INTRODUCTION

This newsletter will address how our lives are to a large extent influenced by the information coded in our DNA and whether that information is expressed or silenced.

The nucleus contains DNA. This substance contains the genetic instructions for the construction and functioning of all cells and higher organisms. The segments of the DNA which contain this genetic information are called genes. The genes are organized within long structures called chromosomes. We can liken DNA to a sentence, the genes to words and chromosomes phrases. There are four letters in the DNA alphabet: A or adenine, C or cytosine, G or guanine, and T or thymine.

DNA is one of three large molecules essential for living things. The other two molecules are RNA and proteins. RNA reads the instructions off of the DNA in a process called transcription. The information is then used to manufacture proteins and other substances.

DNA is structured in the form of a double helix (see illustration). It is tightly wound around a (histone) core just as thread is tightly wound around a spool.

PROTEIN SOURCES

DNA and RNA are not protein, but they serve as templates for synthesis of protein. Protein becomes an important nutrient for maintaining proper operation of the DNA and RNA. Lack of protein to DNA is like depriving a factory of raw material to produce finished products. The word protein means “to be first” because it has long been known that what we see in the mirror is largely protein.

Consumption of poor quality protein can lead to damage to DNA. Science uses the term mutagen to refer to a physical or chemical agent that damages the genetic material, usually DNA. Many mutagens cause cancer.

Certain forms of cooking can introduce mutagens and carcinogens into foods. High temperature broiling and frying of foods like chicken and beef can introduce significant quantities of mutagens into the food. Commercially cooked hamburgers have demonstrated a wide range of mutagenic activity. All protein-rich foods cooked to a well-done state will develop mutagens.

GNLD developed the protogard process to protect or guard protein from damage. The process involves breaking down protein with digestive enzymes at body temperature. Proteins can be broken down with heat, acids or bases, but all of these damage the quality of the protein and may introduce mutagens which can damage the DNA. The first step for healthy DNA functioning is intake of quality protein which has not been seriously damaged by heat.

REFERENCE:


DNA DAMAGE

The DNA is very prone to damage by oxidation. Work by Bruce Ames suggests that the DNA of each cell in the human body receives 10,000 hits from free radicals every day. DNA damage can lead to cancer. Cells usually contain two duplicate pairs of genes. Damage to both genes greatly increases the risk of cancer and creates a major obstacle for the DNA repair mechanisms in the cells.

Antioxidants such as carotenoids can function as powerful protectors of the DNA, decreasing the risk of damage when exposed to harmful substances.

One study showed that supplementation of a diet low in carotenoids reduced oxidative damage within cells.
by 44%. This is probably one of the reasons that diets high in carotenoids from food have repeatedly been associated with a reduction in the incidence of various types of cancers.

REFERENCES:

EPIGENETICS AND DNA

Epigenetics is a word composed of two Greek words meaning “on top of the gene.” The classic definition of epigenetics is the study of changes in gene expression caused by mechanisms other than changes in the underlying DNA sequence which can be inherited. In other words, DNA expression can change while the underlying DNA remains the same.

The word epigenetics can be used more generally to describe anything other than DNA, for example nutrition, which influences the manner in which DNA behaves. That sense of the word will be used here. Changes in DNA expression, in this sense, may last for hours, for the life of the cell or for several generations. From a nutritional standpoint, it is important to realize that nutrients and other factors can alter DNA expression for short or long periods of time.

The power of epigenetics is illustrated by the queen bee. The DNA of a worker bee and of the queen of a hive happens to be identical. Queen bees are fed a special food, royal jelly, which silences or blocks the expression of a key gene. The developing bee becomes a queen rather than a worker.

SHORT TERM EPIGENETIC EFFECTS

Some genes that code the cell for growth can potentially become cancer genes (oncogenes) if they are damaged or switched on. Such genes are called proto-oncogenes. One such gene is called the n-myc gene.

The most common cancer in infancy is called neuroblastoma. Amplification of the activity of the n-myc gene by anywhere from 3 to 300-fold is common in this disease and is correlated with advanced stages of the disease.

Carotenoids are the fat soluble coloring pigments in fruits and vegetables. They have very powerful antioxidant activity. They also appear to have an ability to exert short-term beneficial effects upon proto-oncogenes.

Alpha and beta-carotene have an inhibitory effect upon the n-myc gene in neuroblastoma cells. Three hours after exposure to a relatively weak solution of alpha-carotene n-myc activity of human neuroblastoma cancer cells was reduced by 24%. Within 18 hours activity of the gene dropped to 18% of that in untreated cancer cells. The inhibition peaked at 18 hours.

The researchers concluded that alpha-carotene locked malignant cells in the rest phase of their growth cycle. Higher levels of alpha-carotene actually proved toxic to the cancer cells. Beta-carotene had similar effects although concentrations had to be ten times higher than those used in the alpha-carotene experiments.

This is an illustration of the short term modification of gene expression by a nutrient. A variety of other carotenoids have been shown to inhibit activity of proto-oncogenes and to inhibit cancer growth or to prevent cancer.

Polyphenols and flavonoids are the water-soluble nutritional counterparts of the carotenoids in foods. They appear to have similar activity to the carotenoids. A flavonoid blend in one study slowed the growth of breast cancer cells by over 90%.

Important polyphenols include resveratrol found in grapes and wine, punicalagins found in pomegranate, and catechins found in green tea. These substances have been shown to provide a wide variety of health benefits.

LONG TERM EPIGENETIC EFFECTS

Some epigenetic alterations of gene expression can last a lifetime or several generations. A plastic component called bisphenol-A (BPA) has been shown to increase blood pressure and insulin levels after four days of exposure.

A research team headed by Dolinoy conducted an interesting experiment with agouti mice. These mice are thin and brown when the agouti gene is methylated. They become yellow and obese when the gene is not methylated.

Dolinoy exposed mice during pregnancy to bisphenol A. The exposure resulted in inadequate methylation of the gene. The normally brown mice became yellow and obese. Supplementation with methyl donors (betaine, vitamins B6, 12 and folic acid) or genistein (a flavonoid found in soybeans) protected the mice from alteration of the genes. They retained their brown color and thin bodies. Once the epigenetic change takes place it is relatively stable for a lifetime.

Methyl donors are very important nutrients as they play a key role in whether many genes express themselves or are silenced. These nutrients are often deficient in the diet and deficiencies have been associated with a wide variety of degenerative conditions. GNLD Lipotropic Adjunct is designed to supply a boost for this
category of nutrients. They are also supplied in many multiple vitamins.

Bisphenol A and other pollutants appear to be epigenetic culprits in obesity and diabetes. Newbold found that bisphenol A over a six month period increased the weight of mice by 20% and the body fat by 36%. This study was a followup to Japanese research which found that bisphenol A caused cells that are inclined to become connective tissue to become fat cells.

Another study found that the 10% of a population group with the highest blood levels of six common pollutants had 38 times more diabetes than the 25% of the study group with the lowest blood levels of pollutants.

A wide variety of human diseases have been linked to epigenetic modification of gene expression. This includes diabetes, obesity, cancer, heart disease, and neurodegenerative disorders like Alzheimer’s. In brain disorders epigenetic alterations lead to a loss of cells and deterioration of cell function.

REFERENCES:


Kim, Jim Man, et al., Chemopreventive effects of carotenoids and curcumin on mouse colon carcinogenesis after 1,2 dimethylhydrazine initiation, Carcinogenesis, 1998; 19(1), 81-85.


The illustration on this page by Christoph Bock (Max Planck Institute for Informatics) February 18, 2006, shows a DNA molecule that is methylated on both strands on the center cytosine. Methylation plays a key role in development and cancer. https://commons.wikimedia.org/wiki/File:DNA_methylation.jpg

**OMEGA-3**

Compounds called resolvins and protectins derived from omega-3 fatty acids have the ability to reduce inflammatory responses in the body. In a study of obese mice, resolvins and protectins appeared to be more potent than their omega-3 precursors in improving insulin sensitivity and decreasing the tendency to deposit fat in the liver and other tissues.

These compounds have been shown to be powerful antagonists to the expression of PPARγ, the target of antidiabetic drugs. This gene stimulates uptake and creation of fat by fat cells. The omega-3 fats also induced the expression of adiponectin, a substance which decreases high blood sugars and improves insulin sensitivity.

Omega-3 researchers have concluded that increased intake of these fats would help prevent fatty liver disease, diabetes, arthritis, colitis and a number of other conditions. The omega-3 fatty acids are obviously an important regulator of gene expression and deficiency can contribute to a wide variety of degenerative conditions associated with changes in the manner in which DNA expresses itself.

REFERENCES:

Gonzalez-Periz, Ana, et al., Obesity-induced insulin resistance and hepatic steatosis are alleviated by w-3 fatty acids: a role for resolvins and protectins, The FASEB Journal, June 2009; vol. 23 no. 6, 1946-1957

**TELOMERES**

Telomeres are protein caps on the ends of chromosomes. The word is Greek and could be literally translated “end part.” Elizabeth Blackburn and Joseph Gall identified telomeres and published their research in 1978.

Telomeres set a limit on the number of times a cell can divide. This was first observed by Leonard Hayflick and is now called the Hayflick limit. Cells are normally destroyed when their telomeres are consumed. Most cancers are immortal cells which avoid the normal cell suicide of cells that have lived out their lifespan.

Telomeres are important because they prevent damage to genes near the ends of chromosomes when cells divide. The enzymes which duplicate chromosomes during cell division cannot carry on their duplication to the end of the chromosome. Telomeres are buffers which are consumed during cell division. Telomeres can be replenished by an enzyme (telomerase reverse transcriptase). Unfortunately, this enzyme is only active in germ cells, stem cells and white blood cells.

Telomeres may play a role in preventing cancer since they limit the number of times cells can divide. On the other hand, many cancers have activation of the enzyme which lengthens telomeres. This confers upon them virtual immortality. Cells that use up their telomeres in cell replication lose their vitality and enter into old age. They function poorly and usually die.
TELOMERES & NUTRITION

Telomeres are very susceptible to damage from free radicals. It is estimated that 2 1/2 to 5 times more telomere length is lost as a result of oxidative damage than is lost due to the process of cell replication. This may explain why antioxidants have been associated with increased lifespan and improved health.

Advocates of life extension promote the idea of lengthening telomeres using drugs or gene therapy as a means of slowing aging. There may be a way to do this, but it is possible that lengthening the telomeres might increase the risk of cancer.

The enzyme responsible for lengthening telomeres is considered a new target for anti-cancer drugs since most cancer cells have up regulated activity of this enzyme, which allows them to exceed the Hayflick limit and replicate without inhibition or limitation.

Multivitamin use and increased intake of vitamins C and E have been shown to be associated with a 5.1% longer telomere length of white blood cells in women. The authors of the study commented, “This study provides the first epidemiologic evidence that multivitamin use is associated with longer telomere length among women.” Higher blood levels of vitamin D have also been associated with longer telomeres in white blood cells.

Intake of omega-3 fatty acids may be particularly important in preventing shrinkage of the telomeres. Researchers studying 608 patients with stable coronary artery disease found an inverse relationship between omega-3 fatty acid levels in the blood and the amount of telomere shortening. Every standard deviation increase in omega-3 levels reduced the odds of telomere shortening by 32%. The researchers observed, “…there was an inverse relationship between baseline blood levels of marine omega-3 fatty acids and the rate of telomere shortening over 5 years.”

REFERENCES:
https://en.wikipedia.org/wiki/Telomere