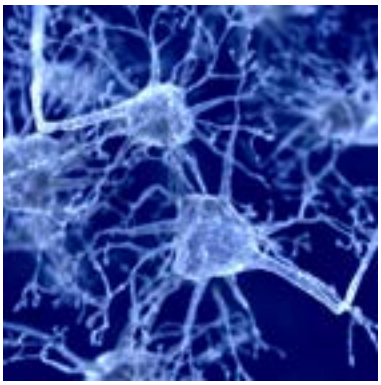
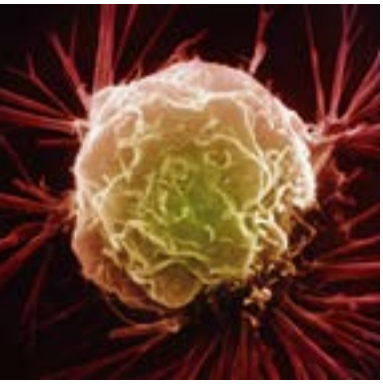
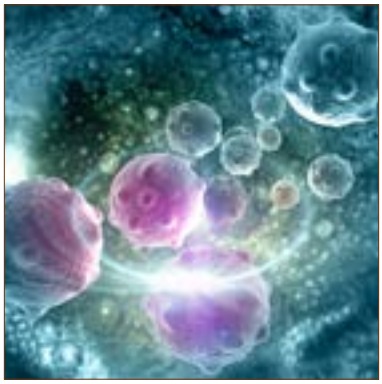
Scientific Tracks & Abstracts
November 27, 2017

Oncology and Biomarkers Summit 2017







Annual Congress on

ONCOLOGY AND BIOMARKERS SUMMIT

November 27-28, 2017 | Atlanta, USA

New biomarkers for prognosis of aggressive prostate cancer

Carlos S Moreno
Emory University, USA

A large number of men are diagnosed with prostate cancer each year, but many will not experience morbidity or mortality as a result of their cancers. Therefore, biomarkers for prostate cancer are necessary to carefully select patients for initial diagnostic biopsy or to facilitate care decisions for men who have already been diagnosed with prostate cancer. RNA-based approaches to biomarker discovery allow the investigation of non-coding RNAs, gene fusion transcripts, splice variants and multi-gene expression panels in tissue, urine or blood as opportunities to improve care decisions. In an effort to identify biomarkers of recurrence, we performed global RNA sequencing on 106 formalin-fixed, paraffin-embedded (FFPE) prostatectomy samples from 100 patients at three independent sites, defining a 24-gene signature panel (Sig24). The 24 genes in this panel have functions in cell cycle progression, angiogenesis, hypoxia, apoptosis, PI3K signaling, steroid metabolism, translation, chromatin modification and transcription. In our validation study, patients with high Sig24 scores had an increased risk of developing metastasis (HR: 3.78, 95% CI: 1.96-7.29, p<0.001) or experiencing prostate cancer specific mortality (PCSM) (HR: 6.54, 95% CI: 2.16-19.83, p<0.001) in an independent validation case cohort set of 235 patients from the Mayo Clinic. The findings of this study demonstrate the applicability of Sig24 for the prognosis of metastasis or PCSM following radical prostatectomy. Future studies investigating the combination of Sig24 with available prognostic tests may provide new approaches to improve risk stratification for patients with prostate cancer.

Speaker Biography

Carlos S Moreno is Associate Professor of Pathology and Laboratory Medicine and Biomedical Informatics at Emory University, where he is a Member of the Winship Cancer Institute in the Cancer Genetics and Epigenetics Program. He has obtained his BS and MS in Aeronautics and Astronautics from MIT and worked for NASA before he earned his PhD in Genetics and Molecular Biology from Emory University in 1998. He specializes in Cancer Bioinformatics and Cancer Genomics and his laboratory has used whole genome expression analysis and next-generation sequencing to identify biomarkers of aggressive disease in prostate cancer.

e: cmoreno@emory.edu

Notes:

Inhibition of breast cancer bone metastasis and pancreatic and colon cancer by synthetic curcumin analogs

Mamoru Shoji
Emory University, USA

Curcumin (diferuloylmethane) is a β-diketone constituent of the turmeric. It is used as a spice to give a specific flavor and yellow color to curry. However, its clinical efficacy is poor because of its low solubility. He worked with professors Liotta and Snyder at the Chemistry department to synthesize a series of novel monocarbonyl analogs of curcumin (MACs) approximately 100 analogs including EF24, EF31 and UBS109. Dr. Shoji's laboratory and the NCI tested the analogs for the anticancer activity. The NCI determined the mean growth inhibitory concentration (GI-50) of EF24, curcumin and cisplatin on the NCI-60 cancer cell panel, which are 0.7 μM, 7.3 μM and 9.5 μM, respectively. MACs do not kill normal breast cells MCF-10A but kill all cancer cells tested (KB-3-1, TU212, MiaPaCa, SE-Mel-28, RPMI-7951, and MDA-MB- 231 cells) at concentrations (0-20 μM). MACs inhibit NF-κB by inhibiting IKK-α and IKK-β. UBS109 inhibited breast cancer metastasis and osteolysis by inhibiting osteoclasts precursors and osteoclasts, but promotes new bone formation by stimulating osteoblast activation. UBS109 and EF24 inhibited four pancreatic cancer cell lines 100% at less than 1.25 μM, whereas gemcitabine did not up to 20 μM. UBS109 significantly inhibited MiaPaCa-2 pancreatic cancer xenografts and colon cancer (HT-29 and HCT-116) xenografts in mice at 25 mg/kg, iv once a week better than a combination of oxaliplatin (5 mg/kg) and 5FU (30 mg/kg) iv.

Speaker Biography

Mamoru Shoji has developed synthetic monocarbonyl analogs of curcumin (MACs) out of the 100 synthetic analogs with Drs. DC Liotta, JP Snyder, BK Adams and other colleagues. He and his colleagues try to move the analogs for clinical trials.

e: mshoji@emory.edu

Notes:

RET oncogene activation in lung adenocarcinoma with neuroendocrine differentiation is mediated through EGFR

Farhad Kosari
Mayo Clinic, USA

Lung adenocarcinoma (AD) accounts for 40% of all non-small cell lung cancers. Achaete-scute homolog 1 (ASCL1) is a neuroendocrine transcription factor specifically expressed in 10-20% of lung AD with neuroendocrine (NE) differentiation (NED). Our recent data demonstrated that ASCL1 was as an upstream regulator of the RET oncogene in AD with high ASCL1 expression (A+AD). RET is a receptor tyrosine kinase with two main human isoforms; RET9 (short) and RET51 (long). We found that elevated expression of RET51 associated mRNA was highly predictive of poor survival in stage-1 A+AD ($p=0.0057$). Functional studies highlighted the role of RET in promoting invasive properties of A+AD cells. Further, A+AD cells demonstrated close to 10-fold more sensitivity to epidermal growth factor receptor (EGFR) inhibitors, including gefitinib and lapatinib, than AD cells with low ASCL1 expression. Treatment with EGF robustly induced phosphorylation of RET at Tyr-905 in A+AD cells with wild type EGFR. Immunoprecipitation experiments found EGFR in a complex with RET in the presence of EGF and suggested that RET51 was the predominant RET isoform in the complex. In the microarray datasets of stage-1 and all stages of A+AD, high levels of EGFR and RET RNA were significantly associated with poor overall survival ($p<0.01$ in both analyses). These results implicate EGFR as a key regulator of RET activation in A+AD and suggest that EGFR inhibitors may be therapeutic in patients with A+AD tumors even in the absence of an EGFR or RET mutation.

Speaker Biography

Farhad Kosari is an Assistant Professor in the Department of Molecular Medicine at Mayo Clinic. His interests are in the discovery and development of clinically relevant biomarkers for prostate and lung cancers. His domains of expertise are Bioinformatics and Molecular Biology, particularly as related to the development of biomarker based assays. His most recent project focus has been in lung adenocarcinomas with neuroendocrine (NE) differentiation (ND-AD). Characterized by the expression of ASCL1, these ND-ADs are a sizable subset of lung tumors that are largely understudied and underappreciated. His group has recently discovered the main drivers in these tumors and is currently investigating therapeutic options for patients with ND-AD.

e: Kosari.Farhad@mayo.edu

Notes:

Adaptive radiotherapy and its clinical application: An institutional experience

Suman Das
Queens NRI Hospital, India

Introduction: Radiotherapy is an integral part of cancer treatment and with the advent of newer technologies it has undergone a paradigm shift. The adaptive radiotherapy or more appropriately adaptive re-planning refers to any strategy that repeats the treatment planning process during treatment in response to anatomic changes in the target volume or the nearby critical structures.

Materials & Methods: Patients with proven evidence of malignancy were considered for radiotherapy with curative intent. The patients were simulated and planned with IMRT radiotherapy technique. After necessary quality assurance exercise they were approved for treatment. All patients were subjected to daily image guidance using CBCT and KV X-ray. During the process, if any patient was observed to have significant variation in planning target volume due to anatomical change, were re-planned. The cases where the use of adaptive radiotherapy has resulted in significant clinical outcome were isolated for presentation.

Results: The adaptive radiotherapy was most commonly used for Head and Neck cancer due to anatomical changes for weight loss or change in the size of the node. These patients were significantly benefited in terms of saving the normal structures being radiated due to the anatomical change. We observed few special cases like Adenoid Cystic Carcinoma (ACC) of bronchus with collapsed lung where the collapsed lung was inflated during treatment and resulted in shifting of GTV medially and the adjacent critical structures. The patient was re-planned and was delivered curative dose of radiotherapy. It was observed that if such patients are not timely intervened the dose delivery to tumor would not be appropriate and the critical structures would get more dose of radiation. These patients were followed up and good clinical outcome was observed. The patient with ACC of bronchus had a disease-free interval of 38 months and she is surviving while writing this paper after 48 months with good quality of life.

Conclusion: The Adaptive re-planning or Adaptive Radiotherapy is a boon to the advancement of radiotherapy. This helps us to achieve better dose delivery to tumors and protection of adjacent normal structures. Though it has proven advantages in head and neck cancer, but it could also be very much useful in certain unusual cases like adenoid cystic carcinoma of bronchus. As per the literature, patients with ACC of bronchus treated with radiotherapy had a median survival of 23 months, where as our patient is surviving after 48 months while writing this paper.

Speaker Biography

Suman Das is a consultant Radiation Oncologist in Queens NRI Hospital Visakhapatnam India. He was granted UICC fellowship at University of Michigan Ann Arbor USA. He has got many publications in various peer reviewed journals of Oncology. He has special interest in Head and Neck cancers.

e: drsumandas@gmail.com

Notes:

allied academies

Annual Congress on

ONCOLOGY AND BIOMARKERS SUMMIT

November 27-28, 2017 | Atlanta, USA

Preclinical diagnosis of Alzheimer's disease

Tapan K Khan
West Virginia University, USA

The pathology of Alzheimer's disease (AD) occurs as a sequence of events that start years or decades before clinical dementia appears. A prolonged phase of preclinical AD has been described in numerous studies. Identification of individuals in the preclinical phase of AD would provide a critical window of opportunity for therapeutic intervention to slow the progression of the disease. Therapeutic interventions are currently focused on the later stages of AD (mild cognitive impairment [MCI] or AD dementia) and most clinical trials of these therapies have failed. Detection of various biomarkers hold enormous promise for identifying individuals with preclinical AD and predicting the development of AD dementia. In addition to AD biomarkers in cerebrospinal fluid (CSF) (Abeta42, tau and phosphor-tau), non-invasive neuroimaging can detect brain atrophy in the medial temporal area (measured by magnetic resonance imaging, MRI) and amyloid plaques (measured by positron emission tomography, PET). These biomarkers are now being used to support the preclinical AD diagnosis in the clinical research setting. Other neuroimaging studies have examined region-specific cerebral blood flow and microstructural changes as biomarkers of preclinical AD. Functional MRI (fMRI), diffusion tensor imaging (DTI) MRI, atrial spin labeling (ASL) MRI and advanced PET imaging have potential applications in preclinical AD diagnosis. In this presentation, we critically evaluate the utility of neuroimaging AD biomarkers in the diagnosis of preclinical AD and propose a comprehensive preclinical AD diagnostic algorithm based on neuroimaging and CSF biomarkers, as well as genetic markers of AD (Figure). Although commonly viewed as an abnormality of the brain, AD is a systemic disease with associated dysfunction in metabolic, oxidative, inflammatory and biochemical pathways in peripheral tissues, such as the skin and blood cells. This has led researchers to investigate and develop assays of peripheral AD biomarkers that require minimally invasive skin or blood samples.

Speaker Biography

Tapan K Khan has expertise in Alzheimer's disease biomarker. He has published numerous research articles in the field of Alzheimer's disease. He was an Associate Professor at the Blanchette Rockefeller Neurosciences Institute (BRNI). Currently, he is a Lead Research Scientist at the BRNI, West Virginia University. He is the Lead Investigator for the development of noninvasive diagnostics for Alzheimer's disease in his Institute. He has published a book, title: *"Biomarkers in Alzheimer's disease"* recently (Academic press). He is also an Associate Editor of the *Journal of Alzheimer's disease.*

e: tkhan@hsc.wvu.edu

Notes:

BRCA1 discovery to precision oncology: The road ahead

Veena N Rao
Morehouse School of Medicine, USA

Statement of the Problem: Breast cancer is the second leading cause of cancer-related deaths among women. BRCA1 mutations results in triple negative breast cancer (TNBC) and high grade serous ovarian cancer HGSOC. Majority of young AA women with BRCA1 mutations have a so-called TNBC with an aggressive phenotype. Currently there is no targeted therapy for TNBC. Our group has reported BRCA1 proteins, unlike the disease-associated proteins to interact with a druggable target Ubc9 which facilitates both the entry of BRCA1 proteins into the nucleus to cause ubiquitination of ER and TNBC tumor suppression. Many BRCA1 missense mutant alleles, termed variants of uncertain significance (VUS) are difficult to classify as benign or malignant. Therefore for a woman who carries a BRCA1 VUS allele, the risk of developing TNBC is unknown.

Hypothesis and Methodology: This work is based on the hypothesis that BRCA1 is a tumor suppressor gene and its coding region can harbor several mutations some of which are driver mutations and others passenger mutations similar to WT BRCA1. We tested this hypothesis by studying the various biological functions of BRCA1 mutant proteins so as to identify the driver mutations that lead to these TNBC.

Conclusion and Significance: Clinically, the ability to predict which of these are driver mutations that can result in TNBC offers unprecedented prospects for early detection to make informed decisions regarding prophylactic measures. The results from this study will stratify the risk for TNBC as well as develop personalized targeted therapy for women with BRCA1-associated TNBC thus reducing the mortality associated with these cancers to achieve health equity for all.

Speaker Biography

Veena N Rao is Professor and Co-Director of the Cancer Biology Program, GCC Distinguished Cancer Scholar in the Department of OB/GYN, at Morehouse School of Medicine. She has completed her PhD in Biochemistry at CCMB, India, Max Planck Institute, University of Edinburgh, and MIT, Boston. She did her postdoctoral work at the University of California, Yale University and National Cancer Institute. She has a long career beginning at University of Pennsylvania, Temple University as an Assistant Professor. She then moved to Thomas Jefferson University as Associate Professor where she identified the BRCA1 isoforms. She became Professor and Co-Director of the Division of Cancer Genetics at Drexel University and was recruited at Morehouse School of Medicine to train minority students in cancer research. Her work led to a patent that can stratify risk for TNBC and to develop targeted therapy for TNBC, a disease which currently has no targeted treatments available.

e: vrao@msm.edu

Notes:

GDF15, potential mediator of resistance and disease progression in breast cancer

Rita Nahta
Emory University, USA

Statement of the Problem: Breast cancer-related deaths are due primarily to drug-resistant, metastatic disease. Identification of molecular mechanisms mediating resistance and invasion will allow new targeted therapies to be developed. Growth differentiation factor 15 (GDF15) is an inflammatory cytokine overexpressed in many types of solid tumors, including breast. Past studies have linked high GDF15 levels with HER2 overexpression, drug resistance and cancer stem cell-like characteristics.

Methods: By IHC and informatics, we examined GDF15 in breast tumor tissues and correlated with clinical characteristics or outcomes. Using 2-d and 3-d cellular assays, we examined the role of GDF15 in breast cancer cell proliferation, epithelial mesenchymal transition (EMT), spheroid growth and invasion. Molecular studies, including genetic knockdown and pharmacological inhibition paired with western blotting and PCR, examined the mechanisms through which GDF15 promoted breast cancer cell invasion.

Findings: High GDF15 is associated with high tumor grade, ER-negative status and HER2 overexpression. Stable GDF15 transfection induces EMT and invasion. Upregulation of transcription factor FoxM1 with subsequent induction of target matrix metalloproteinases (MMPs) is required for GDF15-mediated effects, as FoxM1 knockdown and MMP inhibition rescues invasion and EMT. Further, GDF15 knockdown or pharmacological blockade significantly inhibits invasion of HER2-overexpressing and triple-negative breast cancer cells.

Conclusion & Significance: These findings support further preclinical investigation of the role of GDF15 in breast cancer progression and development of GDF15-targeted therapies for breast cancer treatment.

Speaker Biography

Rita Nahta is an expert in breast cancer pharmacology. She has published extensively on mechanisms of resistance to targeted therapies in breast cancer, with a focus on kinase signaling cross talk and novel combination approaches to treating drug-resistant breast cancer.

e: Rnahta@emory.edu

Notes:

Adipose/Macrophage fatty acid binding protein: A new marker for pro-tumor macrophages

Bing Li
University of Louisville, USA

Tumor associated macrophages (TAMs) play a critical role in cancer development and progression. However, due to the heterogeneity of TAMs, it remains a major challenge to identify clinically-relevant markers for pro-tumor TAMs. Here, we report that expression of adipocyte/macrophage fatty acid binding protein (A-FABP) in TAMs promotes breast cancer progression. While upregulation of A-FABP was inversely associated with breast cancer survival, deficiency of A-FABP significantly reduced mammary tumor growth and metastasis. Furthermore, we demonstrated that the pro-tumor effect of A-FABP was mediated by TAMs, in particular in a subset of TAMs with a CD11b+F4/80+MHCII-Ly6C- phenotype. Mechanistically, A-FABP expression in TAMs facilitated pro-tumor IL-6/STAT3 signaling through regulation of NFκB/miR-29b pathway (Figure). Collectively, our results suggest that A-FABP may represent as a new functional marker for pro-tumor TAMs. Tumor stroma contains heterogeneous macrophages with different phenotype and function, among which A-FABP is highly expressed in the subset of CD11b+F4/80+MHCII-Ly6C- promoting mammary tumor growth and metastasis through NFκB/miR-29b/IL-6 pathway. Thus, A-FABP represents a new functional marker for pro-tumor macrophages and a novel target for macrophage-based tumor immunotherapy.

Speaker Biography

Bing Li has completed his PhD in Immunology at Peking University Health Science Center, Beijing, China in 2004. He has expertise in the areas of obesity, chronic inflammation and mammary tumor development. His research is focused on dissecting the role of fatty acid binding proteins in regulation of metabolism and function of immune cells in different disease models

e: b.li@louisville.edu

Notes:

Evaluation of circulating endometrial cells as a biomarker for endometriosis

Chen Zhang
Peking University People's Hospital, China

Introduction: Endometriosis (EM) is a common disease among women of reproductive age but significantly under diagnosed in the absence of a reliable clinical marker. It has been reported that circulating endometrial cells (CECs) were present in peripheral blood of women with EM, providing clear and specific evidence of the presence of ectopic lesions. However, the clinical value of CECs is still unknown.

Methods: In this study, we established a method with high detection rate of CECs, examined the prevalence of CECs in patients with ovarian EM and compared the diagnostic performance with serum CA125, proposed a hypothesis of the pathogenesis of EM from the new perspective of CECs.

Results: The peripheral blood samples were collected from 59 participants and the blood cells were isolated for immunofluorescence staining via microfluidic chips. The cells that were positive for vimentin/cytokeratin and estrogen/progesterone receptor and negative for CD45 were identified as CECs. The detection rate of CECs reached 89.5% (17/19) in the EM group, which was significantly higher than that of the control group (15% (6/40), $P<0.001$) and was independent of menstrual cycle phases. Furthermore, a positive CEC assay detected 4/5 cases of stage I-II EM. In contrast, a positive CA125 test had limited value in detecting EM (13/19, 68.4%) and only detected one case of stage I-II EM.

Conclusion: In brief, CECs are a promising biomarker for EM with great potential for non-invasive diagnostic assay.

Speaker Biography

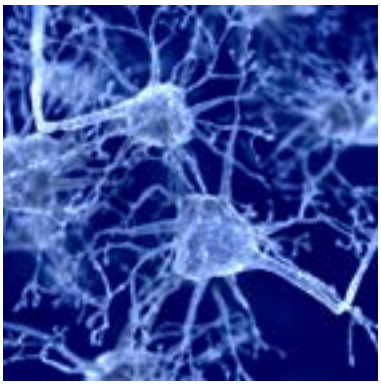
Chen Zhang is working on Ph.D. in Gynecology and Obstetrics at Peking University Health Science Center since September 2016. Her research interest has been on endometriosis and ovarian cancer, mainly focusing on biomarkers research and molecular mechanisms. Combining the characteristics of endometriosis and document reports, she and her team members found an effective and efficient method to detect and identify circulating endometrial cells in peripheral blood utilizing proprietary microfluidic chip which reveals a novel and promising diagnostic approach for endometriosis.

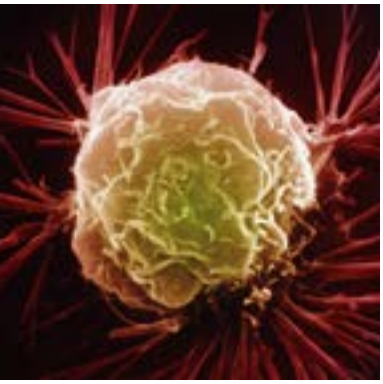
e: zhangchen20080925@163.com

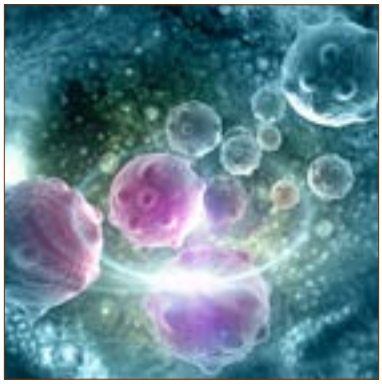
Notes:

Scientific Tracks & Abstracts
November 28, 2017

Oncology and Biomarkers Summit 2017







Annual Congress on

ONCOLOGY AND BIOMARKERS SUMMIT

November 27-28, 2017 | Atlanta, USA

Improving patient outcome through personalized radiation immuno-oncology approaches

Mohammad K Khan
Emory University, USA

Statement of the Problem: New immuno-oncology approaches have emerged, to improve outcome for cancer patients. These approaches involve the use of immune-checkpoint inhibitors (CTLA-4, PD-1, PD-L1, etc), agonists (4-1BB, Ox 40-L), and cytokines (IL2, IL-15), some of which have received FDA clearance. Future direction, now involves using these agents in combination with other approaches. One approach may involve the use of radiotherapy. Radiotherapy has been shown to have "immuno-genic" effects on tumor cells, T cells, APCs, as well as the tumor micro-environment. Post radiotherapy, abscopal effect, has been previously described, and can lead to immune-mediated control of distant sites of disease, when one site of tumor deposit is irradiated. The purpose of our efforts is to improve outcome in our melanoma mouse model, and translate these findings into ongoing clinical trials, involving radiation and immunotherapy.

Methods: We have developed a B16F10GP melanoma human syngeneic mouse model to evaluate the immunological effects of radiation, in combination with various immune-checkpoint modulators and cytokines (Figure 1). In addition, our work also involves the development of tumor exosomes as potential biomarkers of post radiation abscopal response.

Findings: We demonstrate that several elements are needed to maximize the optimum post radiation abscopal response, and that the response is CD 8 T cell mediated. Considerations, such as radiation dose, radiation fractionation, and timing of radiation with various immune-checkpoint inhibitors are important factors to consider when designing clinical trials. Furthermore, tumor exosomes may play an important role as biomarkers in abscopal response.

Conclusion & Significance: Our data suggest that radiation may be one strategy that could improve outcome in patients, when combined with emerging immunotherapeutics, such as PD-L1/PD-1, CTLA-4, 4-1BB, and others. Future clinical trials are needed to translate this, into the clinic, as part of multi-disciplinary approach in the future.

Speaker Biography

Mohammad K Khan has expertise as Radiation Oncologists, and as a Translational Physician Scientist. He treats variety cancer patients, with expertise in skin cancers and hematological malignancies. His research focuses on translating post radiation abscopal effect into the clinic, to improve outcome for cancer patients. In particular, he is interested in developing multi-disciplinary approaches involving radiation and immuno-oncology to improve outcome for cancer patients. He currently leads several efforts that span patient outcomes work, basic sciences work, as well as ongoing clinical trials.

e: drkhurram2000@gmail.com

Notes:

The cytoprotective role of autophagy in CYT997 treated human head and neck squamous cell carcinoma

Yong Teng
Augusta University, USA

Head and neck squamous cell carcinomas (HNSCC) exhibiting resistance to molecular-targeted therapeutics poses a challenge to their effective clinical management and alternate treatment strategies are actively sought to improve results. CYT997, a novel microtubule-disrupting agent, has shown anticancer activity in prostate cancer and other cancer types by inhibiting tubulin polymerization and disrupting cellular microtubules. Here, we report that CYT997 has considerable potential as a novel anticancer agent for HNSCC. CYT997 effectively abrogates mTOR signaling and induces significant cytotoxicity in HNSCC cells. Consequently, CYT997 treatment inhibits cell viability, migration and invasion and induces autophagy-associated apoptosis. CYT997 also suppresses tumor growth of HNSCC in a mouse xenograft model. Combined treatment with CYT997 and the autophagy inhibitor HCQ, but not 3-MA, overcomes autophagy blocked apoptosis and augments the anticancer activity of CYT997 *in vitro* and *in vivo*, suggesting that inhibition of mTOR-dependent autophagy sensitizes HNSCC cells to CYT997-induced apoptotic death. These findings underline the importance of autophagy in the anticancer activity of CYT997 and suggest that CYT997 may represent a potential therapeutic approach to treat HNSCC and pharmacologic autophagy blockade may enhance its efficacy. Therefore, our study has significant impact on the design and execution of effective therapy of patients with HNSCC.

Speaker Biography

Yong Teng was largely engaged in illustrating cancer metastatic signaling cascades and developing animal disease models for gene functional analysis and drug evaluation. Through his team work, he has identified several new molecular targets and signaling pathways which control cancer progression and metastasis and developed several novel anticancer strategies by modulating them. He is trying to bridge three major research themes, tumor microenvironment, autophagic survival and tumor metastasis, with an emphasis on a few central regulators. His ongoing projects seek to shift current research and clinical practice paradigm, which will directly impact the future development of effective therapy for cancer patients.

e: yteng@augusta.edu

Notes:

Hepatocellular carcinoma: The role of host immunity in the regulation of proliferative responses

Natalyn N Hawk
Winship Cancer Institute, USA

Hepatocellular carcinoma (HCC) is the most common primary liver malignancy, with over 600,000 cases annually around the world. Less than 20% of cases are not amenable to curative therapy either surgery or transplant, so the overall outcome of patients with HCC is poor. Cirrhosis of the liver is a major driver in the pathogenesis of HCC in addition to direct proliferative stimuli from hepatitis viruses. The nature of the influence of cirrhosis has emerged as an area of intense study, where the long-term effects of chronic inflammatory states might include creating a host environment driven by a perpetual activation of inflammatory responses which may lead in some cases to abnormal cell proliferation or inappropriate persistence of activation of inflammatory states culminating in malignancy. Recently, PDL1 ligand inhibition with novel therapies that up regulate MHC-1 targeted markers on the malignant cells has shown exceptional promise for various malignancies including melanoma, lung cancer, renal cell carcinoma and sub-classes of colon cancer as well as in hepatocellular carcinoma. The mechanisms remain to be clarified in HCC. However, the impact of cirrhosis in creating the framework within which the host's immune system can benefit from these therapies may be critical in determining how effective these therapies can be. Future study in the area of HCC will highlight how survival/proliferative and immune signaling pathways communicate in the background of cirrhosis compared other conditions and what may be the impact on the ability of driving the key pathogen etic events in the development and progression of HCC as well as influence the therapeutic approaches that are being actively studied to achieve control of this disease and thereby improve survival. In our discussion we will: Provide an overview of the major etiologic factors associated with the development of HCC; Review the major biological and molecular pathways that have been shown to be important in the pathogenesis of HCC and review the current therapies that are in use or in study for treatment; Review the data which demonstrates the impact of host inflammation on the pathogenesis of HCC in the absence versus presence of liver cirrhosis; and summarize the widely used systemic therapies in HCC and refractory HCC and highlight the more promising/actively studied therapies that show reasonable promise in improving the outcomes of patients with advanced and or refractory HCC.

Speaker Biography

Natalyn N Hawk obtained her MD and PhD from Brown University in Providence, Rhode Island, earning her doctorate in molecular pathology as a visiting scientist at M.D. Anderson Cancer Center in Houston, Texas where she identified a molecular complex important in the pathogenesis of chronic myeloid leukemia. She completed residency training in internal medicine at Johns Hopkins Bayview Medical Center in Baltimore, MD. She completed fellowship training in hematology and medical oncology at Emory University which included a one year post-graduate fellowship where she studied the efficacy of dual inhibition of mTOR and EGF receptor pathways as a potential therapy in Non small cell lung cancer. She is an Assistant Professor of Hematology and Medical Oncology at Emory University and is a member of the Gastrointestinal Oncology Working Group of Emory Winship Cancer Institute. She is also a member of the Discovery and Developmental Therapeutics Research Program at Winship Cancer Institute of Emory University.

e: nhawk@emory.edu

Notes:

Identification of novel tumor suppressor through methods of reverse genetics

Zhenglun Zhu
Harvard Medical School, USA

Identifying novel tumor suppressor holds the promise for improving cancer treatment. Forward genetic screening has been the primary method for identifying tumor suppressors and oncogenes. While, the potential of reverse genetics in deciphering genes critical for tumorigenesis has been widely expected, the application of the approaches has reminded limited. By exploring the molecular mechanisms underlying dorsoventral axis formation during early vertebrate embryogenesis, we identified the human homeobox protein VentX as a novel tumor suppressor. We demonstrated that VentX exerts its function through mechanisms of anti-proliferation and pro-differentiation. Importantly, we found that VentX expression can be induced by chemotherapeutic agents and caused apoptosis of cancer cells in p53-independent manner. Taken together, our study revealed the application of reverse genetics in identifying novel tumor suppressors, and the role of VentX as a novel therapeutic target in cancer treatment.

Speaker Biography

Zhenglun Zhu is an expert in Fundamental Biology and Translational Medicine. He is an elected member of the prestigious American Society of Clinical Investigation (ASCI). Dr. Zhu discovered novel principle governing cell fate determination during early embryogenesis and translated the principle into identifying novel tumor suppressor.

e: zzhu@partners.org

Notes:

Circular BANP expression profile and potential function in human colorectal cancer

Feng Yan
Nanjing Medical University, China

Circular RNAs (circRNAs) are recently identified as widespread and diverse endogenous noncoding RNAs that may harbor vital functions in human and animals. However, the role of circRNAs in the process of tumorigenesis and development of colorectal cancer (CRC) remains vague. Here, we characterized the circRNA expression profile from three paired CRC cancerous and adjacent normal tissues by human circRNA array and identified 136 significantly overexpressed circRNAs (>2-fold changes). We further validated one circRNA generated from Exon 5-11 of BANP gene, termed circ-BANP. In addition, RT-PCR result showed that circ-BANP was overexpressed in 35 CRC cancerous tissues. Knockdown of circ-BANP with siRNA significantly attenuate the proliferation of CRC cells. In summary, our findings demonstrated that dysregulated circ-BANP appears to have an important role in CRC cells and could serve as a prognostic and therapeutic marker for CRC.

Speaker Biography

Feng Yan is the Vice Director of Department of Clinical Laboratory in Nanjing Medical University Affiliated Cancer Hospital and Jiangsu Cancer Hospital. The research works focus on the Bioanalytical Chemistry in laboratory medical diagnostics, particularly in detection of tumor markers and tumor cells. She has published 42 papers in Scientific journals. She was the Outstanding Medical Talents, Excellent Medical Talent and Leading Medical Talent of Jiangsu Province.

e: yanfeng1895@163.com

Notes:

allied academies

Annual Congress on

ONCOLOGY AND BIOMARKERS SUMMIT

November 27-28, 2017 | Atlanta, USA

Development of a novel DNA bio-marker for the qualitative and quantitative detection of malayan box turtle (*Cuora amboinensis*) material in traditional chinese medicines

Asing
University of Malaya, Malaysia

Malayan box turtle (*Cuora amboinensis*) (MBT) is a protected species in Malaysia since 2005 and prohibited (haram) animal species in Muslim foods and medicines. The widespread availability of commercial traditional Chinese medicines across Malaysia may offer the opportunity of turtle product trafficking under the covert of halal brands, needing to develop a convenient and reliable method both for the qualitative and quantitative tracing of turtle materials in medicines. Several polymerase chain reaction (PCR) assays have been proposed for the detection of MBT species under various routes but they are based on long-length targets which break down under the state of decomposition, making them unsuitable for the forensic detection in medicines and other potential routes. To overcome this knowledge gap, for the first time, we developed a short length DNA target for the quantitative detection of MBT tissues by SYBR green real-time PCR systems. The assay specificity was checked against 20 different species and DNA biomarker stability was tested under various meat tissue processing conditions, including boiling, autoclaving and micro oven heating under pure and admixed matrices. The limit of detection (LOD) of the SYBR green duplex real time PCR system was 0.00001 ng DNA and 0.001% (w/w) MBT meat under mixed matrices. Finally, 120 traditional Chinese medicines samples were surveyed by SYBR green duplex real time PCR system and 23% of them were found to be MBT-positive (0.00157 to 0.0612 ng/µL), respectively. Thus the methods were suitable for real-world application and they confirmed the widespread speculation that MBT materials are widely used in Chinese medicines and herbal medicines as well as this technique could be applied medical diagnosis science.

Speaker Biography

Asing has completed his PhD in Biology and Biochemistry under the supervisor of Md. Eaqub Ali, Associate Professor, at Nanotechnology and Catalysis Research Centre, University of Malaya, Kuala Lumpur, Malaysia. He has obtained his MS degree in Biochemistry and Molecular Biology under the supervisor of Professor Dwaipayan Sikdar, University of Chittagong, Bangladesh. His research interests are on DNA markers development, Biochemistry, Molecular Biology, Food Science and Pharmaceutical Science. He has contributed and published 17 research articles in top rating research journals. He has 5 conference proceedings and presented oral (3) and poster (2) in prestigious international conferences in Malaysia, Indonesia, Thailand and Singapore respectively. Before being a PhD student, he had worked as research assistant, quality control office in leading Biochemistry and Molecular Biology research laboratory and pharmaceuticals industry in Bangladesh.

e: asing95bio@gmail.com

Notes:

Circulating tissue specific exosome profiles for noninvasive monitoring of immunologic rejection in transplantation

Prashanth Vallabhajosyula
University of Pennsylvania, USA

Statement of the Problem: Organ/tissue transplantation remains the only life-saving, curative therapy in patients with end stage diseases of the heart, liver, kidney, and lungs. Transplant patients are placed on obligatory immunosuppressive medications to prevent organ rejection, thus placing them at higher risk for malignancies and infectious complications. Rejection and immunosuppression-related complications remain the primary causes of morbidity and mortality in transplant patients. Yet to this date, there is a critical need for development of biomarkers for noninvasively monitoring rejection. We proposed that circulating exosomes, microvesicles carrying tissue-specific nucleic acids and proteins, reflect condition specific changes imposed on the transplanted tissue. If so, transplant tissue specific exosome profiling would constitute a novel biomarker platform for monitoring transplant rejection. We studied this concept in animal models of islet, heart, and lung transplantation, and further validated its translational potential in clinical setting.

Findings: In animal models of islet and heart transplantation, we demonstrated that circulating transplant tissue specific exosome quantitative and cargo profiles are significantly decreased early in the acute rejection process. This change was noted to occur in a time sensitive manner, before histological evidence of rejection/ injury to the transplanted tissue. Further, in clinical islet transplantation, transplant islet specific exosomes were reliably tracked in 4 patients over long term follow-up of over 5 years, suggesting that transplant exosomes can be utilized for noninvasive surveillance in the clinical setting. In addition, in heart transplant patients (n=5), we demonstrated that circulating donor heart specific exosomes can be reliably tracked in the perioperative setting.

Conclusions & Significance: Circulating transplant tissue specific exosomes accurately herald early acute rejection in animal models of transplantation. These potential noninvasive biomarkers can also be reliably tracked in the clinical setting. Further investigations may reveal the noninvasive diagnostic potential of transplant tissue specific exosome platform.

Speaker Biography

Prashanth Vallabhajosyula received his Bachelor of Science and Masters of Science in molecular biophysics and biochemistry, along with his Doctor of Medicine degrees from Yale University, New Haven, CT. He completed his residency in general surgery at Johns Hopkins Hospital, Baltimore, MD. During this period, he did a clinical fellowship in upper gastrointestinal surgery at Oxford-Radcliffe Hospitals, Oxford, United Kingdom. He attended the Hospital of University of Pennsylvania for a fellowship in cardiothoracic surgery, and completed a sub-specialization year in aortic surgery, along with endovascular and minimally invasive techniques. His surgical interests are in aortic surgery, endovascular surgery and thoracic organ transplantation.

e: Prashanth.Vallabhajosyula@uphs.upenn.edu

Notes:

Non-correlation between tumor biomarkers levels in peritoneal carcinomatosis

Manuela Stoicescu
University of Oradea, Romania

Introduction: Peritoneal carcinomatosis is considered the end stage of cancer, with different locations. Disseminations of metastases in peritoneum are very dangerous; because the invasion is extended from the primary tumor to peritoneum. Of course, we expect that in this advance stage of cancer the levels of tumor biomarkers to be increase or very increase, in concordance with the severity of the disease.

Material & Methods: Present the situation of a woman patient 73 years old, who suffered a total hysterectomy with bilateral oophorectomy, with one year a half before, for carcinoma of the uterus. The patient refuses radiotherapy and chemotherapy after surgical intervention. After this period of time develop sudden a clinical picture of occlusion of the bowel. An abdominal CT was performed and surprise put in evidence a tumor block in right flank, around the ascendant colon and catch also a few anses of small bowel and fluid collection inside of peritoneal cavity around the liver and around the spleen in medium quantity. The patient suffered surgical intervention, but the tumor block wasn't possible to be removed, was performed only a palliative surgical intervention with ileostoma (contra nature anus), drainage of fluid of as cites and resection of omentum. The analyses of fluid confirmed neoplastic etiology and histopathology examination from omentum confirmed metastases in omentum. After laparotomy, the surgeon observes peritoneal carcinomatosis. The problem was that all the tumors biomarkers performed before surgical intervention were in normal range: CE (carcinoma embryonic antigen) <0,50 ng/mL, feto protein<0,97 ng/mL, CA125<0,5 U/mL, SCC (Squamous Cell Carcinoma) =0,8 ng/mL (normal range<1,5).

Results & Discussions: The most important question is, how was possible to be in normal range all these tumor markers in context of peritoneal carcinomatosis – the end stage of cancer? Confer us safe the normal results of level of tumor markers that the patient isn't in danger or in advance stage of cancer?

Conclusion: The most important conclusion of this presentation is that exist paradoxes a non-correlation between the tumor biomarkers levels and peritoneal carcinomatosis.

Speaker Biography

Manuela Stoicescu is a Assistant professor in University of Oradea, Romania. She has completed her Phd in 2010. She has published various books and was invited as speaker for 12 International Conferences. She is the Member of Romanian Society of Internal Medicine and Romanian Society of Cardiology. Member of Balcanic Society of Medicine. She has published many articles.

e: manuela_stoicescu@yahoo.com

Notes:

allied academies

Annual Congress on

ONCOLOGY AND BIOMARKERS SUMMIT

November 27-28, 2017 | Atlanta, USA

Development of diagnostic and prognostic biomarkers and understanding the signaling using protein interaction network in neurodegenerative diseases

Deepshikha Pande Katare
Amity Institute of Biotechnology, India

Neurodegenerative Diseases (NDs) involve sequentially interacting pathological cascades, including the interaction of amyloid-beta aggregation with plaque deposition, Lewy bodies formation, initiation of seizures, tremor and hyper-phosphorylation of tau protein with formation of tangles. Together with associated processes, such as inflammation and oxidative stress, these pathological cascades contribute to loss of synaptic integrity and progressive neurodegeneration. Today the focus is being placed on the discovery of oxidative stress biomarkers for the understanding of neurological disorders. Inadequacy in disease detection/treatment and the lack of diagnostic and prognostic tools have prompted investigators to turn to proteomics-based biomarker discovery. In the present study, we have developed animal models using zebrafish and Wistar rats for multiple NDs. The differential expression of proteins was analyzed in serum and brain tissue with the disease progression. The behavior studies and biochemical analysis confirmed the desired pathology in the animal model. The differentially expressing proteins were identified and subjected for further validation in humans for the prospective diagnostic/prognostic biomarkers. Further characterization of these proteins will likely shed more light on the mechanisms by which the changes or modification in these proteins and their interaction with the other protein in the pathway. The current study will also contribute to identify the new drug targets for subsequent therapeutic development and also the link between the different NDs. This link can also help in understanding the initiation of all neurological damage.

Speaker Biography

Deepshikha Pande Katare has the research and teaching experience of 21 years and she has been extensively working in the area of Pharmaceutical/Medical Biotechnology. She has Master degree in Genetics with Human Genetics specialization and PhD in Biotechnology. In the past she has worked at NIPER, Mohali, Chandigarh and Hamdard University, New Delhi for about 10 years. Currently she is working as Professor and Head Medical Biotechnology in Amity University. The research area is human health where she is working with collaborators both from India and Abroad as well as PhD scholars registered under her Supervision from multidiscipline specialization. She has undertaken various research projects and successfully guided PhD students in the area of Diagnostic prognostic biomarkers of HCC and Lung cancer and phytosomal formulations and characterization for epilepsy and Parkinson's disease. She has around 42 patents and more than 70 publications in the related area.

e: dpkatare@amity.edu

Notes: