Ontogenetic memory of the cell

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Abstract

Objective: A hypothesis is presented here, that 'in the ontogenetic growth-aging process from conception to death of an organism, each cell has a reducing predefined finite reproductive potential and somatic life span of its own, defined by its temporal occurrence within the life-cycle of the organism'.

Methods : Phenomenological and Reductionist observations. Different species of living organisms have different species-specific finite life spans. In each of the species different cell lines have finite replicative potential, and, different cells have different life-spans.

Findings: The growth-aging process of ontogeny unfolds in a specific biocybernatic process. Either in the native state or explanted or transplanted or cloned or grafted state, the cell has memory of its original age and its remaining replicative potential and somatic life span.

Applications : are in the selection of cell in animal cloning, cell line in tissue transplantation, and the donor for organ transplantation and plant grafting.

***Keywords*:** Cell Memory, Growth - Aging, Culture, Organ Transplant, Grafting, Cloning, Biotechnology

1. Introduction

Sanatana Science states various biotechnology phenomena. Modern science has been elucidating various biotechnology processes.

Gerontology refers to the growth aging process from conception to death. In Organismal Senescence, this turnover system may become inefficient or may exhaust the regenerative capacity of progenitor cell lines, eventually resulting in the accumulation of senescent cells that contribute to aging.

In Cellular senescence [1,2,3] time-dependent accumulation of cellular damage is widely considered to be the general cause of aging [4, 5, 6]. Various mechanisms of aging have been established like Genomic Instability [7] , Telomere Attrition, Epigenetic Alterations [8], Deregulated Nutrient Sensing [9], Stem Cell Exhaustion [10,11] and Altered Intercellular Communication. Cause effect relationship in these mechanisms is not understood. Biological clocks, which objectively measure the biological age of cells and tissues, may become useful for testing different biological aging theories [11]. Comet assay was applied to study radiation induced senescence-linked DNA damage and apoptosis in cell lines of human origin [12]. Stem cells have different potency and therefore accordingly classified as totipotent, pleuripotent, multipotent or unipotent [13]. Studies on aged mice have revealed an overall decrease in cell-cycle activity of hematopoietic stem cells (HSCs), with old HSCs undergoing fewer cell divisions than young HSCs [10].

Adult cells, such as skin or blood cells, have a cellular "memory," or record of how the cell changes as it develops from an uncommitted embryonic cell into a specialized adult cell [14] and have a cell type identity.

The ontogenetic age of the donor cell at the time of the cloning, transplantation, grafting or culture as one of the basic determinant of its longevity in the explanted state, is not well established.

2. Materials and Methods

2.1. Phenomenological Approach

2.1.1. Human Population*: Homo sapiens* may have appeared about 50,000 B.C. At the dawn of agriculture, about 8000 B.C., the population of the world was somewhere on the order of 5 million. By 1 A.D. It reached 300 million. By 1800, however, world population had passed the 1 billion mark, and it has continued to grow since then to the current 7 billion. As per the guesstimates 108 billion people have lived on this planet [15].

2.1.2. Ontogenetic development: of growth-ageing process in billions of people over thousands of years has proceeded in a precise pattern of biocybernatics, and followed a biological clock from conception till death.

2.1.3. Human Life Cycle: The human being starts as a single cell, a fertilized ovum : zygote and ages as it grows to morula, blastocyst, embryo, foetus, neonate, infant, child, youth, adult, old, ending in death [16] (Fig.1).

2.1.4. Self Organizing System: From a single cell at the time of conception, the cell population increases to around 3.5 trillion at the time of birth and evolves into a structural, functional, biochemical social order of 60 trillion living cells at adulthood **(Fig.2), (Table 1).** The living cells grow, divide, and die in a programmed fashion, from toti-potent cell to the differentiated specialized cell lines and cells. Living Entity recycles the resources from the environment for its growth and self propagation.

2.1.5. Life Span of Humans: 108 billion humans ever lived on this earth [15], each had the potential to live for 126 years under natural circumstances, as the number of cell divisions and their longevity , in different cells at different stages of the ontogeny is predetermined. Environmental factors at different ages, and in the same age in different regions are responsible for variation in the life expectancy in different ages and regions.

Figure.1. Humans and animal Life cycles [16]

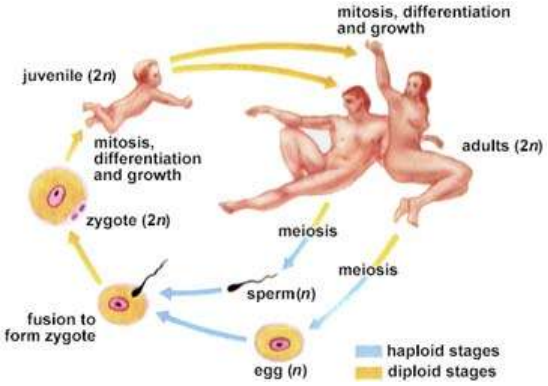

Figure 2. Ontogenesis

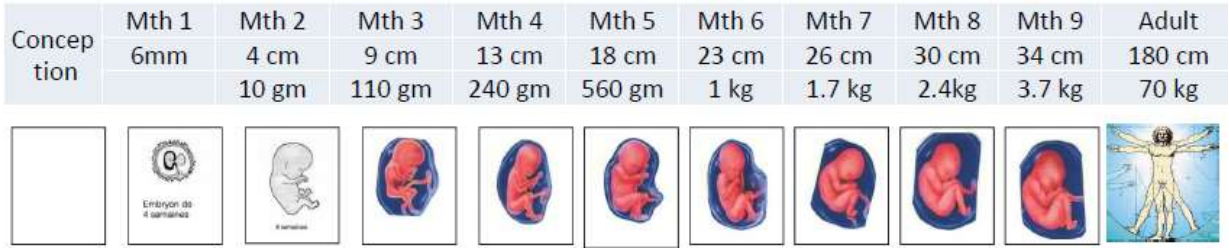

Table 1. Human Cell Population

Number of Cells		Cell Divisions	Volume	Weight	Stage
1			10^3 microns	1 nanogram	Cell
10^6	1 million	21		1 mg	
10^7	10 million	25		10 mg	
10^8	100 million	28		100 mg	
10^9	1 billion	31	$1cm^3$	1 gm	
10^{12}	1 trillion	41	$10cm^3$	1 kg 1 Liter	
37.2-60* 10^{12}	37.2-60 Trillion			70 kg	Human being

2.2. Reductionistic approach

2.2.1. Life Span of Cells: There are around 60 trillion cells in the body. Each type of cell has its own life span. The growth process is the aging process by itself. In the differentiation process cells divide and disappear as cells or stop reproducing and become senescent after a number of reproductive divisions and self-destruct (apoptosis). The average cell will divide between 50-70 times before cell death [17]**.** Though the cell may disappear, the cell lines continue. Differentiation process results in around 200 different types of cells: stem cells, germinal cells, reproductive cells and various somatic cells.

Red blood cells live for about four months, while white blood cells live on an average more than a year. Skin cells live about two or three weeks. Colon cells die off after about four days. Sperm Cells have a life span of only about three days. Brain cells typically last an entire lifetime [18]**.**

2.2.2. Life Expectancy of explanted cells: Doubling potential in vitro with the age of the donor of the postnatal cells was investigated. Human fibroblasts originated from adult donors have a shorter doubling potential than those originated from human embryos [19]**.** Several experiments support the idea that there is a relationship between the limited life span of human fibroblasts and aging of the donor. Cells obtained from human adults early during their life span in vitro have proliferation kinetics similar to those of embryonic cells during the last stages of their in vitro life span [20, 21]; that the potential number of doublings in vitro is inversely proportional to the age of the donor [22].

2.2.3. Life Expectancy of cloned animals: Sheep has life expectancy of 12 years. Dolly was cloned using a cell taken from a healthy six-year-old sheep [23]**.** Dolly lived for six and half years. Dolly had developed arthritis prematurely and type of lung disease which is most common in older sheep. On 2 February 2003, Australia's first cloned sheep died unexpectedly at the age of two years and 10 months. The cause of death is unknown and the carcass was quickly cremated, as it was decomposing. The only study of cloned mammals that have lived long enough to determine any effect on lifespan revealed that the mice involved died prematurely. The research was conducted at the National Institute of Infectious Diseases in Tokyo, Japan, and published in February 2002.

3. Results and Discussion

It was believed that vertebrate cells had an unlimited potential to replicate. Cell immortality was suggested by French Nobel-prize-winning surgeon Alexis Carrel, that all cells explanted in culture are immortal, and that the lack of continuous cell replication was due to ignorance on how best to cultivate the cells [24]. Ross Harrison describes the ability to maintain cells in culture [25]**.**

Later German biologist August Weismann speculated that “death takes place because a worn-out tissue cannot forever renew itself, and because a capacity for increase by means of cell division is not everlasting but finite” [26] . In vitro investigations revealed the finite replicative capacity of normal human fibroblasts which led to interpreting the phenomenon as ageing at the cellular level [27]**.** Cell-division counting mechanism could be involved in ageing was proposed by Hayflick. Hayflick and Moorhead discover the finite lifetime of cultured normal human cells and interpret this finding as a manifestation of human ageing at the cellular level [17]**.** Hayflick describes memory in cultured normal human cells: cells reconstituted from the frozen state remember at what population doubling level they were frozen and undergo further doublings only up to a predetermined maximum [28]. Hayflick recognizes that a direct relationship may exist between the population-doubling potential of cultured cells and the maximum lifespan of species from which they are taken .

Telomeres shorten as cells divide and are therefore considered a measure of aging [29]. Some cloned mammals, including Dolly, have shorter telomeres than other animals of the same age. Roslin Institute scientists claim that the cloned sheep, Dolly, has shorter telomeres than an age-matched control. Is Dolly a sheep in lamb’s clothing?[30]

Time dimension is implied in human life cycle as the human being exchanges matter, space and energy with the environment, all which are time dependent variables. Hence the life spans of the organism and the individual cell are defined. Each of the cell in the life cycle of the organism has an individual finite life span of its own, which is a dependent variable as the function of time in the life span of organism.

The physical structure of organism is constantly changing from conception till death. Every seven years on an average, every cell in the body, except the nerve cell, is replaced by a new cell. The body is rebuilt almost completely anew every seven years. But, the person does not become younger, but ages. The aging process of the organism is the independent variable.

In the differentiation process, which is the growth process as well as aging process, hierarchically from cell to cell, the living state potential and the doubling potential keep decreasing from cell to subsequent cell in different cell lines. Individual cell metabolism keeps decreasing from zygote to cell lines to differentiated cell of an adult to old age. Length of

telomeres keeps shortening. Hayflick Limit is specific to each cell in its ontogenetic developlment. Living State Potential of the organism, function of the organs and the metabolic rate of individual cell, decrease as a function of time, as the organism undergoes gowth-ageing process.

Normal cells are not immortal. Each of the type of the cells have their own life spans in the organism. Even the individual cell remembers the age of the native organism and ages according to the native's age when transplanted or cloned.

Ontogenetic memory of the cell's temporal position in the time line in the life cycle of an organism and the cell or organ or clone's memory of its remaining life span, has the predictive value of the longevity of transplanted organ, cloned animal and grafted plant.

Aging of the transplant is intrinsic to the native Donor's aging. Transplanted organ can live up to the lifespan of the of the balance of the age of the donor. Younger the age of the donor than the recipient, longer the survival of the transplant. The older the donor than the recipient, that much shorter the transplant survival for the recipient.

In cloning, the age of the clone-mother is the determinant of the age, longevity and he remaining life cycle of the cloned tissue or the animal.

In nature or in horticulture grafting, the age of the scion at the time of grafting determines the longevity of the stock-scion plant. It is general observation that in natural grafting, inosculation, both the plants maintain their biological identity and longevity. In horticulture the biological life cycle of stock-scion plant is that of scion plant. The stock plant is the interface, between the scion and the environment with its inherent character of hardiness, sturdiness, pest resistance, dwarfing. In precocity technique grafting of mature scions onto root stocks can result in early flowering and fruiting.

4. Conclusion

The central dogma of the Cell Immortality was replaced by Cell gerontology in scientific experiments. In the present hypothesis, based on phenomenology and reductionism, ontogenetic memory of the cell is proposed, in that each cell in the organism, is an independent organism by itself with the ontogenetic memory of its occurrence and its own longevity and replicative potential, within the time line of the life cycle of organism. Applications are in cell culture, artificial cloning, in-vitro fertilization, tissue explantation, organ transplantaion and plant grafting.

5. Acknowledgement

This work is not funded by any organisation. The author has no conflict of interest.

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The Publication fee is defrayed by Indian Society for Education and Environment (iSee). www.iseeadyar.org

Cite this article as:

Sreenile V. Chirala. Ontogenetic memory of the cell. *Indian Journal of Bioinformatics and Biotechnology.* Vol 4 (1), January, 2016.