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WSCST 2017

Day 1 : January 23rd 2017

10.30am -11.00 am - Registration

11.00 am -11.15 am - Inaugural session

11.15 am -11.30 am - Group photo

Keynote Forum

11.30 am -12.15 pm - Krishna Murthy

Kidwai Memorial Institute of Oncology, Bangalore, India

12.15 pm - 12.45 pm - **Coffee Break**

Session Introduction

12.45 pm -01.15 pm --- **Oral Presentation by *Chenbo Zeng***
Topic :-Sigma-2 receptor ligand as a novel method for delivering a SMAC mimetic drug for treating ovarian cancer

01.15 pm - 02.15 pm --- **Lunch Break**

02.15 pm - 02.45 pm --- **Oral Presentation by *Elise Verron***
Topic :-Innovative nanoformulation of curcumin to prevent breast cancer bone metastasis

02.45 pm - 03.15 pm --- **Oral Presentation by *David Vesely***
Topic :-Cardiac Hormones for the treatment of Cancer

03.15 pm - 03.45 pm --- **Oral Presentation by *Claudio Pusceddu***
Topic :-Percutaneous Cryoablation in the treatment of lung cancer

03.45 pm - 04.00 pm --- **Coffee Break**

DAY 1 END

Day 2 : January 24th 2017

11.00 am -11.30 am	---	**Oral Presentation by *Jixin Dong*** **Topic :-The Hippo-YAP Pathway in Prostate Cancer**
11.30 am -12.00 pm	---	**Oral Presentation by *Howard Yang*** **Topic :- Reproducible genes for breast cancer patient survival prediction**
12.00 pm- 12.30 pm	---	**Coffee Break**
12.30 pm -01.00 pm	---	**Oral Presentation by *Maurizio Memo*** **Topic :-Tropomodulins are new favorable prognostic biomarkers in high-risk Neuroblastoma**
01.00 pm -02.00 pm	---	**Lunch Break**
02.00 pm-02.30 pm	---	**Oral Presentation by *Run-Sheng Ruan*** **Topic :-Clinical and immunological response to in vivo whole cancer cell antigen priming followed by adoptive T-cell therapy in terminal cancers**
02.30 pm - 03.00 pm	---	**Oral Presentation by *Elise Verron*** **Topic :- Gallium as a promising candidate for the treatment ofpatients with bone**
03.00 pm -03.30 pm	---	**Poster Presentation by *Suhn-Young Im*** **Topic :-Mechanism of CK2a activation and its expression in human breast cancer**
03.30 pm -04.00 pm	---	**Poster Presentation by *Seonghui Jang*** **Topic :-Heterogeneous ribonucleoprotein E1 and E2 regulate BC200 RNA-mediated translation inhibition**
04.00 pm -04.15 pm	---	**Coffee Break**

DAY 2 END

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WSCST - 2017

World Summit on Cancer Science and Therapy

at

Singapore on January 23rd-25th, 2017

KEYNOTE FORUM

World Summit on Cancer Science and Therapy

23rd – 25th January 2017, Singapore

Dr S Krishnamurthy

Dr S Krishnamurthy
Professor & HOD of Surgical Oncology
Kidwai Memorial Institute of Oncology.

Breast Cancer in India- Where do we stand and where do we go?

Treatment of Breast cancer has undergone quite an improvisation in the last 20 years since the introduction of molecular biology, immunohistochemistry and availability of targeted therapy.We present our last 6 years' experience in treating 862 Breast cancer patients in a single unit at a Regional cancer centre in India. Total of 862 breast cancer patients have been treated at our institute in a singlesurgical oncology unit from 2010 to 2016. Maximum incidence was observed in the age group 35-64 years (710/82.4%) and least in above 65 years (73/ 8.5%) with almost an equal number of patients coming from rural (51.9%) and urban (48.1%) population. Right sided breast cancer (56%) dominated compared to left (43.4) whereas 0.6% were bilateral. A higher incidence was noted amongst postmenopausal (54.2%) compared to premenopausal women (45.8%). Maximum patients were of Luminal A category (35%) with most of them presenting as Stage II (42.5%) and III (44.4%) disease. Triple Negative tumours contributed to significant 32.7% of the disease. 338 patients were given neoadjuvant chemotherapy before surgical management. 21 patients underwent Breast conservation surgery with Sentinel Lymph node biopsy done in 9 patients with 100% sentinel Lymph node identification rate while the rest underwent modified radical mastectomy. Adjuvant chemotherapy and Radiotherapy was

administered to 437 and 702 patients respectively whereas 198 patients were given targeted therapy. Hormonal therapy was offered to 460 patients based upon their receptor status.In a developing country where health insurance cover and governmental policy is not available for the patients, it remains a challenge to offer the advanced management to all patients attending a regional cancer centre.

Biography

M.ch SURGICAL ONCOLOGY (AUGUST 1994); M.S.GENERAL SURGERY (FEBRUARY 1987); M.B.B.S (JULY 1982). Joined the institute as lecturer in 1987, promoted as assistant professor 1993, professor 2002 and heading the department of surgical oncology since 2015. Teaching super specialty students (8) every year, published 40 articles in national/ international journals, participated in 8 global projects.

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ACCEPTED ABSTRACTS

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World Summit on Cancer Science and Therapy

23rd – 25th January 2017, Singapore

Chenbo Zeng
University/Organization: University of Pennsylvania Perelman School of Medicine

Sigma-2 Receptor Ligand as a Novel Method for Delivering a SMAC Mimetic Drug for Treating Ovarian Cancer

We have developed a new strategy to deliver anticancer drugs selectively into tumor cells by targeting sigma-2 receptors. Sigma-2 receptors are overexpressed in various tumor cells. The radiolabeledsigma-2 receptor ligand, [18F]ISO-1,provided high contrast images of solid tumors in cancer patients by the Positron Emission Tomography (PET). Sigma-2 ligands are rapidly internalized into cancer cells by endocytotic pathways and localize in multiple subcellular organelles such as lysosomes, mitochondria and the endoplasmic reticulum. These data suggest that sigma-2 receptor ligandsare an excellent candidate for delivering anticancer drugs selectively to tumors. We conjugated a sigma-2 ligand, SW43, to a second mitochondria-derived activator of caspase (SMAC) mimetic drug. The resulting compound, SW III-123, successfully delivered the SMAC mimetic to ovarian cancer cells, suppressed tumor growth and improved mouse survival. Mechanistically, SW III-123 induced rapid degradation of inhibitor of apoptosis proteins (cIAP1 and cIAP2), accumulation of NF-κB-inducing kinase (NIK) and activation of caspase-8, -9 and -3. Tumor necrosis factor alpha (TNFα) antibody markedly blocked SW III-123-induced cell death and caspase-3 activity. The data suggest that SW III-123 activated NF-κBand apoptotic pathways. In conclusion, sigma-2 ligands are a promising tumor-targeting drug delivery agent. Sigma-2-conjugated SMC exemplifies a novel class of cancer chemotherapeutics.

Biography

Dr. Zeng obtained her Ph.D. in biochemistry at Iowa State University inthe United States. Since then she worked at Washington University School of Medicineas a postdoc and then as a research instructor until 2013. Currently she is a Research Assistant Professor at the Department of Radiology, University of Pennsylvania, PerelmanSchool of Medicine. Her research has been focusing on development of chemotherapeutic drugs by targeting the sigma-2 receptor.

World Summit on Cancer Science and Therapy

23rd – 25th January 2017, Singapore

Pusceddu Claudio

University/Organization: Oncology Hospital – AOB Cagliari - Italy

Percutaneous Cryoablation in the Treatment of Lung Cancer

Lung cancer is the most commonly diagnosed cancer in the United States and Europe and it is a major cause of cancer death. Surgical resection, when possible, offers the best chance of healing of NSCLC in selected patients and in early stage. In patients not candidates for surgery, chemotherapy and radiotherapy are mainly palliative. Cryoablation is a minimally invasive technique, highly innovative, which has only recently been used in the treatment of primary and secondary lung tumors. Cell death is obtained as a result of rapid freezing followed by slow thawing that causes necrosis of the target tissue. Cryoablation can be proposed with radical intent (curative) in cases of disease limited to the lung; individual tumors no larger than 5 cm or up to 5 multiple tumors confined to no larger than 3 cm each one. The advantages of cryoablation are due to very precise control of the treated area (display of the iceball) sparing the surrounding healthy tissues. The major risks and complications of pulmonary cryoablation are those deriving from interventional treatment such as: local hematomas, pneumothorax, pulmonary bleeding caused by wrong placement of the cryoprobes and infections.

Biography

Dr. Pusceddu Claudio graduated in March 1986 from the University of Cagliari (Italy) and specialized at the same university in Diagnostic Radiology in 1996 and in Medical Oncology in 2004. He has worked in an oncological hospital since 1992, and he has specialized in extra-vascular interventional radiology in the field of oncological disease. Every year he performs more than three hundred procedures (Radiofrequency thermal ablation, Microwave ablation, Cryoablation, Percutaneous screws fixation, Osteoplasty with PMMA injection and combination of these procedures) in cancer patients.

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23rd – 25th January 2017, Singapore

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NMK-BH2, A Novel Microtubule Disrupting Agent, Induces Apoptosis And Autophagy In Cervical Cancer Cells By Binding To Tubulin.

Cervical cancer remains one of the most common causes of cancer-related death among women in developing countries. Microtubules, being a validated anti-cancer drug target, prompted innovation of novel anti-mitotic chemotherapeutics which could overcome systemic toxicity related limitation of the clinically used anti-cancer drugs.

This study aims to explore the detailed anti-cancer mechanism of NMK-BH2, a novel bis-indolyl-hydrazide-hydrazone derivative based on indole scaffold. According to our data, the anti-proliferative activity of NMK-BH2 was selective towards cervical cancer (HeLa) cells compared to normal cells, thus conferring therapeutic advantage of reduced host toxicity. NMK-BH2 caused G2/M arrest followed by mitochondria-mediated apoptosis through depolymerisation of cellular interphase and spindle microtubules. It also induced lethal autophagy, independent of apoptosis, contributing to enhanced cytotoxicity in HeLa cells. Characterisation of NMK-BH2 –tubulin interaction in cell-free system revealed that NMK-BH2 inhibited the microtubule assembly through strong and specific binding to tubulin at a single site, overlapping with colchicine-binding site on tubulin.

In conclusion, the present study suggests NMK-BH2 as an efficient and selective anti-cancer agent endowed with remarkable ability to target the cellular microtubule system, leading to apoptosis and autophagy-mediated cell death in HeLa cells and thus, inspires its establishment as a promising candidate for cervical cancer chemotherapy.

Biography

I, Dipanwita Mukherjee, have been working as Senior Research Fellow (CSIR) at Department of Biotechnology, University of Calcutta (India). I have obtained M.Sc. in Biotechnology (Jadavpur University, India) and received Junior Research Fellowship award from Council of Scientific and Industrial Research (CSIR). I have participated in national and international conferences and seminars for oral and poster presentations and published my research findings in peer-reviewed international journals. My research interest is development of novel chemotherapeutics as potential anti-cancer agents by targeting tubulin-microtubule system and understanding the involvement of autophagy in modulating the therapeutic efficacy of these anti-cancer agents.

World Summit on Cancer Science and Therapy

23rd – 25th January 2017, Singapore

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Gallium as a Promising Candidate for the Treatment of Patients with Bone Metastasesfrom Breast Cancer

Bone metastases of breast cancer typically lead to a severe osteolysis resulting from unbalanced bone metabolism. On the other hand, the semi-metallic element gallium (Ga)is an inhibitor of bone resorption. Thus, using an establishedin vitro model associating conditioned medium from breast cancer cells withosteoclast precursor cells, we exploredGa activity on osteoclastogenesis in an aggressive bone metastatic environment. We first observed that Ga dose-dependently inhibited osteoclastogenesis induced by tumour cells medium. To mimic a more aggressive environment where pro-tumorigenic factors are released from bone matrix, metastatic breast tumour cells were stimulated with TGF-□ , a major cytokine involved in bone metastasesdevelopment. In these circumstances, Ga still inhibited cancer cells medium-driven osteoclastogenesis. Lastly, we evidenced that Ga directly and

strongly impacted cancer cellsproliferation/viability, as well as the expression of major osteolytic factors.

This is the first time that antitumor properties of Ga have been specifically studied in the context of bone metastases. Our data strongly suggest that, through its action against the vicious cycle involving bone cells and tumour cells, Ga represents a relevant and promising candidate for a local deliveryupon the resection of bone metastases from breast cancer.

Biography

After getting her PharmD, she has completed her PhD in 2009 from INSERM-U791 (laboratory of osteo-articular engineering-Nantes University-France) and postdoctoral studies from Nice University School of Medicine (CNRS genetic and physiopathology of bone disorders). She accomplished her academicals mobility in the nanoformulation of anticancer drugs in the University of Sydney(Australia). Her research career is focused on regenerative medicine for bone tissue especially by designing innovative drug-combined systems and evaluating their efficacy and safety. She is lecturer at the pharmaceutical sciences faculty. She has published more than 25 research articles in international reputed journals, 4 chapters of book and has been serving as reviewer of scientific journals.

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23rd – 25th January 2017, Singapore

Ella Y. Tyuryumina

International Laboratory for Intelligent Systems and Structural Analysis (ISSA), National Research University Higher School of Economics, Russia

Alexey A. Neznanov

International Laboratory for Intelligent Systems and Structural Analysis (ISSA), National Research University Higher School of Economics, Russia

On Consolidated Predictive Model of the Natural History of Breast Cancer Considering Primary Tumor and Secondary Distant Metastases Growth

This study is an attempt to obtain reliable data on the natural history of breast cancer growth. We analyze the opportunities for using classical mathematical models (exponential and logistic tumor growth models, Gompertz and von Bertalanffy tumor growth models) to try to describe growth of the primary tumor and the secondary distant metastases of human breast cancer. The research aim is to improve predicting accuracy of breast cancer progression using an original mathematical model referred to CoMPaS and corresponding software. We are interested in: 1) modelling the whole natural history of the primary tumor and the secondary distant metastases; 2) developing adequate and precise CoMPaS which reflects relations between the primary tumor and the secondary distant metastases; 3) analyzing the CoMPaS scope of application; 4) implementing the model as a software tool.

The CoMPaS is based on exponential tumor growth model and consists of a system of determinate nonlinear and linear equations; corresponds to TNM classification. It allows to calculate different growth periods of the primary tumor and the secondary distant metastases: 1) "non-visible period" for the primary tumor; 2) "non-visible period" for the secondary distant metastases; 3) "visible period" for the secondary distant metastases. The CoMPaS is validated on clinical data of 10-years and 15-years survival depending on the tumor stage and diameter of the primary tumor (1. Engel J. et al. Eur J. Cancer. 2003; 39(12): 1794-1806; 2. Engel J. et al. Int. J. Radiat. Oncol. Biol. Phys. 2003; 55(5): 1186-1195; 3. Engel J. et al. Cancer Metastasis. 2012; 31(1-2): 235-246). The new predictive tool: 1) is a solid foundation to develop future studies of breast cancer growth models; 2) does not require any expensive diagnostic tests; 3) is the first predictor which makes forecast using only current patient data, the others are based on the additional statistical data.

The CoMPaS model and predictive software: a) fit to clinical trials data; b) detect different growth periods of the primary tumor and the secondary distant metastases; c) make forecast of the period of the secondary distant metastases appearance; d) have higher average prediction accuracy than the other tools; e) can improve forecasts on survival of breast cancer and facilitate optimization of diagnostic tests.

The following are calculated by CoMPaS: the number of doublings for «non-visible» and «visible» growth period of the secondary distant metastases; tumor volume doubling time (days) for «non-visible» and «visible» growth period of the secondary distant metastases.

The CoMPaS enables, for the first time, to predict "whole natural history" of the primary tumor and the secondary distant metastases growth on each stage (pT1, pT2, pT3, pT4) relying only on the primary tumor sizes. Summarizing: a) CoMPaS describes correctly the primary tumor growth of IA, IIA, IIB, IIIB (T1-4N0M0) stages without metastases in lymph nodes (N0); b) facilitates the understanding of the appearance period and inception of the secondary distant metastases.

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Howard Hua Yang

University/Organization: National Cancer Institute at NIH, USA

Reproducible Genes For Breast Cancer Patient Survival Prediction

We have analyzed the dataset METABRIC to find reproducible genes to form linear and nonlinear models for survival prediction. We drew random half samples from the training data as bootstrap samples and applied the Cox Proportional Hazards Model to analyze the full training data and each half sample with the adjustment for the four clinical variables: age, ER, tumor size, and node. From the analysis of the full training data, we selected top 330 genes (top 1%). We selected 50 genes most reproducible in the analyses of the bootstrap samples with repetition rate greater than 0.36. The 50 selected genes include TFRC (one of 21 Oncotype DX genes) and other cancer genes such as PAWR, PKM2, STAT5Band ANGPT2. We used linear/nonlinear predictors to combine the expression of the selected genes. We used the validation data to examine the generalization performance of the predictors with adjustment for age, ER, tumor size, and node. The nonlinear model gave a signature with HR=1.7, CI:1.39-2.08 and P= 2.552e-07 better than the linear model. The METABRIC data analysis showed that the patients with high expression of STAT5Bhad better prognosis while those with high expression of TFRC had poor prognosis. The analysis of the tamoxifen treatment data showed that TFRC expression can be reduced by taking Tamoxifen without changing STAT5B. Our further understanding about these genes has clinical implications in breast cancer treatment.

Biography:

Dr. Yang received his PhD inProbability and Statistics in 1989 from Zhongshan (Sun Yat-Sen) University, China. Before he joined the NCI as an expert/staff scientist in 2001, he was a productive scientist in signal processing, neural networks and machine learning. Since 2001, he had been focused on biostatistics and bioinformatics in cancer research.

World Summit on Cancer Science and Therapy

23rd – 25th January 2017, Singapore

Prof. Indraneel Mittra

University/Organization: Tata Memorial Centre, Advanced Centre for Treatment, Research & Education in Cancer (ACTREC), Mumbai. India

Biology of Cell-Free Nucleic Acids and Its Role in Initiation And Metastasis of Cancer

Several hundred billion to a trillion cells die in the adult human body daily, and a considerable amount of fragmented cell-free nucleic acids (cfNAs) from dying cells are released into the circulation. Our research has shown that circulating cfNAs can freely enter into healthy cells, accumulate in their nuclei, trigger a DNA damage repair response (DDR) and integrate into host cell genomes by an unique mechanism (http://www.ias.ac.in/article/fulltext/jbsc/040/01/0091-0111; http://f1000research.com/articles/4-924/v1). Similarly, at the tissue level, locally generated cfNAs from dead cells can be taken-up by healthy bystander cells to induce DDR that facilitates their integration into recipient cell genomes. Genomic integration of cfNAs leads to dsDNA breaks, inflammation, chromosomal instability, senescence and apoptosis of recipient cells. cfNAs from cancerous cells can cause oncogenic transformation of NIH3T3 cells which are tumourigenic in immune-deficient mice. These findings raise a new hypothesis of cancer metastasis which posits that metastasis arises from de novo oncogenic transformation of cells of target organs induced by cfNAs arising from apoptotic circulating tumour cells (CTCs). This hypothesis challenges the current dogma that metastasis are produced by growth of CTCs that are lodged in distant organs.

Biography:

Professor Mittra obtained his medical degree from University of Delhi and is a Fellow of the Royal College of Surgeons of England and holds a PhD degree from University of London. He did his post-doctoral training with Dr Renato Dulbecco, Nobel Laureate, at the Imperial Cancer Research Laboratories in London. Professor Mittra is a multi-faceted personality. He is a breast cancer surgeon while at the same time being deeply involved in public health and basic research in cancer. Professor Mittra's current research interests lie in the area of biology of extracellular nucleic acids and their role in ageing, inflammation, degenerative disorders and initiation and metastatis of cancer.

World Summit on Cancer Science and Therapy

23rd – 25th January 2017, Singapore

Jaw Yuan Wang MD, Ph.D

Kaohsiung Medical University Hospital,Kaohsiung Medical University,
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Combining this 6-miRs panel with clinicopathologic factorsor the Detection of Early Relapse in Postoperative Colorectal Cancer Patients

MicroRNA (miR) deregulation is associated with colorectal cancer (CRC) development and recurrence; therefore, miRs may be reliable biomarkers for detecting early relapse postoperatively. Ten candidates were identified using miR arrays: miR-7, miR-31, miR-93, miR-141, miR-195, miR-375, miR-429, miR-494, miR-650, and let-7b. Substantial differences were observed in their expression levels between early relapsed and non-early relapsed CRC patients. Using a miR RT-qPCR, we observed that expression levels of miR-93, miR-195, and let-7b were significantly decreased, whereas those of miR-7, miR-141 and miR-494 showed increases that were more significant in the CRC tissue samples from the early relapsed patients than the non-early relapsed patients. A panel of 6 miRs (miR-7, miR-93, miR-195, miR-141, miR-494, and let-7b), at a cut-off value of 2 deregulated miRs, distinguished early relapsed CRC from non-early relapsed CRC, with a sensitivity of 76.6% and a specificity of 71.4%. By combining this 6-miRs panel with 6 clinicopathologic factors, at a cut-off value of 4, distinguished early relapsed CRC from non-early relapsed CRC, with a sensitivity of 89.4% and a specificity of 88.9%.This study showed that the developed miR panel has the potential to improve predicting early relapse in CRC patients.

Biography:

Prof. Jaw-Yuan Wang is Vice superintendent at Kaohsiung Medical University Hospital (KMUH). He went on to receive further training as a Research Fellow at the State University of New York, Stony Brook, USA. He now serves as Leader of Colorectal Cancer Multidisciplinary Team, Program Director of Robotic Surgery. He is an active member in numerous professional organizations. Besides being a recipient of numerous awards, he has published widely at least 245 peer-reviewed papers and 4 book chapters. He is a reviewer for more than 40 prestigious journals and is now the PI of Biosignature in Colorectal Cancers, Academia Sinica, Taiwan.

World Summit on Cancer Science and Therapy

23rd – 25th January 2017, Singapore

Jixin Dong, Ph.D

Fred& Pamela Buffett Cancer Center and Eppley Cancer Institute, University of Nebraska Medical Center, Omaha, NE68198, USA.

The Hippo-YAP Pathway in Prostate Cancer

Prostate cancer is the most common malignancy and the second leading cause of cancer-related mortality among men in the United States. Although androgen-deprivation therapy (medical or surgical castration) is highly effective for advanced prostate cancer, the majority of patients eventually develop resistance and progress to castration-resistant prostate cancer (CRPC). Unfortunately, most cases of CRPC are currently incurable. The cause of castration resistance is still not completely known. Recent genetic mouse models and studies with cancer patients firmly demonstrated the critical roles of Hippo signaling in cancer development. Yes-associated protein, YAP, is an effector of the Hippo tumor suppressor pathway. The oncoprotein YAP has been implicated in promoting several types of tumor formation, such as liver and skin tumorigenesis and rhabdomyosarcoma.We found that YAP mRNA was upregulated in androgen-insensitive prostate cancer cells (LNCaP-C81 and LNCaP-C4-2) when compared to the androgen-sensitive LNCaP cells. YAP knockdown greatly reduced the migratory and invasive rates of LNCaP-C4-2 cells. Importantly, ectopic expression of YAP was sufficient to promote LNCaP cells from androgen-sensitive to androgen-insensitive in vitro and YAP conferred castration resistance in vivo. Deletion of MST1/2 (core tumor suppressors in the Hippo pathway) or YAP did not affect the prostate development. YAP activation or MST1/2 inactivation was not sufficient to promote prostate tumorigenesis.

Biography:

Dr.Dongobtained his Ph.D. at Zhejiang University, China.He went on to receive further training as a Postdoctoral Fellow at the University of Texas Southwestern Medical Center at Dallas, and then at Johns Hopkins University, Baltimore, USA. Currently he is an Associate Professor at the University of Nebraska Medical Center, Omaha, USA.

World Summit on Cancer Science and Therapy

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Dr S Krishnamurthy

University/Organization: Kidwai Memorial Institute of Oncology Bangalore

Breast Cancer in India- Where do we stand and where do we go?

Treatment of Breast cancer has undergone quite an improvisation in the last 20 years since the introduction of molecular biology, immunohistochemistry and availability of targeted therapy.We present our last 6 years' experience in treating 862 Breast cancer patients in a single unit at a Regional cancer centre in India. Total of 862 breast cancer patients have been treated at our institute in a singlesurgical oncology unit from 2010 to 2016. Maximum incidence was observed in the age group 35-64 years (710/82.4%) and least in above 65 years (73/ 8.5%) with almost an equal number of patients coming from rural (51.9%) and urban (48.1%) population. Right sided breast cancer (56%) dominated compared to left (43.4) whereas 0.6% were bilateral. A higher incidence was noted amongst postmenopausal (54.2%) compared to premenopausal women (45.8%). Maximum patients were of Luminal A category (35%) with most of them presenting as Stage II (42.5%) and III (44.4%) disease. Triple Negative tumours contributed to significant 32.7% of the disease. 338 patients were given neoadjuvant chemotherapy before surgical management. 21 patients underwent Breast conservation surgery with Sentinel Lymph node biopsy done in 9 patients with 100% sentinel Lymph node identification rate while the rest underwent modified radical mastectomy. Adjuvant chemotherapy and Radiotherapy was administered to 437 and 702 patients respectively whereas 198 patients were given targeted therapy. Hormonal therapy was offered to 460 patients based upon their receptor status.In a developing country where health insurance cover and governmental policy is not available for the patients, it remains a challenge to offer the advanced management to all patients attending a regional cancer centre.

Biography:

M.ch SURGICAL ONCOLOGY (AUGUST 1994); M.S.GENERAL SURGERY (FEBRUARY 1987); M.B.B.S (JULY 1982). Joined the institute as lecturer in 1987, promoted as assistant professor 1993, professor 2002 and heading the department of surgical oncology since 2015. Teaching super specialty students (8) every year, published 40 articles in national/ international journals, participated in 8 global projects.

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Tropomodulins are new Favorable Prognostic Biomarkers in High-Risk Neuroblastoma

Neuroblastoma is a pediatric tumor of the sympaticoadrenal lineage of the neural crest characterized by an extreme molecular and clinical heterogeneity, which is the main cause of the unsatisfactory response to standard multimodal therapy. The identification of new and selective biomarkers is crucial to fill the gaps about the biological and molecular mechanisms of neuroblastoma and to improve cancer therapies. This study identified a positive and promising correlation between Tropomodulins (Tmods) proteins and neuroblastoma. Tmods bind the pointed end of actin filaments, regulate polymerization and depolymerization processes, modifying actin cytoskeleton dynamic and influencing neuronal development processes. High expression levels of Tmods positively correlate with high survival probability neuroblastoma patients'. Functional studies on neuroblastoma cell lines demonstrated that Tmod 1 Knockin induced cell cycle arrest, cell proliferation arrest and a mature functional differentiation. Tmod 1 overexpression is responsible of particular cell morphology and

biochemical changes, which direct cells towards a neuronal prognostic favorable differentiation profile. On the contrary, Tmod 1 downregulation caused the loss of mature cell differentiation for the development of neuroendocrine cell characteristics, delineating an aggressive and prognostic unfavorable tumor behavior. This work indicates that Tmods can be the innovative and prognostic favorable biomarkers in high-risk neuroblastoma and contributes to understanding new biological mechanisms to improve personalized therapeutics opportunities.

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Nina Mikirova
Organization: Riordan Clinic

High-Dose Intravenous Vitamin C as Sole Therapy and in Combination with Cytotoxic Chemotherapy in Patients with Cancer

Vitamin C has been shown to protect against oxidant injury at physiological concentrations and has been suggested as having both a preventative and therapeutic role in a number of pathologies when administered at pharmacological levels. In our clinic we treat cancer patients by high doses of vitamin C intravenously (15-75 grams) during 40 years. According to our data,there was positive response to IVC, which was demonstrated by measurements of inflammation (C- reactive protein) andinflammatory/angiogenesis cytokines. 174 cytokines with tumor markers were determined in cancer patients before and after a series of IVC treatments. The average levels (z-scores) for inflammatory and angiogenesis promoting cytokines, that were higher than averages for healthy controls, decreased over the course of treatment. A decrease in the level of inflammation correlated with the decrease in the levels of tumor markers. Clinical studies of chemotherapy with vitamin Cdemonstrated thatIVC does not interfere with anti-tumor effects of chemotherapy. IVC may improve time to relapse, enhance reductions in tumor mass and improve survival in combination with chemotherapy. IVC treatment improves quality of life, physical function, and toxicities associated with chemotherapy. Our Phase I clinical study and other trials indicated that IVC can be administered safely with relatively few adverse effects.

Biography:
Nina Mikirova, PhD, Dr. Mikirova is the Director of research at the Riordan Clinic. After graduation from Moscow State University in Russia, she worked atthe Institute of Bio-Medical Problems and joined the Riordan Clinic in 1997. Her areas of research focus include: the effect of high dosage vitamin C on cancer, inflammation and angiogenesis; energy metabolism of mitochondria in cancer cells; modulation ofthe levels of progenitor and stem cells in circulation by nutraceuticals.

World Summit on Cancer Science and Therapy

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Runsheng RUAN

Organizations: Xiamen Key Laboratory for Translational Medicine in Cellular Theranostics of Cancer, Xiamen University, People's Republic of China

Clinical And Immunological Response to in Vivo Whole Cancer Cell Antigen Priming Followed By Adoptive T-Cell Therapy in Terminal Cancers

Strategies to enhance an antigen specific immunity against cancer have been met with limited clinical success. We adopt a 2-tier protocol coupling active with passive immunization, allowing a prospective clinical evaluation of survival in 31 terminal cancer patients. Treatment commences with subcutaneous inoculation of whole cancer cell antigen followed by re-infusion of ex vivo expanded autologous T cells. Tumour-specific cytotoxic T cells were confirmed via Elispot and Real-time Cell Analyzing (RTCA) Assay, and serum cytokines werealso measured pre and post therapeutically. Statistical tests show tumour-specific T cell response is effectively invoked post treatment. Spearman correlation analysis determined significant association between higher post treatment cytotoxicity scores and longer survival duration in months($R=0.59$, $p=0.005$). This result is mirrored by the Elispot count. Prospective controlled trials are needed to further clarify the role of cancer whole antigen immunization with adoptive cell therapy, but these encouraging preliminary observations suggest that this combination can induce more durable responses to immunotherapy.

Biography:

Professor Ruan received his medical degree from Fujian Medical University and holds a MD degree from Zurich University of Switzerland. He did his post-doctoral training at the Cancer Research Institute of Zurich University Hospital. Professor Ruan is a multi-faceted personality. He is an ENT Head & Neck surgeon while at the same time being deeply involved in applied cancer research. He currently is the Director of Xiamen Key Laboratory for Translational Medicine in Cellular Theranostics of Cancer, and his research interests lie in the area of cellular medicine for cancer immunotherapy.

World Summit on Cancer Science and Therapy

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Shun Young Im

Mechanism of CK2α Activation and its Expression in Human Breast Cancer

The protein kinase CK2α(formerly Casein Kinase II) is implicated in tumorigenesis and transformation. However, the mechanisms of CK2α activation and the role of CK2α in breast cancer remains to be elucidated.

Methods: CK2α activity, phosphorylation, and protein expression were determined in ER+ MCF-7 and T47D, and ER- MDA-MB-231 human breast cancer cell lines. The expression of the various genes involved in reactive oxygen species (ROS) metabolism and CK2α in human breast cancer tissues were investigated using RT2 PCR array (Qiazen), and immunohistochemistry, respectively.

Results: Estrogen increased CK2α activity and phosphorylation in ER+, but not in ER- cell lines, which were inhibited by the antioxidant N-acetyl-L-cysteine (NAC). H2O2 enhanced CK2α activity and phosphorylation. Estrogen increased ROS generation in ER+, but not in ER- cell lines through activation of p38 MAPK. The PCR array demonstrated that, among the 115 oxidative stress-related genes examined, 11.3% genes were downregulated and 2.6% genes were upregulated in ER+/PR+, 7.0% genes were downregulated in HER2+, and 6.1% genes were upregulated in triple negative breast cancer tissues, respectively.Nuclear CK2α protein expression was observed in 100% (15/15), 100% (15/15) and 92% (12/13) of ER+/PR+, HER2+, and triple negative cancer tissues, respectively.

Conclusios: The data suggest that 1) estrogen activated protein kinase CK2α via the induction of ROS/p38 pathway 2) there were no significant differences in the expression of oxidative stress-related gene and CK2a protein among the three different types of human breast cancer cells.

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David Vesely
University of South Florida, Tampa

Cardiac Hormones for the Treatment of Cancer

Four heart hormones, namely atrial natriuretic peptide (ANP), long-acting natriuretic peptide (LANP), vessel dilator and kaliuretic peptide reduce up to 97% of cancer cells in vitro. These four cardiac hormones eliminate up to 80 % of human pancreatic adenocarcinomas, 2/3rds of human breast cancers and up to 89% of human small cell lung cancers growing in athymic mice. ANP intravenously for 3 hours after "curative" lung surgery as an adjunct to surgery results in a two year relapse-free survival of 91% compared to 75% with surgery alone. Their anticancer mechanisms of action involve binding to receptors on the cancer cells followed by 95% inhibition of the conversion of inactive to active rat sarcoma-bound guanosine triphosphate (RAS)-mitogen –activated protein kinase kinases 1/2 (MEK 1/2) (98% inhibition)-extracellular signal-related kinases 1/2 (ERK1/2) (96 % inhibition) in cascade cancer cells. They are dual inhibitors of vascular endothelial growth factor (VEGF) and its VEGF2 receptor (up to 89%) They also inhibit MAPK9 i.e. c-JUN-N-terminal kinase 2. One of the downstream targets of VEGF is B-catenin, which they inhibit up to 88%. These four peptide hormones inhibit the Wingless-related integration site (WNT) pathway 68% and WNT secreted-Frizzled protein is reduced by up to 84%. Signal transducer and activator of transcription 3 (STAT 3), a final "switch" that activates gene expression that leads to malignancy, is specifically decreased up to 88 % by these peptides as they do not affect STAT 1. There is cross –talk between the RAS-MEK 1/2-ERK 1/2 kinase cascade , VEGF, B-catenin, JNK, WNT, and STAT pathways and each of these pathways and their cross talk is inhibited by these peptide hormones. They enter the nucleus of cancer cells where they inhibit the proto-oncogenes c-Fos (up to 82 %) and c-Jun (up to 61%). Conclusion: These multiple kinase inhibitors have both adjunct and primary anticancer effect ANP is one of four hormones synthesized by the ANP prohormone gene.

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Doni Dermawan
Padjadjaran University, Indonesia

The Combination of *Zingiberis officinale var.rubrum* and Piper retrofractum Based on Microencapsulation Technology as an Anticancer Drug

Cancer is a disease that causes high mortality rates in Indonesia and has a tendency to increase. A wide variety of prevention and treatment of cancer has been done in Indonesia but there is no treatment that is really effective. Indonesia has a huge potential in natural resources, including plants that can be used as medicine. Piper retrofractum and Zingiberis officinale var. rubrum are plants which has anticancer activity in the active ingredient. By using the method of literature study, this paper focuses on assessing the activity and effectiveness of the combination of the active ingredient in Piper retrofractum and Zingiberis officinale var. rubrum that have a potential synergistic effects as anticancer in the appropriate dosage form. Curcumin can induces apoptosis of cancer cell and piperine as an antioxidant that inhibits the free radical chain oxidative so it can prevent the oxidative stress. Optimization of the extraction of active ingredients piperine from Piper retrofractum and curcumin from Zingiberis officinale var. rubrum can be done by soxhlet extraction method with solvent ethanol 95%. Soxhlet method yields an efficient curcumin and piperine extraction, the efficiency of solvent and time. The extract that obtained from the extraction process should be standardized to ensure its quality so it implies safety and efficacy of dosage form produced. Effort to maximize the activity and effectiveness as an anticancer, extract can be made dosage form based on microencapsulation technology with variation concentration of core and coating agent using spray drying techniques. The formulation technology of the combination of Piper retrofractum and Zingiberis officinale var. rubrum based on microencapsulation is expected to provide a therapeutic effect that is secure, effective, and efficient against cancer.

Keywords : Curcumin, Microencapsulation, Piperine, Piper retrofractum, Zingiberis officinale var. rubrum

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New Topoisomerase Inihibitor for Breast and Pancreas Cancer

Recently, some authors reported that the Topoisomerase enzymes such as TOPO II is more expressed in aggressive subset of tumors (for example breast tumor that overexpresses HER-2/neu).Based on these evidences recently our group has synthesized a new molecule, called SC4, which inhibits the TOPOII, reducing the proliferation and acts negatively on the cellular migration; furthermore SC4 shown in vivo an antiproliferative effect and a reduction in the systemic toxic effects. We have tested SC4 on two cancer cell lines, that representing the principal "Big Killer" of the oncology: pancreatic cancer human cell (Mia-PaCa2) and triple negative breast cancer human cell

(MDA.MB231). In vitro cytotoxic assays have demonstrated the ability of SC4 to inhibit cell proliferation. The MTT assay , FACs Colony Assay results support the inhibition of proliferation. Likewise, we performed two experimental in vivo to evaluate the SC4 inhibition activity on proliferation and migration, and to assess the degree of safety.

Orthotopic cancer xenograft mouse models and in vivo models of secondary localization (Lung Colonization)confirm the anticancer activity. In conclusion SC4 inhibits proliferation and migration of human tumor cell lines by blocking the activity of TOPO II, and may be considered as a potent inhibitor of tumor growth and invasion in mouse model; for these reasons could be considered a valid prototype for the development of new antineoplastic therapies.

Biography

He has worked as Fellow Researcher at the National Institute of Cancer - I.R.C.C.S. "G. Pascale Foundation" since 2007. In the meantime he was Fellow Researcher at Institute of Endocrinology and Oncology "G. Salvatore" - National ResearchCouncil, a national institute specialized in basic research on tumor biology.From 2002 to 2005 he was a junior clinical Fellow Researcher at San Raffaele Hospital, Cancer Immunotherapy and GeneTherapy Dept., where he worked on the development of anti-cancer vaccines against melanoma based on dendritic cellstransfected with lentiviral vector. His activity led to a clinical trial performed by MolmedSpA (Milan, Italy). From 2005 to2007 he was in charge of the development of oncology murine models for testing new drug candidates at CEINGE Scarl, abiotechnology consortium located in Naples, Italy.He is the author of 30 papers in peer-reviewed international Journals.Giuseppe has a B.Sc, M.Sc in Medical Biotechnology (University of Naples "Federico II", Italy).

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Gregory Lee
UBC Center for Reproductive Health, Vancouver, Canada

Distinct Functional Roles of Cancerous Immunoglobulins in Cancer Immunology

The immune system in cancer cells was revealed with the understanding that immunoglobulins expressed on the cancer surface play important roles in cancer immunology. RP215 monoclonal antibody generated in 1987 against ovarian cancer cell extract was shown to react specifically with a carbohydrate-associated epitope mainly found in the variable region of immunoglobulin heavy chains and expressed on the surface of almost all of cancer cells (designated in general as CA215). Since then, RP215 has become a unique probe to study mechanisms of action by which the cancer cells are affected by these immunoglobulins. Generally speaking, RP215 and anti-human immunoglobulins are equally effective in inducing apoptosis and complement-dependent cytotoxicity reactions to cultured cancer cells and reducing the volume of the implanted tumor in nude mouse animal models. Interaction studies were performed between isolate cancerous immunoglobulins and/or CA215 and human serum proteins, most of which exhibit either anti-cancer or pro-cancer properties. Therefore, it is hypothesized that cancerous immunoglobulins may function to interact with these human proteins for the growth/proliferation as well as protections of cultured cancer cells in human circulations. RP215 may be further developed as candidates of anti-cancer drugs to target most of cancer cells for immunotherapy of human cancer.

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Hafiz Muhammad Asif, (Ph. D)

University College of Conventional Medicine, Faculty of Pharmacy & Alternative Medicine, The Islamia University of Bahawalpur

Prevalence, Risk Factors and Disease Knowledge of Breast Cancer in Pakistan

Breast cancer is the most common cancer in females all over the world with approximately one million new cases each year as well as one of second leading causes of death among females. In Pakistan, the most frequently diagnosed cancer among females is also breast cancer. Breast cancer is more common in Pakistani population as compared to the Western population. In Pakistan every year at-least 90,000 women suffer from breast cancer. One in every nine Pakistani women suffers from breast cancer which is one of the highest incidence rates in Asia. Recently, incidence of breast cancer is 21.5% among all and 45.9% among female patients, reported. Its incidence in Pakistan is 2.5 times higher than that in neighboring countries like Iran and India. Key factors that play role in the development of breast carcinoma are the genetics and environment, the reproductive experience, the effect of endogenous and exogenous hormones in females, the change in immune status, host vulnerability and the biologic determinants of breast carcinoma. The present study is aimed to provide awareness about breast cancer as well as an updated knowledge about the prevalence, risk factors and disease knowledge of breast cancer in Pakistan.

Keywords: Breast cancer, incidence, prevalence, risk factors, Pakistan

Biography

I, Dr. Hafiz Muhammad Asif have completed my Ph.D. in the field of Eastern Medicine (Clinical Methods & Therapeutics) from Hamdard University, Karachi, Pakistan. I have published more than 80 papers in National and International journals. I have attended many national and international conferences and seminars and presented oral and poster presentations. I am member of many national and international academic and learning bodies. I am serving as Assistant Professor in University College of conventional medicine, Faculty of pharmacy & alternative medicine, The Islamia University of Bahawalpur.

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Henry I.C. Lowe

University/Organization: Bio-Tech Research & Development Institute

Tillandsia recurvata: A Natural Plant with Anti-Prostate Cancer Potential Targeting Kinases

Prostate cancer is the second most common cause of death from cancer in men of all ages. The three conventional treatment options include surgery, radiation and chemotherapy. In many cases, these treatments are used in combination. Increased resistance to current chemotherapies by prostate cancer calls for an urgent need to discover and develop new therapeutics that can slow the growth of cancer cells while having lesser side effects on patients. In an effort to discover new anticancer drugs from natural products, several Jamaicanplants were screened for anticancer activity. The Jamaican Ball Moss (Tillandsia recurvata L.) was one such plant that exhibited potent activity against the prostate cancer cell lines in vitro and in vivo. To explore the mechanism of action of the plant material, a crude extract of Ball Moss was screened for interaction with over 450 kinases. The crude extract was active against 5 kinases (kd = 8-14 µg/ml), of which 4 are implicated in prostate cancer onset and proliferation. The kinases are; CSNK2A2, DRAK1, GAK and MEK5. Based on our scientific determination of the molecular target for this potent extract, our lab produced a nutraceutical (Alpha Prostate Formula) for the prevention and treatment of prostate cancer.

Biography

Dr. Henry Lowe, , O.J., C.D., J.P., Ph.D., D.Sc. (Hons.), F.R.S.H, isin medicinal chemistry and has contributed approximately 50 years in the fields of science and technology and the health sciences nationally, regionally and internationally.He has earned several recognitions nationally and regionally, including the Order of Jamaica and Commander of the Order of Distinction. He is an Adjunct Professor in the Department of Medicine, University of Maryland School of Medicine, USA and Distinguished Adjunct Professor of Ethno-medicinal Chemistry, University of Technology, Jamaica. He is a public servant, author, educator and successful entrepreneur.

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Nutrition Therapy For Breast Cancer During Chemotherapy A Qualitative Study onthe Needs of Breast Cancer Patients

The high prevalence and incidence of breast cancer in Indonesia remains a disheartening issue, for it has turned out to be a threat for the quality of Indonesian women's life. Let alone the fact that the patients and their families often lose interest in recognizing the issue of breast cancer, both benign and malignant. Besides, the problem faced by breast cancer patients in determining which kind of diagnosis or best therapy is still overlooked by the patients as well as their family members. This includes their indifference toward the patients' nutrition during chemotherapy, which now thus must be taken into consideration.

This research aims at observing therapy needs in general, particularly that of nutrition of breast cancer patients during their chemotherapy and post-therapy period. This research is the result of qualitative data collected by case study on 17 breast cancer patients undergoing chemotherapy in Al-Ihsan Hospital, Bandung District and HasanSadikin Hospital, Bandung City. These patients have undergone an in-depth interview either on their own or accompanied by a family member.

The result of the qualitative research is obtained through content analysis observation, showing a shallow understanding about therapy, both generally and specifically, regarding the importance of nutrition and the escalation of its amount on the patient and their families. In fact, one of the things that support the patient's immune system during their chemotherapy is the sufficient condition of nutrition. Not only that, the result shows that cancer survivors claim they keep a balanced intake of nutrition during and after therapy. Therefore, it is necessary to make a formula about nutrition needs of breast cancer patients, in the preparatory, momentary, and preempting stage of chemotherapy.

Keywords: nutrition therapy, breast cancer.

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Prognostic Value of Breast Cancer Subtypes Based on ER/PR, Her2 Expression and ki-67 Index in Women Received Adjuvant Therapy after Conservative Surgery for Early Stages Breast Cancer

Breast cancer is the most common malignancy in women, accounting for 29% of all female cancers. it accounts for < 1% of all cancer cases in men. In a population based cancer registries in Gharbia, Egypt, breast cancer was the most frequent cancer among Egyptian females. Prognostic information for the individual patient is based on the analysis of biological markers in the primary tumour including (ER), (PR), (HER2) and Ki67, together with age, tumour size, histological grade and lymph node involvment. Molecular subtyping of breast cancer may provide additional prognostic information regarding patient outcome.

Objectives: To evaluate the prognostic effect of breast cancer subtypes on local relapse rates, distant metastases, and survival in women underwent breast conservative surgery for early stages breast cancer.

Material and Methods:Data of 100 patients affected by early stage breast cancer and treated with breast-conserving therapy were reviewed. Patients were grouped, based on the basis of receptor status and HER-2 status, patients were grouped, as: luminal A (ER + and/or PR+, Ki67 low and HER2-),

luminal B (ER + and/or PR+, Ki67 high and/or HER2+), HER2-positive (ER-, PR- and HER2+) and triple negative (ER-, PR, HER2-). Distribution of variables among subtypes was evaluated with Pearson's test. Survival rates were calculated with life tables; Cox regression stepwise method was used to identify predictive variables of survival.

Results:Median age was (range 18-50) and median follow up time of 40 months (range 36.83-43.17).Breast cancer specific survival and distant metastases rates were different among breast cancer subtypes (both outcomes P= 0.001) , there was significant difference regarding local relapse rates (P= 0.002). Axillary nodes status (P= 0.007), adjuvant therapy (P= <0.001) and breast cancer subtypes resulted prognostic factors of breast cancer specific survival; axillary node status (P= 0.007) and breast cancer subtypes had an impact on distant metastases.

Conclusions: In our study, breast cancer subtype seems a prognostic factor of breast cancer specific survival and distant metastases rates & of local relapse rate. Patients could be submitted to conservative surgery, if feasible, but considering the differences in survivals, patients with worse prognosis should receive more aggressive adjuvant treatment.

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Mostafa I. Waly

University/Organization: Department of Food Science and Nutrition, College of Agricultural and Marine Sciences, Sultan Qaboos University, Muscat, Oman

Functional Foods in the Primary Prevention of Colon Cancer

Increased consumption of refined carbohydrates, sugars, and saturated fats is accompanied by low intake of fruits and vegetables; this dietary pattern is involved in the etiology of different types of cancers, the global cause of morbidity and mortality in the Western countries and gulf region. Colorectal cancer, CRC, is among the primary preventive cancers if adequate intake of antioxidants was provided either by diet, and nutritional supplements. Our research group at Sultan Qaboos University has successfully identified phytonutrients- rich dietary bioactive agents (Date Pit Pomegranate Peel, Mushroom Extract, and Nabag Extract) which provide antioxidant protective effect against oxidative stress-induced CRC, using in-vivo experimental study models. Our results have shown a net subjective improvement in the CRC pathogenesis as evident by a marked decrease in tumor growth, increase in intra cellular glutathione level, and antioxidant enzymes-improved activities. It was concluded that the high intake of plant-based foods might be adopted as a dietary-based intervention approach for the primary prevention of oxidative-stress mediated cancers, including CRC. The mechanism was thought to be by abrogating oxidative stress in carcinogenic cells.

Biography:

Dr. Mostafa Waly obtained his PhD in 2003 in Nutritional Biochemistry from the Department of Biomedical Sciences at Northeastern University, Boston, USA. He is currently holding the position of associate professor, Food Science and Nutrition department, Sultan Qaboos University in Oman. Dr. Waly has received several academic awards and he is an active member in international advisory board of American Society of Nutrition and Experimental Biology of Medicine Society. Dr. Waly is the author of many scientific publications recognized by local and international bodies. His research interests have been in the role of dietary antioxidants and B vitamins in the primary prevention of chronic diseases. Dr. Waly performed several consultancies for UNICEF and WHO.

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Muna Fathy

Association Between Environmental Tobacco Smoke Exposure and Lung Cancer Susceptibility: Modification by Antioxidant Enzyme Genetic Polymorphisms

Environmental tobacco smoke (ETS) is the primary etiologic factor responsible for lung cancer. However, only 10–15 % of smokers develop lung cancer, suggesting a genetic role in modifying individual susceptibility to lung cancer. Antioxidant enzymes and genetic polymorphisms should be considered.

Aim: The present study aimed to evaluate the role of antioxidant enzyme activity and genetic polymorphisms in modifying the susceptibility to lung cancer among individuals exposed to ETS.
Subjects and Methods: A total of 150 male subjects were divided into three groups: 50 lung cancer patients, 50 chronic smokers, and 50 passive smokers. Genotyping of microsomal epoxide hydrolase (mEH) exon 3 (Tyr113Hist) and exon 4 (Hist139Arg) polymorphisms were done by the polymerase chain reaction-restriction fragment length polymorphism technique. MnSOD (Val16Ala) polymorphism was detected by the real time-TaqMan assay. Erythrocyte MnSOD activity was measured spectrophotometrically.

Results: ETS-exposed individuals (both active and passive smokers) who carried the His allele of mEH exon3 have a 2.9-fold increased risk of lung cancer (odds ratio [OR] 2.9, $P < 0.001$). In addition, ETS-exposed carriers of the Arg allele of mEH exon 4 have a 2.1-fold increased risk of lung cancer (OR 2.1, $P = 0.024$). However, no association between the MnSOD Val16Ala polymorphism and lung cancer was detected among ETS-exposed individuals (OR 1.6, $P = 0.147$), although the lung cancer group had significantly lower MnSOD activity than the chronic or passive smoker groups ($P = 0.03$). Conclusions Exons 3 and 4 polymorphisms of the mEH gene may contribute to lung cancer susceptibility through disturbed antioxidant balance. However, this was not thecase with the MnSOD Val16Ala single-nucleotid polymorphism. Antioxidant enzymes may modulate the influence of ETS exposure on lung cancer risk.

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VEGF and IL-6 Profile in Patients with Invasive Breast Cancer

The aim of this study was to investigate VEGF expression in tumour tissue in patients with breast cancer in relation to stromal tissue and normal breast tissue in patients with benign breast disease, and in relation to circulating VEGF and IL-6 levels, preoperatively and postoperatively. Samples from 20 patients with breast cancer and 15 patients with benign breast disease were included. Immunohistochemical staining was used for determining VEGF expression in tissue samples. Measuring VEGF and IL-6 levels was conducted by ELISA.

Differences in VEGF expression between tumour and stroma were significant (p=0,007) and between tumour and normal breast tissue in benign disease patients (p=0,0001), and also between stromal and normal breast tissue (p=0,004). Circulating VEGF were significantly higher in serum from patients with breast cancer than in patients with benign breast disease pre- and post-operatively (p=0,023; p=0,019). VEGF levels were higher postoperatively in serum (p=0,009) and in seroma (p=0,0001). Circulating IL-6 were significantly higher in serum from patients with breast cancer than in patients with benign breast disease (p=0,023) postoperatively. IL-6 levels were higher postoperatively in serum (p=0,015) and seroma (p=0,0001). IL-6 levels were significantly higher in serum from patients with benign breast disease postoperatively (p=0,018). Statistically significant correlation between VEGF and IL-6 in seroma from patients with breast cancer was found (p=0,009).

Results from present study suggest sinergistic activity of VEGF and IL-6 in wound healing process after breast cancer surgery.

Biography

Nahida Srabovic is assistant professor at The Department of Biochemistry, Faculty of Pharmacy, University of Tuzla, Tuzla, Bosnia and Herzegovina.

Nahida Srabovic was born in Tuzla, Bosnia and Herzegovina on 11 January 1982. She graduated from High School in Lukavac and from the University of Tuzla, Faculty of Science with a Bachelor of Chemistry in February 2005. She completed her Master of Science degree in Biochemistry in April 2010 at University of Sarajevo, Sarajevo, Bosnia and Herzegovina. After receiving her education she remained at the Department of Biochemistry, University of Tuzla as teaching assistant and researcher. She completed her PhD thesis in October 2012 at University of Tuzla.

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DNA methylation Analysis of genes in Notch signalling pathway in human glioblastoma FFPE tissues

Gene expression can be disrupted either through genetic or epigenetic alterations. In cancer, over half of tumor suppressor genes are affected through methylation. It can also affect other important signal transduction pathways leading to altered receptor function, altered function of transcription factors, and disruption of normal cell–cell interaction. Aberrant methylation can occur at very early stage in cancer leading to malignancy, hypermethylated gene promoters hold great promise as tumor markers for early detection and their reversible nature provides an effective drug target for gene reactivation.

The Notch signaling pathway is one such developmental pathway governing cell fate decisions, differentiation, cell proliferation and apoptosis. Deregulated Notch signaling is found to have a prominent role in development of various cancers. Glioblastoma is most common primary brain tumor with very poor prognosis despite aggressive treatment regiments. Therefore it is important to study genetic and epigenetic events leading to gliomagenesis and consequent aggressive phenotype to guide new treatment strategies.

The aim of this study was to detect Notch pathway genes potentially regulated by promoter methylation from human glioblastoma FFPE sections. Using methylation specific PCR, we identified Notch3 and JAG2 promoters as hypermethylated and Notch4 with both methylated and unmethylated promoter. Despite methylation, Notch3 showed robust gene expression suggesting its partial dependency on promoter methylation and presence of alternative regulatory mechanisms. However, low gene expression of JAG2 and absence of Notch4 gene expression suggest possibility of epigenetic silencing. This study provides gene expression and DNA methylation profiles of Notch pathway genes in glioblastoma. Epigenetic mechanisms can be used as markers that may guide treatment decisions.

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Exosomal Formulation Enhances Therapeutic Response of Celastrol Against Lung Cancer

Celastrol (CEL), a plant-derived triterpenoid, is a known inhibitor of Hsp90 and NF-κB activation pathways and has recently been suggested to be of therapeutic importance in various cancers. However, the molecular mechanisms of celastrol- mediated effects in lung cancer are not systematically studied. Moreover, it suffers from poor bioavailability and offsite toxicity issues. This study aims to study the effect of celastrol loaded into exosomes against two non-small cell-lung carcinoma (NSCLC) cell lines and explore the molecular mechanisms to determine the proteins governing the cellular responses. We observed that celastrol inhibited the proliferation of A549 and H1299 NSCLC cells in a time- and concentration- dependent manner as indexed by MTT assay. Mechanistically, CEL pre-

treatment of H1299 cells completely abrogated TNFα-induced NF-κB activation and upregulated the expression of ER-stress chaperones Grp 94, Grp78, and pPERK. These changes in ER-stress mediators were paralleled by an increase in apoptotic response as evidenced by higher annexin-V/PI positive cells evaluated by FACS and immunoblotting which showed upregulation of the ER stress specific pro-apoptotic transcription factor, GADD153/CHOP and alteration of Bax/Bcl2 levels. Exosomes loaded with CEL exhibited enhanced the anti-tumor efficacy compared to free CEL against lung cancer cell xenograft. CEL did not exhibit any gross or systemic toxicity in wild-type C57BL6 mice as determined by hematological and liver and kidney function test. Together, our data demonstrate the chemotherapeutic potential of celastrol in lung cancer and that exosomal formulation enhances its efficacy and reduces dose related toxicity..

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Dr. Rania Zayed
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Regulatory T Cells; Key Role Players in Hematological Malignancies

Regulatory T cells (Tregs) are a specialized subpopulation of CD4+ T cells, which act to suppress the activation of other immune cells. Tregs are either naturally occurring or induced.Tregs have crucial role in induction of immune tolerance during infection, pregnancy, transplantation, autoimmunity and neoplasias.They are recently recognized as key component of the tumor microenvironment and important determinant of tumor progression; Tregsare implicated in both solid tumor and hematological malignancies. Thus manipulation of Tregs represents an emerging therapeutic approach to cancer treatment.
The following items will be discussed:

- T regulatory Cells Types and function
- Tregs induction mechanisms
- Identification of Tregs
- Mechanisms underlying the role of Tregs in hematological malignancies
- Manipulation of Tregs as a targeted therapy in hematological malignancies

Biography:
Rania Zayed is professor of Clinical and Chemical Pathology (Subspecialty: Hematology), Faculty of Medicine, Cairo University, Egypt. She practices and teaches at Kasr Al-Ainy Hospitals and School of Medicine, Cairo, Egypt. She had completed the doctorate degree in 2004. She earned certificates in medical education, research methodology, research ethics, scientific writing and communication skills. Research interests include stem cells and hepatitis C virus infection. Professor Rania shared in several national and international conferences in hematology and stem cell research.

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Prevalence of Epstein–Barr Virus Genotypes in Pakistani Lymphoma Patients

The Epstein-Barr virus (EBV) is a herpesvirus infecting more than 90% of the human population. The tropism of EBV for B lymphocytes is evidenced in its association with many lymphoproliferative disorders. Different types of EBV (EBV-1 and EBV-2), classified on the basis of EBNA-2 genotyping, have been reported in benign and malignant pathologies, but there is almost no information about their frequency in the Pakistani population. The aim of this study was to determine the frequency and distribution of EBNA-2-based EBV genotypes in lymphoma patients. Genomic DNA was extracted from formalin-fixed paraffin embedded (FFPE) tissue samples obtained from 73 EBV-DNA-positive lymphoma patients. The ß-globin gene was amplified to assess the presence and quality of cellular DNA from all samples. EBER-1 DNA was detected by PCR to confirm EBV presence in tissue samples. EBNA-1 mRNA relative quantification by quantitative PCR substantiated EBNA-1

mRNA overexpression in 52% of EBV-positive cases in comparison to an EBV-positive cell line control. EBNA-2 genotyping was done by nested polymerase chain reaction (PCR). Among typable samples, EBV-1 was present in 90.7%; EBV-2, in 9.3%. These results show that EBV-1 is the most prevalent type in the lymphoma population of Pakistan, similar to reports from other countries. This definition of EBV epidemiology in Pakistani lymphoma patients represents an important first step in using EBV for prognosis and monitoring treatment response in patients.

Keywords: Epstein - Barr virus; Genotyping; Non-Hodgkin Lymphoma; Hodgkin Lymphoma; EBER-1; EBNA-1;EBNA-2.

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Design, Synthesis and Evaluation of Novel Pyridazine Pharmacophores on Migration and Invasion, A Major Event of Cancer Metastasis

Neoplastic metastasis is a major route where tumour cells transfer from the primary tumourand colonize at other parts of our body to form secondary tumour. Cancer incidences are rising and novel anti-neoplastic compounds with new mechanism of actions are essential for preventing cancer related death. In the current examination, a novel series of pyridazine analogues 6a-m was synthesized and evaluated against metastatic neoplastic cells. Experimental data postulated that compound 6j has potential cytotoxic efficacy with prolonged activity against various cancer cells, including A549, HepG2, A498, CaSki and SiHa cells. Moreover, compound 6j arrests the A549 migration and invasions markedly by counteracting matrix metalloproteinase (MMP)-2 and MMP-9 expressions. Altogether, we concluded that compound 6j down regulates MMP-2 and MMP-9, thereby impairs metastatic cancer cell migration and invasions which can be translated into a potent anti-neoplastic agent.

Key words: Pyridazine; Metastasis; Migration and invasion; MMPs; Cancer.

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An Ounce of Prevention is Worth a Pound of Cure"-Gnrh-Acotreatment Significantly Preserves Fertility and Increases Pregnancy Rate in Addition to Cyclic Ovarian Function.

The late effects of cancer treatment have gained a worldwide interest among hematologists, reproductive endocrinologists, oncologists, and all health care providers, and the protection against iatrogenic infertility caused by chemotherapy assumes a high priority.

Methods:Recent metaanalysesof RCT'sconcluded that GnRHa cotreatmentalong chemotherapy significantly decreasedPOF rate.However, cyclic ovarian function is not equivalent to fertility [pregnancies].Therefore we evaluated thePR after exposure to gonadotoxic chemotherapy+ GnRHa vs controls.We have administered a monthly depot IM injection of GnRH-agonistic analogue to 300 young women exposed to gonadotoxic chemotherapy for malignant or non-malignant diseases, after informed consent, starting before chemotherapy for up to six months, in parallel to, and until the end of chemotherapy. These patients were compared to a control group of 200 patients of comparable age (14-40 years), who were similarly treated [chemotherapy without GnRH-a]. Neither the age, nor the diagnoses, or radiotherapy exposure differed between the two groups. The cumulative doses of each chemotherapeutic agent and the mean or median radiotherapy exposure did not differ between the groups. The patients who have not visited our clinic in the last 6 months were interviewed by phone to verify the data on pregnancies. The study was approved by the institutional RB ethics [Helsinki] committee.

Results: Less than 13% developed irreversible hypergonadotropic amenorrhea in the GnRHa cotreatment group, vs 50% in controls [P<0.001]. The remaining patients resumed cyclic ovarian function, and 90 patients spontaneously conceived 178 times, and were delivered of 129 healthy neonates, in the GnRHa+chemotherapy group. In the control group only 55 pregnancies were reported in 31 patients [P=0.02]. The age of the patients who spontaneously conceived, in the GnRHa group was 14-38 at chemotherapy compared to 14-30 y's in the control group. One patient, in the GnRHa group, spontaneously conceived three times and was delivered of three healthy neonates despite two stem cell transplantations [SCT], 11 years apart. Several patients spontaneously conceived up to six times. GnRH-a cotreatment was beneficial not only against regular chemotherapy but also for lymphoma

patients undergoing SCT in significantly decreasing the POF rate. The possible de-novo formation of follicles by the surviving germline stem-cells brings about a decrease in FSH concentration and return of regular cycles, ovulation, and even gestations. Most relevant to this equivocal and highly debatable issue, is a publication from one of theprevious opponents to GnRH-a use for fertility preservation,reporting that the use of GnRH-a during chemotherapy has significantly increased the probability to conceive [OR= 12.87; P[0.001=. Furthermore, in keeping with our experience, two recent prospective RCT [NEJM, 2015 and JAMA 2016] have found significantly higher pregnancy rate and delivery rate, in addition to significantlyhigher cyclic ovarian function in the GnRHa+chemotherapy group. In addition, they reported either similar orsignificantly higher survival rates of breast cancer patients in the GnRHa+chemotherapy group vs. controls. Two recent expert committees have concluded that GnRHa cotreatment in parallel to chemotherapy is beneficial in minimizing POF rate and increasing pregnancy rate in survivors and recommended its use.

Conclusions: GnRHa cotreatment in parallel to chemotherapy is beneficial in minimizing POF rate and increasing pregnancy rate in survivors. Therefore, it should be offered to every young woman before gonadotoxic chemotherapy in addition to cryopreservation of embryos, ova, and ovarian tissue. Future endeavors may include Sphingosine-1-Phosphate as a novel means for fertility preservation, immunotherapy instead of chemotherapy, and in-vitro maturation [IVM] of primordial follicles from the cryopreserved ovarian tissues to mature metaphase-II fertilizable oocytes for IVF. This may completely omit the risk of reintroducing malignant cells while auto transplanting cryopreserved ovarian tissue.

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Quinacrine Induces Apoptosis in Cancer Cells by Forming a Functional Bridge Between TRAIL-DR5 Complex and Modulating the Mitochondrial Intrinsic Cascade

Death Receptor 5 (DR5) is known to be an important anti-cancer drug target. TRAIL is a natural ligand of DR5, but its drug action is limited because of several factors. A few agonistic ligands were identified as TRAIL-DR5 axis modulators, which enhance the cellular apoptosis. Literature suggest that quinacrine (QC) acts as a DR5 agonistic ligand. However, the detailed mechanism explaining how QC interacts with TRAIL-DR5 axis has not been established. Also focused in vitro and in vivo experimental analysis to validate the hypothesis is not yet performed. In this work, extensive studies have been carried out using in silico analysis (molecular dynamics), in vitro analysis (cell based assays) and in vivo analysis (based on mice xenograft model), to delineate the mechanism of QC action in modulating the TRAIL-DR5 signalling. The MD simulations helped in identifying the important residues contributing to the formation of a QC-TRAIL-DR5 complex, which provide extra stability to it, consequently leading to the enhanced cellular apoptosis. QC caused a dose dependent increase of DR5 expression in cancer cells but not in normal breast epithelial cells, MCF-10A. QC showed a synergistic effect with TRAIL in causing cancer cell apoptosis. In DR5-KD MCF-10A-Tr (DR5 knocked down) cells, TRAIL+ QC failed to significantly increase the apoptosis but over expression of full length DR5 in DR5-silence cells induced apoptosis, further supporting DR5 as a drug target for QC. An increase in the release of reactive species (ROS and RNS) and activation of enzymes (FADD, CASPASES 3, 8, 9 and cytochrome-C) indicated the involvement of mitochondrial intrinsic pathway in TRAIL+QC mediated apoptosis. In vivo study pointed out that TRAIL+QC co-administration increases the expression of DR5 and reduce the tumor size in xenograft mice. This combined in silico, in vitro and in vivo analysis revealed that QC enhances the cellular apoptosis via the modulation of TRAIL-DR5 complexation and the mitochondrial intrinsic pathway.

Biography

Chanakya N Kundu, Associate professor at School of Biotechnology, KIIT University, Bhubaneswar, completed his PhD in Biochemistry from the Indian Institute of Chemical Biology, Kolkata Jadavpur, India. He later joined Texas A&M University, Texas, USA as a postdoctoral research fellow. He worked three and half years on mammalian molecular signal transduction pathways. Afterwards he worked at the University of Florida Shands Cancer Center, Gainesville, USA, for two years on DNA damage and repair pathways in special reference to cancer biology. In prior to join at KIIT University as an assistant professor he worked for one year at Cleveland Clinic Foundation, Cleveland, Ohio, on translational research in colorectal cancer and WNT-ß CATENIN signaling. Currently the focus of his research work is to understand the molecular mechanism of metastasis, angiogenesis in cancer stem cell signaling. He is trying to develop new chemotherapeutic cocktail which will not only inhibits the bulk of cancer cells but also inhibit the cancer stem cell proliferation, angiogenesis as well as reduce the inflammation in cancer patients. He has already published more than 50 peer reviewed research articles in international journal, file two patent, written multiple book chapter, etc. He is the recipient of several award such as young biomedical scientist of India, DBT-CREST,etc by the govt of India.