

THE EFFECTS OF COMMON STRUCTURAL VARIANTS ON 3D CHROMATIN STRUCTURE

The 3D chromatin structure consists of chromatin loops and Topologically Associated Domains (TADs), which control physical interactions between genes and regulatory sequences. The cohesin protein complex and the CCCTC-binding factor CTCF localize to the boundaries of TADs. Structural variations affecting such boundaries disrupt gene-enhancer contacts leading to ectopic interactions between promoters and non-coding DNA and have been shown to cause skeletal abnormalities such as polysyndactyly, and craniofacial abnormalities. By Chromatin Conformation Capture (Hi-C) sequencing of 19 lymphoblastoid cell lines from the 1000 genomes project [Shanta and colleagues \(2020\)](#) studied the effects of common structural variations on 3D chromatin structure. They found distinct signatures depending upon the molecular type of the structural variation. Deletions, which remove TAD boundaries and cause TAD fusion would be rare since they may be under negative selection in the general population. Large inversions (e.g. at 8p23.1) have effects on chromatin interactions that span the inversion breakpoints, and are able to affect 3D structures within a 2 Mb distance.