



REGIONAL CENTRE FOR BIOTECHNOLOGY
Seminar series

Role of Transcriptional Enhancers and their Hierarchical Networks in Gene Regulation

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Wednesday, October 29, 2014
11:00 AM
ATPC Seminar Room



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Abstract

Gene expression is regulated by distal regulatory elements known as enhancers that establish physical contact with the target promoter to control their expression in spatio-temporal manner. ENCODE (ENCyclopedia of DNA Elements) has identified thousands of cell type specific enhancers that populate mammalian genome. However, molecular mechanisms underlying enhancer functions still remain poorly understood. Recently, another layer to this conundrum was added by the discovery of bi-directional non-coding RNAs (lncRNAs) that are transcribed by enhancers and are thus referred to as enhancer RNAs (eRNAs). Different theories evaluating whether these eRNAs are functional or merely a reflection of enhancer activation are just emerging. Understanding molecular link among chromatin architecture, enhancer and these eRNAs is important for developing strategies to target enhancers in “Enhancer Therapy”.

Using genomic techniques, we demonstrate the requirement of eRNAs in target gene activation as well as in looping with promoter. We also observed that eRNAs act in sequence specific manner for such functions. Moreover, these eRNAs recruit protein complexes that are regulatory in nature involving the components of nuclear bodies, suggesting that eRNAs help in orchestrating the transcriptional outcomes of the target loci by repositioning it in the three-dimensional nuclear space. Interestingly, high-resolution map of chromosomal chromatin architecture exhibits a dynamic enhancer-enhancer interactome that seems to regulate target genes in hierarchical order via the mechanisms hitherto unknown. These observations warrant a new model of enhancer function that depends on the co-operative strength of other enhancers that presumably in part determined by the protein complexes recruited by eRNAs.
