

John Harris, former editor of the Journal of Medical Ethics, argues that as long as life is worth living, according to the individual, we have a powerful moral imperative to save life and therefore to develop and offer life-prolonging therapies to those who want them (<u>Source</u>).

Theme of the month: Recent developments in gene therapies for longevity

Introduction

The average lifespan of both and humans varies animals according to many factors. For diet, predation, disease animals, climatic conditions play the and most important roles. In humans, disease and lifestyle, social conditions are the determining factors.



But when it comes to the maximum lifespan of animals, like that of humans, the most important element is the genetic heritage.

We still know very little about the genetic differences that favour or hinder longevity in humans. Studies of genetic characteristics related to longevity have been conducted, including studies <u>of supercentenarians</u>. Although genes such as the <u>klotho gene</u> are sometimes cited, no single gene or group of genes appears to have a very strong positive influence.

A human being who lives in a perfect environment with adequate health care and an exemplary lifestyle would never live past the age of 122. It should be noted that the oldest person in the world has been <u>a woman for almost 40 years</u>, which can be explained by the genetic difference between men and women.

Place a mouse in a mouse paradise. No matter what happens, it won't live past five years. Place a Galapagos tortoise in a chelonian paradise and it will live at most two centuries.

Very similar animals can have very different maximum life spans. For example, the <u>Labord's chameleon</u> of Madagascar is the terrestrial vertebrate with the shortest life span. It lives only 4 or 5 months. While its distant cousin from the same big island, <u>Parson's Chameleon</u>, can live for about ten years.



In other words, we know that few genetic modifications can allow considerable changes in lifespan.

This is one of the reasons why gene therapies are among the most promising therapies for longevity.

What is gene therapy?

<u>Gene therapy</u> is one of the preferred ways to treat genetic diseases, but also certain cancers. It consists of inserting into the patient's cells a normal version of a gene that does not work and causes the disease.

The functional gene then allows the patient to produce again the protein whose deficiency was the source of the disease.

However, three conditions must be met:

- Knowing the gene responsible for the disease, i.e. the function of that gene, so that the cell can be "repaired".
- Allowing the gene to reach and enter the cell with the help of a "vector", most often a virus that has been rendered harmless to the patient.
- And associate the gene with a "promoter", a small DNA sequence that allows it to function once inside the cell.

It is also possible to transform the genetic heritage of subsequent generations. It is conceivable that one day our children could live longer and healthier lives as a result of genetic modification. This raises innumerable ethical questions, some of which have been addressed by the <u>birth of two (or perhaps three) genetically modified babies in China</u>. These issues will not be discussed here.

The gene therapy revolution

<u>In 2000</u>, for the first time in the world, gene therapy demonstrated its effectiveness with bubble babies, children with severe immune deficiency who returned to normal life with the treatment. However, the therapies were slowed down and then virtually halted for more than a decade following the deaths of two patients, including <u>Jesse Gelsinger</u>. However, during this interruption countless lives could have been saved.

Between 2015 and 2020, gene therapy has experienced a considerable boom. Several clinical trials have been conducted to treat certain blood, skin and neuromuscular diseases. Some of these trials have been sufficiently successful to lead to <u>market authorization</u> in the United States



and Europe.

In 2017, a team of European doctors managed to replace 80% of a little boy's epidermis (suffering from <u>epidermolysis bullosa</u>) with gene therapy.

By 2019, about ten gene therapy treatments for rare blood, vision, muscle and certain cancers had received marketing approval in the United States or Europe.

In the same year, the first gene therapy drug (Zolgensma) capable of saving the lives of babies with diseases such as spinal muscular atrophy was put on the US market.

Other treatments for <u>Pompe disease</u>, <u>adenosine deaminase deficiency</u>, <u>beta-thalassemia</u>, <u>acute lymphoblastic leukemia</u>, <u>diffuse large B-cell</u> <u>lymphoma</u>, and <u>Leber's amaurosis</u> have been developed.

However, treatments are still usually aimed at uncommon diseases, generally linked to an "error" in a single gene.

Gene therapy and longevity: Can it delay or reverse age-related diseases including neurodegenerative diseases?

In 2019, a <u>study by George Church and his teams</u> showed favorable results of a therapy acting simultaneously on three genes in mice with various age-related symptoms.

In the same year, an <u>experiment on a gene for telomeres</u> was carried out by researchers from the Chinese Academy of Sciences on mice in 2019. This resulted in a longer life expectancy.

In 2020, <u>mRNA vaccines</u> were used to induce immunity against COVID-19. This method is similar to gene therapy. However, the changes concern the RNA and not the DNA.

In October 2021, <u>BioViva</u>, a biotechnology startup led by E. Parrish, demonstrated that by administering gene therapy to <u>six patients with</u> <u>dementia</u> that a reversal of dementia symptoms such as cognitive impairment could be observed.

The American Elizabeth Parrish is also the first known case of self-testing of a gene therapy targeting ageing processes. The treatment consists of injections of adenovirus, which could extend <u>leukocyte telomeres</u> and thus strengthen muscle mass.

Conclusion

A massive sharing of knowledge, including statistics, about genetic endowments is developing. Investments for a longer healthy life seem to accelerate and improve. <u>The European Union is proposing legislative tools</u> for "altruistic" databases.

Billions of sequencings (total or partial) have been performed on animals, plants and humans. The pooling of these data and their analysis, in particular by means of tools based on artificial intelligence, is continuing. Thanks to genetic modification technologies such as CRISPR, it should be possible to break through the "glass ceiling" of the maximum lifespan for mice and then for humans in the near future.

The good news of the month

The <u>European Longevity Initiative was</u> launched by a non-governmental organization with members in some 20 EU countries.

Its <u>proposal</u> was the most supported of the <u>Conference on the Future of</u> <u>Europe</u> and is still one of the most supported.

The main promoter of the idea is the Hungarian scientist <u>Attila Csordas</u>, who <u>said</u>: " The only real solution (for many, many diseases) is to start treating the root causes of biological aging (...). We have experimental strategies to slow down the rate of accelerated aging and reduce morbidity and mortality in late life. To achieve this in the European Union, we would like to propose effective legal, budgetary, regulatory and institutional commitments to enable science-intensive healthy longevity research and technologies, large-scale geroprotective clinical trials focused on ageing and equitable access to these technologies to increase healthy life expectancy in the European Union."

The <u>European Health Data Space</u> is at the centre of many projects aimed at better exchange of health data for medical and research purposes. An international conference on 19 November on "<u>Innovations in Consumer</u> <u>Longevity Data"</u> is one example.

For more information:

- See: <u>heales.org</u>, <u>sens.org</u>, <u>longevityalliance.org</u> and <u>longecity.org</u>.
- <u>Source of the image</u>