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Commentary
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Epigenetics and Apoptosis in Development and Aging: Retrospective from the End of Last Century

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This story began for us at the end of the decade of eighties when we became involved in studies on hormonal regulation in primary liver and pituitary cell cultures obtained from rats of different age groups: perinatal, prepubertal and adults. These studies continued later in vivo on somaitc and organ growth in rats treated with several hormones. The results of investigations in vivo and in vitro, together with the data of subsequent epidemiological studies have influenced our decision to be associated with Latin-American chapter of International Society for DOHaD (Developmental Origins of Health and Disease) since the year 2009 and till the present time.

One of the main objectives of this Society is to study the phenomena of programming / imprinting and embedding and to evaluate their possible mechanisms. Here we aimed at estimation of the roles of epigenetics and apoptosis in the link of development and aging uniquely studied by this Society.

At present it is suggested that (epi)genetic code is made of 5 and perhaps even 6 nucleotide derivatives (and not 4, as hypothesized in classical studies) [1-4]. The fifth component is 5-methyl-cytosine. In addition to nucleotide (epi)genetic code, there exists probably also quite complex histone code, because of various covalent modifications of these proteins, the most studied being acetylation and methylation [5, 6].

In combination, (epi)genetic and histone codes determine the exact phenotypic patterns of more than 200 types of cells in human and animal bodies from zygote and up to adult state, at least. During the last years a lot of evidence was gathered, as referred to small non-coding RNAs that also regulate gene expression, together with (epi)genetic and histone codes, but their interactions are poorly understood yet.

As for DOHaD concept, there exists already rather firm evidence about epigenetic nature of the phenomena of programming / imprinting (see, e.g., ref. [7]).

What for apoptosis, it represents a phenomenon of programmed cell death and is absolutely necessary for maintaining the homeostasis of tissues in humans and animals. In fact, approximately 10^5 and 10^{10} cells are produced every second and day respectively, and similar numbers should be eliminated by apoptosis in adult state [8, 9].

However, the contribution of apoptosis to developing and growing body is understood much less. The role of apoptosis in aging was already suggested [10], but without sufficient detailing. In relation to DOHaD paradigm, the data on apoptosis are rather scarce yet, but we can already suspect its role in glucocorticoid-indiced growth inhibition [11], responsible, at least in part, for programming / imprinting phenomena [12].

What are the next steps in evaluation of the roles of epigenetics and apoptosis in development and aging? We suggest that, as for the area of stem cells in general, studies on induced pluripotent stem cells may help a lot. Earlier we have already proposed that an expanded version of endocrinology is necessary, because of highly complex nature of bioregulation [13]. In addition, expanded version of gerontology should study the whole ontogeny (and not only its senescent part). Probably, the interactions of expanded versions of endocrinology and gerontology may obtain in near future the critical value of evidence, useful for tissue engineering and regenerative medicine. The advanced knowledge of epigenetics and apoptosis may be very important in this endeavor.

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