The genes of longevity. The death of death. February 2018.

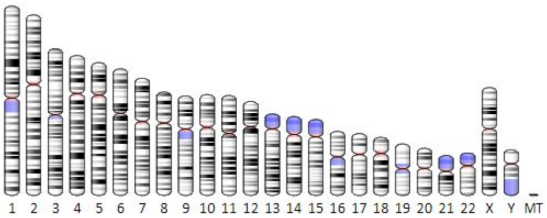
The real issue is the fight against old age and death, (…) truly increasing human longevity. (...) Life expectancy has been increased thanks to antibiotics, better lifestyles and medical advances. In 1900, for example, the life expectancy of French people was 45. Today, on average it is 82. But we still die more or less at the same time. Basically we still die at around 100. (...) What is the philosophical goal now ? The idea is to create a humanity which would be young and old at the same time. As the saying goes: "If the young only knew, if the old only could" – if we can just bring the two together.

*L*uc Ferry (translation), former French education minister and philosopher (Arte, 8 February, 2017)

Theme of the month: Genetics and maximum life span

Introduction

“In the beginning was the gene”, we could perhaps write, concerning the appearance of life. Even if the first stages remain mysterious.



We are probably all the – incredibly lucky – descendants of a common DNA-bearing ancestor which appeared, according to current knowledge, about 3.8 billion years ago.

During the first half of the history of life our distant ancestors, who were as yet neither plants nor animals, probably did not die of old age. They simply divided themselves when circumstances were favorable, or died when nutrients were lacking or when the environment changed too much.

Then life became more complex; living beings became multicellular. Little by little, the genetic heritage transmitted itself from one generation to the next, no longer by simple division, but by fusion of genetic material. Much later this would become the meeting between an egg and a sperm. Individuals thus produced began to age (if they were lucky enough not to die before). Each generation gave birth to new young beings, but the animals (and plants) themselves became ‘disposable’.

Much later again, about 500 million years ago, vertebrates appeared. Then the first primates, 50 million years ago. The first beings which, wearing clothes, would not have surpised you in the Metro, were born barely 300,000 years ago, a ten-thousandth of the history of life on Earth.

We living beings are so different and yet also so similar. From the humblest bacterium born hundreds of millions of years ago, to the largest cetaceans alive today, we are all determined, notably, by 'life's IT': the four molecules of adenine (A), cytosine (C), guanine (G) or thymine (T) that make up deoxyribonucleic acid.

The genetic universality of aging

While in the vegetable kingdom aging is far from universal (many trees have no senescence) for animals there are very few exceptions and for mammals none escapes from it.

What is the purpose of aging in the 'laws of nature'? We don't know for sure, but the most likely thing is that death from old age makes it possible to maintain genetic diversity. If animals did not die of old age, only a small number of genetically very well-adapted ones would survive. That would reduce diversity. In nature, however, in the long term, environmental conditions change quite often. When these changes happen, the most perfectly-adapted animal species, which are therefore too uniform (those which do not age), are 'eliminated'.

It is also genetic diversity that explains sexual reproduction. Without sexual reproduction, living beings would be too similar.

But in nature, some animals can reproduce without sex (even some vertebrates) while aging seems almost universal. So there is one component that remains mysterious.

Of course we are not totally dependent on our genes. But in terms of maximum longevity, maximum lifespan, it is indeed our genes which determine it for the most part.

Maximum lifespans vary considerably from one species to another. A human being living in perfect psychological and physiological conditions would have almost no chance of living longer than 122 years. As for a mouse, it is much less fortunate. Even if it is placed in a 'mouse paradise', it will never live more than five years. The longest-lived mammal is the bowhead whale. It can live at least two centuries; perhaps more.

What genes are responsible for aging?

The metabolism of a human being is colossally complex.The organ which in some ways is the most fragile, the brain, is sometimes referred to as the most complex object in the universe. And yet, among these extraordinary entanglements, certain mechanisms that speed up or considerably slow down aging are probably all down to a few letters of DNA. Here are a few points to consider on this subject:

There are a number of genes that are related to aging and which are present in many animal species. Hence, the FOXO and ApoE genes, which crop up in different animal species, including humans, influence longevity.

Among chameleons living in Madagascar, Furcifer Labordi is the land-dwelling vertebrate with the shortest life in the world (4 or 5 months). Another, larger, chameleon, Calumma Parsonii, which is biologically, and therefore genetically, very similar, can live for around ten years. In other words, small genetic modifications can produce large differences in lifespan.

The chromosome which determines sex also determines maximum lifespan. Mankind's oldest member is always a woman. The oldest woman in the world today is 117, while the oldest man is 'only' 112.

Human longevity has a strong genetic component, especially for maximum lifespans. Family members of centenarians are more likely to become one themselves.

Unfortunately, a study carried out on supercentenarians (people living to 110 or more), has not (yet) allowed researchers to detect common genetic characteristics of human longevity.

How can we change the genes responsible for aging?

The sequencing of the genome of women, of men, the human microbiota and other living creatures is becoming ever simpler and faster, ever more accurate and less expensive.

More recently, potential advances in gene therapy, notably via CRISPR Cas9 techniques, have also accelerated. Diseases of genetic origin can already be treated.

However we are still a long way from a gene therapy to allow a much longer life in good health. Advances in the area of artificial intelligence for medical research allow research into determining more and more precisely the genetic sequences linked to aging in living creatures in general and humans in particular. When progress becomes sufficient to identify useful therapies, it will be necessary to test them in vitro, then on animals and then finally on humans. In this area, as in others, it will be too late for millions of women and men who are very elderly today. The future will tell us which readers will perhaps benefit from them (if they so wish).

Good news of the month : An 800-page document sums up positive developments for longevity research

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This document called *The Science of Longevity* aims to detail the various emerging technologies and industries related to human aging, longevity in good health and other related matters. It was created by, notably, the Biogerontology Research Foundation.

In 2018, aging is still an anonymous enemy in an undeclared war, the authors write. That will less true for those political leaders, representatives of regulatory authorities, investors and other people in positions of responsibility who take the time to browse through what makes for just under 1,000 pages of information.

The report is available in its entirety, free of charge, online (warning: 58MB file). Other reports will follow.

To find out more:

- *Generally speaking, see, notably: heales.org, sens.org, longevityalliance.org et longecity.org*
- *Sources: human chromosome*