

**Significance of research contributions for which the following awards were given to Dr Galande:**

1. National Bioscience award (DBT)
2. Shantiswaroop Bhatnagar Award (CSIR)
3. GD Birla Award (KK Birla Foundation)

The citations for these awards have been appended after the research summary below:

Dr. Galande began his independent career at National Centre for Cell Science (NCCS) Pune in 2001 by testing a hypothesis that SATB1 is a chromatin level functional end point for the PDZ-mediated signal transduction resulting in coordinated gene regulation by studying the PDZ-mediated interactions of SATB1. Since SATB1 is a T-lineage restricted regulator, Galande initially focused on regulation of cytokine genes and discovered that in HIV-1 infected cells, SATB1 is targeted by Tat, the viral transactivator, such that genes under the control of SATB1 such as IL-2 and its receptor are upregulated. The functional interaction between HIV-1 Tat and SATB1 requires its PDZ-like domain, and that the HDAC1 corepressor also binds through the same. Furthermore, Tat competitively displaces HDAC1 that is bound to SATB1, leading to increased acetylation of the promoters in vivo. These results suggest a novel mechanism by which HIV-1 Tat might overcome SATB1-mediated repression in T-cells (Kumar et al. 2005, *Mol. Cell Biol.*). This publication is regarded as one among the important contributions in the area of gene dysregulation upon HIV infection and Dr. Galande has received a number of invitations for delivering talks describing this work in national as well as international meetings. While studying the mechanism of regulation of global gene expression by SATB1, his group found that phosphorylation status of SATB1 governs its mutually exclusive association with HDAC1 and PCAF. Gene expression profiling studies using RNA from cells overexpressing point mutants of SATB1 defective in phosphorylation or acetylation unequivocally demonstrated the importance of these modifications towards the ability of SATB1 to act as a global regulator of gene expression (Kumar et al., 2006, *Mol. Cell*). This seminal study is one of the first reports revealing the molecular mechanism of action of a global transcription factor and chromatin organizer, and is therefore cited in number of reviews pertaining to T cell biology. Galande then set out to define more precisely the role of SATB1 in global gene regulation by identifying its novel partner proteins and identified the promyelocytic leukemia (PML) oncoprotein as a SATB1-interacting protein. Using modified in vivo chromatin conformation capture methodology (3C) combined with chromatin immunoprecipitation (ChIP), he and coworkers demonstrated PML and SATB1 form a novel type of regulatory complex that governs gene regulation in a global manner by establishing distinct chromatin loop architecture (Kumar et al. 2007, *Nature Cell Biol.*). These findings have opened up many avenues to study the link between higher-order chromatin organization and coordinated gene expression. Although SATB1 can act both as a repressor and activator of gene expression, the precise mechanism of how these contrasting activities are manifested at a global level was not clear. Galande's elegantly designed experimental strategy revealed that SATB1 and CtBP1 form a repressor complex by recruiting HDAC1 whereas  $\beta$ -catenin forms an activator complex with SATB1 by recruiting p300 in vivo (Purbey et al., 2009, *Mol. Cell Biol.*). Analysis of occupancy of SATB1 at its genomic targets indicated specific recruitment of these factors and corresponding changes in histone modifications at SATB1 and Wnt targets (Notani et al. 2010, *PLoS Biol.*). These results unequivocally establish SATB1 as a mediator of Wnt/ $\beta$ -catenin signaling and provide mechanistic insights into how two factors

with contrasting activities, namely CtBP1 and  $\beta$ -catenin, cooperate with the chromatin organizer SATB1 to regulate gene expression upon Wnt signaling. These findings have tremendous implications in development, differentiation and cancer. This is one of the most fundamental discoveries from Galande laboratory, which has now been incorporated in review articles written by others. Findings from all of these studies have made significant impact on the chromatin biology-gene regulation community.

Prof Galande's vision has led to the setting up of a **Centre of Excellence in Epigenetics** (CoEE) at IISER Pune in 2010, which has resulted in a network of diverse biologists making use of knowledge and techniques of epigenetics. In particular, the centre was focused on epigenetic modifications underlying variety of biologically important phenomena and their role in gene expression, regeneration, cancer, and behavior. The holistic and multi-pronged approach of this team led by Prof. Galande necessitated more close and effective collaborations that were facilitated by trained manpower and by creation of state-of-the-art facilities. While each group was engaged in contemporary and competitive areas, this Centre of Excellence acted as a catalyst to bring these groups in active interaction – an effort of this kind was unprecedented in modern biology labs in India. The grand scheme of projects proposed by this team of scientists led by Prof. Galande aimed to achieve the understanding of complex mechanisms of epigenetic regulation in various biological processes. This is accomplished using number of different eukaryotic model systems of increasing complexity from Hydra to mouse, so as to gain insights into the evolution of epigenetic regulation. Using these model systems, Galande has dared to tackle important long-standing questions addressing fundamental phenomena in biology. In another landmark study as part of his collaborations, Galande was instrumental in demonstrating age-dependent changes at the epigenetic and behavioral levels in mice challenged with early life stress (Suri et al. 2012, *Biol Psychiatry*). These results have important implications towards treatment of stress related disorders such as anxiety and depression. Further mechanistic studies in this direction are ongoing and the results will be published shortly. Galande is also engaged in another multi-institutional collaborative project to study epigenetic regulation of diabetes and obesity. The results of one of the first set of findings were published in *Cell Metabolism* (Hardikar et al., 2015). He is also involved in collaboration with group of clinician-researchers studying epigenetic alterations underlying type II diabetes by nutritional intervention in human cohort (Khare et al., 2023). During the pandemic his group generated a knockout model of ACE2 receptor to study the effects of long COVID. The results of this collaborative study provided the morphological basis for the sensory and cognitive disabilities caused by the deletion of ACE2 receptors and offer a potential experimental approach to study the neural circuit mechanisms of cognitive impairments observed in long COVID (Mahajan et al., 2023). Prof. Galande is tenaciously working towards fulfilling these long-term projects whose outcomes have potential to become game-changers, albeit after many years. In summary, making best use of his early training in biochemistry, genetics and molecular biology and employing novel strategies, Galande made an early mark in the field of epigenetics and rapidly established himself as a leading epigenetics researcher globally.

# DEPARTMENT OF BIOTECHNOLOGY



## National Bioscience Award for Career Development 2006-07



### DR. SANJEEV GALANDE

*National Centre for Cell Science, Pune.*

**D**r. Sanjeev Galande is presently working as Scientist D at the National Centre for Cell Science, Pune. He obtained his Ph.D in Biochemistry and Molecular Biology from the Indian Institute of Science and did post-doctoral work at the Burnham Institute, La Jolla Cancer Research Centre, USA and Lawrence Berkeley National Laboratory, University of California, USA.

He has studied dynamic changes at the level of chromatin architecture during various immunological phenomena such as activation and differentiation of T cells and pathogenesis of diseases involving T cells. His group identified involvement of a T-lineage-enriched host factor SATB1 during the early events in HIV-1 life cycle. He has contributed a number of innovative technologies for biological research including a novel cassette for expression and purification of recombinant proteins.

Dr. Galande has published papers in peer reviewed national and international journals. He is an elected member of American Association for Cancer Research (AACR) and American Society of Microbiology (ASN). He is a recipient of International Senior Research Fellowship from Wellcome Trust post-doctoral fellowship from United States, Department of Defense Army Medical Research and Breast Cancer Research Program of the State of California, USA.

The National Bioscience Award for Career Development for the year 2006 is conferred on Dr. Sanjeev Galande for his significant findings on dynamic changes in higher order chromatin assembly which governs gene expression in a spatial and temporal manner.

जैव विज्ञान

**डॉ. संजीव गलान्दे**

जैव विज्ञान में वर्ष 2010 का शान्ति स्वरूप भटनागर पुरस्कार, नेशनल सेंटर फॉर सेल साइंस, पुणे के डॉ. संजीव गलान्दे को उच्चतर विन्यास क्रोमैटिन आर्किटेक्चर में होने वाले क्रियात्मक परिवर्तन किस प्रकार जीन अभिव्यक्ति में स्पेशियोटेम्पोरल परिवर्तन करते हैं, को समझने में विशिष्ट योगदान के लिए प्रदान किया गया है। उनके कार्य ने, विशेषतौर पर, T सैल के विकास और विभेदीकरण में Wnt सिग्नलिंग पाथवे की भूमिका में महत्वपूर्ण अन्तर्दृष्टि प्रदान की है।

**Biological Sciences**

**Dr Sanjeev Galande**

The Shanti Swarup Bhatnagar Prize for the year 2010 in Biological Science has been awarded to Dr Sanjeev Galande of National Centre for Cell Science, Pune for his outstanding contribution to the understanding of how dynamic changes in higher-order chromatin architecture lead to spatiotemporal changes in gene expression. In particular his work has provided important insights into the role of the Wnt signaling pathway in T cell development and differentiation.

## **G.D. BIRLA AWARD FOR SCIENTIFIC RESEARCH**

### **Prof. Sanjeev Galande**

**The twenty fourth G.D. Birla Award for Scientific Research for the year 2014 has been given to Prof. Sanjeev Galande, Professor and Team leader in Centre of Excellence in Epigenetics. Indian Institute of Science Education and Research, Pune.**

### **Prof. Sanjeev Galande and his research Work**

Born on 20<sup>th</sup> September 1967, Prof. Sanjeev Galande is Professor and Team Leader in Centre of Excellence in Epigenetics at Indian Institute of Science Education and Research, Pune. Prof. Sanjeev Galande obtained his PhD in Biochemistry from the Indian Institute of Science, Bangalore, India in 1996. As a postdoctoral fellow at the Lawrence Berkeley National Laboratory, USA from 1996-2001, he studied the role of MAR-binding proteins in tumor genesis. He then joined the National Centre for Cell Science, Pune, India in 2001 as a senior scientist.

After joining as Professor at IISER Pune in 2010, he established the Centre of Excellence in Epigenetics and has assembled a team of scientists to study the evolution of epigenetic mechanisms using multiple model systems. Research in Galande laboratory is focused on studying how the dynamic changes in higher-order chromatin assembly govern gene expression in a spatial and temporal manner. To fulfil this, he has established a multidisciplinary program engaged at the interface of biochemistry, molecular biology, bioinformatics, cell biology, proteomics, and genomics.

The packaging of chromatin is hierarchical and its different states are interconvertible depending upon the physiological need of the cell and also contribute in variety of ways to achieve stringent regulation of gene activity. Dynamic nature of chromatin loops is one such mechanism. Technological advances in recent years have provided unprecedented insights into the role of chromatin organization and interactions of various structural-functional components towards gene regulation.

All cells contain identical genome; however, its expression varies drastically from cell type to cell type. In multicellular organisms, DNA is organized with help of basic proteins into an orderly packaged compact

structure called chromatin. The studies from Galande laboratory have provided novel insights into how environmental factors ‘epigenetically’ govern gene expression patterns by virtue of key cellular signaling pathways that affect higher-order assembly of chromatin. Research in Prof. Galande’s laboratory was instrumental in establishing the role of SATB1 in organization of chromatin loop structures and their dynamic nature in response to physiological stimuli.

Epigenetics is defined as the heritable changes that influence gene function without changing DNA sequence. Prof. Galande’s team is particularly interested in studying the implications of epigenetic regulation towards development and differentiation of cells. To accomplish this, they use a variety of model systems such as cells of the immune system, stem cells and cancer cells. They are also interested in studying the global regulatory networks and the dynamic interplay of various cis and trans regulatory elements that dictate patterns of gene expression. The outcome of these studies would be important towards understanding the biology of diseases such as infectious diseases, cancer and other complex disorders such as diabetes.

Prof. Galande is also the recipient of the national Bioscience Award for Career Development 2006 from the Department of Biotechnology, the 2007 Swarnajayanthi Fellowship from the Department of Science & Technology and Shantiswaroop Bhatnagar Award in 2010. He was also elected member of the American Association for Cancer Research in 1999 and American Society of Microbiology in 2005 to 2010. He is an elected fellow of the Indian Academy of Sciences, Bangalore, 2010 and the Indian National Science Academy, 2012.