The Egyptian Journal of Medical Human Genetics (2016) 17, 1–23

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The Egyptian Journal of Medical Human Genetics

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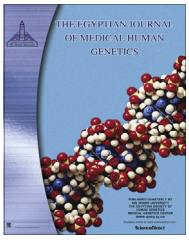

REVIEW

Pathogenetics. An introductory review

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Received 1 July 2015; accepted 7 July 2015
Available online 27 July 2015

KEYWORDS

Pathogenetics;
Mutagens;
Mutation;
Pathogenetic mechanisms;
Anti-mutation mechanisms

Abstract Pathogenetics refers to studying the different aspects of initiation/development/progression and pathogenesis of genetic defects. It comprises the study of mutagens or factors capable of affecting the structural integrity of the genetic material leading to mutational changes that, in the majority of cases, result in harmful effects due to the resulting disturbances of functions of mutated components of the genome. The study of mutagens depicts different types of mutagenic factors, their nature, their classification according to their effects on the genetic material and their different modes of action. The study of mutation involves different types of mutations classified according to various parameters, e.g. magnitude, severity, target of mutational event as well as its nature, which can be classified, in turn, according to whether it is spontaneous or induced, static or dynamic, somatic or germinal mutation etc. Finally, pathogenetics comprises studying and delineating the different and innumerable pathophysiological alterations and pathogenetic mechanisms that are directly and indirectly involved in, and leading to, the development of genetic disorders, coupled with a parallel study of various anti-mutation mechanisms that play critical roles in minimizing the drastic effects of mutational events on the genetic material and in effective protection against the development of these diseases.

Contents

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Peer review under responsibility of Ain Shams University.

http://dx.doi.org/10.1016/j.ejmhg.2015.07.002

1. Definition

Pathogenetics encompasses studying the various factors and different mechanisms involved in the pathogenesis of genetic diseases. It comprises the study of mutagens or factors that can cause change and/or damage of the genetic material, the study of mutations or acquired structural/functional changes of the genetic components at any of its organizational levels that result secondary to the effects of mutagens, the study of the various anti-mutation mechanisms of the human genome/transcriptome/proteome that exert an essential and pivotal role in maintaining the integrity/stability/identity of the genome, the study of the different and varying pathophysiological alterations in cellular functions secondary to the ensuing disturbances of the metabolic-regulatory networks that mediate and control these functions, and the study of the different pathogenetic mechanisms that mediate the development and pathogenesis of genetic defects due to the ensuing changes of the normal structure/function framework of the genetic material.

2. Pathogenesis of genetic diseases

Genetic diseases are caused by harmful mutations. Mutations cause structural changes and consequent functional alterations of the affected components of the genetic material, leading ultimately to a deficient synthesis of proteins or synthesis of defective proteins necessary for mediation of cellular activities. These functional consequences are reflected in disturbed/defective construction of one or more of the metabolic networks that regulate every aspect of cellular functions. As depicted from the cardinal dogma of molecular biology, mutated genome results in the transcription of altered transcriptome which, in turn, causes synthesis of a defective proteome. The defective proteome leads to wide spread pathophysiological alterations that pave the way for the development of various pathogenetic mechanisms responsible for initiation and pathogenesis of genetic disorders. The spectrum of pathophysiological alterations and pathogenetic mechanisms is quite wide and is steadily expanding as more knowledge of the structure/function/behavior/regulation of the genetic material is revealed. However, the basic etiological outline of development of genetic defects, as depicted in Fig. 1, can be summarized as follows (Fig. 1):

(1) Deletion or loss of part of a gene, one or many genes, part of a chromosome, one or more chromosomes, one or more of mitochondrial genes, or even a whole genome.
(2) Duplication/rearrangement of the genetic material.
(3) Deficient/defective transcription of mRNA.
(4) Deficient/defective post-transcriptional modifications of mRNA.