a ***Joint Seminar*** brought to you by

p53 Laboratory & Bioinformatics Institute (BII)

Date : 16 March 2012 (Friday)

Time : 11.00am – 12.30pm

Venue: Aspiration Theatrette, Matrix Building, Level 2M, Biopolis

Co-host: Prof Sir David Lane, p53 Laboratory

Dr Chandra Verma, Bioinformatics Institute

Prof Tanya Das
Professor of Molecular Medicine,
Bose Institute

11:00 am – 11:45 am

Multifocal signal modulation therapy of cancer: 'p53' or 'not p53' – that is the question

The tumor suppressor p53 play an important role in the cell's intrinsic responses to genome instability, including a transient cell cycle arrest, senescence and apoptosis. Since both senescence and apoptosis are powerful tumor-suppressive pathways preventing the uncontrolled proliferation of transformed cells, the network of p53 target genes functions as an important regulator of cancer prevention. To target the 'guardian angel' p53 thus appears to be a critical strategy to energize the process of cancer therapeutics. Our effort to develop a multfocal signal modulation therapy of cancer revealed that apoptosis could be induced in wild type p53-expressing cancer cells *via* activation of SMAR1-p53 loop that mediates Bax transactivation and stimulation of intrinsic death pathway. Even in p53-degraded HPV-infected cancer cells, p53-dependent apoptotic program could be rejuvenated by manipulating pro- and anti-p53 networks, not in isolation but in concert. Interestingly, by changing Ras/p53 balance, cellular micro-environment of drug-resistant cancer stem cells could also be shifted towards apoptosis. Outcome of this study might expand our knowledge in developing a signaling network modulation therapy of cancer by steering a single molecular target - p53, and therefore, provide a highly potential and effective tool in the hands of clinicians.

Prof Gaurisankar Sa
Professor of Molecular Medicine,
Bose Institute

11:45 am – 12:30 pm

Oncogenic Ras and p53: a deadly alliance

Perhaps active-mutant or oncogenic Ras is best known for its ability to induce malignant transformation through the stimulation of uncontrolled cell proliferation and cell survival. It can also sensitize cells to undergo apoptosis although the mechanism by which such oncogenic transformation promotes apoptosis is not well documented. Here we report that genotoxic agent like curcumin inversely regulates super-family PI3K and ATM signaling to converge into the same phenomenon of p53 stabilization and accumulation to confer oncogenic *Ras-transformed cell apoptosis. While under* normal condition, oncogenic Ras signals through Raf/MEK/ERK pathway to resist apoptosis and favor proliferation, this protection is antagonized by intervening in this signal transduction cascade. In fact, targeting *Ras-downstream factors of this proliferative pathway channelizes oncogenic Ras-signaling* towards p38MAPK/JNK1 pro-death circuitry that phosphorylate p53 at Ser33/Ser46 and Thr81 of its transactivation domain required for optimal activation of p53. These results establish a hitherto unexplored role of oncogenic Ras as a molecular switch between growth-promoting and growth inhibitory cascades in which the ultimate balance between these pathways defines cellular homeostasis, leading to survival or induction of programmed cell death.

About the Speakers

Prof. Tanya Das did her Masters in Biochemistry from Kolkata University and received Ph.D degree in Biochemistry from the same University in 1988. Thereafter she joined The Cleveland Clinic Foundation, USA, for her post-doctoral research and returned to India in 1993 to work as a Pool Officer in IICB, Kolkata. She joined Bose Institute, Kolkata, in 1995 where she is now working as a Professor in the Division of Molecular Medicine. Prof. Das is also a visiting scientist of The Cleveland Clinic Foundation, USA.

Research area: Research work of Prof. Das is focused in the area of Cancer Chemoprevention and its Molecular Mechanisms. Her aim is to develop a multifocal signal modulation therapy of cancer by targeting signal networks responsible for cancer development, angiogenesis, metastasis and drug-resistance. Her recent work also aims at identifying the genomic, proteomic and signalomic signatures of cancer stem cells, the origin of all cancers, to develop a molecular engineering-based miRNA therapy.

Awards: Prof. Tanya Das has received National Young Woman Bio-scientist Award for 2004 from DBT in 2004, Seva Samman from Dakshin Kolkata Krira-O-Sangskriti Sangstha, Kolkata, in 2005, Woman of the Year award from Anwesa, Kolkata, in 2006 and Rupa Chakrabarty Memorial Award from Bethune College, kolkata, in 2009. She has been elected as a Fellow of WB Academy of Science, India, in 2011.

Publications: Prof. Das has published more than 100 original research papers and reviews in highly reputed International journals like *Science*, *Oncogene, Journal of Biological Chemistry, Cancer Research, Journal Immunology etc.*

Editorial Board member: Prof. Das is in the Editorial and Reviewing boards of several International journals like *Carcinogenesis, Neoplasia, Cancer Molecules, Cellular Immunology, British J Pharmacology, Cancer Letters, PLoS ONE, FEBS Letters, Molecular Cancer, Cancer Immunology* etc.

Patent: Prof. Das has in her credit two patents on (i) *A process for producing therapeutically active pure curcumin from Curcuma longa Linn*" and (ii) '*A novel system for conducting chemotaxis and durotaxis assays for monitoring cell migration through 3-dimensional matrices'.*

Prof. Gaurisankar Sa completed his Master degree in Biochemistry from Calcutta University in 1983. After obtaining *Ph.D. degree from* the same University in 1990, Prof. Sa joined Dept. of Biochemistry, Virginia Tech, USA, as *Visiting Faculty. Afterwards he moved to The* Cleveland Clinic, USA in 1992 for further research in cell signaling.
He joined Bose Institute in 1995 where he is working as a *Professor in* the Division of Molecular Medicine. Prof. Sa's research interests are understanding the molecular mechanisms of carcinogenesis and development of selective anti-cancer drugs from natural and synthetic sources. In the field of tumor immunology, Prof. Sa has contributed substantially to understand the mechanisms of immune-editing and immune evasion of tumor that is required for escaping from immune-surveillance.

Prof. Sa has obtained several International and National awards for his contribution in Science and humanities. He is the member of various *National and International Scientific societies and expert member* of a number of *Scientific Advisory Bodies. Prof. Sa has published more that 100 original research papers* and reviews in International journals of repute. He has two patents in his credit which is on the process of commercialization. Prof. Sa is also serving as *Editorial Board Member of several scientific journals.*