ACTA SCIENTIFIC MICROBIOLOGY (ISSN: 2581-3226)

Volume 2 Issue 4 April 2019

Review Article

Translational Research – Emerging Epigenetics: A Glowing Gamut Beyond Genetics

S Jeelani[1]*, Amirthaa Priyadharscini R[2] and K Abdul Khader[3]

[1]Reader, Department of Oral Medicine and Radiology, Sri Venkateshwaraa Dental College, Puducherry, India

[2]Senior Lecturer, Department of Oral Pathology and Microbiology, Sri Venkateshwaraa Dental College, Puducherry, India

[3]Senior Lecturer, Department of Oral Medicine and Radiology, Sri Venkateshwaraa Dental College, Puducherry, India

***Corresponding Author:** S Jeelani, Reader, Department of Oral Medicine and Radiology, Sri Venkateshwaraa Dental College, Puducherry, India.

Received: February 18, 2019; **Publication:** March 14, 2019

Abstract

Genetics pioneered by Darwin is an aspiring field of science with remarkable exploration of human existence in health and disease. Interestingly epigenetics is a reflection of Lamarckism wherein various mechanisms related to gene expressions and functions are heritable but with seldom any changes in the DNA sequence. DNA methylation, histone modification, chromatin remodeling and microRNA are the notable mechanisms associated with epigenetics. Alterations in DNA Methylation in the form of hypo methylation or hyper methylation with an impact on proto oncogenes and tumor suppressor genes serve as ideal molecular markers to assess risk, arrive at diagnosis in incipient stages, propose epigenetic based treatment strategies, plan preventive measures and ultimately contribute to the prognosis of the cancer. The role of epigenetics has been extended to explore pathologies related to psychiatry, autoimmune diseases and also in the form of nutrient epigenetics. Thus genes and environment are inseparable part of any human condition and ultimately life as a whole. This article is a tip of the iceberg reflecting translational research with respect to epigenetics.

Keywords: Epigenetics; DNA Methylation; Cancer

Introduction

Cell is the basis of life and the life of cell has interesting curves with balanced check points. Genes play an invaluable role in the identity and functions of cell. Healthy cells live in harmony with the environment. At occasions the impact of environment on genes play a pathetic role in the phase of pathologies especially of unknown origin. Garrod applied the knowledge of genetics to human pathologies around a century back [1]. Contrary to the conventional genetics, Epigenetics is the study of changes in gene activity that do not envisage alterations in the genetic code but still get passed down to atleast one successive generation [2].

Epigenetics is the most important discovery in science of heredity since the gene which has opened new vistas to the understanding of heredity and genetic sciences.

Historical background

Some geneticists quietly acknowledged the emergence of epigenetics as the resurgence of Lamarckism – contradictory to Darwin's theory of evolution where John Baptiste De Lamarck explained this theory through a simple example that animals acquired certain traits during their life time because of their environment. The most interesting example of Lamarckism is of giraffes which are stated to have acquired their long neck as their recent ancestors used to stretch their necks to reach high nutrient rich leaves [3].

Holiday in mid-1990s mentioned the significance of DNA methylation in gene expression [4,5] and Strohman in 1995, emphasized on epigenetic regulation in along with the genome to understand unresolved complex pathologies [6].

Epigenetics

Epigenetics derived from the Aristotelian word 'epigenesis,' pioneered by Conrad Waddington who in 1940 considered Epigenetics as the blossoming scientific field and branch of biology which deals with causal interactions between genes and their products which bring the phenotype into being [7]. Recently epigenetics has been defined as the study of changes in function of genes that are inheritable but without a change in DNA sequence [8].

In the broader sense it implies "on top of or in addition to genetics. It also deals with mechanisms or pathways that initiate and maintain heritable patterns of gene expression and gene function without changing the DNA sequence [9].

Also interestingly genome is different from that of epigenome in that genome defines the complete set of genetic information contained in the DNA of an organism, whereas epigenome refers to the complete set of characteristics of epigenetic pathways in an organism [10].

Mechanisms in epigenetics

DNA methylation, histone modification, nucleosome remodelling, and non-coding RNA-mediated pathways are the different mechanisms associated with epigenetics.

DNA methylation

DNA is the identity of life. Cytosine is one of the five nucleotides in the nucleic acids of DNA and RNA. When a methyl group is covalently added to the fifth carbon of the cytosine ring to form 5-methyl cytosine it is referred to as DNA methylation. CpG sites are DNA sites where a cytosine is followed by and linked via a phosphate to guanine, another nucleotide and denser sites are referred to as CpG islands. The significance of these islands is that these are prominent regions associated with DNA methylation. The function of cells and the differentiation of cells are regulated by DNA methylation. Excessive and insufficient DNA methylation can cause undesirable cellular changes leading to pathologies.

Histone modification

Gene expressions related to transcription are mediated by histones which are globular proteins influencing the integrity of chromatin during transcription. Improper gene expressions resulting from modifications of histones due to addition or deletion of methyl, acetyl, phosphate or ubiquitin groups which in turn can terminate in pathologies [11].

Chromatin remodeling

Chromatin plays a key role for packaging and condensing genomic DNA and in directing the control of the accessibility of DNA for transcription. Chromatin remodelling is an important mechanism associated with epigenetics. The structure of chromatin is assembled through four complexes namely switch mating type/sucrose nonfermenting (SWI/SNF), imitation switch, chromodomain helicase DNA binding and INO80 complexes. Amongst it SWI/SNF complex plays a key role in cellular differentiation, proliferation, DNA repair and replication [12]. It is also involved in immune responses [13] and carcinogenesis [14] and in the prevention of obesity.

MicroRNA

A new class of regulatory molecules that are 18–23 nucleotides in length are MicroRNA which regulate gene expression by translational repression and control DNA methylation and histone modifications [15]. Carcinogenesis has been affected with respect to origin and progression due to modification in proliferation of cell and apoptosis process resulting from aberrant micro RNA

Impact of epigenetics on health

Cancer epigenetics

Aberrations in methylation play a central role in cancer epigenetics. Hypomethylation is associated with the promoters of various proto-oncogenes thereby transforming them to oncogenes. Hypermethylation is associated with the promoter regions of the various tumor suppressor genes. CpG islands are prominent regions associated with DNA methylation. patients. Methylation specific PCR (MSP) is a standard but cumbersome technique used for detection of methylation. In potentially malignant disorders and oral cancer, the methylation status of five genes, p16, p15, hMLH, E-cadherin and MGMT were considered significant in assessing methylation markers. Thus Methylation changes constitute potentially sensitive molecular markers to define risk states, achieve early diagnosis, formulate epigenetic therapeutics, preventive measures and also track the prognosis of the cancer [16].

Epigenetics in neuropsychiatry

Psychiatric disorders such as schizophrenia, bipolar illness, and depression have been connected with Epigenetic mechanisms involving imprinted genes and effects of folic acid. Folic acid contributes to biosynthesis of purines and pyrimidines and production of adequate amounts of SAM (S-adenosylmethionine (SAM) which is required for methylation of DNA and histones [17].

Nutrient epigenetics

Nutrients such as Folate, vitamin B-12, methionine, choline, betaine, water-soluble B vitamins like biotin, niacin, and pantothenic acid can reverse or change epigenetic mechanisms by inhibiting enzymes which catalyze DNA methylation and histone modifications by altering 1-carbon metabolism and leading to two metabolites namely S-adenosylmethionine (AdoMet)5 which is a methyl donor for methylation reactions and S-adenosylhomocysteine (AdoHcy), which is a product inhibitor of methyltransferases [18].

Epigenetics and autoimmune diseases

The impact of epigenetics on autoimmune disease such as systemic lupus erythematosus (SLE) is associated with global hypomethylation of promoter regions, which contain the genes that are

overexpressed in the disease which leads to accentuation of the immune response and subsequently inflammatory response [19-21].

In Sjogrens syndrome miRNAs such as miR-547-3p, miR-168-3p, miR-150, and miR-149 play a key role and their overexpression causes of the downregulation of few mRNAs which are vital for proper immune function and for the downregulation of proinflammatory cytokines [22,23].

Conclusion

To conclude, genetic researchers have lately begun to realize that epigenetic studies might also explain certain health related age old mysteries like the one about twins where it has been observed that one member of a pair of identical twins could develop a particular disease even though the other remains fine throughout the life. In such cases, the genes may be the same but their pattern of expression might have been influenced by epigenetic factors [24]. Genetics was surprisingly considered as an esoteric academic speciality till the completion of Human genome project in October 2004. Craig Venter, one of the most prominent researchers in the genome project, made the following statement when questioned about the influence of the environment on the occurrence of diseases. Genes and the environment have probably the same importance. In each illness, in each human condition there is a different mix of the influence of these two factors. The biological molecule proves that the environment is really an essential part of life, of biology. They are not separated. The people who only look at genes or only at the environment, start out missing the point. Hence it has to be the two of them together [25]. Overall epigenetics is a silent avenue in translational research whose scope is multifaceted in various medical problems recalcitrant to conventional modalities of treatment.

Bibliography

1. Collins FS and McKusick VA. "Implications of the human Genome Project for medical science". *JAMA* 285 (2001): 540-544.

2. Bob Weinhold. "Epigenetics: The science of change". *Environmental Health Perspectives* 114 (2006): A160-A167.

3. Eugene V Koonin and Yuri I Wolf. "Is evolution Darwinian or/and Lamarckism?" *Biology Direct* 4 (2009): 42.

4. Holliday R. "Epigenetics: an overview". *Developmental Genetics* 15 (1994): 453-457.

5. Holliday R. "Epigenetic mechanisms of gene regulation". ed. V Russo, RA Martienssen, ADRiggs, Cold Spring Harbor, NY: Cold Spring Harbor Press. (2002): 5-27.

6. Strohman RC. "Linear genetics, nonlinear epigenetics: complementary approaches to understanding complex diseases". *Integrative Psychological and Behavioral Science* 30 (1995): 273-282.

7. Jablonka E and Lamb M. "The changing concept of epigenetics". *Annals of the New York Academy of Sciences* 981 (2002): 82-96.

8. CT Wu and JR Morris. "Genes, genetics, and epigenetics: a correspondence". *Science* 293.5532 (2001): 1103-1105.

9. Goldberg AD., *et al*. "Epigenetics: a landscape takes shape". *Cell* 128 (2007): 635-638.

10. Jones PA and Baylin SB . "The epigenomics of cancer". *Cell* 128 (2007): 683-692.

11. Van Vliet J., *et al*. "Epigenetic mechanisms in the context of complex diseases". *Cellular and Molecular Life Sciences* 64 (2007): 1531-1538.

12. Simone C. "SWI/SNF: the crossroads where extracellular signaling pathways meet chromatin". *Journal of Cell Physiology* 207 (2006): 309-314.

13. Jeong SM., *et al*. "The SWI/SNF chromatin remodelling complex modulates peripheral T cell activation and proliferation by controlling AP-1 expression". *Journal of Biological Chemistry* 285 (2010): 2340-2350.

14. Reisman D., *et al*. "The SWI/SNF complex and cancer". *Oncogene* 28 (2009): 1653-1668.

15. DP Bartel. "MicroRNAs: genomics, biogenesis, mechanism, and function". *Cell* 116.2 (2004): 281-297.

16. Andrew P., *et al*. "The history of cancer epigenetics". *Nature Reviews | Cancer* 4 (2004).

17. Yong-hui Jiang., *et al*. "Epigenetics and human disease". *Annual Review of Genomics and Human Genetics* 5 (2004): 479-510.

18. Sang-Woon Choi and Simonetta Friso. "Epigenetics: A New Bridge between Nutrition and Health". *Advances in Nutrition* 1 (2010): 8-16.

19. W Lei., *et al*. "Abnormal DNA methylation in CD4+ T cells from patients with systemic lupus erythematosus, systemic sclerosis, and dermatomyositis". *Scandinavian Journal of Rheumatology* 38.5 (2009): 369-374.

20. Q Lu., *et al*. "DNA methylation and chromatin structure regulate T cell perforin gene expression". *Journal of Immunology* 170.10 (2003): 5124-513.

21. Q Lu., *et al*. "Effect of DNA methylation and chromatin structure on ITGAL expression". *Blood* 99.12 (2002): 4503-4508.

22. Alevizos and GG Illei. "MicroRNAs in Sjögren's syndrome as a prototypic autoimmune disease". *Autoimmunity Reviews* 9.9 (2010): 618-621.

23. F Meda., *et al*. "The epigenetics of autoimmunity". *Cellular and Molecular Immunology* 8.3 (2011): 226-236.

24. Hogenson TL. "Epigenetics as the underlying mechanism for monozygotic twin discordance". *Medical Epigenetics* 1 (2013): 3-18.

25. Marc A Shampo and Robert A Kyle. "J. Craig Venter - The Human Genome Project". *Mayo Clinic Proceedings* 86.4 (2011): e26-e27.

Volume 2 Issue 4 April 2019