Learning epigenetic regulation from host-pathogen interaction

12.15 ~ 13.15, Fri. August 3, 2018

Institute of Bioengineering, pr. 60-letya Oktyabrya, 7/1
Conference room, 3 flour, 304

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Biosketch

Dr. Sanjeev Khosla is presently working as a Staff Scientist at the Centre for DNA Fingerprinting and Diagnostics (CDFD), Hyderabad, an autonomous organization funded by the Department of Biotechnology (DBT), Government of India. He received his Ph.D. degree from the Developmental Biology and Genetics Laboratory at the Indian Institute of Science, Bangalore, India where he worked on the correlation of chromatin organisation with genomic imprinting and sex determination in the coccid insects, mealybugs (*Planococcus lilacinus*). After completion of his doctoral thesis he joined as a Research Scientist at The Babraham Institute, Cambridge, UK, where he was involved in analyzing differential epigenetic information inherited from the mother and father in mice and identified regions of allele-specific chromatin organisation within imprinted genes in the mammalian genome. Later he moved to the Wellcome Trust/ Cancer Research UK Institute, Cambridge, UK where he continued his work on the correlation of chromatin organisation with genomic imprinting in mammals. After moving to CDFD in 2002, his laboratory's research focus, in addition to examining parental-allele-specific chromatin conformation associated with genomic imprinting, has been to examine the epigenetic interface between environment and cellular machinery. Work from his laboratory is involved in deciphering the human epigenome and has also elucidated novel functions of the mammalian DNA methyltransferases, Dnmt3l and Dnmt2 in transgenerational inheritance and during environmental stress respectively.

Abstract

The molecular mechanisms involved in the ability of *Mycobacterium tuberculosis* to modulate the adverse immune response require manipulating the host genome, to express only the gene products advantageous to the survival of the bacilli. In the host cell, the transcriptional fate of a gene is determined by its epigenetic state. Therefore, any factor that can alter the epigenome should be able to modulate the expression profile of a cell. Our studies have shown that the pathogenic *M. tuberculosis* has evolved strategies to exploit this pliability of the host epigenome for its own survival. In two different studies we have identified methyltransferases from *M. tuberculosis* that functions to modulate the host epigenome by methylating (i) a novel, non-canonical arginine of histone H3, H3R42 (Rv1988); (ii) cytosines present in non-CpG context within host genomic DNA (Rv2966c) during infection. Similar protein but with ability to directly methylate host histones H3 at another novel lysine residue (H3K14) has also been identified from *Legionella pnemophilia* (RomA). I will be discussing our findings that point to the use of non-canonical epigenetic mechanisms by pathogenic bacteria to hijack the host transcriptional machinery.

Selected publications

1. Yaseen I, Kaur P, Nandicoori VK, Khosla S. Mycobacteria modulate host epigenetic machinery by Rv1988 methylation of a non-tail arginine of histone H3. Nat Commun. 2015 Nov 16;6:8922
2. Yaseen I, Choudhury M, Sritharan M, Khosla S.Histone methyltransferase SUV39H1 participates in host defense by methylating mycobacterial histone-like protein HupB. EMBO J. 2018 Jan 17;37(2):183-200.
3. Sharma G, Sowpati DT, Singh P, Khan MZ, Ganji R, Upadhyay S, Banerjee S, Nandicoori VK, Khosla S. Genome-wide non-CpG methylation of the host genome during M. tuberculosis infection. Sci Rep. 2016 Apr 26;6:25006
4. Sharma G, Upadhyay S, Srilalitha M, Nandicoori VK, Khosla S. The interaction of mycobacterial protein Rv2966c with host chromatin is mediated through non-CpG methylation and histone H3/H4 binding. Nucleic Acids Res. 2015 Apr 30;43(8):3922-37