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Biomarkers of aging. A mini review

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Key words: Aging, biomarkers, EVOLV2, cirRNAS, sCD14, microRNA, Heterochromatin-related aging, Lamin B1, Thyroid Hormone, Exosomes, Ret Oncogene, Germs, Lipids, Melatonine, sirtuins, Growth Factors.

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SUMMARY*: Biomarkers of aging give the true "biological age", which may be different from the chronological age. The main ones are: EVOLV2, cirRNAS, sCD14, microRNA, Heterochromatin-related aging, Lamin B1, Thyroid Hormone, Exosomes, Ret Oncogene, Germs, Lipids, Melatonine, sirtuins and Growth Factors.*

INTRODUCTION

Biomarkers of aging can anticipate utilitarian ability at a later age better than chronological age. Stated another way, biomarkers of aging will give the true "biological age", which may be different from the chronological age. Currently, good health in old age includes studies that explore or combine biochemical indicators such as:

1. Epigenetic changes: they refer to the mechanisms, outside of DNA, which regulate gene expression in cells, such as DNA methylation, histone alteration and RNA not encoded. DNA methylation is associated with aging and chronic diseases in humans. Elevated amounts of DNA methylation have greater danger enhancing a lot of age-associated diseases. Age forecasting models situated on DNA methylation are not only correct about chronological age, but also calculate biological rates of aging. DNA methylation age is described as a valuable

biomarker for prediction of real physical condition in old people and has been displayed to be related with high concentration of insulin, glucose and triglycerides. [1]

2. Genomic instability: when DNA fix procedures cannot correct cell damage. The effect is accumulation of DNA alterations, resulting gene expression deregulation and production of changed proteins leading to cell loss.

3. Telomeres length: telomeres are placed in the finale DNA strand and keep safe the ends of chromosome from harm. Throughout every reproduction, telomeres are reproduced, but not entirely, so they turn into smaller and participate to cellular aging. [2]

4. Mitochondrial disorder: a good biomarker of aging, related with incapacity in the old age, within muscle power reduction.

5. Proteostasis loss: proteostasis develops poor with aging and participates to immune response [2]

6. Cellular aging: aging cells create pro-inflammatory cytokines and chemokines, growth factors and uterine proteases called SASP (Senescence-Associated Secretory Phenotype). SASP has lately come out as a leader and encouraging healing goal for quite a few age-connected states of health, ranging from neurodegeneration to cancer [2,9]

7. Deregulated nutrient detection: genetic alterations in Growth hormone and insulin-like growth factor have been combined to lifespan. In addition, alimentary limitation has been shown to increase life prospect. [2]

8. Autophagy: is more functional in people with a long life and stem cell depletion, thus potential reduction is one feature in the base of aging. [2]

9. Altered intracellular message: as the inflammatory reply grows, additional modes of communication like endocrine, neuronal and immune system turn into dysfunctional.

SPECIFICALLY

EVOLV2: Methylation of ELOVL2 has been shown to be strongly associated with biological age of individuals. ELOVL2 is an enzyme which extends long chains of omega-3 and omega-6 polyunsaturated fatty acids (LC-PUFAs). Repression of Elovl2 accelerates aging in the retina of eye. Deposits are observed under the epithelium of retinal pigment, including C3 complement system, C5b-9 (the complement membrane attack complex, MAC), Htra1 (high temperature requirement A, serine protease family), implicated in the pathogenesis of retinal macular degeneration. [3]

cirRNAs: Circular RNAs (circRNAs) are a forthcoming class of unencoded molecules RNA believed to regulate gene expression and human disease. Three circRNAs (circDEF6, circFOXO3 and circEP300) are related with parental long life. [4]

sCD14: Differentiation unit 14 (CD14) is a glycoprotein which binds lipopolysaccharides and has many roles in microbes classifying and signaling. sCD14 may be a useful inflammatory biomarker, as higher levels are correlated with danger of mental deterioration regardless of vascular risk agents and is commonly used as circulating inflammatory marker. It is correlated with many indicators of brain aging and physical harm, involving total brain degeneracy. [5]

microRNA: New proof has shown that miRNAs direct dermal biogenesis and aging. A few miRNAs are down-regulated in long-term individuals, such as let-7, miR-17 and miR-34 (known as miRNAs associated with lifespan). Analysis of age-related dermal miRNA revealed raised expression of miR-130, miR-138, and miR-181a / b in keratinocytes for the duration of reproductive aging. These miRNAs act by targeting p63 and Sirtuin 1 mRNA. In particular, miR-181a is involved in skin's immune response, characterized in Langerhans cells. In addition, dermal fibroblasts express high concentration of aging biomarkers affecting all phases of cell life cycle, such as l et-7, miR-23a-3p, 34a-5p, miR-125a, miR-181a-5p and miR-221 / 222-3p. Between them, miR-34 family, excited by ultraviolet B radiation, deteriorates collagen amounts in extracellular uterus due to the activity of uterine metalloproteinases enhancing wrinkles formation. [6]

Heterochromatin-related aging (SAHF): Aging cells frequently give heterochromatin structures, a characteristic phenomenon known as Senescence-associated heterochromatin foci (SAHF). SAHF is full of heterochromatin 1c protein (HP1c), anti-silencing function 1 (ASF1), histone H3 lysine 9 trimethylation (H3K9me3) and phosphorylated histone H2AX (H2AX), related to age. [7]

Lamin B1: Lamin B1 is nearly connected to aging. In vitro, Lamin B1 expression is reduced in RS (replicative senescence) and prematurely aged cells induced by various points, such as DNA-damaging drugs, UV radiation, and oncogenes. In vivo, Lamin B1 has a great reduction in the internal aging of skin. [8]

Thyroid stimulating Hormone (TSH): Production of thyroid hormone (TSH) is a strictly controlled process with negative feedback implicating hypothalamus, pituitary gland and thyroid gland. Thyroid-releasing hormone (TRH) is created in hypothalamus. Once liberated, TRH influences pituitary gland, adheres to TRH receptor and provokes the production and excretion of TSH, also known as thyroid thyrotropin. Then TSH binds to TSH receptor (TSHR) and causes TSH production. Thyroid function is central to controlling normal and pathophysiological processes. Changes in TSH function have been correlated with disease as well as with fitness, varying from remarkable longevity in individuals with low thyroid function to lack of viability in people without TSH. [10]

Exosomes: a form of nanoscale vesicles with diameters varying from 30-150 nm, are usually found in biological fluids and central nervous system tissues. They transport proteins with a key role in intracellular communication. Exosomes also carry extended toxic amyloid-beta and hyperphosphorylated tau protein among cells causing apoptosis and participating to neuronal decrease and therefore neurodegenerative disease such as Alzheimer's disease (AD) which occurs mainly in old age and includes progressive cognitive impairment. Tau is a key protein related with AD pathogenesis and secreted extracellularly. In addition, exosomes have a detrimental function in accumulation and deposition of particular incorrect proteins, such as amyloid-beta, tau, prion and α-synuclein. These abnormal proteins can cause neurodegenerative disorders and spread proteins throughout the brain. Exosomes can not only extent pathological proteins but in addition have a detrimental role in neuronal functions fact related to aging. [11]

Ret Oncogene: Gray hair is a characteristic signal of aging in animals and men. Hair follicles without melanocyte stem cells (MSCs) are found. Graying hair with oldness in RET mice is associated with increased mature keratinocytes (KSCs), reduced levels of endothelin-1 (ET-1) expression and reduced receptor expression endothelin B (Ednrb) in MSCs. [12]

Germs: Several germs are also associated with age. These are bacteria of the intestine like Clostridium cluster IV bacteria whose abundance is observed to increase with age. The genus Blautia is also positive associated with age, and in addition it has been shown that Blautia hansenii can be used to predict chronological age. [13]

Lipids: Lipids are of great interest to predict cardiovascular (CVD) disease risk assessment compared to conventional clinical indicators. Despite CVD is age-related, its progress increases with high-fat diet, smoking, sedentary lifestyle and genetic tendency. CVD is one of the leading causes of morbidity and mortality in the world. It has been established that the risk of myocardial infarction is correlated with high Low-density lipoprotein (LDL-C) levels. Many people with normal LDL-C levels continue to develop CVD, which means that only LDL-C as an indicator is not enough to distinguish high-risk patients. Lipids are assumed to contribute to disease-related metabolic dysfunction. Lipids are implicated not only in CVD and chronic obstructive pulmonary disease (COPD) but also in infectious diseases and diabetes. Elevated levels of alkyl forms derived from Phosphatidyl-choline (PC), with shorter carbon chains and double bonds, decreased content in alkenyl forms derived from Phosphatidyl-ethanolamine (PE), with long chain length and high double bonds, have significant role in human lifespan background. Levels of sphingomyelin (SM) d18:1/20:0, SM d18:1/22:0, and SM d18:1/24:0 decline with age while levels of SM d18:1/16:0, SM d18:1/18:0, and SM d18:1/24:1 increase. Elevation of sphingolipids ceramides Cer d18:1/16:0 and Cer d18:1/24:1 also increase with age. Finally, 140 lipids observed are related to age, while a lot are sphingolipids, particular acylcarnitines and phospholipids containing omega-3 fatty acids and omega-6 fatty acids. [14]

Melatonine and sirtuins: Melatonin (MT) and sirtuins (SIRT) are anti-aging fragments which inhibit aging procedure and growth process of diseases associated with age. SIRTs direct transcription and cellular aging by deacetylation of histone target proteins. SIRT1,2,6,7 mammals are found in the nucleus, SIRT1,2 in the cytoplasm and SIRT3,4,5 in mitochondria. SIRT1 is related in the regulation of inflammatory reactions and mitochondrial function, avoiding tissue hypoxia. Reduction of SIRT1 and SIRT6 composition is associated with endothelial cell aging, expansion of atherosclerotic plaques, myocardial and vascular pathology. Vasoprotective properties of SIRT1, SIRT3 and SIRT6, recognizable in endothelial aging suggest a hopeful role in slowing down aging procedure and highlight these molecules as possible implements for curative approaches. [15]

Growth Factors: Age is negatively associated with platelet-derived growth factor-BB and insulin-like growth factor-1. Platelet counts in PRP is positively related with platelet-derived growth factor-BB, transforming growth factor-β1, epidermal growth factor, and hepatocyte growth factor. [16]

Conflicts of Interest: The author declares no conflicts of interest regarding the publication of this paper.

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