# Analysis of the chromatin spatial organization in the human keratin type II gene locus identified potential locus control regions

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Keratins are encoded by 54 genes clustered in two loci at chromosomes 12 and 17. Keratins expression patterns are highly specific for different epithelial cell types and differentiation stages, and are regulated by local microenvironment signals that influence epigenetic state of the keratin loci and activity of individual keratin promoters. Previously, it has been shown that, in mammals, switching of expression pattern within multigene tissue-specific loci are regulated by complex enhancer elements (locus control regions, LCR) characterized by the presence of domains of H3K27ac and H3K4me1 epigenetic marks, binding of numerous transcription factors and chromatin architectural proteins. Here, we applied high-resolution chromosome conformation capture method, C-TALE (Chromatin TArget Ligation Enrichment) to build the map of spatial chromatin organization of 12q13.13 locus in the human epidermal skin keratinocytes at two distinct stages of differentiation. We found that expression switching between keratin 5 (specific for basal epidermal keratinocytes) and keratin 1 genes (actively transcribed in spinous K1/K10-positive keratinocytes) is accompanied by drastic changes in chromatin loop profile inside the locus. Both genes in active state spatially interact with two regions located at 5'- and 3'-flanks of the locus, and loose these contacts upon inactivation. Comparison with publicly available datasets showed that both regions identified possess the features characteristic for LCRs: high level of histone H3 acetylation at K27 position, presence of numerous DNAse I hypersensitivity sites, binding of CTCF and transcription factors involved into keratin transcription regulation. These data potentially denote that transcription switching within keratin gene domain is controlled by two locus control regions forming chromatin loops with active keratin promoters.

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