A Micro-review of Oxidative-Stress Hypothesis and its Effect on Aging

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This review is to look at three different scientific studies that deal with oxidative-stress hypothesis. The studies deal with different recent and relevant discoveries that deal with the effects of oxidative stress. Even though the hypothesis is around sixty years old, there is room for criticism in one way or another, which keeps it from becoming a theory. This article will discuss the role oxidative stress plays in aging, and the hypothesis that it is the driving force behind the aging of a human being. Now while it is a known fact that reactive oxygen species do bond to biomolecules, it is not known whether this is the cause of aging or if it is a biomarker caused by another aging process. This review's purpose is to sum up the procedures and results of the experiments done, as well as discuss how valid the experiments are and how relevant they are to the hypothesis.

Introduction

This micro review focuses on recent advances in the oxidative-stress hypothesis. This hypothesis states that one of the factors that causes aging in humans is reactive oxygen species (ROS), and the interaction they have with important cellular structures that hinders cells overtime. While the cell has structures to eliminate the ROS overtime, the structures get less effective and therefore allow the ROS to bind to different cellular structures. This hypothesis is mainly used to show why different members of the same species age differently. The more ROS a species produces from processes, such as, the metabolic process of mitochondria, the faster the aging process unless there is a reasonable number of enzymes to break down the ROS. This is one of the most widely accepted hypotheses for one of the main causes of aging, because of the relatively large amount of supporting evidence. However, the problem is that scientists aren't sure if the ROS is the cause of aging or if it is just an indicator of some other cause for aging. The three articles will show different sides of this theory by using three articles that deal with, the inhibition of a receptor of lab mice to cause premature aging, the regulator of lab mice to cause the aging of the heart, and the comparison the antioxidant defense and the age of different primate species.

Recent Progress

In the Lee, Liu, et al. article, one of the recent progresses made for this hypothesis is the "premature aging with impaired oxidative stress defense in mice lacking TR4." TR4 is a receptor that helps regulate various genes as well as help to regulate oxidative stress defense. The mice lacking the TR4 gene showed physical features of premature aging such as graying hair. The results of the study show the connection between TR4, cellular stress defense, and aging in mice. To assess the level of oxidation, the level of a common oxidized macromolecule was compared in the experimental mice to the control mice. The study allows for an analysis of TR4 as a main contributor in aging defense. The results show that the TR4 receptor can be restored to the system of the mice before a certain time to increase its longevity of life.

In the Bailey-Down, Mitschelen et al. article, the main progress made for the oxidative-stress hypothesis is that of Nrf2, which is a molecule that helps with vascular antioxidant defense, can be inhibited by a lack of a key regulator, IGF-1. This leaves vasculature vulnerable to

ROS. This vulnerability can cause premature aging of structures such as the heart leading to a variety of cardiovascular diseases. The procedure of this experiment was to shut down the "Igf1 specifically in the liver of mice" and measure the amount of ROS in an aorta using fluorescence. They also compared the cell death using a "cell death detection kit." The results show that inhibiting the function of the liver will also affect the health and aging of the heart.

Csiszar, Podlutsky, et al. researches the oxidative stress hypothesis in primates. This experiment reveals an association between a longer lifespan and a greater antioxidant resistance, which is in accordance to the oxidation-stress hypothesis. Because people are so closely related to primates, researchers conclude that a greater antioxidant resistance will lead to a longer life in primates as well as humans. The mean average of different primate species was used to obtain estimates for each species body mass and age. They also compared the cells of the different species to see which ones had a greater antioxidant defense. In order to do this they exposed the different types of fibroblasts to a variety of oxidation stress inducers.

Discussion

The Lee, Liu, et al experiment is promising for future studies because researchers were able to cause phenotypic changes in the mice that caused premature aging and premature death. There is a main problem in the study though. Since TR4 regulates various genes, it is essential for genomic stability. This fact would make an observer think that maybe it was not the lack of antioxidant defense that caused the aging, but merely some other genomic function that was hindered due to the lack of TR4 receptor. What the study should have done is to find some kind of receptor or enzyme that dealt specifically with antioxidant defense, and that way it would further eliminate the possibility of there being other factors in the premature aging of the mice. Further research that could be done on this subject would be to study other regulators that regulate things similar to TR4, but vary in some way to start eliminating the possibilities of the causes of premature aging.

The Bailey-Down, Mitschelen, et al experiment is a strong supporter of the oxidative stress hypothesis, because a key regulator of antioxidant defense inhibited in a certain area caused that area to age by itself. This effectively shows that ROS is the main cause of aging since a body part without the antioxidant defense aged faster than that of a different body part. Not only is this a big support for the oxygen-stress hypothesis of aging, but it also shows that different parts of the body can age at different rates, further supporting the hypothesis that an extracellular force affects the aging process. One of the main ideas to research further is the possibility of

inhibitors of the Nrf2 regulator besides an endocrine problem. Another thing to look at is if the Nrf2 is the only thing that is inhibited by the Igf1 deficiency. There could be another inhibited process that was overlooked, and therefore the research could be questionable, but there is really no way to do this besides guessing.

The Csiszar, Podlutsky, et al. experiment was interesting because other studies experimented on small laboratory animals with shorter lifespans, however this study was run on a variety of primates. The ability of a different species to defend against antioxidants did seem to affect the life span of that animal, which supports the oxidation-stress hypothesis of aging. The main problem with this experiment however is that multiple species were compared against each other; this makes the experiment inconclusive because there are many more different genomic differences between primate species than just their oxidation-stress hypothesis. The experiment would have been made better if primates were compared not across species, but between a single species. This experiment would have taken much longer, but the results would have been much more conclusive. The changed experiment would also allow for a more in depth observation of the subject instead of using data acquired from a different primary source. While this is a new take on the subject, the lack of controlled tests due to multiple variations across species makes this experiment subject to doubt.

Sixty years later the oxidation-stress hypothesis is still just a hypothesis. Even though all of these experiments support the hypothesis, they each have flaws, which could call to doubt the hypothesis's validity. However, making an experiment that would allow for the conclusion to be without doubt is difficult with current technology because if you inhibit antioxidant defense there will probably be some other process inhibited. Overall these experiments provided support for the hypothesis which will help it on its way to becoming a theory.

References

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