Frequently Asked Questions on Longevity and Rejuvenation

1. What does "rejuvenation" mean?

If you immediately think of cosmetics and skin care when you hear terms like "anti-aging" and "rejuvenation": our topic has nothing to do with that. In contrast to other anti-aging measures, "rejuvenation" here refers to the targeted intervention in the human body to not merely slow down but reverse the biological aging process, which affects not only the skin but all parts of the body and organs. One promising and well-known approach is called "Strategies for Engineered Negligible Senescence "1 (SENS for short), which is now being implemented by an ever-growing industry.

The SENS plan is based on the fact that the human body is nothing other than a complicated machine with moving parts. Machines - defined here as structures that perform certain functions - accumulate damage (i.e. unfavorable changes in the structure) over time as a result of their normal operation. This is due to the laws of physics and can also be observed in everyday life: The longer a car is used, the more it breaks down. Since in machines the function results from the structure, damage, if large enough, leads to problems in the function, and the accumulation of damage leads to a continuous deterioration of the function. Human cells and organs also suffer damage due to constant operation (called metabolism in living beings), which in turn affects the functions of the organism. Unlike a car, our body has many self-repair mechanisms that prevent it from breaking down after a short time. But because these mechanisms are not perfect, more and more damage accumulates over time and at some point exceeds the level to which we can tolerate it: The body starts to have difficulty maintaining its functions (see diseases of old age such as heart attacks, Parkinson's and Alzheimer's) and eventually the body gives up.

So aging is a mechanical rather than a biological phenomenon, but how can we define it succinctly? It is often said that aging is very difficult to define. This is true if you are looking for a definition that suits all purposes, but when it comes to interventions in the aging process, an overall uncontroversial definition is easy to find. A typical one is as follows:

aging is a series of metabolic side effects that change the structure of our bodies in unfavorable ways over time, eventually making them less functional.

The aim of SENS is therefore to regularly repair the molecular and cellular damage to the body (i.e. the above-mentioned "side effects of metabolism") and thereby keep them below the threshold mentioned above.2 That maintenance and repair work for machines can be seen in cars that are already over 100 years old and were originally designed to be roadworthy for only about 15 years, but still function as well as they did when they were completed.3 They still function because people have maintained them with sufficient care. Of course, with humans we have to repair other damage: Whereas in the case of cars, we treat the body shell with rust inhibitors, remove deposits with petrol additives, and replace aged parts with new ones, among other things, in the case of our bodies we have to work with stem cells and the enzymatic removal of waste products, for example (for a concrete description of the necessary therapies, please refer to our answer to the question "How should this work in detail?"). However, the principle is the same in both cases: as long as enough energy is supplied to the system, it is possible to preserve its structure and thus function with the necessary technology.

The researchers pursuing this approach do not want to cure aging like an infection with a single treatment. This would require a profound understanding of human metabolism, which we do not have today - on the contrary, we are only scratching the surface, if at all, because our metabolism is an enormously complex system with countless interactions.2 The goal is much more to control aging by regularly reversing it.4 To do this, they take advantage of the fact that we do not need to know how the damage occurred to be able to repair it. A car mechanic replacing a windscreen does not need to know about the size and composition of the stone that damaged the glass. Nor do we need to know the details of free radical chemistry to render mitochondrial mutations harmless. For the treated, on the other hand, all this makes no difference apart from the fact that the treatment has to be done regularly.

2. **Doesn't this just prolong suffering?**

No. The purpose of rejuvenation therapies is to extend a person's healthy life span. Many people, when they hear the word "age rejuvenation", immediately have the idea that it would only prolong the painful and frail phase of life in which older people find themselves today.5 This is also referred to as the so-called tithonus error6 (tithonus error). However, the therapies we are talking about are about preventing people from getting into this phase of life in the first place. The victory over aging will not prolong this phase but will bring its elimination. So there will simply no longer be a proportion of the population that is weak, sick, and frail because of its age.

Incidentally, theory and data clearly show that it is not even possible to significantly prolong the frail stage of life - and not because frailty is risky.5 The principle is simple: if you only ever repair a man-made machine that is nearly broken to the point where it just sort of works, sooner or later it will still break down because so much damage has accumulated that it is highly susceptible to malfunction. And just like man-made machines, our body is only as strong as its weakest link.

3. **What is meant by "longevity escape velocity"?**

We left out one critical point in our first answer: The "first generation" therapies for humans will not be perfect. So they will repair some aging damage very well, some less than that while others might not work at all. If we simply keep applying the same therapies - no matter how often or thoroughly - the less well or unrepaired damage will continue to accumulate. Ultimately, we will only experience age-related decline and death at an older age.

So, to keep aging at bay permanently, it is not enough to repeat the therapies at regular intervals. We have to improve them in the meantime and apply the improved version the next time. This is where the concept of "longevity escape velocity" (LEV for short) comes into play.7 What is meant by this? The term refers to the rate at which we need to improve the thoroughness of repair over time to prevent the overall level of damage in the body from increasing further - in other words, to keep our biological age, defined as the amount of damage in our body, constant or to reduce it. If we achieve this rate, we would therefore increase the remaining life expectancy of people receiving the treatment faster than time passes during it (for example, by more than one year per year).8 A 52-year-old who has a life expectancy of 80 years (i.e. 28 years remaining) would therefore add more than one year of life during his 53rd year. His life expectancy would increase to more than 81 years and the next year to more than 82. The expected (age-related) end of their life would thus move away from people faster than they approach it.

It is to be expected that once we reach LEV, (global catastrophes and similar scenarios excepted) we will never fall below this rate again, because as therapies become more thorough, the amount of damage that needs to be repaired continues to decrease (after all, the complexity of aging is finite, not infinite). As a result, the remaining damage takes more and more time to reach a critical level and the speed needed to improve therapies also decreases.

Comparison with jumping off a cliff: the remaining life expectancy of a human being is currently constantly decreasing due to aging, just as the distance to the ground decreases in a fall due to gravity. If you jump with a jet engine on your back, the situation is comparable to regular "rejuvenation" spurts: At first, it is inactive - so you fall. If you activate the jet engine in time (i.e. if you are not too old when the first therapies are available - see 100- and 80-year-olds in the sketch - we won't be able to save them with the first therapies because they will already have accumulated too much damage), it will give you lift, slow down the fall and eventually let you climb further and further.

4. What does "robust mouse rejuvenation" mean?

In a nutshell: The successful attempt at very precisely defined life extension in mice. According to the British biogerontologist Aubrey de Grey, the founder of the concept, RMR is achieved when:

at least 20 mice of the species Mus musculus from a strain whose natural lifespan is around three years are rejuvenated by a single treatment at the age of two years (when the first clear signs of age-related mortality appear) to such an extent that their remaining lifespan (one year) is tripled by this treatment alone, i.e. they live to be five years old instead of three.9 In doing so, the mice are expected to spend their additional lifespan in health.

This milestone will most likely lead to a paradigm shift in public attitudes towards rejuvenation therapies, as after such a robust result, no one can believe that reversing aging is impossible. Therefore, from this point on, the project should receive much more support from the public than it has so far and should be subsidized by the government. For a prediction of when we will reach RMR, see our item "How close are we?".

5. Will this make us immortal?

The answer to this question depends on how "immortal" is defined. If it means that life is no longer finite, the answer is yes, because at least theoretically an ageless person could live indefinitely. But if we take the ordinary definition of immortality - the inability to ever die from any cause - it quickly becomes clear that it has nothing to do with our topic: While aging is by far the most common cause of death, it is of course not the only one - accidents, murders, natural disasters and diseases that are not age-related will still exist, to whatever extent, even after the victory over aging. Logically, no longer having to die from aging does not mean that one can no longer die at all.

If we use a probability calculation to determine the average life expectancy of a 25-year-old whose risk of dying in the next year always remains the same (which reasonably reflects the situation of a non-aging person), we arrive at about 1000 years of life. This would mean that some people would live longer and some people shorter. However, there are two bold assumptions in this result: first, that the behavior of the 25-year-old will not change in any way even after several hundred years lived, and second, that we will make no progress whatsoever about all other causes of death (such as road accidents). Practically, therefore, it is impossible to make any meaningful prediction about how long people will live after they have won the battle against aging.

6. Why try to defeat aging at all?

aging kills about 110 000 people every day, causing more than two-thirds of all deaths worldwide.10 To put this into perspective, that's more than 30 World Trade Center attacks - per day! In one year, that's about 40 million deaths, which is more than the entire population of Canada. In the industrialized world, about 90% of people die of age-related causes.11 Moreover, in most cases, and especially in the case of diseases such as cancer and Alzheimer's, death is preceded by a long period of suffering that also affects relatives and caregivers. The happy and contented falling asleep in the circle of the family does not exist in this way; age-related dying is usually associated with severe pain and grief for all involved.

Apart from the humanitarian and moral aspects, aging is very expensive for society: it makes us ill, unable to work, or both, thus causing immense costs in the health system and the labor market. The average citizen of industrialized countries makes more use of the health care system in the last year of his life than in the entire period before, regardless of age at the time of death. This amounts to trillions of euros per year.12 If we defeat aging, old and frail people would become productive again. They could once again contribute to the well-being of society, contributing their knowledge and life experience instead of just consuming wealth. Moreover, young people would no longer have to care for their elderly parents, grandparents, or other relatives.

7. Why not better fight diseases of old age?

So, as we noted in the last section, there are many compelling reasons to intervene medically. But why would it be preferable to fight aging itself, rather than working to combat the diseases of old age that make aging so distressing in the first place? The reason is simple: these diseases are merely the late stages of aging, which is why it makes little sense (and is even very detrimental to medical progress) to consider certain parts of aging, such as Alzheimer's, and "aging itself" separately. The distinction between these aspects has no biological basis but is purely conceptual. We label certain aspects of

aging as a disease, others not. An example of the aspects that are not considered pathological would be the muscle deterioration known as sarcopenia 13 that accompanies aging and often leads to falls in older people, or frailty.14 However, all these individual parts of aging (or diseases) have one thing in common: as things stand, each of us is guaranteed to get them if we do not die of another part first.

As already explained, aging is nothing more than the accumulation of damage, which ultimately manifests itself in the diseases mentioned. But if - as geriatrics is trying to do today - we fight the diseases of aging only in the late stage of life when they have already appeared, the battle is lost from the start. Just as it doesn't do much good to replace the brakes on a rusting car, a blood-thinning drug prevents the formation of blood clots but doesn't address the cause: the deposits in the arteries. That is why these deposits continue to accumulate until they eventually lead to a blood clot or other problems. (We would like to clarify here that we support these treatments - even if they are not very effective in the long run - as they alleviate the suffering of currently old people).

To advocate the treatment of cancer, diabetes, heart attacks, and strokes, but at the same time to reject the fight against aging, is thus to be in favor of medicine, but only as long as it does not work well.

It is true that gerontologists today repeatedly point out that even the slightest delay in aging would create many more health benefits than a breakthrough in the fight against individual diseases. However, policymakers still do not understand this fact - probably because gerontologists, especially in the 1950s, 60s, and 70s, publicly distinguished between aging and age-related diseases to narrow their field of research financially. This strategy has turned out to be a mistake and has led to a fundamental misunderstanding of the implications of each approach.9 Indeed, the SENS approach in particular aims to break this paradigm and prevent age-related diseases by repairing the underlying damage in time or otherwise rendering it harmless.

8. Is aging a disease?

Whether biological aging is "a disease" or not is a semantic question that we should not worry about. aging causes disease and is, therefore, a medical problem, which legitimizes its control.

Even though aging is still not considered a disease in modern medicine,15 the WHO has included in its 11th version of the International Classification of Diseases and "extension code" called "age-related". This makes it possible to designate a treatment as approved or recommended for those who suffer from the disease to be treated and are over a certain minimum age. This sounds subtle but has far-reaching benefits for therapy development about aging.16

9. Don't we know far too little about aging to be able to combat it at all?

No. We still know very little about the aging process as a whole, but we know enough to develop therapies that eliminate, repair or otherwise render harmless the molecular and cellular damage that leads to disease and death (notwithstanding that basic research is constantly providing new insights that inform the development of these therapies).

As we explained in the first response, SENS addresses the damage caused by aging - not the processes that cause that damage, nor the processes that are triggered by the damage. In doing so, we

circumvent our ignorance of the many different mechanisms of aging and their relationships to each other, because we start at a weak link within the chain of events that leads from metabolism to pathology.17

This approach will be rather alien to basic researchers, but natural to engineers. In engineering, it is common to design technologies before we have unraveled the physics behind them. Engineers have been using electricity and semiconductors for a long time before they had a consistent explanation of the forces behind them. It is also easy to find examples of this principle in medicine: Not only have salicylates from willow bark been used for centuries against pain and inflammation, but the German chemist and pharmacist Felix Hoffmann even managed to make these active ingredients more tolerable, although we did not understand the molecular mechanism of action of the drug aspirin developed from them until some 70 years later.18

10. Why should victory over aging be possible in the foreseeable future if we cannot even cure individual cancers (or other diseases)?

The argument that success in the fight against aging is unthinkable because at the moment we are still powerless against so many other diseases (autoimmune diseases, mental disorders, non-age-related cancers, etc.) is based on two flawed assumptions.

The first is that we have no chance of curing these diseases in the foreseeable future. However, the very regenerative medicine we need to defeat aging holds several other biomedical promises and will most likely lead to breakthroughs in other diseases and disabilities. One example of these prospects is pluripotent stem cells,19 which are being researched for the treatment of some of the most fearsome non-age-related diseases and have shown very promising results in studies to date: Type 1 diabetes,20 spinal cord injuries,21 multiple cases of sclerosis,22 ALS (amyotrophic lateral sclerosis),23 cerebral palsy24 and more.

The second is that tackling these diseases must necessarily be easier than tackling aging. However, precisely because of the engineering approach of SENS and its heuristics, the latter, although also a mammoth task, should be easier than, for example, curing autism. After all, as already mentioned, we do not have to intervene in the genome or metabolic processes of any kind. Instead, we can simply reverse the damage in the body regularly and ever more thoroughly.17

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4: See also the TED Talk "A roadmap to end aging" from 2005, which introduces the topic. The "engineering approach", i.e. repairing the damage, is discussed in the book "Niemals alt! How to reverse aging. Advances in Rejuvenation Research" (ISBN 978-3-8376-1336-0) by the biogerontologist Aubrey de Grey and his research assistant Michael Rae.

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