

Nutriepigenomics & Cancer

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Academic Qualifications:

Ph. D. Biochemistry- CSIR-Indian Institute of Toxicology Research (IITR), Lucknow.
(Degree awarded by the Aligarh Muslim University, Aligarh, India).

M. Sc. Biochemistry- Aligarh Muslim University, Aligarh, India.

Research Experiences:

Position Title	Department/ Employer/ Date
Principal Scientist	Department of Biochemistry, CSIR-Central Food Technological Research Institute (CSIR-CFTRI), Mysore, India.
Senior Scientist	Division of Endocrinology, CSIR-Central Drug Research Institute (CSIR-CDRI), Lucknow, India.
Postdoctoral Fellow/ Research Assistant Professor	Department of Dermatology/ Department of Biology, University of Alabama at Birmingham, AL, USA
Research Scientist	New Drug Discovery Research (NDDR), Ranbaxy Research Laboratories, Gurgaon, India

Awards and Honors

- **Keynote speaker** at the National symposium on Metabolic Disorders in Human Health held at the Department of Biochemistry, VCAS for Women, Tiruchengode, Tamilnadu, March 2018.
- **Chaired a technical session** in the International Conference on Cell Death in Cancer and Toxicology” organized by the CSIR-IITR, Lucknow on February, 2018
- **Co-Chaired a technical session** in the annual meeting of SBC(I) 2016
- **Young Scientist Grant** from DST-SERB from 2012-2015

- **Chaired a technical session** on the UGC& DBT-sponsored National symposium organized by the Interdisciplinary Biotechnology Unit, AMU, Aligarh on March 26, 2015
- **Young Scientist Award-2011** by the **Association for Biotechnology and Pharmacy (ABAP)**, India
- **Gold Medal** conferred by the **Association for Biotechnology and Pharmacy (ABAP)**, India for the research excellence.
- **Postdoctoral Research Fellowship** by the **University of Alabama at Birmingham, USA.**
- **Assistant Professor** at the Department of Biology, **University of Alabama at Birmingham, USA**
- **Susan G. Komen for the Cure Travel grant award** for work presented at American Institute for Cancer Research (AICR), held at Washington DC, USA on October 20-21, 2010.
- **Susan G. Komen for the Cure Travel grant award** for work presented at 101 Annual meeting for American Association for Cancer Research (AACR), held at Washington DC, USA on April 17-21, 2010.
- **National Institute of Health (NIH) Travel award** to participate “Dietary Supplement Research Practicum” held at NIH on June 1-5, 2009.
- **Outstanding Visiting Scholar Award-2007”** from University of Alabama at Birmingham, USA.

Professional Memberships

- American Association for Cancer Research, USA
- European Association for Cancer Research, UK
- American Society for Photobiology, USA
- Association for Biotechnology and Pharmacy, India
- Society of Biological Chemists, India

Editorial Board Member

- Non-coding RNA research (Jan 2016-Dec-2019)
- World Journal of Clinical Oncology (Jan 2015-Dec 2018)
- American Journal of Cancer Prevention (Jan, 2013-Dec, 2014)
- International Journal of Cancer Research (2008-2010)
- Pakistan Journal of Biological Sciences (2008-2010)
- Asian Journal of Biochemistry (2008-2010)
- Delivered more than 25 invited talks and presented paper in more than 50 national and International conferences
- Ad-hoc reviewer for many international peer-review journals

Research Interest

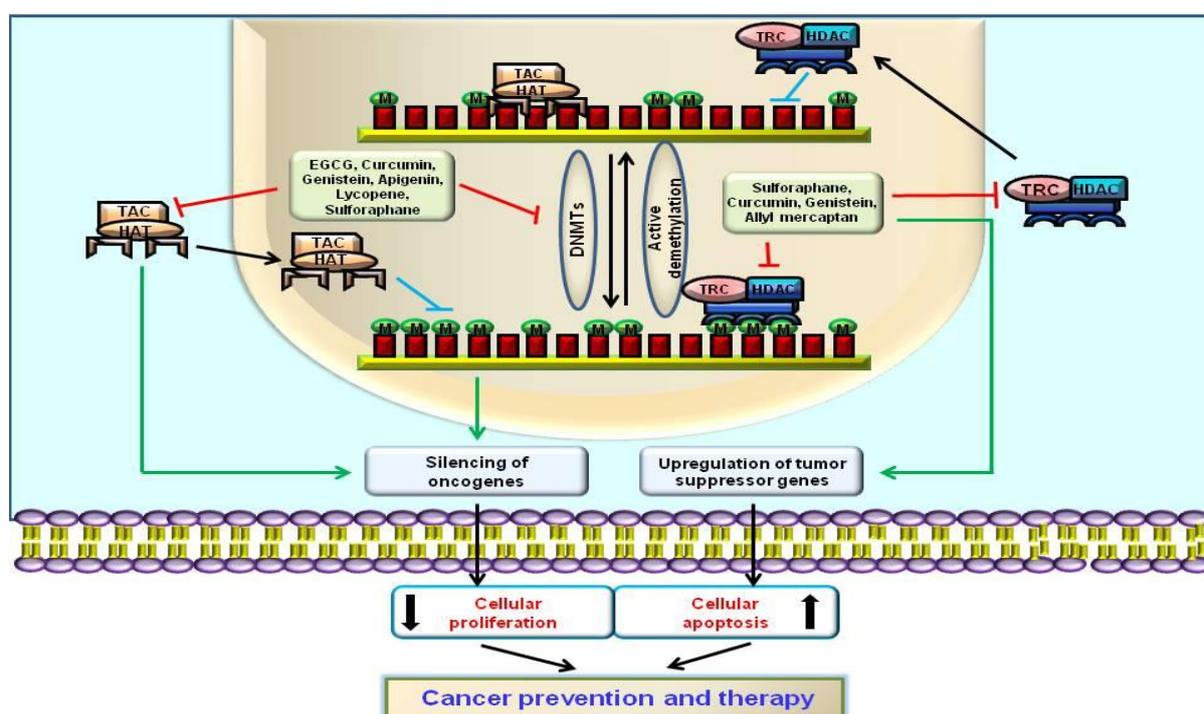
In our laboratory, we mainly focus on exploring the epigenetic role of bioactive diets and dietary supplements on cancer prevention and therapy. We investigate the role of different epigenetic modifications such as DNA methylation and histone acetylation as well as histone methylation changes during the processes of carcinogenesis. We also aim to investigate the epigenetic role of traditional spices and other bioactive diets on the onset of life-style associated diseases including cancer.

Our research interest can broadly be categorized into as follows:

- *Nutri-epigenomics of bioactive diets and to explore their role on cancer and aging*
- *Epigenetic of cancer stem cells*
- *Studying epigenetic targets by bioactive diets including herbs and spices*
- *Developing experimental animal models to study the cancer progression and cancer metastasis*
- *Epigenomics of cancer to explore the novel therapeutic targets*

Current Research

■ *Epigenetic of bioactive diets in cancer prevention and therapy*



Role of bioactive dietary DNMT inhibitors in cancer prevention and therapy. The transcription activation complex (TAC), which contains HATs, binds to the unmethylated promoter and gene transcription takes place. When the gene promoter is methylated by DNMTs, the TAC becomes unable to bind to the gene promoter and initiation of transcription is inhibited. The transcription repression complex (TRC) containing HDACs is recruited to the methylated DNA and the gene is silenced. Bioactive phytochemicals have the capability to inhibit these epigenetic enzymes and thus alter the patterns of gene expression in cancer cells. The bioactive supplements inhibit the process of DNA methylation either by inhibiting the different epigenetic remodelling complexes or by inhibiting the DNMT enzymes. M, methyl group

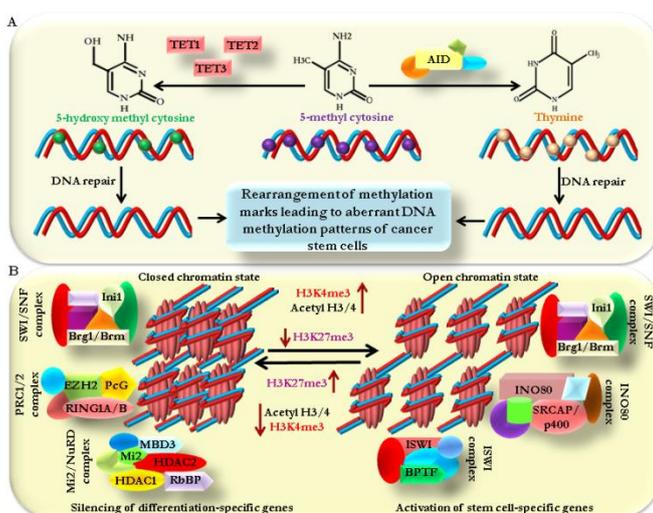
Carcinogenesis is considered to be the outcome of deregulated genetic and epigenetic events. Epigenetic alterations are important as they link the behaviour of cells to their environmental interactions and thus determine the susceptibility of a cell to transforming changes. As these changes do not involve alterations in the genome constructs, these epigenetic events occur constantly during the life of the cells. DNA methylation, histone tail modifications, chromatin remodelling and miRNA-mediated multi-gene silencing are considered to be the major epigenetic changes that are involved in maintaining cellular homeostasis and differentiation states. Multiple studies have revealed that global DNA hypomethylation events are a major characteristic of most of types of cancer and contribute to genomic instability by activating retrotransposons and other silent genomic regions. On the other hand, promoter hypermethylation events occur in important tumor suppressor genes, indicating that it is inappropriate DNA methylation that is important in driving the process of carcinogenesis. Histone modifications also occur, including acetylation and methylation of lysine residues, methylation of arginine residues, phosphorylation of serine or threonine residues, ubiquitination and sumoylation of lysine residues, ADP ribosylation of glutamic acid residues and isomerisation of proline residues, *etc.* These modifications define the patterns of chromatin remodelling, thus determining the resultant gene expression and gene silencing patterns. Bioactive phytochemicals (tea polyphenols, resveratrol, curcumin, genistein and sulforaphane, *etc.*), which are largely non-toxic, have been tested for their role in epigenetic modulatory activities in cancer prevention and therapy. These phytochemicals inhibit the growth of tumors through epigenetic modifications. We have addressed the epigenetic modulatory potential of different bioactive diets in various scientific publications [[Cancer Lett.](#) 2014 Dec 1;355(1):9-17; [Clin Epigenetics.](#) 2010 Dec 1;1(3-4):101-116; [Expert Opin Ther Targets.](#) 2016 Jun;20(6):689-703].

We have previously demonstrated the epigenetic modulatory potential of various bioactive phytochemicals in lung and breast cancer therapy using in vitro and in vivo models

- Cucurbitacin B Alters the Expression of Tumor-Related Genes by Epigenetic Modifications in NSCLC and Inhibits NNK-Induced Lung Tumorigenesis
 - [[Cancer Prev Res \(Phila\).](#) 2015 Jun;8(6):552-62]
- Cucurbitacin B inhibits the stemness and metastatic abilities of NSCLC via downregulation of canonical Wnt/ β -catenin signaling axis
 - [[Sci Rep.](#) 2016 Feb 24;6:21860]
- Cucurbitacin B inhibits breast cancer metastasis and angiogenesis through VEGF-mediated suppression of FAK/MMP-9 signaling axis
 - [[Int J Biochem Cell Biol.](#) 2016 May 19;77(Pt A):41-56]
- Epigenetic reactivation of p21^{CIP1}/WAF1 and KLOTHO by a combination of bioactive dietary supplements is partially ER α -dependent in ER α -negative human breast cancer cells.
 - [[Mol Cell Endocrinol.](#) 2015 May 5;406:102-14.]
- Bioactive dietary supplements reactivate ER expression in ER-negative breast cancer cells by active chromatin modifications
 - [[PLoS One.](#) 2012;7(5):e37748.]

■ Epigenetics of Cancer Stem Cells

Epigenetic alterations including DNA methylation and histone modifications are the key factors in the differentiation of stem cells into different tissue subtypes. The generation of cancer stem cells (CSCs) in the process of carcinogenesis may also involve similar kind of epigenetic reprogramming where, in contrast, it leads to the loss of expression of genes specific to the differentiated state and regaining of stem cell-specific characteristics. The most important predicament with treatment of cancers includes the non-responsive quiescent CSC. Therefore, CSC-targeted therapeutic approaches improve the chances of patient survival by reducing the frequency of tumor relapse. Differentiation therapy is an emerging therapeutic approach in which the CSCs are induced to differentiate from their quiescent state to a mature differentiated form, through activation of differentiation-related signalling pathways, miRNA-mediated alteration and epigenetic differentiation therapy. We have been actively working to address the cancer stem cell therapy by bioactive diets in our laboratory.



Epigenetic reprogramming to achieve stemness. A) The 5-methyl cytosine residues are actively converted into 5-hydroxy methyl cytosine by Ten eleven translocation (*TET* 1-3) proteins. The activation-induced deaminase (*AID*) also converts the 5-methyl cytosine into thymine. These residues are then removed in the

process of DNA repair and a complete DNA demethylation signature is achieved. The rearrangement of these methylation marks leads to differential methylation observed in case of cancer stem cells. **B)** The silencing of differentiation-specific genes is achieved by the compaction of chromatin with the help of *SWI/SNF*, *Mi2/NuRD* chromatin remodelling complexes and *PRC1/2* repressor complexes. The compacted chromatin is enriched in the inactive mark *H3K27me3*, while the active marks, acetyl histone *H3/4* and *H3K4me3* are absent. The stem-cell specific genes are activated by the action of *SWI/SNF*, *ISWI* and *INO80* chromatin remodelling complexes which increase the trimethylation of *H3K4* (*H3K4me3*) and histone acetylation and decrease in *H3K27me3* marks [Biochim Biophys Acta. 2014 Dec;1840(12):3494-3502].

List of Publications

Selected Publications: Articles Published in the Peer Reviewed Journals

[Total publications: 66; International-64; National-02; Corresponding author-23]

[[Google Scholar](#)] [[PubMed](#)] [Total citation-3100; h-index-32; i-10 index-47]

Selected Publications

*Published as a corresponding author

1. Zaman M, Khan MV, Zakariya SM, Nusrat S, **Meeran SM**, Alam P, Ajmal MR, Wahiduzzaman Shahein YE, Abouelella AM and Khan RH (2018) Amino group of Salicylic acid exhibits enhanced inhibitory potential against insulin amyloid fibrillation with protective aptitude toward amyloid induced cytotoxicity. *J. Cell. Biochem.* 119(5): 3945-3956. **Journal Impact Factor (JIF)- 3.5**
 2. Li Y, **Meeran SM** and Tollefsbol TO (2017) Combinatorial bioactive botanicals re-sensitize tamoxifen treatment in ER-negative breast cancer via epigenetic reactivation of ER α expression. *Sci. Rep.* 7(1): 9345-60. **Journal Impact Factor (JIF)- 4.26.**
 3. Shukla S, Sinha S, Khan S, Kumar S, Singh K, Mitra K, Maurya R and ***Meeran SM** (2016) Cucurbitacin B inhibits the stemness and metastatic abilities of NSCLC via downregulation of canonical Wnt/ β -catenin signaling axis. *Sci. Rep.* 6: 21860. **JIF- 5.58.**
 4. Khan S, Shukla S, Sinha S and ***Meeran SM** (2016) Epigenetic targets in cancer and aging: dietary and therapeutic interventions. *Expert Opin. Ther. Targets.* 20(6): 689-703. **JIF- 5.14.**
 5. Khan S, Shukla S, Sinha S and ***Meeran SM** (2016) Centchroman altered the expressions of tumor-related genes through active chromatin modifications in mammary cancer. *Mol. Carcinog.* 55 (11): 1747-1760. **JIF- 4.81**
 6. Shukla S, Khan S, Kumar S, Sinha S, Mohd. Farhan, Bora HK, Maurya R and ***Meeran SM** (2015) Cucurbitacin B alters the expression of tumor-related genes by epigenetic modifications in NSCLC and inhibits NNK-induced lung tumorigenesis. *Cancer Prev. Res.,* 8(6): 552-62. **JIF- 5.27.**
 7. Dighe SU[#], Khan S[#], Soni I, Jain P, Shukla S, Yadav R, Sen P, ***Meeran SM** and ***Batra S** (2015) Synthesis of β -carboline-based N-heterocyclic carbenes and their anti-proliferative and anti-metastatic activities against human breast cancer cells. *Journal of Medicinal Chemistry,* 58 (8): 3485-3499. **JIF 5.48.**
- * Equal correspondence author
8. Sinha S, Shukla S, Khan S, Tollefsbol TO and ***Meeran SM** (2015) Epigenetic reactivation of p21^{CIP1/WAF1} and KLOTHO by a combination of bioactive dietary supplements is partially ER α -dependent in ER α -negative human breast cancer cells. *Mol. Cell Endocrinol.,* 406: 102-114. **JIF- 4.24.**
 9. Khan S, Shukla S, Sinha S and ***Meeran SM** (2013) Role of Adipokines and Cytokines in Obesity-associated Breast Cancer: Therapeutic Targets. *Cytokine and Growth Factor Reviews.* 24: 503-513. **JIF 8.83**
 10. Shukla S, Khan S, Tollefsbol TO and ***Meeran SM** (2013) Genetics and Epigenetics of Lung Cancer: Mechanisms and Future Perspectives. *Current Cancer Therapy Reviews:* 9 (2): 97-110.

11. *Meeran SM, Patel SN, Chan TH and Tollefsbol TO (2011) A Novel Prodrug of Epigallocatechin-3-gallate: Differential Epigenetic *hTERT* Repression in Human Breast Cancer Cells. **Cancer Prev Res.**4(8): 1243-54. **JIF 5.2.**
12. *Meeran SM, Ahmed A and Tollefsbol T (2010) Epigenetic targets of bioactive dietary components for the cancer prevention and therapy. **Clinical Epigen.** 1: 101-116. **JIF 6.22.**

Book Chapters Published

13. Khan S, Shukla S and Meeran SM (2017) Epigenetics in Cancer Prevention and Therapy: Role of Phytochemicals. Book title-Cancer Mechanisms and Therapy. S. Sanyal (Ed.), Apple Academic Press, a Taylor & Francis group, Waretown, NJ, USA.
14. Shukla S and Meeran SM (2013) Epigenetic Factors in Breast Cancer Progression. Book title-Breast Cancer Metastasis and Drug Resistance. A. Ahmad (Ed.), Springer Publications, New York, USA. Page 341-365, DOI: 10.1007/978-1-4614-5647-6_19

Invited Talks: More than 20

PhD Students Mentored: 07; awarded : 02

Master/ M.Tech students' degree awarded: 11

Paper presented in the National and International conferences: 61

Perspective PhD students/PDF's: Interested candidate may apply through institute guidelines and send their CV directly to me by Email at s.musthapa@cftri.res.in