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Epigenetics is Normal Science, But Don't Call It Lamarckian

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Abstract

Genetics is a currently limited by not understanding (or explaining) either how different genes are expressed at different levels in the tissues of multicellular organisms, or predicting gene regulation in unicells. Understanding such regulation is crucial to an understanding of inheritance, and epigenetics seeks to help explain this. There is very good progress in the area, and genetics and epigenetics are best not to be considered as alternatives. Sometimes there can be inheritance of acquired features, and a few authors attribute this to Lamarck. However, nowhere in his book does Lamarck appear to analyze such inheritance, and it appears that this was a general assumption at the time? Lamarck's book is almost exclusively on ideas of relationships between different groups of animals, how they might transform and on the importance of so-called 'nervous fluids'.

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Epigenetics

Epigenetic mechanisms are increasingly being accepted as an integral part of normal science. Earlier genetic studies appear to have assumed that the only changes were 'mutations' as a result of a change in the DNA sequence. If any such changes altered the amino acid sequences then it was effectively a mutation, and if it occurred in a germline cell (including in unicellular organisms) then it could be passed on to subsequent generations. However, it is increasingly apparent that other changes are also important, for example, changes to methylation patterns, and to the histone proteins. Epigenetics was sometimes consider 'additional' to classical genetics, but it is still fully dependent on DNA, RNA and protein sequences, and at least since [1] it has been considered a part of normal science. A richer way is to expand classical genetics to include transfer of information between cellular generations. Indeed, it is hard to imagine a unicellular protist that does not modify some of its protein expression levels as a result of environmental changes-gene regulation is integral to biology.

There is a very general question about the regulation of gene expression levels in both unicellular and multicellular organisms. Unicellular organisms are interesting in that they have different levels of gene expression, depending on their environment. For multicellular organisms (say, plants and animals) there is the very important issue that all cells are considered to have the same genetic information, yet the proteins they are expressing is different. For example, plant cells in roots do not normally express the large numbers of chloroplast proteins; this is a fundamental example.

First we should mention that there are several processes that regulate epigenetics, and that they are widespread in nature. There are at least three classes of responses that modify gene expression, small RNAs, methylation (and hydroxymethylation), and protein modifications (in eukaryotes at least). These organisms have several (five) histone proteins attached to their DNA in pairs, and these form regular structures along the DNA – the nucleosomes, and the tightness of these nucleosomes affects gene expression. There are several interesting modifications to the histone proteins that are found in a very wide variety of deeply diverging eukaryotes [2-4]. We consider these to be present in the universal ancestor of eukaryotes [5], that is, they are general (but not necessarily universal) because they are found in Excavates, which many people consider are ancestral to other eukaryotes [6, 7].

Similarly, an important point is that methylation, phosphorylation, etc. of the DNA and of the histones is a part of normal evolution (at least in eukaryotes that have the nucleosome structure) [8]. One of the most interesting aspects is methylation (and hydroxymethylation) of cytosine, and this is found in many deep branching eukaryotes [9]. Typically there is methylation of cytosine molecules, especially in CpG (cytosine followed by guanine) regions. The role of small RNAs in helping regulate the levels of protein expression is discussed in [10]. The main point here is that protein expression levels are very variable in all cells – it is not just classical genetics that is important; there are many epigenetic mechanisms affecting the differences in protein expression. Epigenetics is a unifying force in biology.

Lamarckism

In contrast to the evidence above, the next theme does not appear as standard science? Often the 'inheritance of acquired characteristics' (for which there is good evidence) is attributed to Lamarck (Jean-Baptiste Pierre Antoine de Monet, Chevalier de Lamarck, 1744-1829). However, I have read again the over 400 pages of the book by Lamarck, published [11], and this is often given as a reference. (An original [5] was written before I had read Lamarck again.) Nowhere in the book do I find any description/proposed mechanism for the 'inheritance of acquired characters', though that inheritance is assumed in many places. Perhaps the closest it comes is on p.113 when he gives two Laws to the effect that there is the loss to unused characters (particularly early in development), and that 'all' changes that affect a character 'through the influence of the environment' will be passed on – there does not appear to be any recognition of germ line and somatic cells here?

It is not even clear from his book whether he accepts progressive evolution', but he must have? He mostly considers extensively 'degradation' from complex to simpler organisms, but the general assumption is that he must have also assumed the opposite, from simpler to more complex. However, most of the time he discuss 'degradation' of complex animals to simpler animals. In the end he recognizes 14 groups of animals. On a positive note, he was apparently the first to recognize a vertebrae/invertebrate division. He also recognized plants as being on a quite different trajectory form animals.

On p.124 he concentrates on the 'will' of the animal – "when the will guides an animal to any action, the organs that have to carry out that action are immediately stimulated to it by the influx of subtle fluids (the nervous fluid). This fact is verified by many observations, and cannot now be called into question." He goes on to suggest that this 'will' will even create the necessary organs. Apparently he assumes that all organisms of a species need to have the same 'will' to change, but again no mechanism is given (how do the organisms/enzymes 'know' that they all want/need to change). There is no reference to germ-line and somatic cells (though there was later disputed that the division existed, [12]. It appears that the general assumption was that any change character would be inherited. In this sense this fits the model, mentioned later, that the *interior milieu* germ-line cells accumulated in the sperm/ova. Lamarck states "every species has been derived from the action of the environment in which it has long been placed … These habits have themselves influenced the parts of every individual of the species".

One of the classic examples of the 'inheritance of acquired characters' is the evolution of the giraffe (p.122), or of long-legged wading birds. He does mention both of these examples (plus some others, including a blind mole and the kangaroo). Basically, we should accept the conclusions of the historians of science [13] that Lamarck, despite being an excellent scientist, did not propose any testable mechanism about inheritance. He was certainly not alone in supporting some evolutionary change; Lacépède, Geoffroy Saint Hilaire, and the professor of geology in Paris (Saint Fond) all favored some idea of species change [14]. Perhaps the main reason his evolutionary ideas received a very negative response at the time was that it required 'materialism' [14], and this was not acceptable to the majority of people at the time.

Lamarck claimed to have very broad interests, and described himself as both a 'naturalist and a physicist' (p.184) though he decided that physical sciences were easier, '… much easier to determine the course of the stars observed in space, and to ascertain the distance, magnitude masses and movements of the planets belonging to our solar system, than to solve the problem of the origin of life in the bodies possessing it, …' (p 184).

It appears that the assumption (at least in Paris in France, though perhaps not necessarily in Brno in the Czech Republic, [15] is that such inheritance of acquired characteristics was the 'norm', and Lamarck was assuming it without testing it, or explaining how it might occur? For example, the French researcher [16] explains some of earlier (18th century) thoughts about 'inheritance'. For example, he points out that Buffon (Georges-Louis Leclerc, Comte de Buffon [17] could not understand how 3D information was passed onto the next generation, so assumed that (somehow) 3-D information from, for example, the structure of the heart was passed on between generations of animals. This (in Buffon's understanding from earlier in the 18th century) was that little 'molds' (the interior milieu) were necessarily passed on between generations –for example, giving the shape of the heart, or of the kidneys, and so on. Nowadays we take it for granted that linear information (for example, the linear information in RNA and DNA and proteins) is sufficient. The laws of chemistry and physics do not have to be passed on between generations; they are in a sense constant and are always present.

Conclusion

One of the main conclusions/recommendations that I have is that we should insist that anyone should actually have read Lamarck's book who wishes to suggest that the 'inheritance of acquired characters' is some sense Lamarckian. Yes, Lamarck was one of the early evolutionists, and should be well recognized as such. However, nowhere in his book does he indicate anything about the mechanisms of evolution, or of the potential of an increase in numbers. We have to accept standards of evidence. It appears that the inheritance of acquired characters it was a general assumption at the time, and Lamarck assumes it, but never really discusses how it might occur.

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