

2nd International Conference on Genomics & Pharmacogenomics

September 08-10, 2014 DoubleTree by Hilton Hotel Raleigh-Brownstone-University, USA

Chromatin and the three-dimensional organization of the human genome

Istvan Ladunga

University of Nebraska-Lincoln, USA

We present specific complexes of transcription factors and histone remodeling enzymes that are highly correlated with the formation of intrachromosomal DNA loops in the human genome. These DNA-loops bring proximal promoter regions into physical contact with distal enhancers, connect co-expressed genes and genes of locus control regions, and responsible for the three-dimensional organization of the cellular nucleus. Our results are based on published recent high-resolution methods of Chromosomal Conformation Capture (HiC, 5C) have revealed tens of thousands of DNA loops within the human chromosomes. We also used ~45 million binding sites of transcriptional regulators and polymerases based on the chromatin immunoprecipitation experiments of the Encyclopedia of DNA Elements Project. We found statistically highly significant and reproducible enrichment of CCCAT-binding factor (CTCF), double-strand break repair protein RAD21, zinc-finger DNA binding protein ZNF143, Yin-Yang 1, and several others. We found that several interconnected DNA-loops bring highly co-regulated genes into 3D proximity despite large distances in sequence. A detailed analysis of the alpha-globin cluster is presented in both pluripotent embryonic stem cells and lung fibroblasts in human and to some extent, in murine cells. In general terms, we present a correspondence between to co-regulation network of the human genome, the patterns of chromatin modifications, the binding sites of the transcriptional regulators, and the three-dimensional architecture of the chromosomes.

Biography

Istvan Ladunga completed his PhD at the Budapest University of Sciences. He served at the Institute of Computer Science and Automation of the Hungarian Academy of Sciences, the Natl. Committee for Technological Development, Hungary, the Dept. Mathematics, Stanford University, the Dept. Human Genetics, Baylor College of Medicine, SmithKline Beecham Pharmaceuticals, and Celera Genomics. He has published 134 patents and copyrights, 35 papers, and a book.

sladunga@unl.edu