Senolytics. The death of death. October 2018. N° 115.

The search for life-prolonging interventions has often been perceived as a purely academic pursuit or as an unorthodox medical enterprise, with few or no practical results.
Yet, in fact, these studies, which explicitly aim to prolong human life, have often been a formidable, albeit rarely recognized, motivation for biomedical research and discovery. Ilia Stambler, June 2014 in The unexpected outcomes of anti-aging, rejuvenation, and life extension studies: an origin of modern therapies

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Theme of the month. Products that destroy senescent cells.

There are many more cells in our body than human beings who have lived on the planet, probably around 40,000 billion. These cells reproduce by dividing, grow, die, absorb and excrete substances... In short, they are living entities that function in our body with a certain autonomy and for an extremely variable duration that can range from a few weeks (120 days for red blood cells) to a whole human life (most neurons).

As far as we know, our cells are directly descended from an organism that appeared nearly 4 billion years ago. More precisely, our cells come from the fusion, two billion years ago, between two descendants of the original organism: the primitive cells and what are today the mitochondria.

When a cell malfunctions, it is normally eliminated quickly. There are many mechanisms that lead to cell death, the best-known being apoptosis sometimes also called "cell suicide".

But it also happens that cells that are harmful to the rest of the body continue to live. The most well-known case is cancer, an "anarchic" multiplication of cells that results in the death of the carrier individual if the body's control mechanisms or adequate therapy do not interrupt the multiplication.

Senescent cells

Another major category of cells in poor health has been the subject of great attention in recent years by researchers working in the field of the fight against aging. These are the so-called "senescent" cells.

Substances used to destroy these cells are called senolytics. The term is based on the word "senescence", i.e. in biology, the process of progressive degradation due to aging, and the word lysis which refers in particular to the degradation of organisms by the action of a physical, chemical or biological agent.

A senescent cell is a cell that does not function effectively for the rest of the body. It has a metabolism whose functioning has harmful consequences for the rest of the body. It accumulates and secretes pro-inflammatory factors that promote the development of age-related diseases.

The objective of the ongoing research is to destroy these cells, but of course without significant negative effects on healthy cells. This is therefore a goal quite close to that sought in the fight against cancer, where it is necessary to eliminate cancer cells without eliminating healthy cells. Products designed to destroy cancer cells are also being tested as senolytics.

Many substances have been tested in recent years on mice and some products are beginning to be tested on humans. Treatment with senolytics results in targeted apoptosis of senescent cells. It should be noted that it is not necessary to remove all senescent cells but only part of them. It is even possible that a treatment that killed all senescent cells would be counterproductive. Successful treatment reduces inflammation. On the positive side, arterial calcification is lower, reducing the risk of atherosclerosis.

To date, a positive effect has been established for mouse health levels in the short and medium term. One experiment yielded positive results with regard to the lifetime of mice, which increased by about 25%.

Tested products

Quercetin (a flavonoid) and Dasatinib reduce the "markers" of senescence in in vitro and animal studies. The anti-cancer drug Navitoclax was also examined as a senolytic.

Another flavonoid, fisetine is currently mentioned very frequently in scientific exchanges related to these new therapies, as are piperlongumine and Bcl-2 inhibitors.

Perspectives and limitations

Senolytics are currently the most frequently cited therapy in the field of research on aging. These are already-existing products, often natural (which are not very expensive to produce), whose mechanism of action is fairly well known and which could significantly extend healthy lifespan.

However, optimism about this should not be excessive. Most experiments on mice to date have not focused on longevity. The first human trials widely announced in the scientific community are only just starting. They will be double-blind and will concern elimination of senescent cells from the joints of osteoarthritis patients.

In this field as in other longevity research, greater public and private investment, faster knowledge sharing and the involvement of more researchers is desirable to enable those who wish to live in good health much longer to do so in as near a future as possible.

The good news of the month: More and more international activities concerning longevity.

There are so many activities informing researchers about human longevity that it is no longer possible to follow everything. Two conferences in Europe have recently taken place and two conferences are taking place in November:

- November 8, 9, 10 the 4th Eurosymposium on Healthy Ageing in Brussels
- November 5, Longevity Forum in London
- October 4-5, the 3rd International Conference on Ageing and

Disease in Nice
- From September 11-14, the Basel Life conference in the Swiss pharmaceutical capital.

To find out more:

- *In general, see in particular: heales.org, sens.org, longevityalliance.org et longecity.org*
- *Image source*