Further Reading


Web Links


Opisn 1 (cone pigments), long-wave-sensitive (color blindness, protan) (OPN1LW); Locus ID: 5956. LocusLink: http://www.ncbi.nlm.nih.gov/LocusLink/LocRpt.cgi?l=5956

Opisn 1 (cone pigments), medium-wave-sensitive (color blindness, deutan) (OPN1MW); Locus ID: 2652. LocusLink: http://www.ncbi.nlm.nih.gov/LocusLink/LocRpt.cgi?l=2652


Gene Distribution on Human Chromosomes

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The distribution of genes in the human genome is strikingly nonuniform. Gene density is very high in GC-rich isochores and very low in GC-poor isochores (isochores are long DNA regions characterized by a fairly homogeneous GC level). Since GC-rich and GC-poor isochores can be localized on human chromosomes, this 'chromosomal compositional mapping' provides information on the distribution of genes on chromosomes.

Introduction

Investigations carried out in our laboratory (for a detailed review, see Bernardi, 2002) have shown that the human genome, like those of all warm-blooded vertebrates, is characterized by a strong compositional heterogeneity. Indeed, these genomes are mosaics of long, compositionally fairly homogeneous regions displaying a broad spectrum of GC levels (GC is the molar ratio of guanine + cytosine in DNA). These regions, called isochores for (compositionally) equal landscapes, range in size from 200 kb to several megabases, and are characterized by very low gene densities in the GC-poor isochrome families L1 and L2, which
Gene Distribution on Human Chromosomes

(a) GC-richest bands

(b) GC-poorest bands

Figure 1. GC-richest and GC-poorest human chromosomal bands. (a) GC-richest bands. From left to right of each chromosome group: T, Chromosome A37/DAPI" and H3+ bands (from Saccone and Bernardi, 2001). (b) GC-poorest bands. The left and right member of each chromosome pair shows the Gema bands and the L1 isochore hybridization respectively (from Federico et al., 2000). Biotinylated H3 and L1 isochore were detected with avidin-FITC and chromosomes were stained with propidium iodide. The H3 and the L1 isochore identify the gene-richest and the gene-poorest chromosomal regions respectively. Note the different localization of the two isocore families, near the telomeres for H3 and more internal for L1 isochore.

form two-thirds of the human genome, and by increasingly higher gene densities in the GC-rich isochore families H1, H2 and H3, which form the remaining third. This strikingly uneven distribution of genes in different isochore families, combined with the possibility of hybridizing compositional DNA fractions in situ, provides an approach for investigating the distribution of genes on chromosomes. (See Evolutionary History of the Human Genome; Isochores.)

Gene-richest and Gene-poorest Bands

H3+ and L1+ bands at low resolution

Ten years ago, in situ hybridization of compositional fractions of human DNA on metaphase chromosomes (Saccone et al., 1992), under suppression of signals from repeated sequences (Alu, LINES), showed that the H3 isochore family produced the highest concentration of signals on a small number of R(verse), or G(iesma)-negative bands. These bands largely coincided with two previously defined group of bands:

- the T(elomeric) bands of Dutrillaux (1973), which are among the most heat-denaturation-resistant R bands and which are located prevalently in telomeric positions, and
- the chromomycin A3-positive/DAPI-negative bands described by Ambros and Summer (1987), which are the GC-richest bands of human chromosomes (Figure 1a).

Our results were of interest because they showed that these two sets of bands were not due to some satellite or repeated sequence DNA. In fact, they corresponded to the regions of human chromosomes with the highest gene concentration. Moreover, the R bands that contain H3 isochores, the H3+ bands, replicate at the onset of the S phase, whereas the R bands containing no detectable amount of H3 isochore, the H3- bands, replicate later; G bands replicate even later (Federico et al., 1998, 2000). (See Chromosomal Bands and Sequence Features; Genome Organization.)

If GC-poorest, gene-poorest L1 isochores are hybridized on metaphase chromosomes, the result that is obtained is very similar to that of a G banding, and a large number of hybridized bands (called L1+ bands) coincided with the darkest G bands (Figure 1b). The data described so far concern the standard 400 band karyotype.

H3+ and L1+ bands at high resolution

If a higher, 850 band resolution is analyzed by using prometaphase chromosomes, it is clear that the bands displayed at low resolution are compositionally very heterogeneous. This is very evident in the case of the GC-richest chromosomes 19 and 22: at low resolution, these chromosomes are completely covered by the H3 hybridization signals, but, at higher resolution, show bands that do not contain H3 isochore (Figure 2). In fact, a chromosomal band at a resolution of 400 bands per haploid genome (R600 and G600 bands) is generally composed of more than two bands at a

Figure 2: Resolut chrom 400, T
resolution of 850 bands per haploid genome (R_{580} and G_{380} bands). For example, the H3^+ band 11q13 (Figure 3) is composed, at higher resolution, of five bands and more precisely of three R_{580} sub-bands (q13.1, q13.3 and q13.5) and two G_{380} sub-bands (q13.2 and q13.4). Thus, H3^+ bands comprise not only R_{580} sub-bands containing H3 isochores, but also G_{380} sub-bands not containing H3 isochores (Figure 3). Moreover, a number of other H3^+ bands showed that only one of the R_{580} bands derived from each one of them contained H3 isochores, as in the case of the H3^+ band 11q23 that yielded only one R_{580} band, 11q23.3, containing H3 isochores (more specifically the distal part of it), whereas the other R_{580} band 11q23.1 and the G_{380} band 11q23.2 do not exhibit H3 isochores (Saccone et al., 1999).

In the case of G banding, at an 850 band resolution, four different types of G bands (on the basis of the degree of staining intensity) were described (Francè, 1994). They were called G1, G2, G3 and G4 bands, from black to pale gray (Federico et al., 2000). In situ hybridization of the GC-poorest L1 isochores indicated that this isochores family is only located on a subset of G bands, which largely corresponded to the G1 and G2 bands (Federico et al., 2000; Figure 3).

Gene Density and Chromosomal Bands

To sum up, human chromosomes comprise four sets of bands: R bands may be very GC-rich (the H3^+ bands) or have a modest GC-richness (the H3^- bands); G bands may be very GC-poor (the L1^+ bands), or have an intermediate GC level (the L1^- bands; Figure 3). Interestingly, the GC-richest bands are preferentially located on telomeric regions and the GC-poorest bands in internal regions of chromosomes (Figure 1).

As far as gene concentration is concerned, H3^+ bands contain more than 15 genes/Mb, with some subregions higher than 30 genes/Mb, whereas the L1^+ bands contain less than five genes/Mb, with some subregions containing one or less genes/Mb (Saccone et al., 2001). This is shown by comparing L1^+ and H3^+ bands with the compositional maps of chromosomes as obtained from the draft human genome sequence. (See Chromosomes 21 and 22: Gene Density.)
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This striking distribution of the GC-richest and the GC-poorest DNA is associated not only with the very different GC levels and gene densities, but also with other features. In fact, the former replicates earlier, is characterized by a more open chromatin, and is more recombinogenic and transcriptionally active compared with the latter. This nonhomogeneous distribution of genes in the chromosomes (and in the nuclei) was also observed in other mammalian and avian species, indicating their conservation in the evolution of chromosomes. (See GC-rich Isochores: Origin; Isochores.)

See also
Chromosomal Bands and Sequence Features
Chromosomes 21 and 22: Gene Density
GC-rich Isochores: Origin
Isochores
1. Isochore Map: Gene-poor Isochores

References


Further Reading


Gene Duplication: Evolution

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Gene duplication is the major source of genetic novelties, because a duplicate copy may be free to change to a new function. Indeed, genome sequencing and statistical analyses have revealed that each eukaryotic genome contains numerous duplicate genes. Furthermore, there is evidence that a genome duplication occurred in the common ancestor of vertebrates and this might have been important for the diversification and organismal complexity of vertebrates.

Introduction

The evolutionary significance of gene duplication was first recognized by Muller (1935), who suggested that a redundant duplicate gene may acquire divergent mutations and eventually emerge as a new gene. However, few examples of duplicate genes were discovered before the advent of biochemical and molecular biological techniques. The development of protein sequencing methods in the 1950s provided a tool for the study of long-term evolution, and by the late 1950s the α and β chains of hemoglobin were recognized as duplicate genes (Rhinesmith et al., 1958; Braunitzer et al., 1961). Later, isozyme and cytogenetic studies added further evidence for the frequent occurrence of gene duplication in evolution (e.g. Markert, 1964; Harris, 1966; Ritossa et al., 1966). Using data from these various types of studies, Ohno (1970) put forward the view that gene duplication is the only means by which a new gene can arise. Although other means of creating new genes or new functions are now known (see Li, 1997), Ohno's view remains largely valid.

Since the late 1970s, there has been ample evidence that gene duplication is the most important mechanism for generating new genes and new biochemical