frontiers FOR YOUNG MINDS

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CAN VITAMINS SLOW DOWN THE BODY'S AGING PROCESS?

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YOUNG REVIEWER:

TIARA

AGE: 10

Some people look younger than their age, others older. Have you ever wondered why? Can we help our bodies age more slowly? Although there seems to be no way to reverse the process of aging, we may be able to slow it down. Improving our diets may help! Humans are born with an internal biological clock within our cells, which reflects the aging state of the body. This is called the epigenetic clock, and it can be changed by what we eat. In this study, we found that women who took supplements of folic acid and vitamin B_{12} had a slower biological aging. More studies on the effects of our diets on the epigenetic clock will help people to live longer and to stay in good health.

EPIGENETICS: TURNING GENES ON AND OFF

The genetic information used to build our bodies and keep them working properly is found in our DNA. That information is organized

in the form of genes. Genes are instructions used to make proteins, which are the building blocks of all our cells. This process of using the information in DNA to make proteins is called **gene expression**. However, cells do not express *all* genes at all times, so our cells need a control system to tell them which genes to express (switch on) and which to switch off. That control system is called **epigenetics** and it is a very complex system.

One of the best understood parts of epigenetics is the process of **DNA methylation**. DNA methylation is performed by a protein called **DNA methyltransferase** (**DNMT**), which adds small chemical units called **methyl groups (CH_3)** to particular places in the DNA sequence (Figure 1). The methylation of the DNA in this way switches genes off. The more spots that are methylated, the more firmly "off" the switch is. Genes involved with maintaining health are increasingly turned off as we age. Turning health-related genes off leads to a greater likelihood of developing diseases as we age.

WHAT FACTORS TURN GENES ON AND OFF?

Although the overall pattern of DNA methylation is similar in most people, the amount of methylation can be increased or decreased by what we eat, by our physical activities, by disease, and by exposure to chemicals or pollutants in the environment. Atmospheric pollution is a concerning problem in many areas of the world and particularly in major cities. This pollution is mostly due to the burning of fossil fuels by factories, power plants, cars, and heaters, and also caused by cigarette smoke. For years, atmospheric pollution has been linked to diseases of the respiratory system, but now that scientists have some understanding of epigenetics, the way these pollutants affect us is better understood. For instance, changes in DNA methylation were identified in diseases related to lung functions in adults exposed to a pollutant called nitrogen dioxide [1]. Also, in children and adolescents,

GENE EXPRESSION

The process by which DNA sequences are read to produce proteins.

EPIGENETICS

The biological mechanism in which gene expression is modified without changing DNA sequences, such as by methylation.

DNA METHYLATION

A biological process in which a methyl group (CH_3), is added to a DNA sequence. Methylation shuts off gene expression.

DNA METHYLTRANSFERASE (DNMT)

A protein capable of DNA methylation.

METHYL GROUP

A small molecule made of one carbon and three hydrogen atoms. It can be added to DNA through a reaction called methylation.

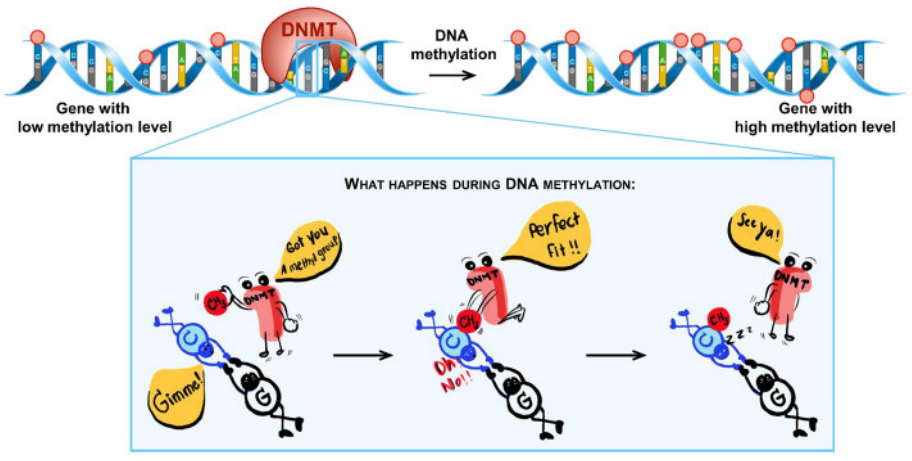

Figure 1

The DNA contained in each cell of the body can be methylated by a molecule called DNA methyltransferase (DNMT). DNMT transfers a chemical group called a methyl group (CH_3), onto the DNA. Methylation of a gene switches it off. The more methyl groups on a gene, the more firmly "off" that gene is.

cases of asthma linked to exposure to atmospheric pollution were associated with changes in methylation levels that could occur *before birth*, showing that pollution can have long-lasting effects on people's health [2].

Fortunately, substances naturally contained in certain foods can combat some of the negative effects of pollution on the body. Several studies have shown that certain vitamins, particularly those of the vitamin B group, can decrease the damage to cells caused by atmospheric pollution. These vitamins act by maintaining a normal level of DNA methylation (Figure 2) [3].

WHAT IS THE EPIGENETIC CLOCK?

BIOLOGICAL AGE

The age corresponding to environment factors like genetics, epigenetics, and lifestyle.

EPIGENETIC CLOCK

A test that calculates a person's biological age using DNA methylation level measurements.

How old are you? This question is easily answered by counting the years since your birth (your chronological age), but what about your **biological age**? Biological age indicates where a person is in their lifespan, based on the damages their cells have sustained. It is interesting that some people look younger than others at the same chronological age, suggesting that factors other than time are at work to cause cells to age. One method researchers have been using to estimate biological age is called the **epigenetic clock** [3]. The epigenetic clock is based on the levels of DNA methylation. As we mentioned earlier, as we age, methylation of our genes, including the genes that keep us healthy and young, increases. So, by measuring DNA methylation at a number of locations on the DNA from several different cells and tissues, and doing some fancy math on those results, scientists can use the epigenetic clock to determine a person's biological age.

Biological age calculated using this method is highly correlated with chronological age [3], which tells us that the epigenetic clock is a good

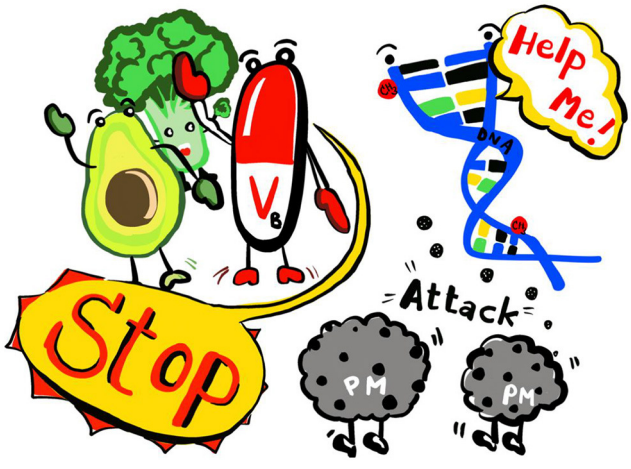

Figure 2

Vitamins can protect DNA against pollution. DNA can be damaged by exposure to pollution, including particulate matter (PM). Pollution can unbalance DNA methylation levels. Methylation changes can cause health problems, but eating a diet rich in beneficial substances like B vitamins can help people stay in good health.

tool for calculating biological age. The epigenetic clock also predicts how quickly diseases like Alzheimer's disease, high blood pressure, diabetes or cancer will get worse. So far, researchers have shown that high-risk lifestyles, like smoking or drinking alcohol, lead to a speeding up of biological aging. On the other hand, a healthy diet can slow down biological aging.

VITAMINS B_9 AND B_{12}

Our bodies need healthy food and a balanced diet to function efficiently. Fruits and vegetables are one of the main food groups containing vitamins. Vitamins are essential for growth, development, and cell function. This means that vitamins help the body to function properly. A long-term lack of a vitamin, which is called a vitamin deficiency, can cause serious symptoms. For example, bleeding gums can result from a lack of vitamin C, and a deficiency in vitamin A causes poor night vision.

B vitamins are important for cell metabolism. Vitamin B_9 is found in dark-green, leafy vegetables such as spinach, broccoli, asparagus and Brussels sprouts. B_9 helps with the synthesis of DNA and RNA, and it is also required for cell division, helping cell growth and development. A deficiency of vitamin B_9 can lead to anemia, which is a problem with blood cell development that leads to poor transport of oxygen and can cause tiredness and weakness. Good sources of vitamin B_{12} are meat, fish, milk, cheese and eggs. Vitamin B_{12} helps to keep blood and nerve cells healthy and also helps to make DNA. Vitamin B_{12} deficiency can also cause anemia. Generally, most people get enough vitamin B_{12} from a balanced diet. However, older adults and people who have a poor ability to absorb vitamins might benefit from vitamin supplementation, which is generally considered to be safe even at high doses.

VITAMINS B_9 AND B_{12} CAN SLOW DOWN THE EPIGENETIC CLOCK

Both vitamins B_9 and B_{12} are involved in biochemical reactions that can increase DNA methylation. However, tiny differences in DNA that naturally exist between individuals, called **single nucleotide polymorphisms** (SNPs) can also play a role in gene methylation. People with a "normal" SNP for the availability of methyl groups have higher methylation levels, but people with a "faulty" SNP in the same location on the DNA have less methylation occurring.

SINGLE NUCLEOTIDE POLYMORPHISM (SNP)

A very small variation in a DNA sequence of an individual.

To understand the impact of B vitamins on biological age, a group of 44 older adults (age 65–75) was studied for 2 years. The diets of study participants were supplemented with vitamins B_9 (400 μg/day) and B_{12} (500 μg/day) for 2 years [4]. To evaluate biological aging, DNA

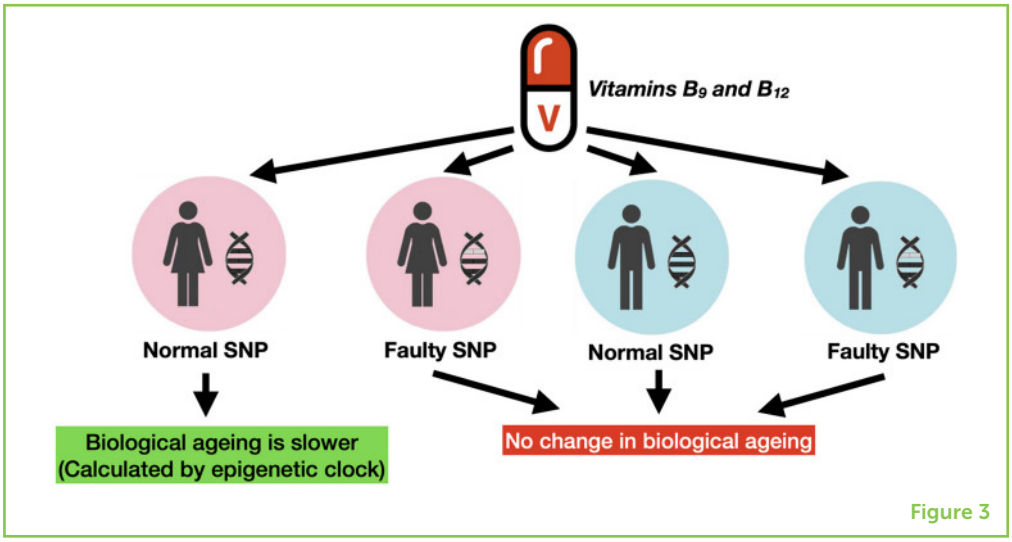

Figure 3

Effects of vitamin B supplementation on biological aging depend on gender and genetics. Following supplementation with vitamins B_9 and B_{12}, female study participants with the normal SNP showed slower biological aging, but females with variant SNP and males did not show a slowdown in biological aging. This means that diet might not affect everyone's epigenetic clock the same way.

methylation levels were analyzed from 353 locations in the DNA, and we put this data into an epigenetic calculator to tell us what their biological age was. In this way, the speed of the epigenetic clock of all participants was generated both before and after supplementation, so that we could compare their real age with their biological age.

Our results showed that, after supplementation, women who carried the normal SNP (the variant that produces a higher methylation activity) had epigenetic clocks that were running slower than those of women with the faulty SNP (Figure 3) [5]. However, the epigenetic clocks of women with the faulty SNP and men were not affected by vitamin supplementation. These results show that the effects of vitamins B_9 and B_{12} appear to be gender and SNP-specific. Although there is no formal evidence for it, the methylation increase observed in women with the normal SNP could have turned off some specific pro-aging genes, with the result of limiting their biological aging over the time of the experiment.

CONCLUSION

Diet plays a role in epigenetic changes, especially in DNA methylation. By looking at the epigenetic clock, we found that vitamins B_9 and B_{12} can slow down biological aging in a gender and SNP-specific manner. Although not everybody is affected by vitamins B_9 and B_{12} supplementation in the same way, our results are encouraging because they mean we might eventually be able to help people to live longer, healthier lives by changing their diets. To achieve this goal, personalized balanced diets could be designed based on the analysis of people's DNA methylation levels. But until we can do this, it is important that we all eat healthy foods, with plenty of vitamins, to keep our epigenetic clocks running properly!

ORIGINAL SOURCE ARTICLE

Sae-Lee, C., Corsi, S., Barrow, T. M., Kuhnle, G. G. C., Bollati, V., Mathers, J. C., et al. 2018. Dietary intervention modifies dna methylation age assessed by the epigenetic clock. *Mol. Nutr. Food Res.* 62:e1800092. doi: 10.1002/mnfr.201800092

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YOUNG REVIEWER

TIARA, AGE: 10

I am a 5th grader. I like to read books and my favorite school subject is library but if that does not count as a subject, I would say reading and if that does not count, then my favorite subject has something to do with reading. My favorite book series is "The Land of Stories" by Chris Colfer. It is a fiction and has everything I like such as fictional dimensions and magic. All the fairy tale characters like Cinderella, Sleeping Beauty, and Rapunzel are in it. My favorite TV show is "Just Add Magic." Soccer is my favorite outdoor play.

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My name is Dr. Chanachai Sae-Lee and I am a medical researcher in the Faculty of Medicine at Siriraj Hospital, Mahidol University, Bangkok, Thailand. My research is mainly focused on epigenetics (DNA methylation) and molecular mechanisms related to human diseases and cancers. I also investigate the effect of nutrition (or dietary constituents) on DNA methylation and the epigenetic clock. *chanachai.sae@mahidol.ac.th

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My name is Julien De Biasi and I am a Ph.D. student at the University of Northumbria at Newcastle in the UK. My research work focuses on the analysis of the effects that Maillard reaction products, substances generated in food during heat treatment, can have on the composition and metabolism of the human intestinal microbiota, and how this relates to inflammatory diseases.

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John is a professor of human nutrition at Newcastle University in the UK. In addition to teaching students about nutrition and health, he carries out research on nutrition and aging and on the risk of age-related diseases. He was one of the founding members of NuGO—the European Nutrigenomics Organization—that has pioneered the use of modern molecular methods for studying how what we eat affects our health. John is using those methods to investigate links between our eating habits and common diseases, including colorectal cancer.