Cell thermoregulation and origin of homeothermic animals

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ABSTRACT

Temperature has a fundamental influence in all chemical and biochemical reactions. It influences reaction rates, equilibrium amounts, viscosity, solubility, molecular arrangements and numeric other parameters. Temperature is important for all physiological processes. Maintaining the relative constancy of the internal temperature (temperature homeostasis) is a necessary condition for normal life. Some living beings maintain temperature homeostasis in the body due to external sources of energy (poikilothermy), others due to the energy of food consumption (homeothermy). However, it is unknown the origin of homeothermic organisms. Despite the fundamental similarity of the mechanisms of the central organ-based physiological thermoregulation, even among the higher vertebrates exists poikilothermy and homeothermy animals. It is assumed that homeothermy is not the result of the evolution of physiological mechanisms of thermoregulation. Homeothermy is the result of the evolution of non-coding DNAs in the genome, some of which formed the so-called chromosomal heterochromatin regions (HRs). Chromosomal HRs constitutes the material basis of cell thermoregulation, which is responsible for the removal of excess thermal energy from the nucleus into the cytoplasm. Homeothermic organisms, unlike poikilotherms, capable of faster and more efficient leveling of temperature difference between the nucleus and the cytoplasm with all the ensuing consequences.

Key words: Homeothermy animals; Cell thermoregulation; Heterochromatin; Temperature homeostasis

INTRODUCTION

Virtually, the life, which is known to science, with rare exceptions, is possible generally at positive temperature, and its highest forms – birds and mammals – are able to keep a relatively high temperature in the body preserving a very high level of metabolism. Temperature has a fundamental influence in all chemical and biochemical reactions. It influences reaction rates, equilibrium amounts, viscosity, solubility, molecular arrangements and numerous other parameters. Temperature is important for physiological processes as well as cell maintenance and function. However, by the mechanisms of heat loss the organism and individual cells apparently DIFFER. As is known, the external heat flow from a body is performed by way of radiation, conduction, convection and evaporation of water. Apparently, of these mechanisms, the cell, in particular the cell nucleus can use only the heat conduction. In our opinion, in the elimination of heat surplus from the cell the cytoplasm and nucleus are different. The nucleus, in contrast to the cytoplasm, cannot conduct heat directly in the extracellular space, from where the heat is taken by the circulating flow of sap, lymph and blood. Thus, the nucleus can conduct heat only in the cytoplasm.
The hypothesis of cell thermoregulation (CT) was proposed to explain elimination of the temperature difference between the nucleus and cytoplasm when the nucleus temperature becomes higher than the cytoplasm temperature [1-3]. The nucleus can conduct heat only in the cytoplasm. With this, the nucleus has two options for the dissipation of heat surplus: either by increasing its volume or increasing the heat conductivity of the nuclear envelope. As the first option is limited, and the second one is hampered because of thickness of the cell membranes, apparently the higher eukaryotes took advantage of the opportunity of a dense layer of peripheral condensed chromatin (CC) as heat conductor for a more efficient elimination of the temperature difference between the nucleus and cytoplasm. The CC localized between a nucleus and cytoplasm is made of different types of chromosomal heterochromatin regions (HRs). The density of the CC packing depends on the type and quantity of chromosomal HRs in its structure that can affect upon its heat-conducting ability. In higher eukaryotes the structural basis of CT consists of chromosomal C-heterochromatin regions (C-HRs), except for three species of higher primates (Homo sapiens, Pan Troglodytes and Gorilla gorilla), in its genome, in addition to the C-HRs have Q-heterochromatin regions (Q-HRs).

**Origin of homeothermic animals**

In the literature we failed to find special theories or hypothesis about the origin of homeothermy organisms [4]. Works devoted to this problem are limited to descriptions of chemical and physiological mechanisms of maintenance of relative constant temperature in a body with indication of pros and cons of homeothermy for organisms. Regarding the possible genetic mechanisms of homeothermy there is no information at all. Thermoregulation on organism level relates to the most studied section of physiology and its basic principles are well known. However we have few data concerning mechanisms of maintaining temperature homeostasis at the level of individual cells.

As is known birds and mammals as well as humans should maintain extremely high level of metabolism in order to preserve relatively constant body core temperature. This is possible during regular organism supply with food reach in calories only. Whereas poikilothermic animals start their active living only after heating their bodies to some extent under sun rays. This raises the question of how homeothermic organisms manage to maintain temperature homeostasis at the level of individual cells, when after taking high-calorie food (in addition to solar radiation), the temperature in the cell nucleus will inevitably rise first.

The role of the circulatory systems (CS) has been discussed in maintaining temperature homeostasis. However, the CS cannot influence directly the temperature inside the cells, as they are linked with the CS indirectly - through the intercellular space. Thus, the CS influence on inner cellular temperature homeostasis is limited and its effect, in general, comes to transferring surplus heat from the intercellular space. That is why it seems that the problem of maintaining the inner cellular temperature homeostasis is solved by cells themselves, and we call it the cell thermoregulation [1,2].

How then is CT performed in homeothermic animals? We will try to illustrate of this issue by the example of two organisms, human and crocodile, typical homeothermic and poikilothermic organisms. Let's start with how crocodiles eat. As known, at one time crocodiles can eat up to 23% of their body weight. Crocodiles are well adapted for long-term fasting. Without food adult crocodiles in case of emergency can live about one year. While the mammal predators of the same size as crocodiles daily require approximately 5 – 10 times more food. At the same time, about 90% of the calories obtained from food are spent only on maintaining a constant core temperature in the body.

It is believed that birds and mammals have become warm-blooded because of their ability to maintain a very high level of metabolic intensity and the presence of a 4-chamber heart. However, it seems to us that the level of intracellular metabolism is not determined by the ability of animals to produce high-calorie food or its availability. The ability of cells to remove excess heat from the nucleus to the cytoplasm in a timely manner is extremely important in order to avoid undesirable consequences of high thermal energy for such vital genetic processes as repair, recombination, replication, transcription, rearrangement, packaging and etc of DNA. And this is possible only through CT using a dense layer of CC in interphase cells [1,5].

But this does not mean that CT is an effect exclusively of chromosomal HRs. As is known, in the chromosomes of higher eukaryotes except C - and Q-HRs there are G+ and Q+ bands, which make up more than half of their length. It is believed that in the composition of chromosomal G+ and Q+ bands can be
and C - and Q-heterochromatin materials, the so-called intercalary heterochromatin. Even if G+ and Q+ bands do not contain C - and Q-heterochromatin materials, the fact that they are tightly packed in the body of mitotic chromosomes convinces that they can also participate in CT.

As part of the issue discussed here, we specifically note that if, indeed, in the composition of G+ and Q+ bands there are a number of C - and Q-HRs, their amount in each of these chromosomal sites should be constant not only in the karyotype of the individual, but also species as a whole. This is evidenced by the constancy of the distribution pattern, size, localization and alternation of G+ and Q+ bands along the length of each homologous chromosome in the normal karyotype. However, chromosomal G+ and Q+ bands, regardless of whether they contain in C- and Q-HRs are required to participate in CT, although quantitatively determine their contribution to body heat conductivity is difficult because of their constancy for each species [6].

We believe that the CC should be the densest domain in bird and mammal cells among higher vertebrates. This confidence is due to the fact that the clearest differentials staining (C-, G - and Q-bands) give the human mitotic chromosomes, then other higher primates, and then the rest of the mammals. Bad or not differential staining gives chromosomes of reptiles and amphibians. By the way, only C-bands can be obtained on plant chromosomes. Referring to the ability of chromosomes to give a differential staining, we have in mind the well-known fact that C+, G+ and Q+ bands represent the densest areas of mitotic chromosomes, enriched with heterochromatin and other types of non-coding DNAs, which constitute the physical basis of CC. Our assumption about the highest density of CC in human cells among mammals is due to the fact that: a) the human genome has all known types of constitutive heterochromatin (C - and Q- HRs); (b) among the higher primates, the highest amount of chromosomal C-HRs is found only in the human karyotype [6].

We assume that the chromosome segments of the higher eukaryotes have undergone their own evolution in the direction: C-heterochromatin → G+ and Q+ bands → Q-heterochromatin as response of a cell nucleus for the demand of multicellular organisms in denser packaging of non-coding DNA for the increase of the heat-conducting effect of CC between the nucleus and cytoplasm [1-3]. For example, at a later stage of evolution of the mammals in Africa in the ancestors of three higher primates (Homo sapiens, Pan troglodytes, Gorilla gorilla) besides C-heterochromatin, a new type of constitutive heterochromatin, Q-heterochromatin, appeared [10,11]. Obviously, this is related to the increase of the metabolism intensity in their organism, and, accordingly, the further improvement of the intracellular thermoregulation. In this case the Q-heterochromatin is not only a new type of constitutive heterochromatin, but possibly an additional 'center of condensation and attraction' for more dense packaging of adjacent inactive chromat in, thus, increasing the heat conducting effect of CC in the interphase cell of three higher primates [2].

If our reasoning really has to do with real events in animal evolution, then for example, it's not difficult to explain why the crocodile didn't become a homeothermic animal. It is believed that this large reptile poikilothermic because it has a 3-chamber heart because of arterial blood is poorly saturated with oxygen, and such an organism cannot maintain a high level of metabolism. However, it can hardly be seriously considered that this disadvantage can be added to the lack of high-calorie food. It seems to us highly probable that the main cause of poikilothermy in a crocodile is the peculiarities of its karyotype; as in all reptiles crocodile chromosomes, give a bad differential staining. This means that in such cells the density of CC is low, which complicates the effective transition of excess metabolic heat from the nucleus to the cytoplasm. Perhaps a crocodile lies for so long after the reception of the next portion of food not because of problems associated with digestion (for example: lack or few of food processing enzymes), and due to the fact that excessive physical activity may cause a risk of overheating of the body. Homeothermic animals solve this problem by efficient removal of excess metabolic heat from the interphase nucleus to the cytoplasm with a dense layer of CC, that is, they have a more perfect intracellular thermoregulation.

We don't have any comparative studies on density of the CC in the cells of homeothermic and poikilothermic vertebrates. And yet there is one study that indirectly supports our assumption. So, Bernardi and Bernardi [7] extensively studied the guanine-cytosine (GC)-rich isochores of cold-blooded (fishes, amphibians and reptiles) and of warm-blooded (birds and mammals) vertebrates. Both the non coding DNA and the sequences that code for proteins (structural genes) turned out to be much richer in GC in warm- than in cold-blooded animals. Though for the time being we do not know how the GC-rich
isochores could influence the appearance of homeothermy, nevertheless all the above data indicate the existence of a relationship between DNA composition and the appearance of warm-blooded organisms.

CONCLUSION

Birds and mammals have become homeothermic animals, perhaps not because they have the most developed systems of physiological thermoregulation. Their homeothermy due to the evolution of the chromosomal bands and HRs (see above), which, in the end, are the most dense of all condensed chromatin that exist in animal cells. Due to this, the removal of excess thermal energy from the nucleus has become more effective than that of poikilothermic animals with all the ensuing consequences.

Of course, there will be opponents who believe that mechanisms of physiological thermoregulation, for example, in human are sufficiently perfect; otherwise he could not master almost all the land on Earth so rapidly and effectively.

We suppose that during his evolution man, possibly owing to chromosomal Q-HRs, had an additional and very flexible tool to ensure more effective thermoregulation, allowing him to master almost all the oikumene [8,9]. In essence, all that was said comes to one simple thought: how does man as a homeothermic being differ from other mammals as concerns preservation of a constant internal environment the main component of which is temperature homeostasis.

As far as we know, H. sapiens is not only devoid of a more or less large anatomic structure, but also has no protein or enzyme that has no analogue in the animal world. The fundamental structural characteristic of man is the presence of chromosomal Q-HRs in its genome which he has inherited together with the chimpanzee and the gorilla – from one common ancestor. In this context the only difference of H. sapiens is the wide quantitative Q-HRs variability in his genome.

Apparently, the physiological thermoregulation functions relatively independently from CT as evolutionally new adaptive system. From our point of view, CT can be the missing link, which should fill the "gap" between the thermoregulation systems, functioning at the molecular level and the whole organism.

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REFERENCES