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Brief Report

Epigenetics, Epiproteomics and Paleoanthropology -

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This brief note is devoted to highlight the possible, remarkable role that epiproteomics might play in paleoanthropology following, in an analogical way, the same contextual role played by epigenetics, with which should profitably cooperate.

Epigenetics is the study of heritable phenotypic changes which arise without changes of genomic sequence, but mainly through environmental influences which give rise to a variability in the gene expression. The chief molecular mechanisms with which epigenetic phenomena take place, are in the context of reversible covalent chromatin modifications, amongst which are DNA methylations, histone acetylations and miRNA (that regulates just gene expression) modifications. Furthermore, epigenetic mutations (above all, DNA methylations), most of which are reversible, have also a greater rate than genetic ones, due to the major sensibility on environmental conditions by the former which stress gene expression [1-4].

Epigenetic transformations account for the differences between primates and humans which share commonly about 99% of DNA, and has also contributed to domestication of animals. Epigenetic data have shown that above all methylations processes have contributed to phenotypic variations during human evolution, having acted more on gene expression rather than on protein sequences. Nevertheless, if one limits to consider only these outcomes, some incongruities may stand out by the comparison between some primates (like orangutans) and humans. Furthermore, there also exist gene sequences of primates and humans, lying at the protein level, having epigenetic diversities [3-5].

As epigenetics plays a very crucial role in the phenotypic manifestations from the genotype, it is obvious that protein formation – which is more dynamical than gene phenomenology – is closely related to epigenetic mutations. Likewise to genomics, the study of expression, interaction and communication (or information exchange) of all proteins contained into a cell, is said to be *proteomics*. Moreover, the analogical parallel to the pattern of epigenetics gives rise to the so-called epiproteomics meant as the study of the effects, as consequences, of the influences of environment (post-translational modifications, in short PTMs) in the protein formation from proteotype (analogous to genotype), which may be heritable as epigenetic marks for those related genomic traits epigenetically influenceable. In particular, we recall that proteins are fundamental for the working of memories, some of which operate just in a similar manner to viral mechanisms [6] as well as they may modify RNA. Early fetal brain development is a highly complex and tightly regulated process. Consequently, small alterations can lead to severe phenotypes such as cortical malformations, epilepsy and intellectual disability. Further, structural and functional brain alterations are reflected in the protein composition of cerebrospinal fluid.

So, to sum up, epigenetics refers to a “heritable” phenomena in which the phenotypic changes are independent of DNA sequence, while epiproteomics is the Post-Translational Modifications (PTMs) that involve histone acetylations, SUMOylations, phosphorylations and ubiquitinations. In turn, the PTMs might regulate various biological processes by means of the modulation of chromosomal structures or regulating the binding of chromatin [7]. Histone methylation is a dynamic process with a key role in development and differentiation. Aberrant levels of histone methylation are likely to play a causal role in tumorigenesis. The outcomes of methylation on histones are highly context dependent and can be associated with different gene expression status. Histone methylation is then intimately associated with transcriptional regulation by influencing

chromatin architecture, recruiting transcriptional factors, interacting with initiation and elongation factors, hence affecting RNA processing [8]. The epiproteomics studies therefore all the Post-Translational Modifications (PTMs) regarding the proteins of a cell or organism [9].

However, proteins are amongst the major promoters and regulators of biological processes; their identity and function are defined by the unique sequence of amino acids which structure them, and may elicit multiple functions on the basis of their interaction with other proteins. Therefore, it is of central interest in biology to determine the interactions and cooperation of proteins (whose set is said to be proteome) as a function of cell state. Thus, protein-protein interactions (whose net is said to be interactome) play an essential role in many biological processes in living systems; current research indicates too that alterations in the interactome network are relevant for many human diseases including neurodegeneration. Most human diseases involve changes in the composition or functions of proteins in one form or another: for instance, as has already been said, structural and functional brain alterations are also reflected in the protein composition of cerebrospinal fluid.

Proteome stronger depends on environmental influences, is time-dependent and more cell-specific than genome. It is important and useful to define a protein expression pattern as the main outcome of the phenotype, varying by Post-Transcriptional Modifications (PTMs). Functional and expressive proteomics tries to study structure and functions of expressed proteins of a cell or tissue. Proteins are however much more liable to environmental conditions and variations than gene sequences. Furthermore, it is very important to determine, where is possible, protein families, their formation and phylogenetic evolution which seems to play a stronger role than that of genome code, in giving rise families and super-families of proteins [10-12].

It is therefore relevant and fruitful to consider epigenetics and, above all, epiproteomics as applied to paleoanthropology to study human evolution, and vice versa. Indeed, proteomics should be taken into account besides and jointly to epigenetics, in that there exist proteins which are not predictable on the basis of genome sequences only, as well as it is able to consider also that key intercellular signalling closely related with gene expression and cell phenotype. In conclusion, epigenetics and epiproteomics should give valuable insights to paleoanthropological research [13,14].

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