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ISSN: 2161-1041
Hereditary Genetics: Current Research

Review Article

Preliminary Examination of the Principle of Self-Organization in Multicellular Organisms: How Traits are formed

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ABSTRACT

Multicellular organisms organize themselves according to two principles; first, the equilibrium between the driving force of unstable state cells and apoptosis or senescence and second, the mutual equilibrium between the functional requirements of different types of cells. For the first principle, we deduce that stem cells at different levels have their own growth limits, which are determined by two factors, the ability of the stem cells to enter an unstable state (specifically, the ability of cells to divide and differentiate) and the rate of cellular senescence, loss of function and finally, apoptosis. The superposition of stem cell limits at different levels over each other can amplify small differences at the genetic level. Moreover, the growth limits of different organs are different, which lead to different individuals having completely different appearances. The second principle is that the sum of the specific output functions of an organ must be equal to the overall demand for the function to be provided by the organ. If negative entropy input can meet this equilibrium, defects in certain genes will cause these defective individuals to become larger or develop other morphology.

Keywords: Unstable state cells; Growth limit; Stem cells; Traits

INTRODUCTION

The field of biology is based on the widely accepted idea that genes determine traits. With the exception of a few traits that can be directly explained by simple genetic segregation, how most traits arise continues to be an important question. Several models and papers explaining biological phenomena from the fields of physics and mathematics are based on the doctrine of gene regulation. Despite the increasing number of reports of regulatory mechanisms, experiments guided by these models have failed to yield the expected results. What could be the problem? The problem is that the process from genes to phenotypes requires the expression of genes into proteins, formation of cells from those proteins, formation of an organism from those cells and the organism to manifest a phenotype. This means that two steps are involved to get to phenotypes from genes however, our biological system bypasses these levels by connecting the genes directly to the phenotype in a single step. Except for a few phenotypes, the vast majority are traits that cannot bypass these two levels. In the previous article, we used the catastrophe model to explain the cellular level; in this article, we will explore the principle of self-organization of multicellular organisms at the multicellular level and some resulting issues.

EQUILIBRIUM BETWEEN THE DRIVING FORCE OF UNSTABLE STATE CELLS AND SENESCENCE OR APOPTOSIS

The key to understanding this question is investigating the driving force of the development of an individual from fertilized egg to adulthood to death [1]. As the human body is a dissipative structure, it can obtain a large amount of negative entropy from the environment; this negative entropy ensures the development and growth of the human body [2]. Starting from a fertilized egg, the human body's specific phenotypes have converted the negative entropy obtained from the environment into cell division

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Received: 19-Jul-2023, Manuscript No. HGCR-23-22261; **Editor assigned:** 24-Jul-2023, PreQC No HGCR-23-22261 (PQ); **Reviewed:** 07-Aug-2023, QC No. HGCR-23-22261; **Revised:** 14-Aug-2023, Manuscript No. HGCR-23-22261 (R); **Published:** 21-Aug-2023, DOI: 10.35248/2167-0358.23.12:252

Citation: Cao Z (2023) Preliminary Examination of the Principle of Self-Organization in Multicellular Organisms: How Traits are Formed. Hereditary Genet. 12:252.

capacity, that is, the cell's ability to enter an unstable state. As the organism develops, fully differentiated cells gradually appear that serve specific functions and these cells basically do not have the ability of differentiation and division. If the negative entropy input of an individual organism can be fully met when the individual organism develops, it would have the ability to grow forever, but there is no tendency for higher organisms to grow indefinitely.

In the course of the experiment we observed the following phenomena:

- From the process of cell culture, any cell line will mutate and age after a long period, leading to division and reduced differentiation ability. Even tumor cells are not immortal and cells in living organisms are also subject to this process. Most tumor cells are difficult to grow in primary cultures. Their growth and proliferation was not strong. After purification into single tumor cells, most of these cells proliferated for several generations and then showed a stationary phase similar to that in diploid cell cultures. Only after passing this stage did the cell acquire immortality and grow smoothly from generation to generation. This showed that the immortality of *in vitro* tumor cells was obtained after *in vitro* culture [3-5].
- From different tissue culture cell lines, most fully differentiated cells do not have the ability to differentiate and cannot be cultured indefinitely. Human embryonic diploid fibroblasts can be cultured for 30-50 generations without freezing and repeated passages, equivalent to 150-300 cell proliferation cycles and can sustain a survival period of approximately one year before senescence and apoptosis. If the donor is an adult or senescent individual, the survival period is shorter; if other cells are cultured, such as hepatocytes or kidney cells, the survival period is even shorter and the cells can only be cultured for a few dozen generations [6-8].
- Human cells undergo constant renewal, different organs have different rates of cell renewal and some cells are not renewable.

Based on the above points, we find that there is an equilibrium between the driving force of the unstable state cells to generate new cells and senescence and apoptosis; this equilibrium determines the growth limit of the organism. The individual reaches this equilibrium when it reaches its developmental apex. The stem cells that comprise the different organs of each individual have different abilities to enter unstable states, their unstable cells have different driving forces to produce new cells and the growth limits of these organs are different, resulting in individuals having completely different appearances. This limit is determined by two factors: the ability of stem cells to enter an unstable state (specifically, the ability of cells to divide and differentiate) and the rate of cellular senescence, loss of function and finally apoptosis.

Here we introduced a parameter Cao Index (CI). The number of times per unit time that a certain type of cell enters the unstable state. This parameter indicates the ability of each cell to generate the next level of cells and to divide. This parameter may have a high correlation with the Potential Energy of Cell (PEC) per cell.

$$CI \propto 1/PEC$$

Different individuals of the same species, starting from their respective fertilized eggs, divide to form various layers of stem cells and finally differentiate into various specific functional cells. This process is driven by inputting negative entropy to generate negative potential driving force; the CI of each individual stem cell at different level is different and finally their growth limits are different, which determines the form that each gene can achieve under normal circumstances. For any set of genomes, this is its standard form. However, in reality, because the input of negative entropy is finite and individual development is not possible without external influence, there is a difference between the specific form of an individual and its standard form.

As the unstable state cells exist for a short period of time, we are not sure what indicator can be used to express their quantity, thus we chose stem cells, a class of cells that can enter the unstable state more easily, as the count indicator. Stem cells were classified according to developmental stages: embryonic, perinatal and adult stem cells and by differentiation potential: totipotent, sub-totipotent, pluripotent and unipotent stem cells [9]. From the fertilized egg to the fully differentiated cell, there are at least four levels of unstable states; the fertilized egg itself is also an unstable level hence, we considered the fertilized egg; totipotent, sub-totipotent, pluripotent and unipotent stem cells and differentiated cells as six levels, of which there were five unstable states and each unstable state had a CI. The author is 1.66 m in height. Assuming my growth limit is n, there is another person whose growth limit is 1.05 n at each level, then their height should be $1.66 \times 1.05^5 \approx 2.12$ m. If their growth limit is 1.1 n at each level, their height is $1.66 \times 1.15 \approx 2.67$ m. This is why Yao Ming and I have minor genetic differences resulting in a huge height difference.

MUTUAL EQUILIBRIUM OF THE ACTUAL FUNCTIONAL REQUIREMENTS OF DIFFERENT CELL TYPES

Another principle that the human body follows during development is that each cell has a specific function and the sum of the specific Function Output (FO) of an organ must be equal to the overall Functional Requirement (FR) for that function provided by the organ.

$$\sum FO = \sum FR$$

We know that housekeeping genes are a class of genes that are stably expressed in all cells and whose products are essential for the maintenance of basic cellular life activities, such as microtubulin, glycolytic enzyme lineage and ribosomal protein genes. Housekeeping genes are a class of genes that maintain low levels of methylation and are always in an active transcriptional state. There have been 575 such genes reported in humans [10], which means that a fully differentiated cell needs to express only 575 genes to survive; the expression of most of the remaining genes are for external functions, which we can call export cells. For cells that enter the unstable state (we are unsure if different layers of stem cells are in the unstable state at all times, this needs to be verified experimentally), besides these genes that are essential for survival, there are several

genes that need to be expressed to maintain the unstable state and the remaining genes are required for external function therefore, we think most stem cells basically do not show their function externally and we call them input cells.

This condition is necessary to be met for the standard morphology of the set of genomes described in the previous section. If this equilibrium is disturbed, the individual must make adjustments based on the two principles mentioned above, resulting in morphological changes, which determine the specific standard form of any set of genes. However, because differentiated cells maintain a steady state over a large range, there is a large range of regulation of starting functional output hence, this equilibrium is relatively easy to maintain (stable cells have a large regulatory range) [1].

A NEW DEFINITION OF GENETICS

Genetics generally refers to the phenomenon where genes expressing the corresponding traits in the parents are transmitted to the offspring through asexual or sexual reproduction, such that the offspring acquire the genetic information of their parents. In practice, we find that most of the offspring are not identical to the parents and there are even individuals that are completely different. When individuals with these characteristics appear, there is always a tendency to explain them in terms of variation. Is this explanation necessarily correct? When two individuals are crossed, the two sets of genomes recombine to form a new genome and this new combination leads to changes in the ability of stem cells at different levels and tissues to enter the unstable state, causing changes in their growth limits. This causes the offspring to manifest traits that are completely different from those of the parents and even some striking phenotypes. The author argues that this is a plausible explanation for genetic variations.

GENETIC DEFECTS CAN LEAD TO POSITIVE BODY SIZE GROWTH

Theoretically, each person carries a large number of genetic mutations. We assume that an individual has a genetic mutation that causes a decrease in the output capacity of an organ. If negative entropy input is unlimited, this organ needs to grow to balance the overall demand. This causes the functional demand of this organ on other organs to increase, causing other organs to grow as well. After re-equilibration, a new equilibrium form will be created and this individual will undergo morphological changes. If the negative entropy input can satisfy the re-equilibrium, the individual will become larger in body size. Therefore, another reason for the large difference between Yao Ming's body type and the author's may be that he has certain genetic defects that cause overall growth.

DISCUSSION

Genetic determination of traits is a fundamental principle of genetics and most traits in multicellular organisms are quantitative traits, except for a few traits. Quantitative traits are those traits in which differences in performance between individuals can only be distinguished by quantity and in which variation is continuous. It has two main characteristics: the variation is continuous and the variation is susceptible to environmental conditions. Its main characteristics are: first, individual differences are difficult to describe and require measurement; second, variation is continuous in a population; third, quantitative traits are often controlled by multiple genes and four quantitative traits are sensitive to environmental effects [11]. If this theory proposed by the author holds true, it seems that most quantitative traits and specific genes do not have a large degree of correlation. Instead, it seems that the collective behavior of many genes that are needed for the expression of these traits rather than their specific functions. In other words, replacing some of them with other genes will not affect these phenotypes as long as they do not affect the cellular potential. That is to say, for example, height, weight and other traits are the collective behavior of all genes and there may be some genes that play a greater role, but I emphasize here that these traits are the collective behavior of all genes.

For any individual of human, the genome, in theory, is highly plastic and can become all types of people, from Shaquille O'Neal to Albert Einstein. We can deduct from this theory that expressing some genes in a certain type of stem cell can increase or decrease the potential of the cell, making it easier or harder for this stem cell to enter the unstable state, allowing the individual to produce a change in the trait. If this theory holds true, anyone can become the person they want to be according to their own ideas. By the way, if the genes of a mouse, pig or fish were expressed in combination in a human manner, would the resulting organism be closer to a human or to the donor species? The author feels that it would be certainly close to human, but may have some rather peculiar physical characteristics.

CONCLUSION

The study delves into the principle of self-organization in multicellular organisms and its implications for genetic traits. It challenges the traditional understanding that genes alone determine specific traits and argues that the process from genes to phenotypes involves multiple levels of complexity. The study presents the evidence of suggesting that the equilibrium between the driving force of unstable state cells and senescence or apoptosis is crucial in determining the growth limit of an organism. Moreover, the study introduces the concept of the "Cao Index" (CI), representing the ability of cells to generate the next level of cells and divide. It proposes that this index may have a high correlation with the potential energy of cells. The equilibrium of functional requirements among different cell types is also explored, highlighting the importance of maintaining specific functions in individual cells to ensure overall organ functionality. The study redefines genetics, moving away from the conventional idea of variations and emphasizing

the collective behavior of genes in determining quantitative traits. This challenges the notion that specific genes alone lead to certain traits and proposes that the expression of many genes contributes to the manifestation of a particular phenotype. Additionally, the study suggests that genetic defects can lead to positive body size growth if the negative entropy input is sufficient to sustain the new equilibrium form. It opens up possibilities for further research and challenges the conventional understanding of genetics and its role in determining individual characteristics.

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