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### On the Evolution of Thermoregulation

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#### Abstract

The role of temperature in biological life is obvious, because, with rare exceptions, life is possible only in conditions of positive temperature. All forms of life in one form or another have the ability to control body temperatures (thermoregulation). As is known, mammals have the most developed thermoregulation system. It is generally believed that among mammals, humans have the most developed thermoregulation. Confirmation of this statement is the fact that only humans have managed to master and populate all climatogeographic zones of the Earth. However, the question of why mammals have the best thermoregulation system still does not have a complete answer. The organ-based (organismal) thermoregulation system of mammals includes the hypothalamus in the brain, as well as the sweat glands, skin, and circulatory system. At the same time, the question remains little studied, how did the organismal system of thermoregulation arise in the process of evolution and how did it turn out to be the most developed in mammals? We believe that cell thermoregulation, which appeared before the development of the organismic level of maintaining temperature homeostasis, apparently played a decisive role in the emergence of the most developed thermoregulation system. An attempt is made to substantiate this point of view by the example of the evolution of the thermoregulation system in man.

**Keywords:** Evolution of Thermoregulation; Cell Thermoregulation; Origin of Circulatory System; Chromosomal Heterochromatin Regions; Human Thermoregulation; Human Body Heat Conductivity

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#### Introduction

The role of temperature in biological life is obvious, because, with rare exceptions, life is possible only in conditions of positive temperature. All forms of life in one form or another have the ability to control body temperatures. Prokaryotes, in response to extremely high or low temperatures, produce heat or cold shock proteins, respectively, in

order to protect proteins from denaturation. Ectothermic animals (amphibians, fish, lizards, other reptiles, etc.) are able to use external sources of thermal energy (the sun) to maintain a positive temperature in the body. They emit much less heat to maintain their body heat, and have a low metabolic rate. Endothermic animals (all mammals and birds) produce most of the heat mainly due to the metabolism of their body and produce the necessary amount of heat to maintain their body heat. These animals have a very high level of metabolism. Mammals

use thermoregulation to keep the body within a limited temperature range. This is important for health, because it allows cells, tissues, organs and processes in the body to work effectively.

Thermoregulation, also called heat regulation, is the biological mechanism responsible for maintaining a steady internal body temperature. As is known, mammals have the most developed thermoregulation system. The organ-based (organismal) thermoregulation system of mammals includes the hypothalamus in the brain, as well as the sweat glands, skin, and circulatory system. However, the question remains poorly understood, how did the organismal system of thermoregulation arise in the process of evolution and how did it turn out to be the most developed in mammals, especially in man and other higher primates?

We believe that cell thermoregulation, which appeared before the development of the organismal level of maintaining temperature homeostasis, apparently played a decisive role in the emergence of the most developed thermoregulation system. Below, an attempt will be made to justify the possible role of cell thermoregulation by the example of the functioning of the thermoregulation system in human, as the most well studied homeothermic organism. By cell thermoregulation, we mean the process of equalizing the temperature difference between the nucleus and the cytoplasm when, for one reason or another, the temperature of the nucleus in the interphase cell begins to exceed the temperature of the cytoplasm. In this case, the heat transition from the nucleus to the cytoplasm is carried out through a layer of condensed chromatin located around the nuclear envelope. As is known, condensed chromatin is a chromosomal heterochromatin region (HRs), which have been found to be able to form structures with the highest thermal conductivity in the interphase cell [1,2].

From our point of view, the known (behavioral, morphological and physiological) mechanisms of adaptation in higher eukaryotes to changing environmental temperature conditions appeared

on the basis of cell thermoregulation. As is known, prokaryotes respond to the effects of extremely high or low temperatures at the gene level by producing special proteins (heat shock or cold shock proteins). In eukaryotes, in the process of evolution, in response to changing temperature conditions of the environment, in addition to the gene, a thermoregulation system has already emerged at the level of individual cells. We have not been able to find special studies devoted to the origin of the circulation system (CS) in the process of evolution, despite the fact that its anatomy and physiology are one of the most studied areas of biology and medicine. The fact is that CS is the first and main link in maintaining temperature homeostasis in higher eukaryotes, without which the organ-based thermoregulation system cannot function. We believe that the CS originated in macroscopic organisms in which cell thermoregulation was already functioning. To understand our idea, it is necessary to distinguish between the existences of two types heat transfer in the body of macroscopic organisms: the short and long-distance transfer of the thermal energy. It is obvious that the transfer of the thermal energy for short distances arose earlier than long distance transfer and it became possible with the emergence of the eukaryotic cells when metabolic processes began to occur in two relatively isolated domains: the nucleus and the cytoplasm. Obviously, this new circumstance laid the prerequisite for the emergence of a temperature difference between the nucleus and the cytoplasm, which must be timely leveled in order to maintain a relatively constant temperature environment in the cell, which we call cell thermoregulation [1,3]. We will address this issue in more detail below.

Let's try to comprehend when and why the long-distance transfer of the thermal energy (LDTTE) could emerge. It is not difficult to imagine that the necessity in the LDTTE became possible with the emergence of the large multi-cellular animals with sufficiently high level of metabolism when in the process of the life activity in different parts of the body sections with different temperature started to

appear. It is natural that under such conditions the organism will strive, in some way, to balance the differences in temperature in the body and, apparently, in the final end the natural selection had preserved precisely the circulatory systems (CS) as means of the far distance transfer of heat. The following three components should be included in the composition of any CS: 1) the circulatory fluid (which is usually blood); 2) the retractable organ which functions like a pump and provides for the running the fluid through the whole body (the heart or modified blood vessel); 3) the tubes inside which the fluid circulates (usually blood). It is considered that CS serves for the transportation of gases (O<sub>2</sub> and CO<sub>2</sub>), nutrients, hormones, ions and waste products of metabolism, and its role in maintaining temperature homeostasis is considered as a secondary process. We believe that CS arose primarily to maintain temperature homeostasis in the body of macroscopic animals and it is the most important link (element) of organismic thermoregulation. Since we discussed this issue in detail earlier here, we will limit ourselves to presenting some the main provisions from this work [3].

Since on the origin of the CS in the process of the evolution there are no special researches, we have no choice other than to speculate on the basis of the data on the fluid circulation in the body of the animals in order to have the most probable picture. So, the Protozoa have no special system for implementing the circulation of substances; the nutritive materials, products of metabolism and respiratory gases - they simply diffuse through the cytoplasm and in the final end reach all the parts of the cell. The central cavity implements the transport and digestion function in the Coelenterata. As a result of the alternate outstretching and contraction of the body the contents of the central cavity gets intermingles and the circulation of substances takes place. The earthworms and forms of the animals close to them have the well-defined CS consisting of the plasma, blood cells and vessels, though the latter have not yet been identified as the arteries, veins, and capillaries. There are five

pairs of “hearts” in the front part of the body – small pulsating tubes, which drive the blood from the spine vessel of the abdominal cavity and which encloses the system of the blood circulation. The contractions of the muscles of the wall of the body help these “hearts” to maintain the blood circulation in the body. All the comparatively large invertebrates (the bivalve mollusks, squids, crabs, insects) have the blood CS consisting of a heart, blood vessels, plasma and blood cells. The CS system of all the vertebrates is mainly constructed in a similar way. In the course of the evolution from the lowest fish-shaped forms of the vertebrates up to man the major changes took place in the heart and were associated with the respiratory mechanism – with the transformation from the gills breathing to the lungs breathing. From the above mentioned it might seem evident that the CS had emerged in response to the requirement of the organism of the multi-cellular animals in the transfer of the nutrients and gas exchange through the whole body, that is, the answer might seem to suggest itself.

However, we believe that the initial cause in the origin of the CS was as follows:

- 1) The simple physical processes such as the emergence of some macroscopic Metazoa of the permanent part with the various temperatures in the processes of their vital activity;
- 2) Existence of the intercellular spaces filled with the tissue fluid which re-flow from one part of the body into the other with the availability in the organism of the parts of various temperatures or pressures.
- 3) Availability of the contractive muscle cells in the body walls both with the Coelenterate, hydra and animals similar to them.

The fact that the CS has initially emerged not for the transfer of O<sub>2</sub> and CO<sub>2</sub> across the whole of the organism is confirmed by such examples as:

- a) The gas exchange with the Arthropod is carried out through the system of the tracheas, that's why their CS are not used for transfer of the respiratory gases. Their blood (hemolymph) is colorless and it contains no hemoglobin;

b) The Annelida, owing to the availability of the coelom the body wall are separated from the internal organs which provides the independence of the movement of such formations as the intestine. In this way, in the Annelida the CS implements the connection between the digestive tube and the body walls, that is, it does not serve for the transfer of the respiratory gases;

c) In closed CS (with the Echinodermata, Cephalopoda, Annelida, vertebrates) along the whole way the blood is put into special vessels which does not come into the direct contact with the cells of the tissue. The entrance to this closed loop system and exit from it is implemented only through the intercellular fluid. An animal with a closed CS has a third fluid, blood, in addition to its intra- and extracellular fluids;

d) The skin breathing with the many vertebrates can be added and even be replaced by breathing with the lungs or gills;

e) The CS are lacking or underdeveloped with the sea animals. They have no erythrocytes in their hemolymph, Hb is in the dissolved state in it.

Thus, in the process of evolution, in addition to the already existing two levels (molecular and cellular) of thermoregulation, a third organismal one appeared, which, in addition to heat, began to transport nutrients, hormones, ions, waste products of metabolism and blood cells [3]. We believe that normally the basic elements of the organismal thermoregulation function more or less the same in all individuals in the population. There is no evidence in the literature that there is hereditary variability in the functioning of the organ-based thermoregulation system at the population level. Whereas short distance transfer of heat energy, the material basis of which is condensed chromatin, is subject to quantitative variability [1-3]. The fact is that condensed chromatin, which is the highest form of organization of the chromosomal heterochromatin regions (HRs) in the interphase nucleus, consists of various non-coding, short, highly repetitive sequences of nitrogenous bases subject to wide variability at

the population level. Two types of chromosomal HRs are known: C- and Q-HRs. Chromosomal C-HRs invariably exist in the genome of all eukaryotes, whereas Q-HRs are present in the karyotype of only three higher primates (*Homo sapiens*, *Pan troglodytes* and *Gorilla gorilla*). At the same time, it is very important to emphasize that among these three primates, only human populations have a wide quantitative variability of chromosomal Q-HRs [4,5]. This circumstance turned out to be very important for us in understanding the reasons why humans and other higher primates were the owners of the most developed thermoregulation system [2,6].

A remarkable feature of the human genome is that: a) chromosomal C-HRs are present without exception on all its chromosomes, whereas Q-HRs can be found only on seven autosomes and the Y chromosome; b) unlike chimpanzees and gorillas, which also have chromosomal Q-heterochromatin, in the human karyotype Q-HRs may be completely absent without visible phenotypic or other manifestations; c) in the population, the number of Q-HRs in the human karyotype ranges from 0 to 10, whereas in chimpanzees and gorillas it varies within very narrow limits (from 5 to 7). We believe that this circumstance (the magnitude of the variability of the Q-HRs number) is very important in the short distance transfer of heat energy. Let's try to substantiate this statement by the example of a man.

We have repeatedly shown that the number of chromosomal HRs in the human genome determines the level of heat conductivity of the human body [2,7]. At the same time, the hereditary variability of the heat conductivity of the human body in the population is affected by the number of Q-HRs in its karyotype. The fact is that according to the total number of chromosomal C-HRs, human populations do not differ significantly from each other [8,9]. It is considered that a human has the most developed thermoregulation. Confirmation of this statement is the fact that only man has managed to master and populate all climatogeographic zones of the Earth.

However, the question of why exactly a human has the best thermoregulation system still does not have a complete answer. The fact is, according to the structure and functioning of the organ-based thermoregulation system, a human does not fundamentally differ from other mammals. After all, most of the knowledge on the mechanisms of maintaining temperature homeostasis in humans has been obtained from animal models. One way or another, no anatomical structure or physiological system associated with thermoregulation has been found in humans, which would be completely absent in other homoeothermic organisms. From our point of view, human still has a feature that distinguishes him from other mammals, including higher primates. By this statement we mean the features of its genome. In particular, a) in the human genome there are both types of constitutive heterochromatin known to science (C- and Q-heterochromatin); b) only in the human population there is a wide quantitative variability of chromosomal Q-HRs; c) chromosomal bands (G- and Q-bands) after differential staining are best manifested in the human karyotype, then in higher primates and other mammals. To be even more precise, the human genome, unlike other mammals, has an additional number of HRs, since interstitial heterochromatin is present in the G- and Q-bands; d) the number of chromosomal Q-HRs in the human genome depends on the geographical latitude or altitude of the permanent residence of this population; e) there is a close relationship between the number of chromosomal HRs and the level of human heat conductivity (for details see [2-5,7,11]).

Therefore, to the question: why does man have the most developed thermoregulation system among mammals, we would answer like this: a) among the higher primates, man has the highest body heat conductivity due to the presence of all types of chromosomal HRs in his genome; b) individuals in the population differ in body heat conductivity due to the wide variability of the amount of chromosomal Q-HRs in the genome; c) the wide variability of human body heat conductivity in the population allowed him to master almost all climatogeographic zones.

What consequences could these features of the human genome lead to? The presence of the largest number of chromosomal HRs in the human karyotype allows maintaining a very high level of cellular metabolism among all mammals. And this is possible provided that excess metabolic heat from the cell nucleus is efficiently removed and this depends on the total amount of chromosomal HRs in the condensed chromatin around the nucleus. In fact, it was this circumstance that made possible the emergence of homoeothermic animals in general up to the presence of intelligence in humans in particular [2,10,12]. The existence of individuals in a population with different body heat conductivity allowed for a human to adapt to different temperature conditions because: a) people with high body heat conductivity tolerate heat better due to their ability to effectively dissipate excess thermal energy into the environment; b) individuals with low body heat conductivity are better cope with the cold because of their ability to better retain heat in the body. Therefore, there are no people who are able to adapt to different extreme temperatures equally well due to the fact that they differ in the number of chromosomal Q-HRs in the genome. In other words, a human managed to master all climatogeographic zones not as the owner of the most perfect organ-based thermoregulation system among mammals, but because there are individuals in the population who differ from each other in the level of heat conductivity of their bodies, which is a phenotypic manifestation of cell thermoregulation.

Thus, the human thermoregulation system functions at three levels: molecular, cellular and organismic. The most ancient is the molecular level, and apparently it has not undergone significant changes in the process of evolution and continues to function at the gene level. The greatest evolutionary changes seem to have undergone cell thermoregulation, since its material basis is very variable non-coding highly repetitive DNA, which arose with the advent of eukaryotes. Therefore, it can be assumed that the organismic level of thermoregulation occurred on the basis of cell

thermoregulation and it arose with the emergence of a circulation system when permanent areas with different temperatures appeared in the body of macroscopic animals.

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