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In Silicon Valley, researchers are working to reverse aging. That works for mice. Human studies are now being conducted

Because research into age-related diseases such as Alzheimer's, Parkinson's or cardiovascular diseases is making little progress, scientists want to combat aging itself. What sounds like a feverish dream of technology optimists is based on solid scientific foundations. Who is working on which breakthrough?

Gioia da Silva, Mountain View

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Gray hair just for fun? Australian cricket fans dress up to look like Richard Benaud, a cricketer and sports commentator. Sydney, January 2019.

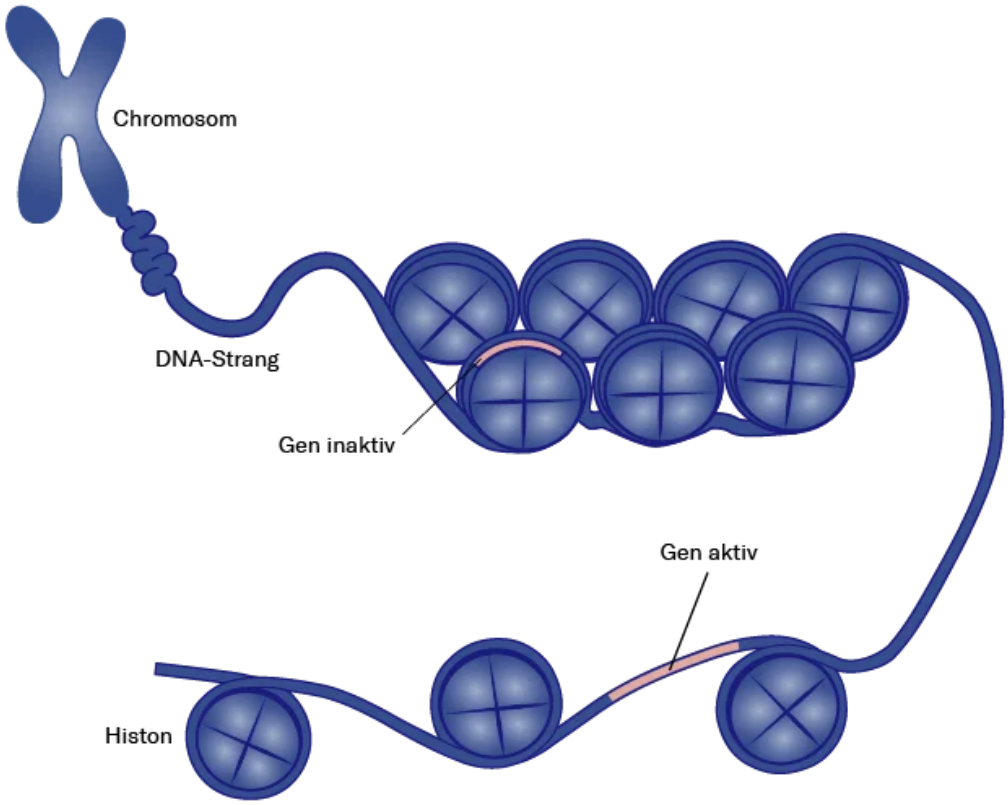
Dan Himbrechts/EPA

Maiko Hermsmeier turns the microscope a little further down. "Now it's sharp," says the molecular biologist and points to the screen next door. There are dozens of dots glowing red, they are human skin cells. Hermsmeier and her team have just successfully rejuvenated her.

Hermsmeier works for Turn Bio, a startup based in Mountain View, in the heart of Silicon Valley. The company is a Stanford spin-off founded by researchers who have been working towards a breakthrough for decades. Now he has succeeded, in the laboratory of the medical professor Vittorio Sebastiano.

Sebastiano and his team have discovered how they can not only stop the aging process in human cells, but even reverse it. To do this, they repair the epigenome, i.e. the system that decides which functions individual cells take on.

What is the epigenome?



Source: nature.com NZZ / cke.

How does the epigenome work?

The epigenome determines which genes are active and which are not. Unlike DNA, which contains the blueprint for the entire body and is present in exactly the same way in every cell, the epigenome in a skin cell is very different from that in a brain or muscle cell.

It's best to think of the epigenome as a system of ill-fitting DNA curlers. In cell biology, the curlers are called histones, which are specialized proteins.

Strands of hair, i.e. sections of DNA that are very close to the curler, are inactive. Strands of hair, i.e. sections of DNA that are further away from the curlers, can interact with their environment. You are active. The combination of active genes decides which function a cell has – whether it is a skin cell or a muscle cell, for example.

As we age, the curlers get loose. They lose small stretches of DNA or hold on to more DNA than they should. Thus, cells that were once young and healthy become diseased because they contain small errors in the epigenome. This can trigger cancer, Alzheimer's or cardiovascular diseases.

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Using mRNA technology, researchers can restore the epigenome from an old, faulty form to its original, young form. They inject a cell with an RNA blueprint for a specific protein. When the cell implements the blueprint, an endogenous instrument is created that enters the cell nucleus and repairs the epigenome. For the cell, the therapy is a kind of help for self-help at the molecular level.

The procedure works not only within individual cells, but also in tissues. In 2020, Sebastiano and his team were able to prove that muscle strength can be restored in old mice in this way. And other researchers have been able to restore sight in old, blind mice . "Now of course we hope that what works in mice will also work in humans," says Sebastiano.

Initial indications suggest that this could be the case. Turn Bio has already succeeded in reversing the aging process in human skin, muscle and blood cells.

side effect cancer?

However, there are skeptics about the enthusiasm of the founders, after all the technology is still young and risky: If the therapy works too long or too strongly, it can cause cancer. This was shown by a study with mice in 2013. For this reason, among other things, Alejandro Ocampo, assistant professor at the University of Lausanne, recently told the magazine of the Massachusetts Institute of Technology (MIT) that, in his view, epigenome therapies will probably not be "nearly" for approved for human use.

Turn Bio is undeterred by these risks. Instead, the company is working to find the right dosage and better control the process of epigenome repair. As is so often the case with scientific breakthroughs, this could happen "in the near future" or never at all.

In any case, Sebastiano is confident. It could even be the case that in the future epigenome therapy will not only be able to rejuvenate individual cells and tissue parts, but the entire human body, says the researcher.

No more gray hair

The startup is currently working on more modest goals: skin therapy. Sebastiano expects epigenome repair to restore youthful skin. This should speed up wound healing in the elderly. There are also various cosmetic applications. This includes the hope that a therapy will let gray hair grow back to its original color, says Anja Krammer, CEO of Turn Bio.

In the Turn Bio laboratory, samples of human skin are rejuvenated.

Gioia da Silva

Clinical trials with volunteer test subjects should start in the next two years, says Krammer. There is a lot of interest in this, the company keeps a waiting list of people who would like to take part in a study.

There is a practical reason why Turn Bio is only now developing a therapy that primarily serves the beauty industry. Sebastiano says they want to try the new technology on a part of the body that is particularly easy to observe. The skin will thus become the entry-level organ for research into epigenome therapies.

Not immortal, but healthy longer

Scientific projects such as those by Sebastiano have taken aging research a big step forward in recent years. Tony Wyss-Coray, a neuroscientist at Stanford University, says this has sparked a kind of immortality hype in parts of the public. However, age research is not about delaying death indefinitely. Rather, one wants to improve the quality of life of people in old age.

In fact, many people today suffer from diseases that are triggered by aging: Alzheimer's and other forms of dementia, arthrosis, Parkinson's, cardiovascular

diseases. According to the current state of knowledge, these diseases cannot be cured. However, if it were possible to control the aging process, they might not break out in the first place, the researchers hope. The result: we live longer and are in good health longer.

With this long-term goal in mind, Wyss-Coray is working on a blood-based therapy. He has shown that when old mice are given blood plasma from young mates, they become healthier, stronger, and better able to remember where their food is hidden. To do this, Wyss-Coray uses blood plasma, i.e. the yellowish liquid with proteins and hormones that remains of blood after all the body's own blood cells have been filtered out. The procedure works particularly well when the blood plasma comes from young, athletic mice.

Blood and blood plasma from those who have recovered from Covid 19 (pictured) help treat the sick. Does the blood of young people make old people young too?

Vito Corleone / Imago

Blood of boys against Alzheimer's

Blood plasma therapy is also being tested on humans. Alkahest, another Stanford University spin-off, administered blood plasma infusions from young donors to people with Alzheimer's disease in initial clinical studies. First results are promising. Wyss-Coray says several study participants were able to prepare

their own meals again after the infusions and would have better remembered that they should take medication regularly or pay their bills.

According to Wyss-Coray, the tests that have taken place so far cannot yet be evaluated statistically. In other words: the positive results could still be a coincidence. A larger, so-called phase 3 study with a sufficiently large number of participants is now being planned, which should enable a statistically significant evaluation. If the study is successful, Alkahest, now bought by the Spanish company Grifols, would probably apply for approval for a blood plasma therapy. That could be the case in three, four or five years, Wyss-Coray estimates.

"The idea that blood transfusions could reverse aging is an ancient idea, but it seems like science fiction to many people," says Wyss-Coray. "But only if we try it out under scientific conditions will we find out whether it doesn't work after all."

Animals that do not age

California, with the tech cluster of Silicon Valley and the burgeoning health research community of San Diego, seems to be a region where ideas are energetically promoted that might otherwise be deemed unrealistic and not pursued. Wyss-Coray says there are now dozens of startups in California trying to translate aging research into practice, as well as several funds and venture capitalists funding such ideas. At the moment, however, no therapy has been approved that can effectively combat aging, so all investments are still associated with high risks.

Nevertheless, the interest of donors is huge. Analysis firm InvestTech currently estimates the longevity market at around $25 trillion. Wealthy celebrities such as Amazon founder Jeff Bezos or Google founder Larry Page also invest: According to various media reports, Bezos finances the rejuvenation startup Altos Labs, which, like Turn Bio, works on epigenome therapies. Page founded a company called Calico in 2013, which is now researching aging with a budget of billions.

Über Calico ist wenig bekannt, die Firma kommunizierte bisher kaum nach aussen. Man weiss allerdings, dass sie vor einigen Jahren eine grosse Kolonie von Nacktmullen gekauft hat. Die Tiere ähneln Mäusen, leben aber um die dreissig Jahre – also rund zehnmal so lange wie Mäuse. Der Grund: Nacktmulle scheinen

nicht zu altern. Sie entwickeln keinen Krebs, und weder ihre Fruchtbarkeit noch ihre mentalen Fähigkeiten lassen im Alter nach. In der freien Wildbahn sterben sie an Infektionskrankheiten, werden gefressen, verdursten oder verhungern. Im Labor sterben sie nach einem langen, gesunden Leben von einem Tag auf den anderen. Warum, blieb den Forschenden bisher ein Rätsel.

Was Calico über die Tiere herausgefunden hat und ob sich dies auch auf den Menschen übertragen lässt, hält sie allerdings geheim. Medienanfragen bleiben unbeantwortet.

Ist die Pille schon erfunden?

Eine weitere kalifornische Forschungseinrichtung, das Buck Institute for Research on Aging, untersucht derweil ein Medikament, das überraschend positive Nebenwirkungen zeigte. Die Pille Metformin wird seit über sechzig Jahren Diabetikerinnen und Diabetikern verschrieben. In den 2000er Jahren merkten Ärzte, dass viele der Millionen Patienten, die das Medikament regelmässig einnehmen, nicht nur länger leben als andere Diabeteskranke, sondern sogar länger als eine gesunde Kontrollgruppe.

Das Medikament scheint das Risiko für Herzkrankheiten und Krebs zu senken und die Patienten trotz fortschreitendem Alter mental fit zu halten. Warum dies gelingt, ist allerdings unklar. Inzwischen ergab eine Studie zwar, dass Metformin bei gesunden Personen den Muskelaufbau eher hemmt, als ihn zu beschleunigen. Trotzdem forscht das Buck-Institut weiter an der Pille. Dieses Jahr soll eine Studie mit 3000 gesunden Personen beginnen.

Sollten die Therapien aus der Altersforschung jemals zugelassen werden, könnten Menschen künftig 120 oder 150 Jahre alt werden. Ob bis dahin das Älterwerden an sich als Krankheit gilt?

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