e-ISSN: 2322-0139
p-ISSN: 2322-0120

RESEARCH AND REVIEWS: JOURNAL OF PHARMACOLOGY AND TOXICOLOGICAL STUDIES

Commentary on Epigenetics role in Human Diseases

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Commentary

Received: 18/05/2015
Accepted: 20/05/2015
Published: 31/05/2015

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Keywords: Epigenetics, DNA methylation, genomic expression, Phenotype, pathogenesis

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The predominant epigenetic mechanisms consisting of DNA methylation, chromatin modifications and non-coding RNA have huge and chronic effects on health and aberrations in these processes will typically contribute to disease [1-4]. However, various advances in epigenetic-based disease prevention and therapy are on the horizon and will revolutionize medication and clinical practice [5-7].

Epigenetics is that study of heritable changes in genomic expression that are not created by modification of gene nucleotide sequences. There is increasing evidence that epigenetic changes are necessary within the etiology or progression of a large range of diseases [8-12]. The technologies available to examine the mechanisms and consequences of epigenetic modifications have risen exponentially. The stimulant for this has been the rapid increase in our understanding and appreciation of the importance of epigenetic changes on phenotypes and in the etiology of diseases, allied to technological breakthroughs that have created it possible to undertake large-scale epigenomic studies. This chapter summarizes number of the contemporary methods used to study epigenetics and highlights new techniques and strategies that have significant potential for future epigenetic and epigenomic studies [13-16].

The dysregulation of genes is in many instances responsible for the initiation and development of cancers of various origins. However advanced analysis of cancerous cell genomes provides insights to possibilities other than mutations that favor a tumorigenic phenotype [17-21]. Epigenomic studies have shown that gene expression can be regulated independently of the DNA sequence by modifying specific bases or chromatin residues and the changes are central to tumorigenesis. The epigenetic marks are heritable and reversible and consequently enzymes that regulate these changes are potential targets for cancer therapy. Inhibitors of epigenetic enzymes can restore the gene expression imbalances set by the epigenetic marks, restoring pathways that initiate cellular differentiation and apoptosis necessary to inhibit tumor. Enzymes such as the DNA methyltransferases (DNMTs), histone acetyltransferases (HATs), histone deacetylases (HDACs), histone methyltransferases and histone demethylases that regulate epigenetic pathways through drug-based inhibitors.

Epigenetic modifications are essential throughout development and postnatal life. Some of these modifications are inheritable and modulate gene function in the offspring, whereas alternative epigenetic modifications regulate gene function without being inherited [22,24]. Aberrations in these modifications lead to abnormal development, even life threatening and a wide variety of disease conditions which include cancer. Machinery that establishes, maintains, and modifies the epigenetic patterns is fairly complex, involving hundreds of proteins [25-28]. Because of the central role played by epigenetic

machinery in development, one would expect many neurodevelopmental disorders related to mutations in genes encoding. Research on those mutations will reveal the role of epigenetics in neurodevelopment [29-31].

Common severe neurobehavioral diseases, like schizophrenic psychosis, bipolar disease, and autism spectrum disorder (ASD) arise from a combination of genetic and environmental factors that impact and are impacted on by the epigenome. All phenotypes as well as disease have epigenomic components. Abnormal functioning of the epigenetic mechanisms causes many congenital neurobiological disorders. Recently, environmental factors, such as nutrition, drugs, and psychological pressure, have been viewed to result to epigenetic changes. Furthermore, epigenetic changes caused by environmental stress in adolescence will persist through adulthood and should be transmitted across generations [32-34].

Autoimmune disorders are also characterized by strong environmental determinants. Epigenetic profiles in cells are influenced by environmental conditions additionally as by aging, reinforcing the observed relationship between age, environmental factors, and pathology development. Additionally, women are characterized by a more incidence of autoimmune diseases, probably related with X-chromosome inactivation, a vital epigenetic event [35].

Obesity is one of the chronic debilitating multisystem diseases due to environmental influences on present living style, such as food and exercise, on overweight liability indicate a strong role for non-genetic factors. Few overweigh disorders and the modulation of phenotype by diet in mouse models have hinted at these epigenomic possibilities [36].

Epigenetic regulation has been clearly implicated in the aetiology of some human disorders. Epigenetics plays major role in the origins and expression of mental disorders. The total life span of human, the brain remains flexible as well as responsive. Many functions of brain are accompanied at the cellular level by changes in gene expression. Epigenetic mechanisms like histone alterations and DNA methylation stabilize gene expression, which is important for long-term storage of information. Some drugs that are used to treat mental illness work by changing gene expression. Those modifications ocur in gene expression are stabilized through epigenetic mechanisms (DNA methylation and histone modification), reversing the effects of the disease [37].

Type-2 diabetes is a polygenic, multifactorial disease characterized by hyperglycemia due to impaired insulin secretion and action. Epigenetic mechanisms, further as polymer methylation and histone modifications, may provide a link between environmental factors and also the genome, and thereby affect the risk for type-2 diabetes. Current research has shown that non-genetic risk factors for type-2 diabetes, like aging, overweight, and less immunity power, are associated with epigenetic changes in target tissues for the disease [38]. Moreover, patients with type-2 diabetes show differential DNA methylation compared with non-diabetic individuals, proposing that epigenetic mechanisms may play a main role within the pathogenesis for the disease [39].

Cardiovascular diseases, like atherosclerosis and heart disease, are major public health issues and leading causes of mortality within the world. Several risk factors for the disease, e.g. smoking, hyperlipidemia, and high blood pressure, have been identified, however the mechanism of the disease development remains processed [40-44]. Epigenetic modifications in cardiovascular system identified the crucial role within the pathogenesis of cardiovascular disease [45]. Epigenetic modification will directly or indirectly influence vascular cell growth, migration, and apoptosis. Some microorganisms like bacterial and viral infections frequently cause epigenetic alterations in host cells [46-49].

Epigenetic factors like DNA methylation plays major role in gene expression regulation. Defects in DNA methylation might result in disorders affecting embryogenesis, genomic desgin and cancer. Epigenetics could be a quickly developing area of human genetics [50-56]. In the same approach that sequencing the human genome has accelerated analysis into inherited diseases and cancer, it is anticipated that initiatives to stipulate the normal human epigenome will enhance progress towards higher understanding of the role of epigenetics in human disease [57-60].

Acknowledgement
I would like to acknowledge the support of my colleagues Rakesh M, Sateesh V in assisting with proper guidance. This content is reviewed and approved by Murali M.

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