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Genetic Polymorphism

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Synonyms

SNP; Single nucleotide polymorphism

Definition

The human DNA is exposed to a number of changes, these changes are frequently carried out in one or few nucleotides called mutations, which can be caused by errors in the mechanisms of DNA replication and repair as well as by environmental factors; and these mutations can have deleterious effects and cause disease. These mutations can result in polymorphisms that provide allelic variation between individuals and diversity of species; to be considered as such its frequency should be higher in one of its alleles at 1%.

Introduction

Since the discovery of the polymerase chain reaction (PCR) began in the 1990s, the Human Genome Project which aimed to completely sequence the human DNA published in 2001 a first draft (Lander et al. 2001; Venter et al. 2001) to 2004 published new results delivering 99% sequence of the human genome. These developments show that the human genome consists of 2.85 billion nucleotides, packaged in two sets of 23 chromosomes, one set inherited from each parent. Human DNA appears to encode only 20,000–25,000 protein-coding genes. Were also revealed the existences of ten million single-nucleotide polymorphisms (SNPs) (Hattori 2005).

The Variation in the Human Genome

The human DNA is exposed to a number of changes which can be translated or not in the onset of disease; these changes are frequently carried out in one or few nucleotides called mutations, which can be caused by errors in the mechanisms of DNA replication and repair as well as by environmental factors; and these mutations can have deleterious effects and cause disease. These mutations can result in polymorphisms which provide allelic variation between individuals and diversity of species; to be considered as such its frequency should be higher in one of its alleles at 1% (Brookes 1999).

Individual phenotypic variability and individual susceptibility or resistance different diseases are mostly due to the SNPs and in a lesser degree

V. Zeigler-Hill, T.K. Shackelford (eds.), *Encyclopedia of Personality and Individual Differences*,
DOI 10.1007/978-3-319-28099-8_754-1

insertions, deletions, repeated sequences, and/or chromosomal arrangements.

In general it is believed that the genes were almost always present in two copies in a genome. However, recent discoveries have revealed that large segments of DNA ranging from thousands to millions of bases can vary in copy number. These copy number variations (CNVs) may include genes that lead to imbalances. For example, now found genes believed that always occur in two copies per genome become sometimes present in one, three, or more than three copies; in some rare cases the genes are missing altogether.

Applications of the study of polymorphisms are diverse and, on the one hand, are used for try to explain the origin of the populations to rebuild part of their evolutionary history. On the other hand, they are widely used in fields such as medicine and the study of complex diseases.

Single-Nucleotide Polymorphisms (SNPs) and GWAS

For the study of complex diseases have used the approach genome-wide association studies (GWAS), which is a high-performance methodology that allows geneticists to scan a large set of SNPs (≈0.1–5 million SNPs) that extend throughout the human genome in an unbiased way, using powerful statistical methods to study the associations between a disease phenotype and a representation of all common variations in the genome. These SNPs are not considered causal, but function as a label of the variation of a common haplotype in a particular region of the human genome (A global reference for human genetic variation 2015).

Successful approach GWAS was made possible by the HapMap project, a large-scale effort that has extensively characterized the variation of the human sequence(Hirschhorn and Daly 2005; The International HapMap Consortium 2005) in addition to the development of high-density genotyping arrays gives a score of alleles for a large number of SNPs in parallel across the genome(International and Consortium 2003; Manolio and Collins 2009).

Because they do not have a prior hypothesis in the GWAS, you may discover new insights into the biology of a given phenotype, without any prior knowledge of its function; since it came on the scene in late 2005 which has found a number of loci for various diseases, for now the challenge is to understand the biological mechanisms underlying these loci and the way they confer risk for certain diseases.

Another challenge is that the design approach GWAS is based on the common disease, with a hypothesis common variant, where it is postulated that the genetic component of complex diseases is largely attributable to a moderate number of common variants, each which only accounts for a small proportion of risk in a population. An example of this is that we have identified many loci for obesity; however, it explained very little of the apparent heritability −10% of estimated heritability has been explained by the more complex traits before using GWAS; therefore, there is much debate about what missing heritability of most complex diseases; it has been hypothesized that this shortfall is made up of much rarer variants, copy number variants (CNVs), and epigenetic changes that are not detected in the bandwidth of GWAS.

Current product genotyping arrays available in the market are generally based on the HapMap and only provide complete coverage of common variants with minor allele frequency greater than 5%.

Copy Number Variants

The copy number variants (CNVs) are products of genomic rearrangements, resulting in deletions, duplications, inversions, and translocations.

Current studies reveal that CNVs comprise at least three times the total nucleotide content of SNPs. Since CNVs often include genes that may play a role in both human disease and drug response (Weber and Wong 1993). Understanding the mechanisms of formation of the CNV can also

help better understand the evolution of the human genome.

Identifying the global map of CNV may have different implications in medical research, such as the identification of genes associated with common diseases, as with the technologies used to date had not been integrated into their analysis.

As studies of SNPs, the mapping of CNV can be used in family studies; the data generated will also contribute to a reference sequence of the most accurate and comprehensive used by all biomedical scientist human genome.

Conclusions

New DNA sequencing technologies that allow rapid and low cost – of expected – in conjunction with sequencing projects "personalized" genome may be the future to capture most of the variation in the human genome.

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