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HealthCare
MARKEY CANCER CENTER
NCI Cancer Center

International Symposium on Breast Cancer Research

Date

Monday, February 27, 2017

Venue

National Center for Cell Sciences (NCCS) Auditorium

Registration

Symposium is open to all without registration charges. Registration is mandatory.

Registration Link: https://goo.gl/forms/HppHjLF9vS2vFZPG2

Contact

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ORGANISERS

- **Markey Cancer Center (MCC), University of Kentucky College of Medicine, Lexington, USA** is an NCI-supported institute with a broad mission to reduce cancer morbidity and mortality of cancer through a comprehensive program of cancer research, education, patient care and community outreach. MCC research programs range from cancer epidemiology and etiology, molecular expression and regulation, cancer prevention, early detection and treatment.

- **National Centre for Cell Science (NCCS), Pune, India** is an autonomous organization aided by the Department of Biotechnology, Government of India with a mandate of serving as a national repository of animal cell cultures, undertaking research in cell biology and human resource development.

- **Prashanti Cancer Care Mission (PCCM), Pune, India** is a DSIR-SIRO certified non-profit NGO and public charitable trust active in the domain of cancer education, training and research along-with providing affordable cancer management to the community.

International Symposium on Breast Cancer Research

Scientific Agenda

8.00 am – 9.00 am Registration

Time	Speaker	Topic	Affiliation
Session I : Welcome and Opening Remarks			
9.00-9.05 am	Dr. Shekhar Mande	About NCCS	Director, NCCS
9.05- 9.15am	Dr. Vivek Rangnekar	About MCC	Associate Director, MCC
9.15- 9.20 am	Ms. Laleh Busheri	About PCCM	CEO, PCCM, Pune
Session II : Welcome and Opening Remarks **Chairperson : Dr. Vivek Rangekar**			
9.20 – 10.00 am	Dr. Chaitanyanand Koppiker	Current and Future Breast Cancer Management	Director, PCCM, Pune
10.00 -10.40 am	Dr. Rajiv Sarin	Genetic Predisposition to Breast Cancer	Director, Genetic Clinic, ACTREC, Navi Mumbai
10.50-11 am Tea Break			
Session III : Breast Cancer Biology **Chairperson : Dr. Sudha Gangal**			
11.00 -11.20 am	Dr. Kathleen O'Connor	Integrin Signaling in Breast Cancer	Professor, MCC, Lexington, USA
11.20 -11.40 am	Dr. Jyothi Prabhu	Synergistic Interactions between Integrins and Growth Factor Receptors Mediate the Clinical Progression of Breast Cancer	Associate Professor, St. John's Research Institute (SJRI), Bangalore
11.40-12.00 noon	Dr. Gopal Kundu	Therapeutic Targeting of Osteopontin and Associated Genes in Breast Cancer	Scientist G, NCCS, Pune
12.00 – 12.20 pm	Dr. Xen Ru	Extra Cellular Matrix Network in Breast Cancer Progression	Associate Professor, MCC, Lexington, USA
12.20 – 12.40 pm	Dr. Mayurika Lahiri	A Central Role for DNA-dependent Protein Kinases in Transformation of Breast Epithelial Cells following DNA Damage	Associate Professor, Indian Institute of Science Education and Research (IISER), Pune

12.40 – 1.00 pm	Dr. Manas Santra	Protein Phosphatase 1 Regulatory Subunit p90/MAPK Pathway Feedback Loop Regulates Breast Cancer Malignancy	Scientist D, NCCS, Pune
1.00 pm- 2.00 pm Lunch Break			
Session IV : Breast Cancer Clinical and Translational Research **Chairperson : Dr. C.B. Koppiker**			
2.00 – 2.20 pm	Dr. Nikhil Hebbar	Bench to Bedside Research on Tumor Suppressor Expression and Inhibition of Cancer Metastasis	Research Scientist, MCC, Lexington, USA
2.20- 2.40 pm	Dr. Beenu Verghese	Updates on Breast Cancer Radiology	Chief Radiologist, PCCM, Pune
2.40- 3.00 pm	Dr. Aju Mathews	Optimizing Adjuvant Therapy for Women with Breast Cancer	Assistant Professor, MCC, Lexington, USA
3.00- 3.20 pm	Dr. Chetan Deshmukh	CDK Inhibitors in Breast Cancer Therapy	Consultant Medical Oncologist, PCCM, Pune
3.20-3.40 pm	Dr. Manoj Bhat	Cellular and Metabolic Factors Influencing Chemotherapy	Scientist, G, NCCS, Pune
3.40 – 4.00 pm	Dr. Gautam Sharan	Radiation Therapy in Breast Cancer	Consultant Radiation Oncologist , PCCM, Pune
4.00 pm -4.20 pm Tea Break			
Session V : Genomics and Breast Cancer **Chairperson : Dr. Kathleen O'Connor**			
4.20- 4.40 pm	Dr. Ramesh Hariharan	Our Experiences with Genome Sequencing for Clinical Applications in Breast Cancer	CEO and Founder, Strand Life Sciences, Bangalore
4.40 – 5.00pm	Dr. Nandini Sahasrabuddhe	Utility of Multi-gene panel in Investigation of Key Mutations in Triple-Negative Breast Cancers"	Principal Scientist, PierianDx, Pune
5.00 – 5.20 pm	Dr. Anamika Krishanpal	Large-scale -Omics Data Integration to Gain Insights into Breast Cancer	Senior Scientist, Persistent Life Sciences, Pune
5.20 – 5.40 pm	Dr. Aarti Desai	Comprehensive Solution for Analysis of Copy Number Variations in Breast Cancer	Senior Scientist, Affymetrix, Bangalore
Vote of Thanks : Dr. Vivek Rangnekar			

SPEAKER PROFILES

Dr. Chaitanyanand B. Koppiker, Medical Director, Orchids Breast Health Clinic, Pune

Dr. Chaitanyanand B. Koppiker is a Breast Oncosurgeon and the Medical Director of Orchids Breast Health Clinic, Pune which is a one-of-its kind Integrated Center of Affordable Excellence for Breast Cancer. He is also the Founder Director of International School of Oncoplastic Surgery- a joint initiative with the Breast Oncoplasty Training Program, University of East Anglia, UK. Outside of Tata Memorial Hospital, Mumbai, Dr Koppiker was the first Oncosurgeon in Pune to lead the establishment of the 1st Integrated Cancer Center namely the Budhrani Cancer Institute, Pune and Inlaks and Budhrani Hospital, Pune, He then helped set up 2 more reputed cancer centres' first as the Director of the Ruby Hall Clinic Cancer Center and then at Cancer Clinic and Research Center at Jehangir Hospital, Pune. Dr. Koppiker has been an International Investigator in several important Breast Cancer clinical trials and leading a translational research group with active collaborations with premier national and international research institutes. Dr. Koppiker is also the Founding Director and Managing Trustee of Prashanti Cancer Care Mission, -a non-profit NGO working in Pune active in cancer education, training and research in addition to providing free or affordable cancer treatment and rehabilitation to underprivileged cancer patients.

Dr.Rajiv Sarin, Director, Cancer Genetics Unit, Principal Investigator, ACTREC, Navi Mumbai.

Dr. Rajiv Sarin is the Former Director of ACTREC. He is a Clinician Scientist working as a Professor of Radiation Oncology, In-Charge of Cancer Genetics Unit and a Principal Investigator at TMH & ACTREC. His research interests include Cancer Genetics, Breast Cancer, Head Neck Cancer & Translational Radiation Biology including Radiation Modifiers and Fractionation. He established the Cancer Genetics Clinic and Lab at TMC and is the PI of the ICMR Centre of Advanced Research in Cancer Genetics & Genomics and one of the lead Indian investigators in International Cancer Genome Consortium (ICGC). He is the Chair of Scientific Committee that recently published the 2017 ICMR Guidelines on Breast Cancer Management in India. He is the Executive Editor of Journal of Cancer Research & Therapeutics.

Dr. Sudha Gangal, Research Advisor, Integrated Cancer Treatment and Research Centre, Pune

Dr. Sudha Gangal did her PhD (1963) in the then Indian Cancer Research centre Mumbai (now ACTREC, Kharghar Mumbai) and her post-doc work in Prof Merchant's lab in University of Michigan on a NIH fellowship. After returning from USA, in 1966 she established the first Cancer Immunology Lab in the country. Her group's work mainly involved studying T cell anti-cancer response in human oral cancer patients. She established 4 oral cancer cell lines and made monoclonal antibodies against TAAs expressed on oral cancer cell lines. Dr. Gangal has mentored about 25 MSc and Ph.D students and published more than 150 papers in National and International journals. She has authored 2 popular books, 'Principles and Practice in Animal Tissue Culture' and 'Basic and Clinical Immunology'. She is Fellow and ex-Council Members of two prestigious National Science Academies of India, viz. Indian National Science Academy, New Delhi (INSA)' and 'Indian Academy of Sciences, Bangalore (IASc)'. She has served as President, Indian Immunology Society, Indian Association for Cancer Research and Indian Women Scientist's Association. She is also an editorial board member of several national and international biomedical research journals. After retirement, she has served as Research Director at Wadia Children's Hospital Mumbai, Vice President at Moving Academy of Medicine and Biomedicine, Pune and Emeritus Professor at Rajiv Gandhi Institute of Biotechnology.

Dr. Kathleen O'Connor-Associate Director of Cancer Education, Markey Cancer Center University of Kentucky Lexington, Kentucky, USA

Dr. Kathleen O'Connor received her Ph.D. from Case Western Reserve University and Post-doctoral training, Harvard Medical School. Her research focuses on how integrin signaling promotes carcinoma invasion and metastasis with special emphasis on the integrin $\alpha6\beta4$. Integrin $\alpha6\beta4$ confers an invasive and metastatic phenotype in many types of carcinomas. She originally discovered links between integrin signaling and the cAMP pathway, and also determined that integrin $\alpha6\beta4$ could stimulate the small GTPase RhoA leading to lamellae formation and enhanced invasion. We have further expanded our work to include investigations on how integrin $\alpha6\beta4$ modifies the transcriptome toward an invasion signature. Through these studies, we have identified the first transcriptional targets for NFAT1 and NFAT5 in cancer and provided evidence that integrin $\alpha6\beta4$ can stimulate select demethylation of the promoters of pro-metastatic genes, including S100A4/metastasin, amphiregulin and epiregulin. The overarching goal of our work is to better understand the contributions of integrin $\alpha6\beta4$ to tumor invasion and understand how this "oncogenic" function differs from its normal functions in order to better target integrin $\alpha6\beta4$ and pathways it influences for therapeutic intervention.

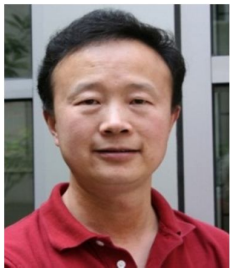
Dr. Jyothi Prabhu, Associate Professor, St. John's Research Institute (SJRI), Bangalore

Dr. Jyoti has received her M.D. (Pathology), DCP certification and a Ph.D. in Molecular Pathology from SJRI. Over the past 8 years Dr. Prabhu has been part of a team that has established a cohort of 460 Indian women with breast cancer with a median follow-up of more than 5 years with only a 3% loss-to-follow-up. This team has established rigorous quality-control measures for the extraction and characterization of nucleic acids from formalin-fixed-paraffin-embedded specimens. Her primary interests are the molecular determinants of chemoresistance and metastasis in Breast Cancer. The interactions between tumor epithelium and the stroma are of particular interest with a long term goal to develop clinically useful assays using the markers identified for selection of patients for specific therapeutic strategies

Dr. Gopal Kundu- Scientist G, National Centre for Cell Science (NCCS), Pune

Dr. Gopal Kundu has obtained his Ph.D. in chemistry from Bose Institute, Kolkata, India (1989). He did his post-doctoral research in US from 1989 to 1998. He joined as Scientist-D at National Centre for Cell Science (NCCS) in 1998 and at present he is Scientist-G. His area of research at NCCS is tumor biology, cancer stem cells, angiogenesis, cancer therapeutics and nanomedicine. He has received Fellows Award for Research Excellence from USA; National Bioscience Award; Shanti Swarup Bhatnagar Prize; International Award in Oncology, Greece; International Young Investigator Award, USA and 7th National Grassroots Innovation Award, Rashtrapati Bhavan, India. He is Fellow of National Academy of Sciences and Indian Academy of Sciences. He has published in Nature Medicine, Science, PNAS, Cancer Research, J. of Invest. Dermatology, JBC, TCB, Oncogene, Nanomedicine etc. and one US patent. He serves as Editorial Board Member of several high-impact journals in the field of cancer research.

Dr.Ren Xu, Associate Professor, Markey Cancer Center, University of Kentucky, Lexington, USA



Dr. Xu got his Ph.D degree from Shanghai Institutes for Biological Sciences, Chinese Academy of Science, and then he received training in mammary gland biology at the Lawrence Berkeley National Laboratory under Dr. Mina J. Bissell prior to the faculty appointment at UK Markey Cancer Center. The long-term goal of Dr. Xu's group is to investigate tumor microenvironment in breast cancer development and progression, thereby identifying potential therapeutic targets and biomarkers for breast cancer treatment. His group showed for the first time that tumor extracellular matrix (ECM) microenvironment is regulated at the transcription network level by Hsp47 and microRNA in human breast cancer tissue utilizing *ex vivo* and *in vivo* mammary tumor models. The research in his group has been published in JCell Biology, Cancer Research, Mol Cell Biol, J Cell Sci, Nature Cell Biol, J Clinical Investigation, etc.

Dr. Mayurika Lahiri, Associate Professor (Biology), Indian Institute of Science Education and Research, P (IISER), Pune.

Dr.Mayurika Lahiri did her PhD from University of Wolverhampton, UK. She spent her postdoctoral years first at Tufts University, and then at Massachusetts General Hospital Cancer Center, Harvard Medical School, USA. She joined IISER Pune in 2008 and her laboratory is engaged in studying the molecular mechanism underlying transformation following DNA damage or inflammatory factors in breast epithelial cells using three-dimensional breast acinar cultures as a model system.

Dr. Manas Santra, Scientist D, National Centre for Cell Science (NCCS), Pune

Dr. Manas Kumar Santra did his Ph. D. in the field of Biophysics and Biochemistry from Indian Institute of Technology, Bombay in 2006 and did his postdoctoral research from University of Massachusetts Medical School, USA. He joined at NCCS as Scientist D in 2010 and presently working as scientist E. He is recipient of ISCA young scientist award, Young Innovative Biologist Award, Ramalingaswami Fellowship. His area of research is elucidation the role of RING-finger E3 ligases and protein phosphatases in breast cancer malignancy. He has 34 publications in credit in peer reviewed journals including Nature, Molecular Cell, PNAS (USA) and Cancer research.

Dr. Nikhil Hebbar, Research Scientist, Department of Toxicology and Cancer Biology, University of Kentucky, Lexington, Kentucky, USA

Dr. Nikhil Hebbar is a cancer research scientist in the Department of Toxicology and Cancer Biology at the University of Kentucky. He obtained a Masters' degree in Biochemistry from the University of Mumbai following which he worked as a Research Associate at the Novel Drug Discovery Program for Cancer Biology at Piramal Life Sciences Limited. He completed his PhD in Toxicology from Dr. Vivek Rangnekar's lab at the University of Kentucky. His research interests include development of novel cancer therapeutics through a chemical biology and immune-oncology based approach. More specifically his work involves studying the role of tumor suppressor protein Par-4 and exploiting its ability to specifically target cancer cells in lung, prostate and breast cancer model systems.

Dr. Beenu Verghese, Chief Radiologist at Orchids Breast Health Clinic (OBHC), Pune

Dr. Beenu Verghese is a Chief Radiologist at OBHC Consultant Radiologist at Cloud Nine Hospital, Pune. She has 19 years of experience in Clinical Radiology Teaching and Practice. She received her Medical Education from B.J. Medical College, Pune and advanced post-graduate training from K.E.M Hospital, Pune.

Dr. Aju Mathew, Assistant Professor, Division of Medical Oncology, University of Kentucky Markey Cancer Center, Lexington, Kentucky, USA

Dr. Aju Mathew MD, MPhil, FACP is an American Board certified medical oncologist, hematologist and internist. He serves as an and has expertise in the management of patients with breast cancer. He serves as the co-director of the fellowship training program in Hematology and Medical Oncology. Apart from clinical activities and teaching, he also serves as the institutional principal investigator to several cooperative group and industry-sponsored clinical trials.

Dr. Chetan Deshmukh, Chief Medical Oncologist, Orchids Breast Health Clinic (OBHC), Pune

Dr. Chetan is the Chief Medical Oncologist at OBHC, Pune. He also leads the Medical Oncology Department at the Deenanath Mangeshkar Hospital, Pune and serves as an Honorary Oncologist at Sasoon Government Hospital, Pune. Dr. Deshmukh is certified as an Oncologist by European Society of Medical Oncology (ESMO). After the basic medical education and post-graduate training at B.J.Medical College, Pune , he underwent advanced trained as a Senior Resident at Tata Memorial Hospital, Mumbai followed by training in Cancer Clinical Research at Cairns, Australia. He has 12 publications in National and International journals. He has specialized in treatment of various solid tumors, lymphomas and Bone Marrow Transplantation. At present, he is also a PI on multiple clinical trials in Breast Cancer.

Dr Manoj Bhat, Scientist G, National Centre for Cell Science (NCCS), Pune

Dr. Manoj Bhat completed my under graduate, graduate and PhD in Biochemistry from the University of Mysore. Subsequently, as a post-doctoral Fogarty fellow in National Cancer Institute, National Institutes of Health, Bethesda, and briefly in Institute of Human Virology, Baltimore, MD, USA, he received training in Cell Biology/ Cancer biology. Since 1998, Dr. Bhat is at NCCS and pursing research activities in the areas of Cancer Chemotherapy, Diabetes and Obesity. Over past decade, his group has been exploring the impact of metabolic disorder on Cancers and Chemotherapy by utilizing *in-vitro* and *in-vivo* model systems. Also, the metabolic flexibility of cancer cells is being investigated actively.

Dr. Gautam Kumar Sharan, Chief Radiation Oncologist, Orchids Breast Health Clinic, Pune

Dr. Gautam Sharan is the Chief Radiation Oncologist at OBHC, Pune and also the Head of Radiation Oncology department at M. N. Budhrani Cancer Institute, Inlaks & Budhrani Hospital in Pune, Maharshtra. He is also DNB coordinator for DNB Radiotherapy course at his department with a teaching experience of more than 10 years. Dr Gautam Sharan is a Life Member of Association of Radiation Oncologists of India (AROI). He is Member of Executive Committee, Maharashtra Oncology Group and Life Member of Indian Cooperative Oncology Network (ICON). Dr. Gautam Sharan is co-author of two book chapters, and has published extensively and presented his work at several national and international conferences. He was awarded MD Radiotherapy from Institute of Medical Sciences, Banaras Hindu University, Varanasi, India in 2004. He received his MBBS degree from Rajendra Medical College, Ranchi University, Ranchi, India in 1997. He has done senior residency at Maulana Azad Medical College & Associated Lok Nayak Hospital, Delhi, India and worked at Rajiv Gandhi Cancer Institute and Research Center, Delhi and Artemis Health Institute, Gurgaon before shifting to Pune in 2009.

Dr. Nandini Sahasrabuddhe, Principal Scientist, PeirianDx India Pvt.Ltd. Pune

Dr. Nandini Sahasrabuddhe is a cancer biologist and has employed multiple Omics approaches to study breast and lung cancer. She carried out her doctoral work at the Johns Hopkins University and Institute of Bioinformatics. She has published over 35 research articles in international peer reviewed journals. Currently, she is working as a Principal Scientist at PierianDx India in the domain of clinical genomics data analysis and interpretation software and services. At PierianDx, she leads the clinical interpretation and knowledgebase team for analysis of Next Generation Sequencing-based complex genetics tests. She is actively involved in collaborative research with Prashanti Cancer Care Mission.

Dr Anamika Krishnapal, Senior Scientist, Persistent Life Sciences, Pune

Dr. Anamika Krishanpal is leading the genomics and bioinformatics group at Persistent Labs, a non-profit R&D unit of Persistent Systems Limited, Pune. This group is working on multiple projects aimed at understanding cross talk between different biomolecules in cancer using various bioinformatics approaches. She has received her PhD from Indian Institute of Science (IISc), Bangalore. Her doctoral work included genome wide analysis of signaling molecules particularly protein kinases using bioinformatics and homology modelling approaches to understand their specificity, diversity and regulation. In her post-doctoral stint at IGBMC, Strasbourg, France she studied epigenetics and transcriptional regulation in higher eukaryotic systems using next generation sequencing approaches.

Dr. Aarti Desai, Technical Sales Specialist, Affymetrix (Thermo Fisher), Bangalore

Dr Aarti is responsible for the commercialization of the clinical and gene expression arrays in the APAC region. In this role she is responsible for engaging with channel partners and customers to understand their research areas of interest and offer the most suitable Affymetrix solutions. Aarti Desai has a Ph.D. in molecular biology from University of Houston and postdoctoral fellowship in mouse genetics at the Wadsworth Center. She has extensive experience in handling transcriptome data from multiple high throughput genomic technologies, particularly, microarrays.

ORGANISER PROFILES

Dr. Vivek Rangnekar, Alfred Cohen Chair of Oncology, Markey Cancer Center, University of Kentucky College of Medicine, Lexington, Kentucky, USA

Dr. Vivek M. Rangnekar is a Professor in Radiation Medicine, and Associate Director at the Markey Cancer Center. He has over 25 years of research experience in cancer biology and signaling, and in moving bench research to clinical trials. He serves as Senior Editor of *Cancer Biology and Therapy*, on the Editorial Board of *Genes and Cancer*, and as chartered member of the BMCT Study Section at NIH. His research projects have received continuous funding from NCI since 1990. He has published over 100 research articles and edited two volumes of a book focused on programmed cell death.

Dr Padma Shastry, Principal Scientist, National Centre for Cell Science (NCCS), Pune

Dr. Padma Shastry is a Principal Scientist (ex-Scientist G) in National Centre for Cell Science (NCCS), Pune. She is PhD from Bombay University, India and did her post- doctoral studies at University of Alberta, Edmonton, Canada. Her research interests are in cancer biology and currently the projects are focused on understanding studying drug resistance/ sensitivity in gliomas using different experimental models, elucidating the signal transduction pathways in proliferation, survival and invasion for identification of molecules for drug targets. She has publications in international peer reviewed journals

Dr. Santosh Dixit, Clinical Research Scientist, Prashanti Cancer Care Mission, Pune

Dr. Santosh Dixit is a Clinical Research Scientist at the Center for Translational Breast Cancer Research, Prashanti Cancer Care Mission. At present, he is actively involved in the design and conduct of multiple interdisciplinary projects in Breast Cancer with a translational focus. Dr. Dixit has over 10 years of experience in translational biomedical research with special emphasis on preclinical and clinical drug development. His other areas of professional interest include clinical pharmacology, pharmacogenomics and regulatory aspects pertaining to the development of drugs and biomedical devices. He has received a Ph.D. in Pharmaceutical Sciences (University of Cincinnati, Ohio, USA) and Post-doctoral training at Vanderbilt University, Nashville, Tennessee, USA and University of Western Ontario, London, Canada.

ABSTRACTS

AB-1- Session II -Dr. Chaitanyanand B. Koppiker

Current and Future Breast Cancer Management

Breast Cancer (BC) occurrence is alarmingly on the rise in India with new cases detected across various age-, socio-economic and urban-rural strata. The disease is acquiring an urban and young profile with peak incidence around 45 years. In his presentation, Dr. Koppiker will provide a 360 degree view on the multimodal nature of Breast Cancer management ranging from patient self-examinations to regular mammography screening, advanced diagnostic and surgical options, targeted chemotherapy and radiation treatment plans, post-treatment vigilance and patient rehabilitation. Recent global perspectives on Breast Cancer management will be put forth vis-a-vis the Indian scenario. The emerging importance of Breast Oncoplastic Surgery to improve treatment outcomes will be discussed. In addition, Dr. Koppiker will discuss few of the important emerging and future global trends in Clinical practice as well as translational biomedical research in Breast Cancer.

AB-2- Session II – Dr. Rajiv Sarin

Genetic Predisposition to Breast Cancer

Breast Cancer is the leading female cancer in large parts of the world including urban India. The major risk association for breast cancer are related to the hormonal milieu. Genetic predisposition for breast cancer occurs due to high penetrance germline mutation in one of the several tumour suppressor genes (BRCA1, BRCA2, TP53, STK11, CHEK2, PALB2, ATM etc.) or from low penetrance alleles in several dozen genes which interact with environmental agents. Identification of mutation in a high penetrance gene helps in confirmation of the syndromic diagnosis, surveillance and prophylactic preventive surgery in mutation carriers. Breast or ovarian cancers in individuals with BRCA1/2 germline mutations also derive benefit with targeted therapy (PARP inhibitors) and from platinum agents. Founder mutations in BRCA1, BRCA2 and CHEK2 have been identified in several populations around the world. Different syndromes and the genes found to be mutated in the Indian population and the founder mutations identified in specific geo-ethnic groups in India will be discussed. Genetic testing algorithms and issues in clinical management of mutation carriers will be discussed.

AB-3- Session III-Dr.Kathleen O'Connor

Integrin Signaling in Breast Cancer

Triple negative breast cancer (TNBC) remains the most deadly form of breast cancer due to a dearth of targeted therapies and a more aggressive clinical course. Integrin $\alpha6\beta4$ is a pro-invasive molecule that is highly expressed in most TNBCs where it amplifies signals from the microenvironment to drive the most aggressive traits of these cancers. Integrin $\alpha6\beta4$ promotes tumor progression in part by altering the transcriptome through specific DNA demethylation and upregulation of multiple factors that drive tumor invasion, metastasis and proliferation. Whole genome bisulfite sequencing (WGBS) revealed that integrin $\alpha6\beta4$ signaling promotes an overall hypomethylated state and site specific DNA demethylation of enhancer elements within the proximal promoters of these genes; we find that integrin $\alpha6\beta4$ mediates these events by stimulating base excision repair (BER) pathway. We further discover that integrin $\alpha6\beta4$ can stimulate rapid repair of DNA through multiple DNA repair pathways and enhance activation of the ATM/ATR pathways, which are critical for sensing DNA damage and subsequent repair. We further show that integrin $\alpha6\beta4$ signaling enhances mutant p53 phosphorylation, which is in turn required for DNA repair. Importantly, integrin $\alpha6\beta4$ expression and p53 mutation rates are high in TNBC where they tend to co-exist. Therefore, while many known signaling functions mediated by integrin $\alpha6\beta4$ that promote invasive properties have been established, our work demonstrates that integrin $\alpha6\beta4$ can dramatically impact the epigenome of cancer cells, direct global DNA methylation levels toward a hypomethylated state, and impact DNA repair.

AB-4- Session III- Dr. Jyothi Prabhu

Synergistic Interactions between Integrins and Growth Factor Receptors Mediate the Clinical Progression of Breast Cancer

Integrin mediated signalling, is essential for cell adhesion and migration, and is thought to play a crucial role in invasion and metastasis of breast cancer. ITGB6 which is absent in normal breast epithelium is expressed in a subset of breast cancer specimens. Interaction between integrins and oncogenic growth-factor receptors such as HER2 and EGFR, have been implicated to play important role in tumor progression. We have examined the expression and interaction of integrins and growth factor receptors in both HER2+ as well as hormone receptor positive breast cancers using a combination of human tumor specimens as well as experimental cell-line systems such as MCF-7.

AB-5- Session III- Dr. Gopal Kundu

Therapeutic Targeting of Osteopontin and Associated Genes in Breast Cancer

Breast cancer is a complex disease and most cancer treatments are limited to chemotherapy, radiation, and surgery. Substantial advances in breast cancer treatments have resulted in significant decrease in mortality. However, existing breast cancer therapies often result in high toxicity and nonspecific side effects. Therefore, better targeted delivery and increased efficacy of drugs are crucial to overcome these effects. Osteopontin (OPN), a chemokine like protein plays crucial role in regulating the oncogenic and angiogenic potential of various cancers including breast. Several groups have demonstrated the role of OPN in regulating the cell signaling that ultimately controls breast tumor progression and metastasis covering all the hallmarks of cancer. During last several years, we have demonstrated that both tumor and stroma-derived OPN regulate breast tumor growth and angiogenesis through induction of pro-angiogenic and metastasis associated genes. Our data also revealed that OPN regulates p70S6 kinase dependent ICAM-1 expression and JAK/STAT3 signaling leading to breast tumor growth. Our recent data showed that OPN controls HIF-1alpha dependent VEGF expression in response to hypoxia and breast tumor angiogenesis. Thus targeting OPN and its regulated signaling network could be novel therapeutic strategies for the management of breast cancers.

AB-6- Session III- Dr. Ren Xu

Extra Cellular Matrix Network in Breast Cancer Progression

Despite recent advance in early diagnosis and adjuvant therapy, treatment of triple negative breast cancer (TNBC) remains a significant challenge because of the high incidence of metastasis and relapse after treatment. Signaling from extracellular matrix (ECM), an essential component of the tumor microenvironment, is required for TNBC progression and metastasis. However, it is not known how cancer cell-deposited ECM proteins and ECM signaling in cancer cells are regulated and promote TNBC metastasis/relapse. We recently identified Hsp47 as a hub of the ECM transcription network. Hsp47 is a molecular chaperon that regulates secretion and deposition of ECM proteins. Increased Hsp47 expression has been detected in TNBC and is associated with cancer metastasis. Silencing Hsp47 restrains the aggressive phenotype of TNBC cells in 3D culture and inhibits tumor growth and lung colonization in the xenograft model, indicating that increased Hsp47 expression is crucial for the TNBC progression. These results suggest that Hsp47 promotes TNBC metastasis by inducing collagen deposition in cancer cells. These studies challenge the current concept that ECM proteins are produced by stromal cells in cancer tissue, and significantly expand our understanding in the function and regulation of cancer cell-produced ECM during cancer progression.

AB-7- Session III- Dr. Mayurika Lahiri

A Central Role for DNA-dependent Protein Kinases in Transformation of Breast Epithelial Cells following DNA Damage

Breast cancer, on a global scale, is the leading cause of death in women. Interestingly only 15% cases are due to inherited mutations, implying that there are various other factors that contribute to the development as well as progression of cancer. DNA damage by various agents (exogenous as well as endogenous) is known to result in genomic instability. One such class of compounds is the alkylating agents, which is widely used in cancer chemotherapy as well as present in environmental pollutants. These agents have also been used to induce mammary tumors in rats. Though the histopathological data of these tumors suggests resemblance to human

tumor specimens, there are no reports pertaining to the mechanism of tumor induction. In this study, we have studied the effects of alkylating agents (MNU, N-methyl-N- nitrosourea) on breast epithelial cells using 3D acinar cultures as a model system. We observed that exposure of mammary epithelial cells to alkylating agents transformed the cells. Methylation damage induced epithelial-mesenchymal transition (EMT)-like phenotype along with disruption of the basolateral polarity as well as induced invasion. Further, the damage also resulted in the acquisition of ability to survive in anchorage independent conditions. Attempt to decipher the mechanism of methylation damage induced transformation revealed the central role played by DNA-PK in facilitating the process. In conclusion, our study provides evidences for the carcinogenic potential of alkylating agents and identifies the novel role of DNA-PK in transformation of breast epithelial cells.

AB-8- Session III- Dr. Manas Santra

Protein Phosphatase 1 Regulatory Subunit p90/MAPK Pathway Feedback Loop Regulates Breast Cancer Malignancy

Breast cancer is one of the leading causes of death claiming millions of life and still counting. In this study, we identified p90, a regulatory subunit of protein phosphatase 1, as a potential tumor suppressor in breast cancer model system. p90 potently inhibits the proliferation of breast cancer cells by inducing apoptosis and retards the tumor growth in mouse xenograft. Our results revealed that it suppresses the tumor growth through inactivating the MAPK-Erk signaling pathway. It interacts with MEK and Erk, promotes dephosphorylation of MEK and Erk and thereby inactivating the Ras-Raf-MEK-Erk pathway. In addition, we found that p90 is stabilized significantly under various genotoxic stresses and it regulates the DNA damage response through the regulation of H2AX activity. Further, results reveal that ATM is essential for the stabilization of p90 under genotoxic stresses. Expression level analysis showed that p90 is highly suppressed in higher grade of breast cancer cell lines as well as in human patient samples. We found that a significant inverse correlation exist between p90 expression and MAPK activity in highly metastatic cell lines and breast cancer patient samples. Further we speculate that Ras-Raf-Erk pathway suppressing the expression level of p90 through epigenetic gene silencing process. Our results demonstrate that p90 and Ras pathways are in feedback loop. Results taken together suggest that p90 may be a putative tumor suppressor.

AB-9- Session IV- Dr. Nikhil Hebbar

Bench to Bedside Research on Tumor Suppressor Expression and Inhibition of Cancer Metastasis

Breast cancer is a heterogeneous disease often composed of therapy-sensitive and emerging therapy-resistant cancer cells. Recent studies have indicated that the pro-apoptotic, tumor suppressor protein Par-4 (also known as PAWR) is downregulated in breast tumors from geographically distinct areas of the world, including North America (USA), South America (Brazil), Europe (United Kingdom), and Asia (India). Such patients with Par-4 downregulated in their tumors show recurrent disease and reduced survival. Our studies have identified a novel domain of Par-4 that is released from therapy-sensitive breast cancer cells undergoing apoptosis and that induces apoptosis of therapy-resistant cancer cells. Moreover, clinical trials with an FDA-approved anti-malarial drug indicate systemic expression of Par-4 in cancer patients. Par-4 secreted in response to this FDA-approved drug is essential for apoptosis and inhibition of lung metastasis of breast cancer. Collectively, downmodulation of Par-4 is associated with breast cancer recurrence, either at the primary or distant metastatic sites, and FDA-approved drugs that elevate Par-4 levels in circulation can be potentially repurposed for inhibition of breast cancer metastasis.

AB-10 - Session IV- Dr. Beenu Verghese

Updates on Breast Cancer Radiology

In her talk, Dr. Beenu will review the biological principles associated with Breast Imaging modalities inclusive of ultrasound, mammography and MRI. The clinical implications of these imaging modalities will also be discussed with few case studies. Advances in Breast Biopsy techniques will also be discussed. Dr. Beenu will highlight the important facets of Breast Cancer Community screening while sharing experiences from an ongoing project in Pune. In addition, she will discuss the ongoing efforts aimed at creation of a Radiology database of Breast Cancer at Orchids Breast Health Clinic.

AB-11 - Session IV –Dr. Aju Mathew

Optimizing Adjuvant Therapy for Women with Breast Cancer

Less is more in breast cancer. We have moved from radical mastectomies to lumpectomies and extensive lymph node dissections to sentinel node assessments. The development and validation of genomic assays in breast cancer have resulted in reduced adjuvant chemotherapy use. However, recent publication of anti-estrogen therapy trials (ATLAS, aTTom, SOFT, TEXT) have suggested that longer duration of treatment with tamoxifen or stronger estrogen suppression may lead to improved outcomes; albeit at the cost of significant toxicities. Additionally, the EBCTCG meta-analysis showed that adjuvant use of bisphosphonates improves breast cancer-specific outcomes. While we have now moved to a stage where we do less for our patients with breast cancer in an adjuvant setting, clearly, some patients need more. In my talk, I will discuss various approaches to personalize treatment strategies for our patients so that adjuvant therapy in the management of breast cancer can be optimized. I will also discuss current areas of investigation pertaining to the field of early-stage breast cancer.

AB-12 - Session IV Dr. Chetan Deshmukh

CDK Inhibitors in Breast Cancer Therapy

Hormone therapy targeting estrogen receptor (ER) is the principal treatment for ER-positive breast cancers. However, many cancers develop resistance to hormone therapy while retaining ER expression. Identifying new druggable mediators of ER function can help to increase the efficacy of ER-targeting drugs. Cyclin-dependent kinase 8 (CDK8) is a Mediator complex-associated transcriptional regulator with oncogenic activities. Expression of CDK8, its paralog CDK19 and their binding partner Cyclin C are negative prognostic markers in breast cancer. Pre-clinical research has elucidated that CDK inhibition can lead to effective tumor regression. Selective inhibitors of CDK4 and CDK-6 (e.g., Palbociclib) have entered clinical practice for effective treatment of ER positive and Her-2 negative breast cancers. Dr. Deshmukh will discuss various aspects related to the clinical development of CDK Inhibitors inclusive of various clinical trials and management of associated toxicities.

AB-13 - Session IV- Dr. Manoj Bhat

Cellular and Metabolic Factors Influencing Chemotherapy

The medical need for advances in cancer treatment with surgery, radiotherapy and conventional cytotoxic chemotherapy has made only a modest overall impact on mortality. Hence the significance of discovering new targets, pathways and strategies for therapeutic intervention in cancer is extremely important. Metabolic disorders like diabetes and obesity alter the risk of developing variety of cancers, and the associations are biologically plausible. Also, cancerous tissues show a high level of glucose uptake and metabolism and it is likely this phenotype is required for rapid proliferation tumor cells. Recent demographic explosion of metabolic diseases has complicated the effectiveness of chemotherapy. Because of these, chemotherapy has turned out to be increasingly complicated and therefore, the anticipated success rate is much below than expected. The understanding of molecular events those contribute to enhancement in drug-induced cell death will not only help in better understanding the inter- relationship between cancer and chemotherapeutic drugs but also will improve sensitivity and specificity of the treatment.

AB-14 - Session IV- Dr. Gautam Kumar Sharan

Radiation Therapy in Breast Cancer

Dr. Sharan will review the biological principles and current guidelines for radiation therapy in Breast Cancer management. State of the art Radiotherapy Techniques such as VMAT, IGRT and IMRT along with 3DCRT will be discussed to highlight the synergistic role of ionizing radiations in the management of Breast Cancer in various scenarios such as chemotherapy, biological therapy, and hormone therapy. He will also elaborate the mechanisms behind radiation-induced fibrosis and methods to mitigate the side-effects. Recent and future trends in personalized Breast Cancer radiation therapy will be discussed. In addition, Dr. Sharan will present results from on-going research projects that assess Radiation therapy outcomes after Breast Oncoplastic surgery.

AB-15 - Session V-Dr. Ramesh Hariharan

Our Experiences with Genome Sequencing for Clinical Applications in Breast Cancer

The talk will describe our experiences and results in using genome sequencing and big data analysis for genomic diagnoses of rare diseases, inherited cancer risk, as well as modulation of cancer treatment.

AB-16 - Session V- Dr. Nandini Sahasrabuddhe

Utility of Multi-gene panel in Investigation of Key Mutations in Triple-Negative Breast Cancers

Breast cancer is the most common cancer amongst women in India. TNBCs are an aggressive subtype difficult to treat and exhibit higher rate of recurrence and mortality. Indian women show higher prevalence of TNBCs compared to the western population. Lack of reliable markers along with paucity of targeted therapy demands an in-depth investigation of the mutational profile of Indian TNBC patients. As an initial step, we decided to focus on key cancer-related genes and carry out targeted sequencing using Next-generation sequencing approach. Multi-gene panels offer number of advantages which include compatibility with archival tissue, multiplexing capability and high coverage. We carried out MiSeq-based NGS analysis of 62 TNBC samples using Illumina's TruSeq Amplicon Cancer Panel (TSCAP). Mean coverage of 1000X was achieved. Positive control samples were used for analytical validation of the NGS data analysis pipeline. VAF of as low as 3% was identified with confidence. As reported previously, PIK3CA hotspots were identified in several samples. We also found a number of TP53 mutations across samples. Interestingly, subset of samples harbored mutations in KIT and kinases alike. Further correlation of the mutational profiles with clinical parameters is ongoing. Our findings warrant validation in large cohorts and indicate utility of multi-gene panels in discovery of potential new targets in challenging diseases like TNBCs.

AB-17 - Session V- Dr. Anamika Krishnapal

Large-scale -Omics Data Integration to Gain Insights into Breast Cancer

With the advent of next generation sequencing technologies, the landscape of genome-wide studies for understanding complexities in biological systems is growing at an unprecedented scale. Humongous amount of genomics, transcriptomics, proteomics and epigenomics data is currently being generated but biologists are struggling severely in managing, integrating, visualizing and analysing the data coming from these multiple sources in order to get 'actionable insights'. Genes, transcripts, proteins, metabolites and other macro/micro molecules systematically collaborate to perform complex cellular processes and studying only single -omics data will never fully unravel the complexities of a biological system. Therefore, a systematic analysis of multi-layered, multi-omics data is imperative for the holistic understanding of the complex biological processes. Using Breast Cancer as a case study, we present a multi-omics approach for the integration and analysis of large-scale high-throughput data to gain biological insights into the disease biology.

AB-18 - Session V- Dr. Aarti Desai

Comprehensive Solution for Analysis of Copy Number Variations in Breast Cancer

Affymetrix high throughput genomic microarray solutions empower researchers to perform not only cutting-edge basic research but also take their discoveries to clinical practice. Affymetrix gene expression arrays have facilitated the identification of gene signatures of Breast Cancer with prognostic and diagnostic value. Deep transcriptome analysis of challenging RNA samples such as those obtained from FFPE has been achieved. In recent years, copy number analysis in solid tumors, high resolution cytogenetic analysis and flexible genotyping analysis is rapidly gaining importance in cancer diagnosis, prognosis, and therapy selection. Affymetrix OncoScan™ FFPE Assay Kit is capable of determining highly accurate copy number changes and allelic imbalances, including loss of heterozygosity (LOH) in solid tumors from limited amounts of highly modified and degraded FFPE-derived DNA. The talk will discuss the diverse array of cutting-edge genomics tools developed by Affymetrix for translational research and routine clinical application in breast cancer.

Journal

Markey Cancer Center

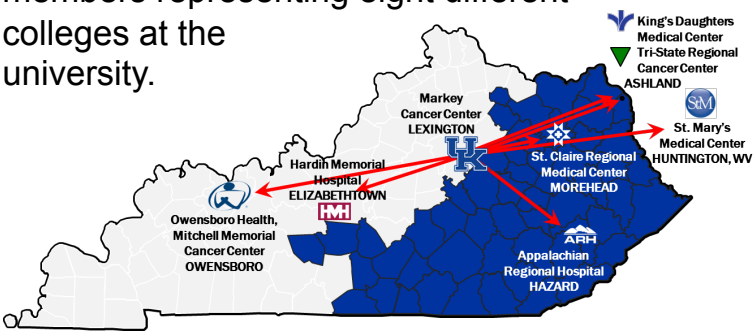
Lexington, Kentucky

Our Mission: To reduce cancer mortality in our state and region through a comprehensive program of cancer research, treatment, education, and community engagement.

We have four research programs and seven shared resource facilities that work closely to achieve this mission.

Our research network (shown below) spans seven hospitals across our catchment area, covering more than half the state of Kentucky, with a focus on Appalachian Kentucky. Our affiliate network currently includes 15 hospitals and is focused on bringing high-quality clinical care to cancer patients.

We foster a culture of education and transdisciplinary collaborations with 116 members representing eight different colleges at the university.

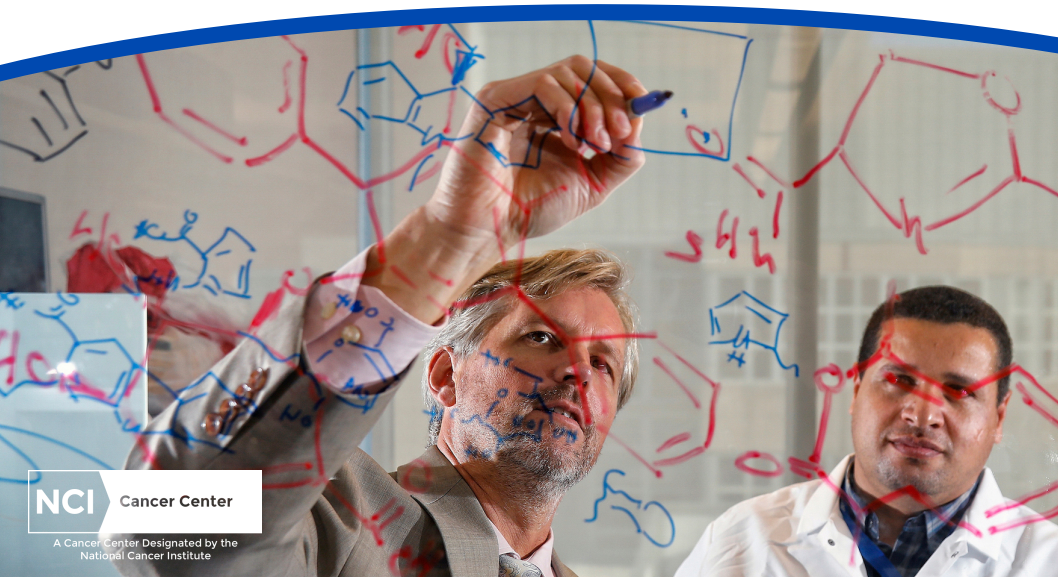


Research Programs

- Cancer Cell Biology and Signaling (CS)
- Genomic Instability and Epigenetics (GE)
- Cancer Prevention and Control (CP)
- Drug Discovery, Delivery, and Translational Therapeutics (DT)

Shared Resources

- Oncogenomics
- Cancer Research Informatics
- Redox Metabolism
- Biostatistics and Bioinformatics
- Flow Cytometry and Cell Sorting
- Biospecimen and Tissue Procurement
- Behavioral and Community-Based Research



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HealthCare
MARKEY CANCER CENTER
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College of Health Sciences

College of Medicine

College of Pharmacy

College of Nursing
Our Goal is to Help You Realize Yours

University of Kentucky College of Public Health