+} exchange controlling cell hydration is a primary mechanism for carcinogenesis

Overhydration of cells is a hallmark for early detection of cancer. However, the nature of the metabolic mechanism, the dysfunction of which leads to decontrolling of cell hydration and generation of Warburg phenomena in cancer cells, has not been elucidated yet. Na^+/K^+-ATPase, having a central role in metabolic regulation of cell hydration, has three catalytic isoforms with different affinities to ouabain and functional activities. Among these isoforms, the α3 isoform, with the highest affinity to ouabain, isn't involved in ion-transporting process and has an intracellular signaling function. It is known that α3 isoforms of Na^+/K^+-ATPase, which are absent in non-excitable cells of healthy animals, are highly expressed in cancerous cells. Based on this, the expression of these isoforms is considered as one of the early hallmarks for carcinogenesis. However, by our previous work it has been shown that all 3 isoforms are present both in tumor and non-excitable tissues of mice carrying sarcoma-180. It has also been shown that α3 isoform, which is absent in non-excitable cells of healthy animals, appears in non-cancerous tissues of women with breast cancer, as well as in all non-excitable tissues of mice carrying sarcoma-180 tumor. Moreover, it has also been shown that this expression of α3 isoform is accompanied by cell hydration. Based on these data, it has been hypothesized that the dysfunction of intracellular signaling system controlling cell hydration could serve as a primary mechanism for carcinogenesis. To check this hypothesis, in non-excitable tissues of healthy and sarcoma-180 carrying mice (including tumor tissues), dose-dependent ouabain effects on Na^+/K^+-pump activity, cell hydration, intracellular cyclic nucleotides (cGMP and cAMP), glycolysis rate (lactate concentration in blood and lactate dehydrogenase activity), membrane permeability for protons, Na^+/H^+, Na^+/Ca^{2+} exchange and cell proliferation by means of electrophysiological, isotope, immunoassay and microscopic methods were studied. These studies have brought us to conclusion that the dysfunction of α3 isoform-dependent cGMP-activated Na^+/Ca^{2+} exchange in forward mode, which controls Na^+/K^+-pump activity, cell hydration, membrane permeability for Na^+ and Ca^{2+}, glycolysis activity and cell proliferation, is a primary mechanism for generation of cell overhydration and Warburg phenomena leading to carcinogenesis. Therefore, α3 isoform-dependent cGMP-activated Na^+/Ca^{2+} exchange in forward mode has been suggested as a novel therapeutic target for early stage of carcinogenesis.

Speaker Biography

Vagharsh Khachikyan has received his PhD in Cancer Therapy at Yerevan State Medical University. Currently, he is a Physician at National Center of Oncology named after V A Fanarjyan and a Senior Scientist and Lecturer at UNESCO Chair in Life Sciences at Life Sciences International Postgraduate Educational Center. He also conducts lectures on oncology at UNESCO Chair in Life Sciences. His research includes the study of the dysfunction of intracellular signaling system responsible for cancer generation. He has participated in many international trainings and conferences.

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E Shyam P Reddy

Morehouse School of Medicine, USA

Decoding of non-coding DNA and non-coding RNA: Noncoding RNA-encoded novel peptides/proteins regulate migration of cancer cells

Only two percent of the human genome was shown to code for proteins and the rest of the 80–90 percent was shown to transcribe into non-coding RNAs. Micro RNAs (miRNAs) and long noncoding RNAs (lnc RNAs) fall into this category of non-coding RNAs. Recently, it was shown that noncoding RNA codes for peptides that regulate the expression of active mature miRNAs in plant cells. Here, we demonstrate the presence of an ORF in non-coding RNAs which codes for peptides or small proteins that show novel biological properties in human cells. We show noncoding RNAs-encoded peptides/ proteins (miPEPs) have homology to breast cancer tumor suppressor and to proteins that promote longevity and health span. They also inhibit the migration of cancer cells by regulating epithelial to mesenchymal transition of these cells. These miPEPs have the potential to serve as diagnostic markers for metastasis and can also be used as therapeutic agents to many cancers. We have also discussed how these novel peptides/proteins encoded by noncoding RNAs are evolved in nature and their potential role in cancer and other human diseases. Thus, these novel tumor suppressors will revolutionize the future biology, diagnosis and therapy.

Speaker Biography

E Shyam P Reddy is a Professor and Director, Cancer Biology Program, Department of OB/GYN, Morehouse School of Medicine, Georgia Cancer Center for excellence, Grady Memorial Hospital, Atlanta, Ga. He carried out his PhD work at the Center for Cellular and Molecular Biology, Hyderabad, India and at Max Planck Institute for Biophysical Chemistry, Gottingen, West Germany. His PhD work was published as two papers (back to back) in the prestigious Nature journal for which he was awarded National Young Scientist award by the Prime Minister of India. He obtained postdoctoral training in Molecular Biology at Yale University, CT (Dr Weissman, PNAS member).

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Michael Retsky

Harvard TH Chan School of Public Health, USA

Perioperative use of NSAID might prevent early relapses in breast and other cancers: An upstream approach

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 five 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 micro-metastases, 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. We suggest this would be most effective for triple negative breast cancer and be especially valuable in low and middle income countries. Similar bimodal patterns have been identified in other cancers suggesting a general effect.

Speaker Biography

Michael Retsky (PhD in Physics from University of Chicago) made a career change to cancer research 30 years ago. He is on Staff Member at Harvard TH Chan School of Public Health and Faculty at University College London. He was on Judah Folkman's Staff at Harvard Medical School for 12 years. He is Editor of a Nature/Springer book on the breast cancer project published July 2017. He was the first person to use what is now called metronomic adjuvant chemotherapy and is a founder and for 10 years was on the Board of Directors of the Colon Cancer Alliance. He has published more than 60 papers in physics and cancer.

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