Genome-wide study of chromatin remodeling factor CHD8 role in transcription

Alicia Subtil-Rodríguez[1], Elena Vázquez-Chávez[1], Manuel Rodríguez-Paredes[2], María Ceballos-Chávez[1], Jose Ignacio Martín-Subero[3], Manel Esteller[2], Jose C Reyes[1]

1 Andalusian Center for Molecular Biology and Regenerative Medicine (CABIMER-CSIC), Molecular Biology, Sevilla, 41092, Spain.
2 Bellvitge Institute for Biomedical Research (IDIBELL), Cancer Epigenetics and Biology Program (PEBC), Barcelona, 08907, Spain.
3 Biomedical Research Center Esther Koplowitz, CIBEK, Barcelona, 08036, Spain.

CHD8 (Chromodomain-Helicase-DNA binding protein 8) is a member of the chromodomain helicase DNA-binding (CHD) subfamily of enzymes, which also belongs to the SNF2 family of ATP-dependent chromatin remodelers. Previous studies of our group showed that depletion of CHD8 impairs cell proliferation. We also demonstrated that CHD8 controls the expression of cyclin E2 (CCNE2) and thymidylate synthetase (TYMS), two genes expressed in the G1/S transition of the cell cycle. In order to identify CHD8 target genes, in the present study we performed a ChIP-on-chip genome-wide analysis. The results show that CHD8 binds to over 1,900 genes and its recruitment is preferentially located at transcription start site (TSS), first exon and first intron. Remarkably, ChIP-on-chip results show a great correlation between CHD8 occupancy and the presence of histone H3 di- and trimethylated at lysine 4 (H3K4me2 and H3K4me·) activation marks, suggesting that CHD8 is mainly involved in transcription activation.

Interestingly, the analysis of annotated transcription factor binding sites in DNA sequence indicates that a high number of CHD8 target genes are also regulated by E2F, a transcription factor involved in cell cycle regulation.

Ongoing studies will address the functional regulation and implications of CHD8 in coordination with E2F to regulate target genes and cell cycle.