Abstract of Presentation

Presentation Title

Role of transcription elongation factors and elongation control in differentiation and maintenance of stem cells

Name (Underline the family name)
Yuki Yamaguchi and Hiroshi Handa

Abstract

We have identified and characterized a number of transcription elongation factors, mainly from biochemical perspectives. Particularly, NELF and DSIF induce promoter-proximal pausing of Pol II, and a growing number of genes are found to be subject to this type of transcriptional regulation. Moreover, recent studies by others have provided evidence that, in ES cells, a number of key developmental genes are controlled by the combination of repressive epigenetic marks (e.g., methylation of histone H3 K4 and K27) and promoter-proximal pausing of Pol II.

To understand the physiological significance of transcription elongation factors, we generated Nelf-A knockout mice and found that a complete lack of Nelf-A leads to embryonic lethality shortly after implantation, whereas heterozygous mice appear to be normal. To examine the role of NELF in ES cells more precisely, we established ES cell lines overexpressing Nelf-A in a tetracycline-inducible manner. Consequently, Nelf-A overexpression was found to increase the expression of Oct4 and Nanog, and to increase the proliferation rate of ES cells. Genome-wide analysis for the genomic binding sites of NELF is also underway, and preliminary analysis has identified hundreds of candidate target genes, among which there are many confirmed targets and Oct4. A more detailed study should provide an important insight into the role of transcription elongation factors and promoter-proximal pausing of Pol II in the differentiation and maintenance of ES cells.