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TPR, chromatin organization, gene expression and cell development

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The area around nuclear pores is enriched in open chromatin. Transcriptional factors and super enhancer sequences localize there during cell differentiation, activating sets of genes specific for a given tissue. Nucleoporin TPR is crucial for the enrichment of open chromatin around nuclear pores, however its role in gene expression and cell development has not been described yet. Here we show that depletion of TPR results in aberrant morphology of murine proliferating C2C12 myoblasts (MB) and differentiated C2C12 myotubes (MT). Our CHIP-seq data revealed that TPR binds to Myosin heavy chain (Myh) gene and majority of olfactory receptor (Olfr) genes in C2C12 MB, and its binding pattern changes upon differentiation into MT. Both Myh and Olfr are expressed in muscle cell and regulate the muscle formation and morphology. We show that TPR affects expression of both Myh and Olfr genes, however in a different manner. Here we discuss possible pathways by which TPR regulates expression of bound genes.

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Effects of selective degradation of the cohesin complex on higher order chromatin structures studied with live cell and super-resolved fluorescence microscopy

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Current models postulate that cohesin is essential for the organization and shaping of the genome into chromatin loops/domains 1. Hi-C data based on large cell populations showed that cohesin loss eliminates all loop domains 2. Here we aimed to investigate the effect of cohesin loss on the preservation/alteration of higher order chromatin structures on the single cell level using super-resolution microscopy and live cell studies. As reference structures we chose replication domains (RDs), first detected in S-phase nuclei as replication foci. RDs stably persist as basic units of higher order chromatin domains (CDs) throughout interphase and during subsequent cell cycles 4. Methods &