Spacial Organization of Genomes: Insights on coordinated regulation of Biological Pathways

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Human genome sequencing was one of the biggest breakthrough in biomedical history. However, not all the expected information was found in genome linear sequence. It is been widely accepted that genome structure also plays an important role in its function. So the development of chromosome conformation capture (3C) technology and the subsequent genomic variants thereof have enabled the analysis of nuclear organization at an unprecedented resolution and throughput. The technology relies on the original and, in hindsight, remarkably simple idea that digestion and religation of fixed chromatin in cells, followed by the quantification of ligation junctions, allows for the determination of DNA contact frequencies and insight into chromosome topology. Hi-C is an unbiased (all vs. all) chromosome conformation capture technique that generates a list of intra and inter-chromossomal contacts which can help to solve the genomic tridimensional structure. Analysing Hi-C data retrieved from public repositories (like Genome Expression Omnibus - GEO) we aim to identify if genes in spacial proximity have the same regulation and expression patterns. As a model study, we first analyze a K562 Hi-C experiment obtained from GEO (acession number GSE-63525), where we: first - identified intra-cromossomal loops and which genes are in each loop, than we look for inter-cromossomal contact points between those loops. Comparing the correlations between genes locates in loops that are in contact to a random set of genes. A more consistent correlation was identified between genes in spacial proximity than random group. Moreover we identified that some genes - e.g. TIE1 (chr1) and TEK (chr9) - both located near the contact points between chromossomes 1 and 9 - are member of the same superpathways. This patterns indicates that spacial localization of genes may play an important role in the coordinated expression of the protein machinery necessary to a determined biological pathway. As a perspective, we also aim to identify the evolutionary patterns that leads to this intrincated spacial organization.