GENE ORGANIZATION

Revealing relationships

The distribution of genes along chromosomes is not random, but what determines gene order? Building on their previous evidence that broadly expressed housekeeping genes cluster, Martin Lercher and colleagues investigated whether there is an interaction between gene-expression patterns and the mosaic structure of the human genome.

Using a combination of serial analysis of gene expression (SAGE) technology and expressed sequence tag (EST) data to examine gene order and base composition, they found that there was a correlation between how broadly a gene was expressed and the local nucleotide composition of the surrounding genomic area — broadly expressed genes lie in GC-rich regions (isochores). Although GC content has been associated with CpG density and housekeeping genes are often located near to CpG islands, CpG preference alone could not account for this correlation. This work therefore supports the idea that there is a relationship between the expression breadth of a gene and isochores.

The authors also found that R bands and the lightest staining G bands (cytogenetic chromosome bands that contain the most GC-rich regions) were the preferential location for broadly expressed genes, although further work indicated that at least part of this correlation was independent of GC.

So, Lercher and colleagues have provided direct evidence of a relationship between gene-expression patterns and base composition and chromosome structure. Their findings are consistent with an adaptive hypothesis in which selective pressures have driven housekeeping genes to concentrate in genomic regions with structural properties that might facilitate access to the transcription machinery.

In a second paper, Jeanne Lawrence and colleagues also looked at higher level genome organization, in particular at whether specific protein-coding genes cluster together at common nuclear structures.

The authors found that different genes and transcripts can associate with the same SC-35 domain — a domain that is enriched in mRNA metabolic factors — at the same time, even if they are distant from each other on different arms of the same chromosome. This finding is contrary to the idea that metabolic factors accumulate on the transcripts of individual highly active genes.

Lawrence and colleagues saw that the gene-rich early-replicating R bands associated with SC-35 domains more frequently than the gene-poor G bands, and that the association between the R bands and the SC-35 domains was more intimate.

Because of the close direct linkage of some genes with SC-35 domains, the authors suggest that the association of a chromosomal neighbourhood with an SC-35 domain could be influenced by the presence of a highly expressed and spliced gene. And they explain that the gene-rich R bands form more contacts with the SC-35 domains because they have more domain-associating sequences. This work presents a "fundamental and new concept relating nuclear and chromosomal organization" in which SC-35 domains act "…as functional centers for a multitude of clustered genes, forming local euchromatic 'neighbourhoods'."

Natalie Wilson

References and links

ORIGINAL RESEARCH PAPERS Lercher, M. J. *et al.* A unification of mosaic structures in the human genome. *Hum. Mol. Genet.* **12**, 2411–2415 (2003) | Shopland, L. S. *et al.* Clustering of multiple specific genes and gene-rich R-bands around SC-35 domains: evidence for local euchromatic neighborhoods. *J. Cell Biol.* **162**, 981–990 (2003)

FURTHER READING Lercher, M. J. *et al*. Clustering of housekeeping genes provides a unified model of gene order in the human genome. *Nature Genet*. **31**, 180–183 (2002) | Moen, P. T. *et al*. Repositioning of muscle-specific genes to the periphery of SC-35 domains during skeletal myogenesis. *Mol. Biol. Cell* (in the press).

WEB SITES

Jeanne B. Lawrence's laboratory:
http://www.umassmed.edu/cellbio/faculty/lawrence.cfm

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http://www.bath.ac.uk/bio-sci/lercher.htm