The Egyptian Journal of Medical Human Genetics (2014) 15, 99–101

Ain Shams University

The Egyptian Journal of Medical Human Genetics

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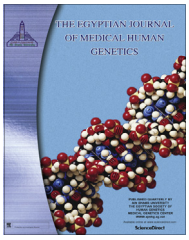

EDUCATIONAL CORNER OF THE ISSUE

Basic concepts of medical genetics, formal genetics, Part 1

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Received 23 October 2013; accepted 26 October 2013
Available online 15 November 2013

KEYWORDS

Formal genetics;
Genetic maps;
Structural genomic maps;
Functional genomic maps;
Experimental genetic maps

1. Basic concepts of formal genetics

The definition of formal genetics is still a matter of contention. However, it can be defined as a branch of basic genetics concerned with deducing and figuring out relevant genetic data from constructed figures that contain specific genetic information. These informative figures include, for instance, constructed family pedigrees, linkage maps and chromosomal maps. Many aspects of applied and clinical genetics have been clarified by analysis of information databases collected from studies of formal genetics of certain diseases and of specific experimental researches, e.g. construction of chromosomal maps of gene loci based on information gathered, formerly, by human–mouse hybridization studies, and currently by in situ hybridization experiments. Progress in disclosing interspecies genetic similarities and dissimilarities, which represent major targets of research of comparative and evolutionary genetics, depends largely on species-specific genetic databases that are gathered and analyzed within the context of formal genetics [1]. Although clinical maps composed of pathognomonic combinations of signs, symptoms and specific pathological findings pointing to specific disease entities represent the simplest of formal genetic maps, they are not considered, strictly, of formal genetic concern. However, when compared to, and analyzed with, other informative maps, like linkage maps and chromosomal maps, clinical maps have major diagnostic significance in recognition and localization of undefined genes underlying, and possibly involved in, pathogenesis of certain disorders and malformations.

2. Scope of formal genetics

Formal genetics is confined to studying genetic maps, whether represented as figure or text interface data. Relevant aspects of formal genetics pertaining to medical genetics include genealogical study and analysis of data provided by the family pedigree, delineation of classical/traditional/Mendelian and non-classical/non-traditional/non-Mendelian patterns of inheritance, construction and analysis of structural and functional genomic/transcriptomic/proteomic maps, chromosomal maps, maps of gene loci, linkage maps, association maps, genomic structural variants (SVs) maps and experimentally induced and constructed maps, which comprise many types like restriction fragment length polymorphism maps, radiation hybrid

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Peer review under responsibility of Ain Shams University.

Production and hosting by Elsevier

http://dx.doi.org/10.1016/j.ejmhg.2013.10.001

Table 1 Scope and applications of common formal genetic maps.

Type of genetic map	Relevance to medical genetics
1. Family pedigree	Genealogical study reveals pattern of inheritance, type of genetic disease, participation of non-genetic factors in pathogenesis of the disease, etc.
2. Structural genomic (DNA) maps	Provide information on number and distribution of unique genic and unique tandem repeats of non-genic parts or domains of DNA, intergenic regions and repetitive sequences, gene density, etc.
3. Functional genomic maps	Provide information on distribution of functional genic sequences, non-functional sequences like pseudogenes and duplicated non-functional genes, transposons, pyknons, mutable hot spots of DNA, imprinting centers, etc.
4. Genomic structural variants (SVs) maps	Reveals human genetic variations and their possible linkage with specific human diseases. Also, they are of particular significance in many fields of study of comparative and evolutionary genetics
5. Ribonucleic acids (RNA) maps	Constituent databases of structure and function of different types of RNA: messenger RNA (mRNA), ribosomal RNA (rRNA), transfer RNA (tRNA) and different species of small or microRNAs
6. Transcriptome maps	Provide databases of (mRNA): structural variations, rates of transcription, of translation and of turnover and decay. Differential characteristic alterations of post-transcription modifications in specific disease states. Comparative analysis of mRNA maps can reveal possible causative gene mutations as well as possible underlying pathogenetic mechanisms
7. Chromosome maps	Reveal details of chromosome topology, e.g. type of chromosome, gene loci, distribution of telomeres and of ribosomal gene repeats, chromatin type and variations, etc.
8. Gene maps	Clarify the size, base sequence, number of exons and introns, distribution of hot spots and of CG sites, sequence type and organization of promoter region of the gene, etc.
9. Proteome maps	Depict constituent structural and catalytic proteins. Specific proteome maps can be constructed for specific states, e.g. oncoprotein maps of malignant cells. These can further be classified and delineated according to specific tumor type, e.g. oncoprotein map of hypernephroma, of multiple myeloma, etc.
10. Linkage maps	Reveal recombination frequency of different types of genetic markers, e.g. genes – traits – proteins – DNA markers, for identifying location of genes relative to each other on chromosomes, etc.
11. Haplotype maps	Provide comparative data about inter-individual single nucleotide polymorphism to determine the likely locations and haplotypes involved in pathogenesis of, or predisposition to, specific diseases, reveal presence and incidence of linkage disequilibrium of certain haplotypes, etc.
12. Inter-species hybridization maps	Allow for assigning or (mapping) specific genes to specific chromosomes and even to certain chromosome segments
13. Restriction fragment length polymorphism (RFLP) maps	Used for diagnosis of point mutations that alter a restriction site, and for comparative purposes, e.g. paternity testing
14. Radiation hybrid maps	Provide data about relative positions of specific genic and DNA markers on specific chromosomal regions based on frequency of chromosomal breakage induced by radiation
15. Probe-specific maps	Reveal widespread inter-individual as well as inter-species and intra-species genomic and transcriptomic differences, provide critical data for population, comparative, experimental and evolutionary genetic studies and researches
16. Genotype maps	Correlate specific genotypes with specific disease states, thus providing crucial information relevant to provisional clinical diagnosis, effective prophylactic management and genetic counseling
17. Phenotype maps	Depict pathognomonic diagnostic combinations of disease-specific signs and symptoms for genetically-determined and genetically-mediated disorders

maps, inter-species hybridization maps and probe specific maps (Table 1). Analysis of formal maps of specific DNA markers, which include single nucleotide polymorphism, microsatellite polymorphism and tandem repeat polymorphism maps, in addition to many others, provide fundamental information crucial for framing better and proper understanding of the structure and function(s) of the human genome, transcriptome and proteome [2].

3. Formal genetic maps

As referred to, genetic maps (Table 1) are databases represented as text or graphic interface figures aimed at providing important, beneficial and crucial clues relevant to nearly all fields of human genetics including medical genetics [3].

4. Applications of formal genetics

The bioinformatics databases represented as, and included within, different types of formal genetic maps have a wide range of applications in many fields of basic, clinical, diagnostic, therapeutic, prophylactic and applied genetics. Construction of the family pedigree of patients with genetic diseases or of families seeking counseling advice, and genealogical analysis of history, clinical and other types of data represented by its informative symbols, to derive relevant genetic information, like possible pattern of inheritance, and to calculate recurrence risk figures in future offspring, constitutes the first step in approaching patients and families having genetic disorders, and represents the simplest and most direct of these applications [4].

Progress in analysis of structural organization of the human genome generates a flood of information leading to characterization of new formal maps of specific DNA markers and regions of both structural and functional significance. These maps represent bioinformatics databases that can have crucial impact on many aspects of basic as well as of clinical medical genetics. For instance, exome maps comprising detailed information of exons of genes can be constructed and used for both intra and inter-species comparative purposes. Similarly, within the context of pathogenetics, comparison of exome maps of patients with specific idiopathic genetic disorders with those of normal subjects represents a revolutionary promising approach that can have many diagnostic applications in clinical genetics. Other types of molecular maps that can be constructed based on available as well as on the rapidly accumulating databases of human genome structure, e.g. introme maps, pyknon maps, transposon maps, telomere maps and maps of pseudogenes, can also have a wide spectrum of applications in many fields of medical genetics [5].

The significant beneficial effects and applications of structural genetic maps in different fields of medical genetics call for construction of parallel databases of functional genetic maps that characterize critical functional markers and transcriptionally active regions and sequences of the human genome. Examples of such functional maps can, possibly, include proteome maps comprising both structural protein and enzyme, or catalytic, protein databases. Comparative analysis of these functional protein maps in normal subjects and in patients affected with specific genetically-determined disorders and idiopathic diseases caused by, still, unidentified etiological mechanisms, might prove helpful in revealing the underlying patho-proteomic abnormalities responsible for development of the specific pathophysiological alterations that characterize the clinical phenotype of each of these diseases. In addition, in a way similar to that of reverse engineering, comparative analysis of normal and abnormal proteome maps of specific genetic disorders can disclose underlying pathogenetic mechanisms, patho-transcriptomic differences and causative genetic mutations possibly involved in mediating the pathogenesis and development of these disorders.

References

[1] Pierce Benjamin A. Genetics. A conceptual approach. 2nd ed. Gordonsville, VA, USA: W.H. Freeman & company; 2005.
[2] Anthony Griffiths JF et al. Introduction to genetic analysis. 9th ed. Gordonsville, VA, USA: W.H. Freeman & company; 2007.
[3] Eberhard Passarge. Color atlas of genetics. 3rd ed. Stuttgart, New York: Thieme; 2007.
[4] Rédei GP. Encyclopedia of genetics, genomics, proteomics and informatics. 3rd ed. New York, USA: Springer; 2008.
[5] Alberts B et al. Molecular biology of the cell. 4th ed. Hamden, CT, USA: Garland Science; 2002.