dCellular Theories of Aging

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There are multiple theories of aging, which include evolutionary, molecular, cellular, and systemic theories. The focus of this entry will be on the cellular theories of aging. There are two main categories of theories of cellular aging, error theories and programming theories. The error theories suggest that aging is a result of an accumulation of errors as an outcome of environmental insults that leads to damage at various levels of the cell. Error theories also propose that imperfect repair mechanisms are a factor that leads to cellular aging. The second category, programming theories, suggest that aging is a genetically programmed event. However, these two broad categories of theories are not mutually exclusive, for example, altered proteins can alter gene expression. Specific theories of aging from the two main categories will be discussed.

Error theories include Wear and Tear, Waste Production, and Cross-Linking. Dr. August Weismann developed the wear and tear theory in 1882, suggesting that cells and tissues have important parts that wear out as a result of aging. The Waste Production theory suggests that there is a build of of toxic substances as we age, such as lipofuscin. Lipofuscin is the build up of nonenzymatic glycosylation, which can be oxidized to form massive cross-links between lipids, nucleic acids, and proteins. Cross-linking is the linking of two or more molecules by a covalent bond. For example, it is proposed that collagen cross-linking decreases the elasticity of tissues as an individual ages. Next is the cross-linking theory, which suggests that an accumulation of cross-linked proteins damages cells and tissues, which leads to the slowing down of bodily

processes, which ultimately results in aging. This theory was proposed by Johan Bjorksten in 1942.

Somatic DNA Damage Theory is another error theory and suggests that damages occur continuously in the DNA of living organisms. Some damages are repaired, while others are not and accumulate over time. This is a result of inadequate cell repair mechanisms, such as DNA Polymerases that cannot correct defects as rapidly as they are produced. Additionally, genetic mutations occur more frequently and accumulate as an individual ages, which can result in malfunctioning cells and deterioration. This theory suggests that damage to the genetic code results in aging.

Another error theory is the Free Radical theory, which suggests that free radicals result in damage to the macromolecular components of the cell. As a result, there is an accumulation of damage that causes cells to stop functioning, which causes progressive deterioration of tissues and organ systems. Macromolecules include lipids, nucleic acids, proteins, and sugars, which are all susceptible to free radical attack. Free radicals are ions with an unstable configuration, because they have an unbalanced electron. Their unstable nature makes them highly reactive to other molecules, because they will take an electron to balance themselves, creating another free radical in the process.

Programming theories are the other major theories of cellular aging. These theories propose that aging is programmed. Telomere shortening is the main programming theory, also known as the Cellular Senescence Theory, which suggests that telomeres are the mitotic clock. In other words, with every cell division, it is thought that a small amount of DNA is lost at each chromosomal end (telomeres), causing shorter telomeres after each cellular division. Research suggests that as we age, we have a decreased capacity for cellular division. This led to the theory

that telomere length regulates the replicative life span of the cell and contributes to aging. However, research suggests that DNA replication is not the only factor of telomere loss. Oxidative stress can accelerate telomere loss. Therefore, telomeres do not shorten at a constant rate, but rather shorten in response to oxidative stress. Other programming theories include Codon Restriction, Repetitive DNA Loss, and Terminal Differentiation.

There are multiple factors of cellular aging, and there is currently no consensus on the causes of aging. However, these theories are not mutually exclusive. Aging is an extremely complex process. However, if we can develop an understanding of how these theories interact, then it may be possible to foster successful aging and increase human lifespan.

Further Readings

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