第3回 疾患エピゲノムコアセンターセミナー

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Nucleolin is a key protein required for the transcription of genes involved in cell division and proliferation.

Nucleolin (NCL) is a highly conserved protein in eukaryotes enriched in the nucleolar compartment. NCL depletion in the cell induces a quick stop of transcription by RNAPI and a fast arrest of cell proliferation and division. NCL interacts with rDNA chromatin and is required for the maintenance of the euchromatin state and transcription elongation of rDNA. To better understand NCL function in cell proliferation, we performed a ChIP-seq analysis of NCL in HeLa cells and coupled this analysis with a transcriptomic study of the genes that are either up- or down regulated when the expression of NCL is repressed by siRNA. This integrative analysis of NCL ChIP-seq and microarray data show that NCL is present on the promoters of some of the genes that are up- or down-regulated in NCL depleted cells. A search for motif identified the same 10 bp palindromic sequence enriched in both the top up- and down-regulated genes. This motif was previously identified in the promoters of genes involved in cell cycle regulation and protein synthesis. We have also developed a transgenic mouse model that allows the constitutive or inducible inactivation of the NCL gene. Using these models we show that NCL is an essential protein required for early embryonic development and in adult.

Altogether, our data indicates that NCL is a key protein to coordinate the transcription by RNPAI and RNAPII of genes required for cell division and proliferation.

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