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Looking for chromosome spatial organization rules in microarray gene expression data

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Background

There is increasing interest in how a genome is spatially and temporally organized within the cell nucleus. Evidence supports the idea that basic nuclear functions, such as transcription, are structurally integrated. Several studies demonstrated non-random, gene density- and/or chromosome size-related radial positioning of chromosomes that may provide additional level of gene expression regulation. Chromosome positioning shows probabilistic rather than deterministic nature. We have used the large sets of human gene expression data and rat hippocampi gene expression data from public repositories to explore relations between gene expression and genomic context.

Materials and methods

We have used several approaches to identify clusters of co-expressed genes. A graph-based data-mining approach efficiently identified frequent co-expression clusters in 105 assembled human microarray datasets [1]. Average linkage hierarchical clustering was applied to broad dataset of 79 tissue microarray measurements [2]. K-median clustering grouped high-density oligonucleotide gene array time-series measurements from rat hippocampi with kainic acid-induced status epilepticus [3]. The potential transcription modules have been integrated with gene position and density information. Literature relationship based tools have been used for functional analysis.

Results

We identified and functionally annotated distant genomic clusters within co-expression clusters. The number of such groups of genomic clusters is statistically higher than random. Co-expression clusters contain statistically fewer chromosomes than random. Co-expressed genes from different chromosomes are characterized by similar local gene density. In different expression datasets, different chromosomes do group within co-expression clusters. This has been observed for similar, medium gene-density, low density and acrocentric chromosomes. Analyses are being extended to study of genomic environment of positional clusters within co-expression clusters e.g. transcription factor binding sites, repeats, replication time.

Conclusion

Co-expressed genes show inter-chromosomal groups of positional clusters when analyzing broad data from many tissues as well when analyzing data from individual tissue. Genes from particular chromosomes show higher than random expression correlation. These large-scale microarray data-mining findings enrich our knowledge of the overall organization of human genome and allow interpretation in the nuclear architecture context. Candidate genes for spacial interactions in rat hippocampi will be further examined by in-situ experiments.

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