Epigenetics and Metabolism – an Interesting Relation

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Abstract

In biotechnologies, genetics is an important issue in preserving the animal and plant species, and also in medical diagnostic. Epigenetic is one branch of genetics that studies the variation of phenotypic traits which can be the consequences of different factors, especially the environmental factors. And, because of the epigenetic is dealing with the gens, which are biochemically defined by proteins' metabolism, we can say that there is a special inter-relation between epigenetic and metabolism. Changes in the metabolism of some biochemical compounds can be transferred to gene expression – which can be also altered. The latest experimental studies published in different scientific journals proved that epigenetic is closely related to the phenotypic traits and to the environment.

Keywords: epigenetic, biotechnology, metabolism

1. Introduction

"Epigenetics" as a term in the literature data was covered in the early 1940s by developmental biologist Conrad Waddington. He tried to explain "the interactions between genes and their environment – which leave their mark on the phenotype characteristics. Later, in 1975, Holliday and Pugh tried to explain Waddington's hypothesis by attempting to make changes at the molecular level, by altering covalent DNA bonds — including cytosine-guanine dinucleotide (CpG) methylation. [1].

A few decades later it was shown experimentally that genomic fingerprinting is a complex and multi-factor dependent mechanism. Thus, a definition has been formulated that describes epigenetics as the processes by which hereditary changes in gene expression occur, which produce changes in DNA sequence – for example by DNA methylation and/or chromatin remodeling [2, 3].

More and more in-depth studies of the genome, and the term "epigenomics" has been defined as a study of the effects of chromatin structure – referring to the chromatin folding pattern and attachment to the nuclear matrix, the arrangement of DNA around nucleosomes, and changes covalent occurrences in histone tails (by acetylation, methylation or phosphorylation), but also changes due to DNA methylation [4].

But, if we think engineering and economics point of view, epigenetics in animal sciences combines animal husbandry technology with the benefits of genetic improvement – which is applied to increase productivity – fact that can be translated into qualitatively or quantitatively better production [5-8].

Intensive animal husbandry combined with genetic gain in higher yields (quantitative or qualitative) or referring to genetic phenotype selection, have often negative consequences on fertility and diseases resistance [9, 10].

Also, some farmers with the idea of intensive development and growth have used antibiotics and thus, over time, the animals' resistance to

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antibiotics has increased, which also affects human consumption.

Epigenetic regulation of gene activity is a branch of genetics that still needs to be developed and depended by experimental studies, so as to clearly establish the environmental consequences of epigenetic gene programming.

Next-generation-sequencing (NGS) technologies reveals very important discoveries and are an ideal tool for the biochemical study of the chemical changes in DNA possibility, with direct consequences on genetic information that can be reflected on the quality of animal breeds [11].

2. Epigenetics and environment – development and evolution

Waddington, cited by Norouzitallab and her collaborators, first introduced the term "epigenetic landscape" – which presented the various metabolic pathways that a cell can follow throughout the differentiation process [12]. The expression or repression of particular genes, the presence or absence of a certain environmental index, but also the genotype-environment interaction mediate the biochemical pathway that the cell will follow at a certain point of divergence. The "epigenetic landscape" is an expression which explain how gene regulation influences phenotypic development due to environmental variations. “Genetic assimilation” is a specific process, during which the phenotypic variation induced by the environment is involved constructively on the genetic characters and is maintained even in the absence of the initial environment signal. These is influenced epigenetic and having causes of hereditary differences that are not always dependent on DNA sequence changes [13, 14].

An epigenetic trait is defined as a stable hereditary phenotypic trait that results from changes at the chromosomal level without the appearance of changes in the DNA sequence. Interactions between the host and the pathogen are processes that involve dynamic and competitive interactions. In a certain environment, living organisms are surrounded by various species of microorganisms (including pathogens: bacteria and viruses) and have a significant evolutionary impact on the host throughout life. In the case of a pathogen, the healthy host cell acts selectively to restrict or eliminate the negative effects. Thus, many pathogens have evolved by modifying their phenotypic plasticity in order to cope with retaliation by the host cell [12, 15].

In figure 1 presents the influence of nutrition and some chemical, biological or physical hazardous agents on gene regulation.

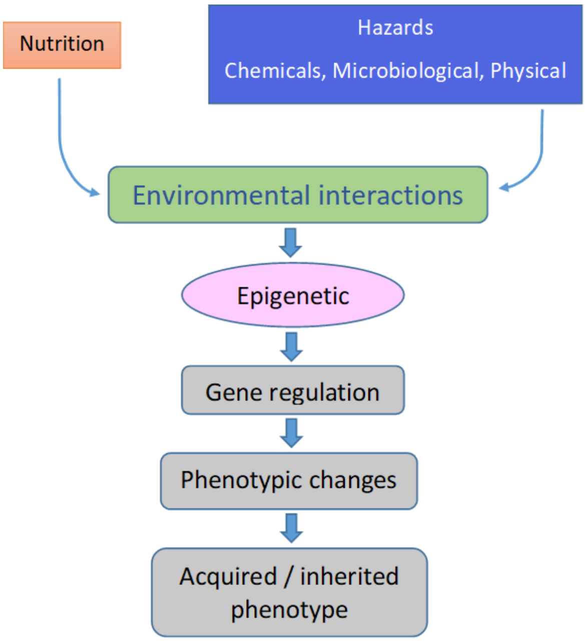

Figure 1. Environmental factors and epigenetics

Environmental factors can modulate positively or negatively the phenotypic characteristics. Nutrition and also different chemicals (toxic substances, drugs, and others), biological (some pathogens or antibiotics) or physical (for example, radiations) hazards can modulate the epigenetic with changes in phenotypic characteristics.

Various experimental studies show that stress causes transgenerational effects on various organisms, with changes at the cell level. The effects of environmental stress on the appearance and inheritance of phenotypic traits are reflected over three subsequent non-stressed generations [16].

The nutritional status of an organism throughout its development has a critical role in regulating the epigenome, which modulates the growth and health of the body – both within a generation and between generations. Experimental studies have shown that the state of nutrition during the preconception and periconception period influenced certain phenotypic traits, such as health and development).

The results of some biochemical experimental studies have suggested that, in the early stages, epigenetic reprogramming of innate or formed immune effectors in response to exposure to a particular biotic stress, may play a key role in certain specific molecular mechanisms that increase the resistance phenotype, with long-term effects.

3. Epigenetics and Metabolism

Each cell in living organisms manages environmental variations (regarding nutrition or hazards), with rapid and stable modification of genetic expression. The key to these adaptive processes is the chromatin polymer - which is a dynamic set of DNA, made up of nucleoproteins that regulate transcriptional competence through structural adaptation and unique compartmentalization of the genome. Covalent epigenetic modification involves functional modulation and structural reorganization of chromatin, which is increasingly being studied in human and animal health and disease [17].

The immediate cellular environment, through its components, determines the epigenetic architecture of chromatin. The integration of global, subcellular and external metabolic information directly influences the process of gene regulation.

Metabolic information is closely related to chromatin modification, which represents for the cell the regulatory and coding elements for certain genes involved in metabolism. After DNA replication, the biochemical process of 5-carbon methylation of cytosine (5-methylcytosine) nucleotides adjacent to guanine residues is associated with gene suppression, essentially contributing to the etymological interpretation of epigenetics [18].

Also very important are covalently post-translational changes made dynamically and deleted from the N-terminal tails of histone proteins chromatinized by specific enzymes and enzyme complexes. From a biochemical point of view, methyl modification is a decisive factor in gene regulation, especially when the process is attributed to arginine and lysine residues by histone methyltransferase enzymes. The transcription process depends primarily on the site of methylation of the histone tail.

Important information comes from the epidemiological and clinical observations that are due to the processes of gene disorder in metabolic disease, and which suggests that the stability of epigenetic changes may confer future cellular memories. Such examples of long-term persistence are presented in the literature referring to continuous vascular damage in patients with diabetes, after several years after effective glycemic control [19, 20].

More recently, experimental evidence has been reported linking developing fetal nutrition and chromatin changes that form the basis of pathological gene expression related to adult disease. Thus, it is shown that cellular metabolism with chromatin-dependent genes changes [21, 22].

Metabolic disease and metabolic dysfunction - in both animals and humans, are carefully studied, and the experimental results of various researchers show that dietary factors confer epigenetic changes that are associated with developing disease and adulthood.

Chemical compounds considered intermediates in diet and cellular metabolism are enzymatic cofactors that can modify chromatin, thus integrating metabolic information and controlling the transcriptional process.

The continuous change in the concentration of some metabolites signals the cell and the metabolism in order to continuously adjust the gene expression that modifies the chromatin dynamics by modulating the epigenome. Thus, general metabolic changes can modulate the epigenome by subcellular synthesis of a specific metabolite and by varying its concentration [23].

The importance of metabolism and epigenetics is also associated with extensive cell proliferation, which is linked to cancer. Thus, to ensure the energy and anabolic requirements necessary for increased proliferation, tumors develop the ability to reprogram the metabolic pathways of nutrient acquirement. Cancer cells have the ability to alter their metabolic profile during tumorigenesis and metastasis, through a unique program of metabolic plasticity. Thus, certain metabolic changes are highlighted at the epigenetic level. Intermediate metabolites formed in metabolic processes (e.g. glycolytic cycle and oxidative phosphorylation), are used as cofactors or substrates for various enzymatic reactions that catalyze transcriptional regulation and epigenetic changes [24].

In cancer metabolism, the reprogramming of metabolic pathways takes place first of all with the qualitative and quantitative modification of the metabolites. Some metabolites are used as co-factors or substrates for essential enzymes to epigenetic changes. Also, metabolites are produced or brought to the nucleus by translocated enzymes into the nucleus. Finally, the cell produces onco-metabolites that modulate the activity of potent epigenetic enzymes, which determines the evolution of the tumor [25, 26].

As presented in this scientific paper, the metabolism and environmental factors are very important in epigenetics – both in animals and humans [27]. Therefore, having in view all the aspects presented above, better knowledge leads to better prevention, treatment, or better coordination in applied biotechnologies.

4. Conclusions

More or less, last decades studies and researchers have been demonstrated the importance of applied knowledge in molecular biology, not only for genetic improvement and biotechnology, but also for the prevention and treatment of acute and chronic diseases. There is much more to be studied about the epigenetic regulation of gene activity, about how the environment is related to the epigenetic programming of genes, and about the contribution of epigenetic programming to the disease etiology of some human and animals.

In biotechnologies is important to identify which are the specific genes that are subject to epigenetic regulation because their epigenetic signature may be used as a potential marker for early diagnosis and of course an efficient treatment.

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