Monthly letter of <u>Heales</u>

The Death of Death – N° 128 November 2019

Products and drugs against senescence

My goal as a scientist is to prolong life. My grandparents are heart patients and I want to help them. And make them live forever. (Belgian newspaper, De Morgen, November 12, 2019, translation). Laurent Simons is 9 years old, born in Ostend, Belgium and studying at the University of Eindhoven in the Netherlands. In a few days, he is expected to become the youngest academic in the world. And he may also soon become one of the most brilliant longevists on the planet.

Theme of the month: Medicines (and other substances for longevity)

Many researchers have been working for decades to slow down aging, or even one day to make possible real rejuvenation mechanisms.

Many avenues of study are being explored and different products are being studied. This letter provides a fairly extensive list of promising substances. Be careful, these products should not be used for yourself



without medical advice and are often not available without a prescription.

Senolytics

Senolytic drugs are said to allow us to get rid of cells that are at the end of their life-cycle.

Remember that our cells are programmed to divide a certain number of times, but as we age, they stop multiplying (or multiply with errors) before dying and being eliminated by our immune system.

The problem is that, as we get older, this "cleaning" system becomes less and less effective. On the other hand, these cells at the end of their life could be eliminated by senolytic drugs. They have the ability to eliminate our aging cells without affecting healthy cells, which helps us fight cellular aging and as a result all the chronic diseases associated with aging. Currently, these drugs are still in the experimental stage – started in 2015 by Jim Kirkland, a researcher at the Mayo Clinic.

The best known products are <u>dasatinib</u>, <u>quercetin</u> and <u>fisetin</u>.

The mixture of dasatinib and quercetin improves the health of older mice and extends their lifespan. First short clinical trials have also been conducted in humans and are promising. Some side effects have occurred. While quercetin is found in apples or onions, dasatinib is originally an anti-cancer drug.

Metformin

Metformine is an old, cheap drug that has been widely used to regulate blood sugar levels in diabetic patients for decades. Today, it could perhaps reduce age-related diseases and improve longevity.

From the biguanide family, this drug treats type 2 diabetes orally. Its interest, for these non-insulin dependent diabetics, is to lower blood sugar levels without increasing insulin secretion. In addition, insulin is now known to reduce inflammation in the body.

For several years now, anti-aging medicine specialists have been studying the case of metformin to combat health problems associated with aging. In particular, it is said to reduce <u>glycation</u>, a process in the body linked to metabolism of sugars and which degrades our proteins, causing the loss of flexibility in our supporting tissues and accelerating overall aging.

Metformin is also known to promote the effects of rejuvenation and cellular regeneration, known as autophagy. This is a process during which a cell can repair its defective components (a true autonomous overhaul). It has been shown that other substances such as resveratrol, green tea or rapamycin also promote this autophagy, as does fasting, <u>as does simply fasting</u>.

Even if a study shows less impact of degenerative diseases (<u>linked to aging</u>) in treated diabetics, and fewer cancers, thanks to this product, as for all other currently available products the impact on maximum lifespan (beyond 95 or 100 years) is low or even zero.

Rapamycine



Easter Island or "Big Rapa" is known for its 900 enigmatic stone statues. This is also the name Canadian researchers have given to "Rapamycin", a molecule produced by the Streptomyces hygroscopicus bacteria. Rapamycin or "Sirolimus" has been used since 1999 as an immunosuppressive drug against organ transplant rejection including Pfizer's "Rapamune".

Different strains of mice have their health improved and their lifespan increased by rapamycin, starting at different life stages. Tests are underway in dogs (<u>"Aging Dog" study</u>). The side effects of rapamycin make it difficult for human use as a preventive measure to progress.

Statins

Researchers from the University of Naples have shown that statins can slow down the cellular aging process by preventing telomere shortening. Telomeres are sections of DNA that cover the tips of chromosomes and protect them from damage associated with aging. Statins can activate an enzyme called "telomerase" which extends the length of the telomeres. This length is a fairly well known index of longevity.

Already used in the treatment of heart disease, diabetes and cancer, statins could also be used in anti-aging therapy. But the sometimes serious muscle side effects of statins mean that current use for prevention remains moderate.

NAD+

Cells have the innate ability to repair DNA damage - which happens, for example, every time our skin is exposed to the sun. However, this ability tends to decrease with age.

Researchers have discovered that the metabolite oxidized nicotinamide adenine dinucleotide (NAD+), which is naturally present in every cell of the human body, plays a key role as a regulator of protein-protein interactions that control DNA repair.

For example, treating mice with a NAD+ precursor improves the ability of their cells to repair DNA damage caused by exposure to sunlight or aging.

"We have never been closer to creating a safe and effective anti-aging drug. It could even be available in just three to five years if the tests are successful," <u>Professor David Sinclair</u> has said.

Hormones

The decrease in our hormones is certainly one of the most marked and early effects of aging. From the age of 30, hormone production decreases with significant consequences.

Among those that are best known, here are the most important ones whose levels decrease with aging: <u>DHEA</u>, <u>melatonin</u>, estrogens, progesterone, testosterone, pregnenolone, growth hormone and cortisol.

While it is medically accepted that a rise in hormone levels is accompanied by a significant increase in fitness, <u>hormone replacement therapy</u> is not a panacea.

While growth hormone has a clear and positive effect on the skin, bones and muscles, no one has yet been able to increase the lifespan of mice and rats with growth hormone, or at least their maximum lifespan. Thus, these positive effects are probably accompanied by side effects as well, which remain to be identified. The recent regrowth of the thymus through injecting growth hormone and DHEA (and other substances), "accompanied by a decrease in biological age" (measured by the methylation of DNA from blood cells), therefore leads to some caution on long-term effects.

A balanced diet is important, especially for a sufficient supply of <u>proteins and</u> <u>amino acids</u> (especially after 65 years of age), but also of certain vitamins and minerals involved in the production of hormones in our endocrine glands.

Aspirin

Doctors have known since the 1990s that aspirin appears to reduce the risk of cancer; in the case of colorectal cancer, the risk reduction is at least 40%, but researchers do not fully understand the nature of this protective mechanism.

Two scientists from the Swiss University of Basel examined the link between lifestyle and genome aging in 546 women over 50 years of age. They determined that aspirin slows down the aging of the genome, particularly by fighting against changes that play a role in the development of tumors. However, the researchers warn that it would not be wise to start taking aspirin regularly just to fight cancer, given the <u>side effects</u> that can accompany taking the drug. The

<u>conclusions of this study</u> are published in the Journal of the National Cancer Institute.

Overall, it is considered that low-dose aspirin ("half a baby aspirin": one hundredth of the dose taken for headaches), taken during meals to avoid ulcers, has a positive effect for people at proven cardiovascular risk, and neutral (and possibly negative) in other cases.

Vitamins

Years of poor nutrition accelerate the aging process. Vitamin and mineral deficiencies can have harmful effects on the health of the elderly. Recent studies indicate that some vitamins have antioxidant properties and prevent the oxidation process. These vitamins are vitamins A, E, C and Beta-carotene. Thanks to these properties, they can delay the aging process.

They also prevent the degeneration of blood vessels, heart joints and eye lenses.

Known as an antioxidant and anti-aging vitamin, vitamin B1 plays an important role in the normal functioning of the nervous system, carbohydrate regulation and good digestion.

Antioxidants

There is a lot of talk about taking these famous antioxidants that must protect us from "free radicals" and accelerated aging.

To understand antioxidants, it is necessary to understand free radicals (FR). These are produced during reactions involving oxygen (breathing, digestion, muscular effort, defences against infection, etc.). They are various molecules with in particular one "excess" electron, which makes them particularly unstable and reactive. As long as an antioxidant system has not stopped the process, free radicals will "contaminate" other molecules, which then become free radicals in a chain process. This contagion of the "excess electron" is called oxidation.

An imbalance in our anti-radical defences may be linked to a lack of antioxidants in our diet. In particular, overcooking and food preservation destroy a large number of antioxidants.

Certain factors (<u>like aging, smoking, and obesity</u>) will increase the production of Antioxidants are found in a large number of foods, their sources are very varied. However, plants, permanently exposed to the sun's UV rays, have had to develop powerful antioxidants to survive, especially polyphenols and carotenoids. For these reasons, a diet rich in undercooked fruits and vegetables is healthy.

Foods rich in antioxidants:

- Vitamin C: pepper, guava, sorrel, lemon, orange, kiwi, cabbage, papaya, strawberries...
- Vitamin E: sunflower oil, wheat germ, soya, corn, butter, margarine, eggs, etc.
- Vitamin A: liver, butter, eggs...
- Selenium: fish, eggs, meat...
- Zinc: seafood, meat, wholemeal bread, green vegetables
- Coenzyme Q10: soy, beef, small fish, spinach
- Lycopene: tomato and red fruits
- Astaxanthine: krill, shrimp, crustaceans with red pigment
- Alpha-lipoic acid: spinach, red meat, broccoli
- Polyphenols (flavonoids and tannins in particular): all colored fruits and vegetables, berries, wine, teas...

Other substances with antioxidant potential:

- Some B vitamins: B1, B5, B6,
- Some amino acids: acetyl L-carnitine, methionine, cysteine, taurine...
- Omega 3 fatty acids
- Hyaluronic acid
- <u>Methylene blue</u>
- <u>Flavonoids</u>

Unfortunately, in the United States, studies on the intake of vitamins or dietary supplements by citizens have not yielded <u>positive results</u>.

In conclusion

The inventory that has been compiled here is incomplete. Many other products are still considered by some to have the potential to promote a longer life, for example certain proteins, <u>resveratrol</u>, <u>sirtuins</u>... For all these substances, the question of dosage is of course fundamental, "not too much, not too little" as well as the study of the combined effects of several products (see in particular the "polypill" projects and the <u>Data Beta test</u>).

Currently nowhere in the world is a public or private organization systematically examining the positive lifetime impact of these many substances, either for laboratory mice or for humans.

The extreme administrative and legal complexity, paradoxically, makes testing more difficult today than in the past. An awareness of the importance of these studies could be accelerated thanks to the recent attraction for senolytics, the development of more automated tests using artificial intelligence and, above all, a long-term awareness of the possible gains in public health and well-being.

The good news of the month: a Longevity Week in London

Among the many conferences held around the world, those held from 11 to 15 November during <u>Longevity Week in London</u> were particularly promising. They saw meetings between potential investors, scientists and politicians, mainly from the United Kingdom, of course, but also from the United States.

To find out more:

• See: heales.org, sens.org, longevityalliance.org and longecity.org