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24th International Conference on
Cancer Research and Pharmacology
&
International Congress on
Structural Biochemistry, Stem Cells and Molecular Biology

August 5-6, 2019 | Singapore

Keynote Forum

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CANCER RESEARCH AND PHARMACOLOGY
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STRUCTURAL BIOCHEMISTRY, STEM CELLS AND MOLECULAR BIOLOGY
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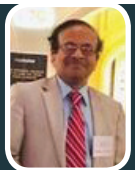
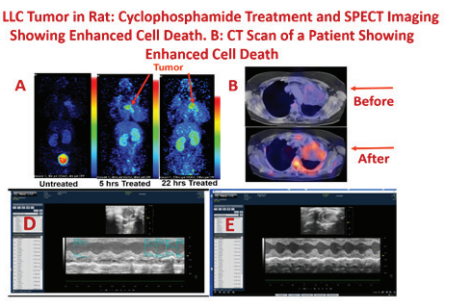


Raghu Pandurangi

Sci-Engi-Medco SolutionsInc, USA

Noninvasive risk stratification of patients using predictive biomarker apoptosis index of tumors

Statement of the Problem: Human tumors are heterogeneous which evoke different responses from different treatments. Current animal models used in cancer research are xenografts which would not mimic human tumors. A noninvasive imaging modality to assess cell death in target and non-target organs simultaneously may help to overcome the heterogeneity and may identify a biomarker which can be used to predict the efficacy and toxicity of treatments. Apoptosis Index (AI) is the measure of cell death in tumor, the modulation of which reflects how it responds to therapy. For example, we and others have shown that lower the spontaneous AI, lower the response and vice versa from the treatments irrespective of the nature of treatments. We have developed a novel technology "A Priori Activation of Apoptosis Pathways of Tumor" (AAAPT) which raises AI of spontaneous tumors above a threshold level in order to evoke a better response from therapy.



A: LLC Tumor in Rat: Cyclophosphamide Treatment and SPECT Imaging Showing Enhanced Cell Death. B: CT Scan of a Patient Showing Enhanced Cell Death

Ultrasound Imaging of Rat Heart: C: Doxorubicin Treatment: Ejection Fraction (EF): < 44.5, D: AAAPT+ Doxorubicin, EF >60 %: Conclusion: A-B: Prediction of Efficacy of chemotherapy: C-D: Prediction of Cardiotoxicity of Chemotherapy

Methodology & Theoretical Orientation: Cancer cells have ability to enhance survival pathways (e.g. NF-kB and PARP) and down regulate the cell death pathways (e.g. CD95, ASK1) for their survival. Hence, we have designed new technology to target these pathways to sensitize those resistant tumor cells using targeted activation technology. We have used clinically oriented SPECT and Ultrasound Imaging techniques to assess AI as a predictive biomarker of efficacy and toxicity of chemotherapy respectively.

Findings: SPECT imaging of Lewis Lung Carcinoma (LLC) showed an enhanced cell death (higher AI) post treatment by Cyclophosphamide while, US imaging reversed the cardiotoxicity by doxorubicin by using AAAPT as a neoadjuvant to Doxorubicin.

Conclusion & Significance: The noninvasive assessment of AI (measure of cell death) by SPECT combined with US imaging can be used to risk stratify patients in terms of who responds to which therapy earlier compared to tumor regression timelines.

Biography

Raghu Pandurangi started his scientific career Ph.D in spectroscopy followed by post-doctoral training at Radiology and Internal medicine, University of Missouri, Columbia where he remained as a faculty for 10 years. He was a principle investigator position in Shering AG, Germany where he directed and involved in 2 FDA approved drugs (AccuTect and NeoTect). He was a team leader at Mallinckrodt directing apoptosis imaging. He became an entrepreneur in 2013 inventing AAAPT technology for improving FDA approved drugs. Currently, he is the Founder, President and CSO of Sci-Engi-Medco Solutions (SEMCO) and Amplexi-LLC, recipient of several NIH grants and awards.

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Wen-Sheng Wu

Tzu Chi University, Taiwan

Hydrogen peroxide inducible clone-5 mediates positive feedback ROS-JNK-c-jun signaling for HCC progression

The poor prognosis of hepatocellular carcinoma (HCC) is due to high recurrence rate mainly caused by intrahepatic metastasis. Hic-5 (hydrogen peroxide inducible clone-5) which belongs to the paxillin superfamily can be stimulated by a lot of metastatic factors including transforming growth factor (TGFβ) and hepatocyte growth factor (HGF), which further regulate epithelial mesenchymal transition (EMT), migration and invasion. The molecular mechanisms for Hic-5 to trigger EMT and tumor progression appeared to be closely associated with its impact on signal transduction. Our recent report demonstrated that Hic-5 not only can be a poor prognosis marker for HCC but also served as a mediator of the reactive oxygen species (ROS)-c-jun-N-terminal kinase (JNK) signaling pathway for HCC progression. Notably, Hic-5 appeared to locate both upstream and downstream of ROS-JNK cascade. In our recent study, a more comprehensive Hic-5-ROS-JNK positive feedback pathway has been established. Specifically, Hic-5 may interact with regulators of NADPH oxidase such as Rac-1, Traf4 and nonreceptor tyrosine kinase (Pyk2) for activating NADPH oxidase and ROS generation, leading to JNK phosphorylation and transcriptional activation of Hic-5 mediated by c-jun/AP-4. The Hic-5 thus induced in turn re-activates the ROS-JNK signal cascade. This positive feedback circuit is essential for elevating mesenchymal transcriptional factors such as Snail, Zeb1 and matrix degradation enzyme MMP9 and decreasing the epithelial marker E-cadherin (Fig.1). Currently, the missing links in both the upstream and downstream of Hic-5-NADPH oxidase-ROS-JNK-c-jun pathway are being clarified. Moreover, whether knockdown of Hic-5 *in vivo* may decrease HCC progression in a SCID mice are being investigated. Our study will benefit designing a more effective target therapy aiming at Hic-5 against HCC.

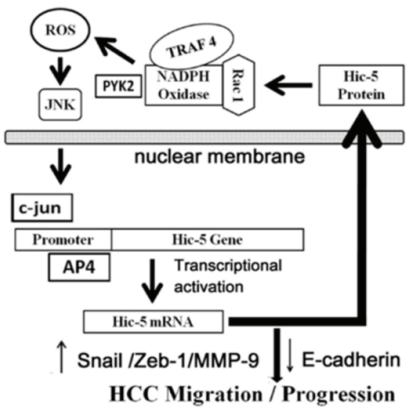

Figure 1. Hic-5 mediated positive feedback NADPH oxidase- ROS-JNK-c-jun cascade, regulating EMT markers. Hic-5 transcription can be induced by ROS-JNK-c-jun pathway which may in turn interact with Rac1 and Traf4, triggering activation of NADPH oxidase, ROS generation and JNK phosphorylation thus sustaining the signal transduction. The positive feedback Hic-5-ROS-JNK signaling circuit further upregulates Snail, Zeb-1 and MMP-9 and downregulate E-cadherin for triggering HCC migration and progression of HCC

Biography

Wen-Sheng Wu graduated from institute of biochemistry Taiwan University getting PhD degree on 1988. He carried postdoctoral research at department of research, veteran general hospital Taipei and department of Medical technology Kaohsiung, Taiwan. He is now a professor in Department of laboratory medicine and biotechnology, college of Medicine, Tzu Chi University. His research interest are. Signaling and transcriptional mechanisms for tumor progression and Target therapy against cancer.

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Mukesh Pandya

Jaihind College, India

Role of biochemistry in industrial wastewater treatment processes

Developments in production technologies have resulted in the concentrated highly concentrated streams of wastewater with high BOD and COD levels a challenge to treat effectively. Biological treatments are widely practiced to treat wastewater containing wide range of organic pollutants by Aerobic and Anaerobic process. The key to success of Biological Processes are Microorganisms which carry out versatile Biochemical reactions to degrade simple to complex, aliphatic to aromatics and recalcitrant organics under ideal physico-chemical conditions in nature.

Although these treatment programs are cheap, but the plants are operated without Optimization as well as understanding the Biochemistry of Microbial Metabolisms and parameters for maintaining metabolic balances.

Aerobic and Anaerobic process were studied for different Industrial Wastewater from Petrochemical and specialty products and Palm Oil Mills and optimum operating conditions were determined. The main key to these studies were types of microorganisms in biomass developed, their co-metabolism and enzyme profiles which transform organics and reduce BOD, COD and TOC levels.

Physico-chemical conditions for growth and multiplication of active bacteria biomass and management of biomass activities were the key for successful operation of both Aerobic and Anaerobic Treatments plants. Analysis for pH, BOD, COD, TN, AN, Alkalinity, VFA TDS MLSS, MLVSS were the key parameters for maintaining high activity of Biomass for achieving 95-99% reduction in BOD and COD levels with discharge levels much below Environment Standards.

Valuable from wastewater in terms of Biogas, Biomass and recycle of treated wastewater were difficult earlier but now easy and Industries are moving ahead with Zero Discharges approach. In this both GHG emissions as well as conservations of water are achieved.

This paper highlights case studies w.r.t various approaches in treatment of wastewater from Industries using Biochemical and Physico-chemical parameters to enhance and economize the treatment programme. Application of Biomass engineering for conversion of organic solids waste from Palm Oil mills to compost as soil conditioner. Results on various studies carried out will be presented during the conference.

It was observed that Biochemical balance w.r.t Biomass, Organic loading, Nutrient balance, and physico-chemical parameters-maintained effectiveness of treatment programs. Methane contents in Biogas could be achieved in a range of 60-65% with > 90% reduction in BOD and COD. Balance of Microbial consortium for efficient aerobic and anaerobic process gave sustainable efficient and economical treatment efficiencies.

Biography

Mukesh Pandya retired as Professor and HOD after 4 decades of teaching at Jai Hind College affiliated to University of Mumbai. He specialized in Industrial collaboration over 3 decades for wastewater Treatment, Design and development of total solution. His expertise was for low cost robust treatment programme for Industries in India and overseas which are running effectively. Guided students for PG and Doctorate programmes in the field of Microbial Biotechnology.

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Entissar S AlSuhaibani

King Saud University, KSA

In silico modeling of Bcr-Abl oncoprotein isoforms in chronic myelogenous leukemia

Chronic Myelogenous Leukemia (CML) is a cancer of the white blood cells. It develops, when a hematopoietic stem cell in the bone marrow acquires a Philadelphia (Ph) chromosome carrying the BCR-ABL fusion oncogene. The fusion of the ABL gene on chromosome 9 with the BCR gene on chromosome 22 results in the formation of two p210BCR-ABL onco-protein isoforms, b2a2 and b3a2, due to the head-to-tail fusion of p160BCR and p145ABL proteins. b2a2 and b3a2 differ in sequence by a 25 amino acid insertion and a Glu903Asp substitution. The oncogenic potential of p210BCR-ABL protein isoforms is due to the fact that the normally regulated tyrosine kinase activity of p145ABL becomes unregulated in both b2a2 and b3a2. p145ABL is a non-receptor tyrosine kinase that plays an important role in signal transduction and the regulation of cell growth. At the N-terminus, p145ABL contains the SH3, SH2 and SH1 domains. The SH2 and SH3 domains regulate tyrosine kinase function of p145ABL and the SH1 domain is responsible for the tyrosine kinase activity. The SH3 domain has a negative regulatory effect on the tyrosine kinase function. Deletion of SH3 or mutation in SH3 eliminates the tyrosine kinase activity of p145ABL. In silico modeling, using Psipred and ExPASy servers, was used to determine the secondary structural elements of these onco-protein isoforms. The structural elements of the two proteins were found to be different in the five □-helices (□25, □́, □26, □27 and □29) and nine β-strands (β12, β13, β15, β́, β17, β30, β□, β34 and β35) which comprise the SH1, SH2, SH3 and DNA-binding domains which can result in different roles played by the two isoforms in mediating signal transduction during the course of Chronic Myelogenous Leukemia. Both p210BCR-ABL proteins can cause pleiotropic effects on many signal transduction pathways that can affect cell survival, disease progression, genomic stability and hematopoiesis.

Biography

Entissar AlSuhaibani is a Professor of Genetic at King Saud University. Her research interest is the cytogenetic effect of radiation. She is involved in many research projects founded by many research institutions. In 2010, she was awarded as a Fellow for the 2010 L'Oreal UNESCO Pan Arab Regional Fellowships. She presented and participated in the various regional and international scientific conferences. She received gold and silver medals from different international expiations for the patent of the Invention of the Sister Chromatid Exchange staining SCE staining. She involved in many community activities to encourage Saudi females to engage in science field. Also, she is member of international and local scientific societies.

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