# Translated Transcript:
## Extending life and health expectancy, the new Saudi ambition

With annual investments of more than $1 billion, Saudi Arabia has become a leader in the field of geroscience and biology of aging. The Hevolution Foundation wants to develop treatments that would allow healthier aging by delaying biological decline.

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Pushing back old age, illness and, possibly, death is the new mission in which Saudi Arabia has invested itself. Through the Hevolution Foundation, the kingdom has committed to paying more than one billion dollars a year to boost longevity research, and to develop treatments that address the very causes of aging.

Based in Riyadh, the Hevolution Foundation is a non-profit organization launched in 2022 and funded by the Saudi government. It is the world's second largest funder for research on the biology of aging and geroscience, behind theNational Institute of Aging in the United States.

Its ambition does not stop at stimulating research; it also wants to support the production and distribution of new treatments in order to accelerate their arrival on the market. Essentially, these treatments would allow a healthier aging, by delaying biological decline.

A significant majority of health costs are related to elderly and aging populations, notes Dr. Mehmood Khan, President and CEO of the Hevolution Foundation, in an interview with Radio-Canada. “[However], investments go to disease research, once they have

arrived. This is important, since it affects a large part of the population, but if we want to change the future, we have to think about what we can do differently."

Rather than subsidizing work on aging-related diseases such as cancer, Alzheimer's or Parkinson's, the foundation has chosen to focus on a still small but promising field of research, that of the biology of aging. This science aims to improve knowledge of the mechanisms of aging, in order to be able to modify them.

Because even today, several shadow areas persist on the subject of aging.

For example, from a cellular point of view, we do not understand why, as we age, the proportion of proteins present in cells across our bodies decreases, says Dr. Khan, a specialist in endocrinology and nutrition, who has worked for several years at theMayo Clinic and Medical School, Minnesota, before holding leadership positions in research and development at Takeda Pharmaceuticals and PepsiCo. "As a result, we lose muscle mass, the bones lose their density… Because we become more fragile, we are more at risk of falling, we become weaker, the immune system loses its vitality. Why is it like that?"

It is to these types of questions that Hevolution wants to help find answers.

**The cost of aging**

Typically, in a developed country like Canada, people live in good health until the age of 65, explains Marc Prentki, a full professor at the Faculty of Medicine at the University of Montreal.

After that, we start to have problems: diabetes, obesity, cardiovascular disease, cancer, Alzheimer's, Parkinson's, etc. It can last a long time, up to 10-15 years, and it costs the health system immensely.

In Canada, in 2022, seniors accounted for 46.9% of health spending or $158 billion according to the Canadian Institute for Health Information.

Considering the rapid aging of the Canadian population, the associated costs will continue to increase in the coming years. According to Statistics Canada, 18.5% of the country's population was 65 years and older in 2021. According to projections, this rate could reach 23.4% by 2030.

"In most developed countries, society can no longer afford to provide all the required services [to sick elderly people]. This is a challenge facing health systems, for example in the UK and Canada. They can no longer bear these costs," Dr. Khan notes.

Making aging treatments accessible to the greatest number, all over the world, is also part of the Hevolution Foundation's mission. Because no matter where they come from, people almost all want the same thing for their old age.

They want to continue to be physically, mentally and financially independent. They do not want to depend on anyone to move in their daily lives. Without running a marathon, which would be extreme, they want to be able to go to the bathroom by themselves. They want to do their shopping, see their friends, be present cognitively, he says.

What is important to them is not to live longer—but to live longer *in good health*.

**Enthusiasm in the United States**

The arrival of this unexpected player somewhat surprised the geroscience community, but he quickly rallied the scientific community, especially in the United States. It already has many partnerships, including the National Institute of Aging (NIA), the American Federation of Aging Research (AFAR), research institutes and universities. He also set up an office in Boston.

The majority of the 150 scientists who received grants from the Saudi Foundation are in the United States.

“Amid a range of global problems and causes, Hevolution Foundation chose to address the far reaching, yet under supported, field of aging research. Hevolution Foundation’s funding and advancement of aging research will have a tremendous impact on the science of aging and increases the likelihood of new breakthroughs,” said Stephanie Lederman, Executive Director of AFAR, in a written statement to Radio-Canada.

The Hevolution Foundation wants to democratize treatments against aging and make them accessible all over the world.

For many researchers, the arrival of Hevolution represents an unexpected opportunity in a field of research that has long been underfunded and attracted few young talents, explains Dr. Khan.

This is also one of the foundation's challenges: attracting talent and convincing them that they can make a difference in an emerging field of research.

According to David Sinclair, professor in the department of genetics at Harvard Medical School and a well-known figure in geroscience, things are starting to change.

20 years ago, research on aging was not well respected, he explains. “Now, I estimate that 10 times more students want to join my laboratories. There seems to be a gain in interest each year among the public, but also among established scientists.  Saudi

Arabia's huge investment of money through Hevolution has shown the world the great potential in this line of research and that there is something very important that is going on."

Together with his team, he developed a gene therapy for cell renewal. Their research, which was the subject of an article in the prestigious scientific journal Nature, first focused on the eye, before being extended to other organs.

It was discovered that by activating three genes found in embryos [Yamanaka OCT4, SOX2 and KLF factors] and introducing them into the eye of an old animal, tissues are renewed. It makes them younger, healthier, and it heals them, explains Professor Sinclair.

"It was able to restore vision in mice and improve that of monkeys. We have also been able to reverse the aging process in the muscles, brain and kidneys so far."

Professor Sinclair's technology is now at the stage of development. Clinical trials on humans are planned to start in August.

"We can't wait to see if it will be possible to use epigenetic reprogramming to treat something as severe as blindness ...We should know if it works to improve vision in humans in about a year."

**Little known in Canada**

The enthusiasm caused by Hevolution in the scientific community in the United States has not reached Canada, where the foundation is still little known.

Marc Prentki, Full Professor in the Department of Nutrition at the University of Montreal, is the only researcher in the country to have obtained a scholarship from the organization. It is the discovery of a new metabolic pathway involved in aging that earned this biochemist, specialized in diabetes and obesity and affiliated with the Research Center of CHUM, generous funding.

A new enzyme (glycerol-3-phosphate phosphatase) of the metabolism has been discovered that acts as a machine to detoxify glucose or nutrients when they are in excess, explains Professor Prentki, director of the Montreal Diabetes Research Center.

The tests were carried out on the C. elegans worm and gave very promising results.

"We have seen that it delayed aging, especially in conditions of metabolic stress," Dr. Prentki notes.

In addition to its detoxifying properties, the glycerol derivation pathway would allow caloric restriction to be mimic, without affecting food intake and fertility, Professor Prentki discovered.

“Calorie restriction is the best way, regardless of the body, to prolong life and health,” Prentki says. “For example, when you give fewer calories to a small worm, it can live twice as long. You do the same thing with a mouse; it will live 15 to 20% more. It's huge. In humans, it translates into 15-20 years.”

For the next four years, the researcher will receive $350,000 per year, plus indirect costs, to test his discovery on mice.

“It's really a substantial sum,” he says. “It allows us to have a bigger team.”

**Ethical issues**

However, the evolution of research on aging raises many ethical questions. The origin of the funds is one of them.

Is it ethically appropriate to accept so much money from Saudi Arabia, a country whose policies, including women and human rights, are denounced? Should scientists be concerned about this?

It is difficult, in a context of research funding that is modest on several topics, to criticize researchers, says Charles Dupras, assistant professor and head of bioethics programs at the École de santé publique de l'Université de Montréal.

“They have legitimate motivations to want to advance science, to make the population benefit from the knowledge that will be generated. Is it up to them to really search, criticize or select funds according to their origin? We can ask ourselves the question. But I would avoid putting this extra burden on their shoulders,” Dupras notes.

Beyond the country, there are several other elements to consider regarding the origin of the research funds, says Professor Dupras. Therefore, he does not believe that a single entity should be pointed out.

He mentions in particular the example of Altos Lab, a private organization with researchers in its team who have developed epigenetic tests for aging.

Now, they seek to develop tools, modes of intervention, to reverse the process of biological aging. They are aimed at rejuvenation, explains Professor Dupras.

Who are they financed by? By Jeff Bezos, of Amazon, to the tune of billions. Jeff Bezos was also singled out for his business practices and with employees.

Even today, several shadow areas persist on the subject of aging.

From an ethical point of view, Charles Dupras considers it essential to question the motivations and interests pursued by private organizations that finance research and companies specializing in biotechnologies. Especially since the latter have tend to multiply over the past ten years, in particular because of the enthusiasm aroused by the biology of aging in Silicon Valley.

Dupras asks: “Is it motivations for the public interest, for the common good, for public health, or is it commercial interests? There are commercial interests, no doubt.”

In the case of the Hevolution Foundation, Charles Dupras finds the approach interesting in the promotion of research. “They are concerned not to talk only about lengthening life expectancy. They talk about aging well, and increasing the quality of life during advanced ages,” he notes.

Although he believes that partnership with private organizations can be positive, Professor Dupras questions himself. “Why do we need foundations to fund research? The foundations have missions with specific objectives. It is not the government that makes choices for the common good, for that of society, when it is foundations that give. Shouldn't it be government entities that decide where to prioritize research funding?”