The Human Aging Process:

Gene Loss as the Primary Cause

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Scientists from the Molecular Biology Division at the University of California, Los Angeles, explain the research demonstrating that gene loss is the primary cause of the human aging process. This article is the first of several which provides a biological explanation for the potential for low level chemical/pesticide exposure (and even recreational drug use) to contribute to accelerated aging of the human system.

BACKGROUND:

Every cell in the human body contains approximately the same 30,000 genes. They are located in every heart cell, every brain cell, every immune system cell, every skin cell, etc. While the majority of these genes are responsible for passing on hereditary traits to offspring, most people are unaware that there is an extremely important group of about 4,000 genes active at this moment controlling - guiding - instructing - any particular cell's function. For example, in the human liver, an estimated 200 liver genes are "turned-on" to guide the function of each liver cell. In our immune system's white blood cells, these 200 "liver genes" are of course not necessary and therefore, are literally "turned-off." However, on a different part of the DNA molecule there is another set of approximately 200 genes which are "turned-on" (active) controlling all aspects of the immune system cells. These 200 genes are controlling such things as - how each immune cell communicates with other immune cells - how each immune cell makes essential compounds such as interferon and interleukins to fight viruses and cancer - how well the cell can differentiate between foreign cells and friendly "self" cells - or how effectively some immune cells can identify and destroy cancer cells on the spot. In other words, your immune system cells have an extremely complex and important job for maintaining health every second you are alive.

Early Stages of Illness

When enough of these 4,000 genes become weakened or damaged in any way, we then begin to experience any of a multitude of subtle health effects. This could be something as subtle as dry skin (if the genes that control skin oil output are not functioning up to par), to catching colds easier and having them for a longer duration (if your immune system monocytes,

a type of white blood cell, did not identify and eliminate the first viruses which entered your body).

Obviously, when a large number of important genes are damaged, the consequences could be uncontrolled growth of cells, otherwise known as cancer (when the growth genes are damaged) - mental illness (when the genes controlling brain cell function are damaged) - and even death (if our immune system genes are so damaged that they cannot control our white blood cells well enough to protect us from pneumonia bacteria or viruses).

SOURCES OF FAILURE

Our gradual move toward aging has been identified as occurring due to four major categories:

1) GENE REPRESSION

The first of these is gene repression (the switching off) of genes whose products are needed to maintain function. Genes work as chemical messengers. They send out natural chemical messages which are essential for telling the different parts of the cell what to do. If any important gene is turned off temporarily, that cell will not be working at optimum efficiency for as long as the gene is turned off. The possibility exists that some genes may be temporarily turned off due to nutritional deficiencies or toxic insults (alcohol, smoking, pesticides/chemicals, etc.). Removal of the problem source would then allow the gene to literally turn itself back on.

2) INTRACELLULAR COMMUNICATION AND SPATIAL REARRANGEMENTS:

The second source of decreased function derives from the spatial relationships between working parts of the system. Because there is an optimum spatial arrangement of the parts of a cell, tissue, organ system or body with respect to each other (an arrangement that provides for the rapid transfer of materials from one part of the cell to the other), any change in physical relationships or in barriers to diffusion, will result in some decrease in optimum function.

3) ACCRETIONAL DEFECTS:

The third contributing source of dysfunction during aging is the accumulation of waste materials composed of nonfunctioning or poorly functioning parts of the system. For example, the human liver must acquire 70% damage before abnormalities appear in routine blood tests. One of the liver's jobs is to remove "bilirubin" from a person's blood. Bilirubin is a natural by-product produced when red blood cells end their life cycle. When bilirubin reaches high level a person is

said to have "jaundice." Bilirubin is itself harmful to the brain if it accumulates to high enough levels in the blood. One of the many different jobs performed by the liver is to remove bilirubin from the blood. If the liver's billirubin removal cells are not functioning properly - billirubin can then concentrate in the blood which results in damage to the health of the individual.

Similar problems happen with the human kidneys. It is estimated that 90% of your kidneys must be damaged before abnormalities appear in blood tests of kidney function. Therefore, you can be exposed to kidney damaging circumstances for many years, but have no idea that gradual damage is occurring since you must reach the 90% damage point before you start feeling ill.

4) DEPLETIONAL DEFECTS

The final type of change that is responsible for the aging process is the physical loss of functioning parts. Such loss may involve any working part of the body such as loss of cells in muscles, the heart, the thymus gland, the brain - anywhere. Finally, the most important loss involves the loss of working parts of individual cells, including their genetic information stores.

There is a small amount of evidence that suggests that long-lived species are better able than short lived ones to counteract the effects of damaging substances or agents (e.g. free radicals or UV irradiation as reflected in "unscheduled" DNA repair (Hart and Setlow, 1976).

Free radicals are believed to be particularly destructive agents. The most common of these ubiquitous substances are the radicals .OH and .OOH. The first of these is derived from hydrogen peroxide (HOOH) when half of the molecule is reduced to water.

Free radicals have also been found to have damaging effects upon your DNA. It is well documented that the mutations caused by treatment with ionizing radiation are greatly increased in number at a particular dose if oxygen is present in the medium in which the organisms are irradiated.

Gene Loss as the Primary Cause of Aging

As stated by the scientists in this article (pg.298),

".... genetic damage (particularly gene loss) is almost certainly a (or probably the) central cause of aging."

The first studies on human DNA dosage in regards to age indicated a very substantial loss of DNA from the human tissue as a function of age (Johnson et al., 1975). This study was subsequently expanded to include 29 individual human hearts. The previous results were again validated (Strehler et al., 1979a). The evidence indicates that 0.5% of the original amount of DNA is lost per year from the human heart. An even greater loss of DNA (0.7%) was then demonstrated in two separate regions of the human brain (hippocampus and sensori-motor cortes). Moreover, the rate of loss per year is 5-7 times more rapid from dogs' tissues than it is from the same human tissues. This number is very similar to the ratio of the maximum longevities of these two species (120 years vs. 20 years, a 6/1 ratio) - which implies that this loss limits the maximum lifespan of both species.

Comparison of Lifespan, Functional Loss and DNA Loss

Humans vs. Dogs

Tissue	Species	DNA Loss
Lymphocytes	Man	0.45% per year
Brain -- SS Cortex	Man	0.79% per year
Brain -- Hippocampus	Man	0.80% per year
Heart Muscle	**Man**	**0.60% per year**
Brain	Dog	2.10% per year
Muscle	Dog	3.20% per year
Heart Muscle	**Dog**	**3.30% per year**
Average DNA Loss	Man	0.61% per year
Average DNA Loss	Dog	2.87% per year

Studies of humans after age 30,

show the rate of DNA loss to be at about 0.97% per year.

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