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Review article

Differential Transcriptomic and Proteomic Analysis between Embryonic Cells and Aged Cells Confirms that Embryo is a Plethora of Rejuvenating Molecules

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ABSTRACT

Regenerative medicine has a wide scope, started with direct transplantation of various stems cells into the tissues or organs for functional restoration. In a further development, molecules of Stem cells are used for the treatment of organ function restoration, but they are the source for a few tissue growth factors. As they have limited scope, there is a need for comprehensive methods in treating age-related organ function restoration.

Sexually reproducing organisms pass through the different stage at which it starts their life from zygote to till it becomes a complete organism. Tissue differentiation and organogenesis are not life-long processes; they occur only at the embryonic stage that follows specific gene signatures. Every organ and tissues are unique in their functions; they need specific gene expressions and their proteins for differentiation and development.

Recent studies of comparative transcriptomic analysis of adult human Mesenchymal Stem Cells (MSCs) derived from dental pulp and adipose tissues showed that dental pulp-derived MSCs exhibit gene expression signatures of neuronal growth while adipose tissue-derived MSCs exhibit signatures of angiogenesis and hair growth. This confirms that Stem cells are a limited source for growth factors

This review emphasizes the transcriptomic and proteomic comparison between aged tissue cells and embryonic tissue cells. This comparative compositional analysis is a fruitful approach for tracing rejuvenating or anti-aging and growth factor for the whole organism.

Keywords: Embryonic stage; Fetal stage; Rejuvenating molecules; Comparative analysis

Abbreviations: MSCs: Mesenchymal Stem Cells; cEBP-α : CCAAT/Enhancer-Binding Proteins (C/EBP)-α ; BRM: Biological Response Modifier (chromatin remodeling factor); GDF11: Growth Differentiation Factor

INTRODUCTION

Age of atoms on the earth is almost equivalent to the age of early earth [1] and these age-old atoms constitute evolutionarily wide verity of organisms as well as many of number organisms of same species. Elemental a unity of all living organisms confirms that all living organisms are alike but their molecular composition reflects the evolutionary rank and life span of the organisms. It is also confirmed that organisms life span equal to the age of so many macromolecules in that organism.

The continuity of life is an evolutionary necessity [2] which lasts for millions of years, in two different ways. One way is evolving into other forms of living organisms by modifying their

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complexity and another way is the continuation of life through the process of reproduction. The process of gametogenesis, fertilization and embryogenesis are natural mechanisms of undoing aging. The entire process of rejuvenation mechanism of an organism starts at the gametic stage and continues up to the embryonic stage with some exceptions. Interestingly, fertilization capacity of gametes even after the middle age is also a promising aspect.

Birth and death are more chemically simplified as death is a matter of decomposition of macromolecules and redistribution of elements" and birth is a matter of refreshment with existing elements, this broader understanding may help in finding a solution for senile complications as well as the expansion of life. Although there are some apparent variations in anatomical resemblance, a wide range of lifespans ranging from few days to 5000 years. Even though different species have variable metabolic rates, there is also a numerable number of unifying features like Chemical unity of living organisms, the universality of genetic code [3] and continuity of life as a whole through billions of years. In fact, all living organisms work under the ambit of physical and chemical laws of nature.

All these unifications inspire to achieve longer lifespan [4] like bristlecone tree lifespan over 4500 [5]. Years in plant kingdom and Arctica Islandica clam for more than 400 years in the animal kingdom. These many thousands of years of the longevity of different organism underscore the emerging hope for an extension of the current life span.

There are a number of aging theories based on age-related molecular changes [6] and structural changes are identified only in adult cells. Polyunsaturated fats replaced with monounsaturated fats [7] changes in telomeres length [8], decreased mitochondrial efficiency [9] debilitation of cytoskeleton function [10]. DNA damage [11] and decrease of gene expression [12] there is no appropriate way to combat against aging complications. All current theories have limitations [13].

Every organism from its early young age to late middle age produces gametes [14] these gametes after fusion and fertilization in the female organism after embryogenesis gives birth to new offspring. This entire process occurs in certainly aged organism, which can also redefine as a matter of natural rejuvenation. During these activities, so many factors are involved and get expire at different phases that are required for cell division, tissue differentiating and growth. These three process more pivotal for tracing both signaling pathways as well as molecules responsible for growth and rejuvenation [15]. Current studies have focused only on the adult organism at which there may be unavailability of tissue-specific differentiating and growth factors [16] of all somatic cells.

First comparative experiment by Hozumi. N and Tonegawa. S between embryonic cell DNA and adult lymphocyte DNA [17] has established first direct evidence for rearrangement of genes that codes antibodies result in combinatorial diversity between the constant chain and variable chain that leads to antibody diversity. Recent fundamental experiments show Comparative transcriptomic analysis between mesenchymal stem cells and stem cells of adipose tissue of human confirms the availability of various growth factors. This experiment paved a way to extend the comparative transcriptomic and proteomic analysis between cells of the embryo at different stages and cells from different tissues of the aged organism.

Our hypothesis is analogous and more comprehensive to these studies. In our study, we are about to compare the embryonic cell with aged to identify the factors involved in the embryo at different stages of development, where all tissue differentiation and organogenesis occurs. Production of a new organism in the adult organism itself is an anti-aging mechanism.

Transcriptomic and proteomic comparative study help in tracing the molecules that are active in the process of tissue differentiation, organogenesis, and development in the embryonic stage. Tissue differentiation and organogenesis, not a lifelong process that occurs only at the embryonic stage that follows specific gene signatures

These determined molecules studied proteomic analysis will also be useful for the restoration of age-associating enervated organs. Organ function restoration is in-turn an elongation of life span.

ADVANTAGES OF EMBRYONIC CELL MOLECULES OVER STEM CELLS

Organ function restoration is simpler then organ synthesis from stem cell and the replacement because it is a complex process and it does not have any influence on organisms aging. It has been proving by transfusion adult blood transfusion in severe injuries. Many lower vertebrates have considerable regeneration capacity [18] of their organs but they have a life span, so creation early embryonic molecular environment is the optimal solution for the entire organism's refreshment. Some of the vertebrates like salamanders have considerable regeneration [19] adult vertebrates regenerate their limbs after amputation.

The regeneration is initiated by epimorphosis [20] a process which is characterized by dedifferentiation and high proliferation of the local cells. The process of epimorphosis starts with migration and proliferation of the epithelial cells immediately after amputation of the limb. Under epidermis, mesenchymal cells (muscle, cartilage, and bone) lose their phenotype and start to dedifferentiate into blastemal cells. These cells act as progenitor cells regenerate the limb. Evolutionarily humans have lost the ability of limb regeneration [21] but they have the capacity of regeneration for other tissues like liver, bone, connective tissue wound healing capacity after injuries and surgical resurrection. Additionally, young children and adults have the ability to regrow their fingertips.

In recent years with the advent of stem cell technology, stem cells from various sources have been using to repair organs like kidney [22]. Current trends in chronic kidney disease treatment are more refined, that includes protein molecules from vesicles from stem cells in amniotic fluid. This study emphasizes the molecular approach rather than the whole stem cell [23] Non-dividing cells like nerve cells, muscle cells need cell repair rather than cell replacement. They have the limitation with Immunological compatibility and individual genome variation.

In another novel development for the restoration of both obstructive and non-obstructive azoospermia testicle function by using stem cells, and extending this advancement we can usage of early embryonic molecules that are involved in organogenesis of the testis is best option to restore testicular function and maintain the genetic uniqueness instead of using stem cells from another individual.

FUNDAMENTAL EXPERIMENTS THAT ENSURES THIS REVIEW PROPOSAL

This hypothesis relays on several experimental results that are helpful to extend to studies further, for a comprehensive solution for senile complications as well as the expansion of life span. Irina and Michael's experiment is a historical experiment that laid a foundation for anti-aging molecular studies [24]. In this experiment, they established parabiotic pairings between young and old mice (Heterochronicparabioses) with parabiotic pairings between two young mice or two old mice (isochronicparabioses) as controls.

A decline in skeletal muscle stem cell (satellite cell) feature due to loss of notch signaling leads to loss of regeneration of aged muscle cell [25]. In parabiosis, animals develop vascular anastomoses and thus a single, shared a circulatory system. In this heterochronic parabiosis study, they noticed the restoration of muscle regeneration and muscle stem cell activation in aged animals this study also confirmed the decreases for this two factors cEBP-a and chromatin remodeling factor (BRM) play an inhibitory role of regeneration. A decline in skeletal muscle stem cell (satellite cell) feature due to loss of notch signaling leads to loss of regeneration of aged muscle cell. In another study, Vascular and Neurogenic Rejuvenation found in aged mouse brain by Young Systemic Factors [26] to the aged recipient. They are isolated factors in young blood that induce vascular remodeling, culminating in increased neurogenesis and improved olfactory discrimination in aging mice. Further, we show that GDF11 alone can improve cerebral vasculature and enhance neurogenesis. The identification of factors that slow the age-dependent deterioration of the neurogenic niche in mice may constitute the basis for new methods of treating age-related Neuro-degenerative and neurovascular diseases.

Nielsen conducted the experiments on blood transfusion by transfusion of young blood to the aged organism [27]. This study of young blood transfusion confirmed the role of GDF-11 factors by culturing age muscle and hepatic cells from mouse under the supplementation serum from young mouse dramatically enhances the proliferation of aged cells in a controlled manner. These experimental outcomes confirmed the improvement in muscle cells, hepatocytes regeneration, and reversal of cardiac hypertrophy and improved remodeling of aged bone. Sara Reardon's remarkable experiment isolated a protein from umbilical cord blood plasma young human that can improve memory function of the brain in aged mice. The first time a protein from human cord blood has shown its effect in the mouse. It is the latest evidence that transfusion of 'young blood' can reverse symptoms of aging like memory loss, decreased muscle function and metabolism, and loss of bone structure [28].

Another contrary experiment, a single heterochronic blood exchange reveals rapid inhibition of multiple tissues by old blood; their experiment confirms the result against the rejuvenating properties of young blood and points to old blood or molecules within the old blood that promotes the aging process. Their study suggests that young organisms blood itself will not work as effective medication, as said by Irina Conboy. It is more appropriate to say that there are inhibitors in aged organism's blood, so they emphasized more the focus on molecules present in aged organism's blood that promotes aging mechanism [29]. These special experiments of young blood transfusion have its own limitation on anti-aging, as many growth factors and tissue, differentiation factors expire before birth so they are not available in young blood. Apart from young blood, embryo also needs more attention, where so many growth and differentiation factors were available in specific stages of the embryo. We also emphasize the study should go beyond stem cell i.e., up to embryonic cell molecules.

A very recent study that authenticates this proposal is a comparative transcriptomic analysis of human mesenchymal stem cells of the dental pulp and adipose tissues [30]. In this study, dental pulp-derived MSCs expresses only neuronal growth factors, while adipose tissue-derived MSCs express two types of factors they are angiogenic and hair growth factors.

CONCLUSION

Parabiosis circulatory connection experiment between young and aged organism confirms that the aged organism's organs recovered from senility to some extent. If the young blood restores the aged organism tissue functions, then embryo would also be the precious source for rejuvenating molecules, as it is still in the formative stage for all organs.

In the aged female, a newly fertilized egg develops into the zygote. This zygote further develops into an embryo, then embryo further develops into the fetal stage and then into a young organism. Tissue differentiation and organ development start in the embryonic stage; hence, we have to consider the whole mechanism of embryogenesis as a natural process that restarts the young features. Mitotic division in the embryonic stage is unique, as the differentiation of tissues occurs, but whereas the mitotic division in adult tissues results in the same type of tissues.

Every embryo has the extended lifespan but every renovated tissue or organ should work in the ambit of stipulated age. Experimental evidence of stem cells and their molecular applications in the restoration of tissue and organ functions invoke to focus more on an embryo to trace the molecules that are involved in tissue differentiation and organogenesis and their development. With the above information, we propose a review article for a future experiment that confirms the embryo as a source for rejuvenating molecules. For this, we have to execute a comparative transcriptomic and proteomic analysis between cells of early differentiated tissues in the embryonic stage and different tissues aged organism will be helpful to identify the molecules promotes rejuvenating mechanisms which in turn useful for the anti-aging mechanism.

Differentiation of every tissue cell line needs differential gene expression so transcriptomic and proteomic comparative analysis between embryonic cell lineages and aged cell lineages would help in tracking of specific molecules. It will be useful to estimate the half-life and specific function of those molecules at the embryonic stage, as they are available only in the formative stage of the embryo.

Apart from the age and telomere lengths of chromosomes in the cells of carrying mother, every embryo possesses full-length telomere in their chromosomes. This comparative study helps to reveal the mechanisms involved in preservation of optimal telomere ends in the embryonic stage.

Finally, these factors are helpful in the clinical application of renewing of the aged whole organism at the tissue level. Study state of the organism and tissue homeostasis are remarkable pieces of evidence for the availability of tissue factors related to differentiation and growth during the embryonic stage. The rejuvenating aged organism needs to explore the embryo for the molecules responsible for the development of a new organism. Reproduction of new individual in a certain aged organism against aging features is nothing but a rejuvenating mechanism that operates at the embryonic level, so the embryo is a plethora of rejuvenating molecules.

AUTHOR CONTRIBUTION

Prasad SRP: Developed the intellectual content and drafted the manuscript; Rentala S: Given his extensive support in writing this article; Sreedhar S: contributed his efforts in proofreading of manuscript; Reddy BR: Supervised the drafting of this manuscript; Reddy AK and Kumar SD: provided critical feedback and helped to shape the manuscript; Radha Krishna N: involved in organization of references.

CONFLICT OF INTEREST

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter discussed in the manuscript. All authors discussed and finalized the manuscript.

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