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SPECIFIC WORK GUIDE ON "ETERNAL LONGEVITY?"

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Introduction

Throughout life, living beings are born, develop, reproduce and die. Each living being has a specific life cycle; there are beings which live for days and others, like many plants (trees), whose life cycle is very long. In the case of human beings, until at least the middle of the 19th century, the average lifespan might be between 30 and 40 years, and although there were people in that era (and other prior ones) who lived longer, the average age was as indicated. With the improvement of medical practices such as surgery, hygiene, vaccination, antibiotics, etc. … the average lifespan has gradually increased and it is now said that human beings are born, develop, reproduce, age and die.

In a recent work (Cell 2016 167, 915-932) a drawing is shown (Figure 1) indicating the different stages in the life of a human being. This work deals with Aging and Longevity, and a possible difference between both terms can be found in the fact that at the same age, in aging there are more problems in functioning, whereas longevity can be understood as the existence of a better quality of life. The work aims at analyzing aging from two viewpoints; the social and the biological.

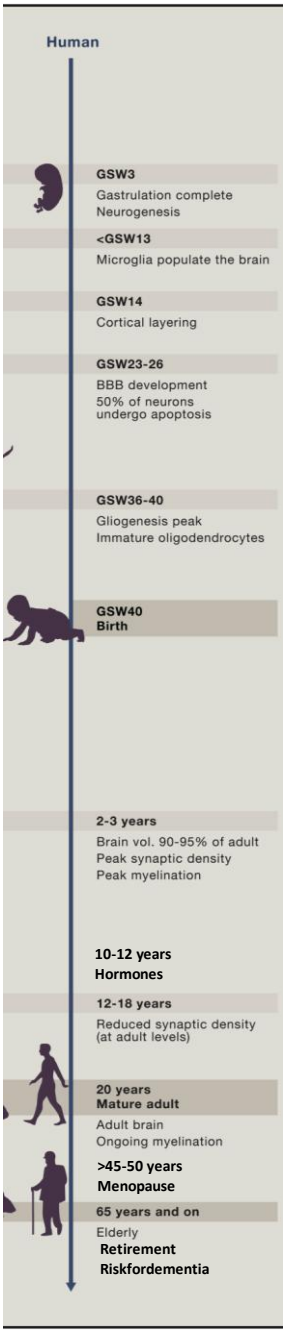
This part of the summary is going to focus fundamentally on the biological aspects of aging.

Stages in life

It all begins with a single cell, the zygote, which contains the mother's and father's genes which have been inherited by the one who will be the new human being. This human being's genes are going to have great importance in the different stages of the person, including the phase of aging.

Cell replacement and aging

The zygote is a cell which splits into two cells, which split again into four cells and so on, consecutively, until an individual forms with 103 or even 104 cells (depending on how big one is). In order to give rise to the adult individual, the cells have split (proliferated) and have differentiated into different cell types in order to form different tissues and organs.



Just like living beings, it has a half-life, the different cells also have a half-life, which might be different depending on each cell type. We replace them every so often, fundamentally in what we know as our body's periphery, that is to say, everything that is not the central nervous system. Thus, throughout life, the cells which make up the skin, the intestines, the bones … are replaced, while most of the cells of the central nervous systemcan have the same lifespan as the individual who has them, without being replaced.

Replacement in the peripheral cells occurs when a non-functioning cell, which disappears due to different types of cell

death, is replaced by other cells called stem cells which, after differentiating with the shape of the deceased cell, are going to carry out its function. The problem is that each tissue or organ has a limited number of stem cells and when the niche of these cells is used up, only the pre-existing cells remain, aging upon going past their half-life and deteriorating in their morphology and in their function. This deterioration can be more or less swift, corresponding to more or less swift aging.

Genes and aging

Changes or mutations in certain genes can give rise to premature aging. Mutations in the LMNA gene which encodes the proteins known as lamins A and C (present in the cell nucleus) can give rise to the type of disease known as progeria. Progeria gives rise to rapid aging.

Moreover, an accumulation of mutations in the genome which can take place during life (somatic) can favor the presence of premature aging. The so-called Werner and Bloom syndromes are examples of how the accumulation of damage in the genome can lead to aging. Additionally, modification (methylation) of the genome's components can regulate the time it takes aging to appear.

Markers of cellular aging

As indicated earlier, the lack of cell replacement can lead to changes in the cell which are related to their aging. These changes include the erosion of chromosome telomeres, while a reduction of the size of the nucleoli (structures present in the cell nucleus) can favor a lengthening of the cell life.

Another marker related to cellular aging is the loss of functionality of the organelle known as the mitochondrion, involved in providing the energy which is required for several metabolic processes. Additionally, the replacement of the proteins present in the cells slows down with cellular aging, so the half-life of the proteins also becomes longer and this aging of the proteinsenables their modification and loss of function.

Among these functions which are altered are the ones related to intercellular communication.

Aging can be delayed or reversed

Human beings' way of life, throughout the different stages of their existence, is highly related to their way of aging, as human aging will possibly be explained from a social viewpoint. Moreover, possible methods are currently being studied torejuvenate aged cells, or when this is not possible, to substitute old, damaged organs withprostheses. Regarding cellular rejuvenation, the procedure which is being experimented with is based on the description made by Japanese Nobel Prize winner Yamanaka, indicating that the process by which the zygote (see beginning of this article) can differentiate in specific cells can be reversible and that the process of cellular differentiation, which ends up in aging, can be reversed in a first step, an aged differentiated cell being able to become a rejuvenated differentiated cell.

Different possible mechanisms for the aging of peripheral tissues and for the central nervous system

It should also be noted, for future commentaries, that factors which can be negative and which can favor aging and a lack of functionalityin what we have calledperiphery, like the cholesterol levels or thesignaling of insulin, are required for the adequate functioning of the neurons within the central nervous system.

Finally, making changes to certain blood components has been suggested with regards to rejuvenation of the organism.

How to prolong a living being's life

As an aspect complementary to what was previously indicated, we wanted to refer to the use of invertebrate models, such as the worm (C.elegans), to study the factors which can be involved (and which we can experiment on) in the aging and the length

of the lifespan and which is fundamentally related to what is known as calorie restriction.

Lastly, we finish by commenting that aging is a risk factor forneurodegenerative processes, cancer or cardiovascular problems.

Debate topics

- Aging can be delayed and/or reversed
- How do you maintain the quality of life in longevity?
- How does stress affect aging?
- Is there a relationship between calorie restriction (eating less) and living longer?
- How does the aging of the brain differ from that of other parts of the organism?

Information sources

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