Synopsis of Original Research Paper

Topological analysis of the transcriptional regulatory regions of the human type I collagen α2 chain (COL1A2) gene

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Previously we have shown the presence of two polymorphic dinucleotide repeats in the human type I collagen α2 (*COL1A2*) gene, one in the 5' flanking region (upstream repeat) and the other in the 1st intron (1st intron repeat) and that the co-presence of these two repeats stimulates expression of the gene, and a specific haplotype of the two microsatellites of the human *COL1A2* gene correlates with susceptibility to systemic sclerosis.

A major part of the DNA double helix within cells exists in the right-handed B-form conformation. Structural transition from the B-form to the left-handed Z-form DNA at dinucleotide repeats is proposed to play an important role in the transcriptional regulation of various genes.

To investigate the association of the change of higher-order structure such as the transition from the B- to Z-form DNA (*B-Z transition*) with the two repeat regions and its role in transcriptional regulation, we performed two-dimensional (2D) gel electrophoretic analyses of constructs containing or not containing the repeat regions. The results indicated that constructs containing both of the repeats led to a structural transition from B- to Z-form but that the construct lacking either of them did not. Additional 2D gel analyses using several constructs containing either of the two repeats showed that this structural transition occurred only in the upstream repeat, but not in the 1st intron repeat. Total number of supercoil relaxation was measured among the constructs with different combinations of several repetitions of the two repeats. The result supported the idea that B-Z transitions occurred only in the upstream repeat regions. Our findings therefore indicate that the upstream repeat region has the ability to convert its conformation from B- to Z-DNA but that the 1st intron repeats did not, although both of the dinucleotide repeats are indispensable for enhancing transcriptional activity of the *COL1A2* gene.