

CLINIQUE  
LA PRAIRIE

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SWITZERLAND

# LONGEVITY SCIENCE REPORT I

MAY 2022

## *Introduction*

There are many things that we need for a long and healthy life. Medical assessments, good nutrition, mental wellness, regular physical activity, low stress levels, good sleep are all essential. Nowadays we also know that epigenetic mechanisms are key to regulate many genes and bring the body's responses to the optimum levels. For over 20 years, our scientific committee has been collaborating with international experts and clinicians in the fields of research medicine and biosciences, contributing to our unique approach for Predictive and Precision Medicine. We are pleased to introduce our new series of **Longevity Science Report** in which our scientific committee and experts will regularly share articles.

This is the **first issue**, and we hope you will enjoy reading about some latest advance in developing predictive tools for optimal aging, wellbeing and longevity, based upon behavioral, environmental, medical and (epi)genetic factors.

With best regards from Montreux

*Simone Gibertoni*  
CEO

*Olga Donica*  
Head of Innovation and Research



ARTICLE N°1

## *Why do we age, and how can the aging process be inhibited?*

In the 19th century, August Weismann hypothesised that somatic cells could not regenerate indefinitely. It was validated in 1960 with research demonstrating that fibroblasts have a replication limit and then become senescent. Later, this limit was associated with telomere shortening.

In 1957, George Williams hypothesised that genes that are beneficial to development, maturation and fecundity have traits that, once growth is complete, are harmful to the organism and contribute to senescence later in life. All these findings are not reciprocally exclusive.





Recent advances in biotechnology and science have led to a growing body of scientific evidence showing that aging is inextricably linked to senescence. During the different phases of body's life, there is a progressive loss of the regenerative potential of somatic cells in many vertebrate species in contrast to simple unicellular organisms and a few primitive invertebrates that display no sign of aging. Apparently, the greater complexity of multicellular organisms translates evolutionary to an increasingly loss of regenerative potential. Eight weeks after birth, mammalian somatic cells are already less able to regenerate, as shown by their inability to heal a wound without leaving a scar. Subsequently, in adulthood, the regenerative potential of somatic

cells gradually decreases until death and is accelerated in the case of chronic tissue damage giving rise to chronic pathology. The "Weismann barrier" defines the limit of both immortality and the regenerative potential of somatic cells.

*At the molecular level, several cell signalling pathways have been identified as playing a crucial role in maintaining cell homeostasis, particularly those related to metabolism*

Nutrient and energy-sensing cell signalling pathways are intimately connected to senescence. It has been shown that activation of cell

signalling pathways associated with cell growth and division (anabolism) is linked to an increase in age-related low-grade chronic inflammation and the development of chronic diseases. In contrast, inhibition of these pathways leads to improved health and longevity, for example with cellular interventions associated with energy production and storage (catabolism), acting on stress resistance. Both anabolic and catabolic cell signalling pathways are linked and self-regulate to maintain cellular homeostasis.

*For example, chronic overeating, lack of physical activity or sleep issues leads to an imbalance in these cell signalling pathways resulting in overactivation of the growth and division cell signalling pathways at the expense of those related to stress resistance involved in somatic cell maintenance and regeneration.*

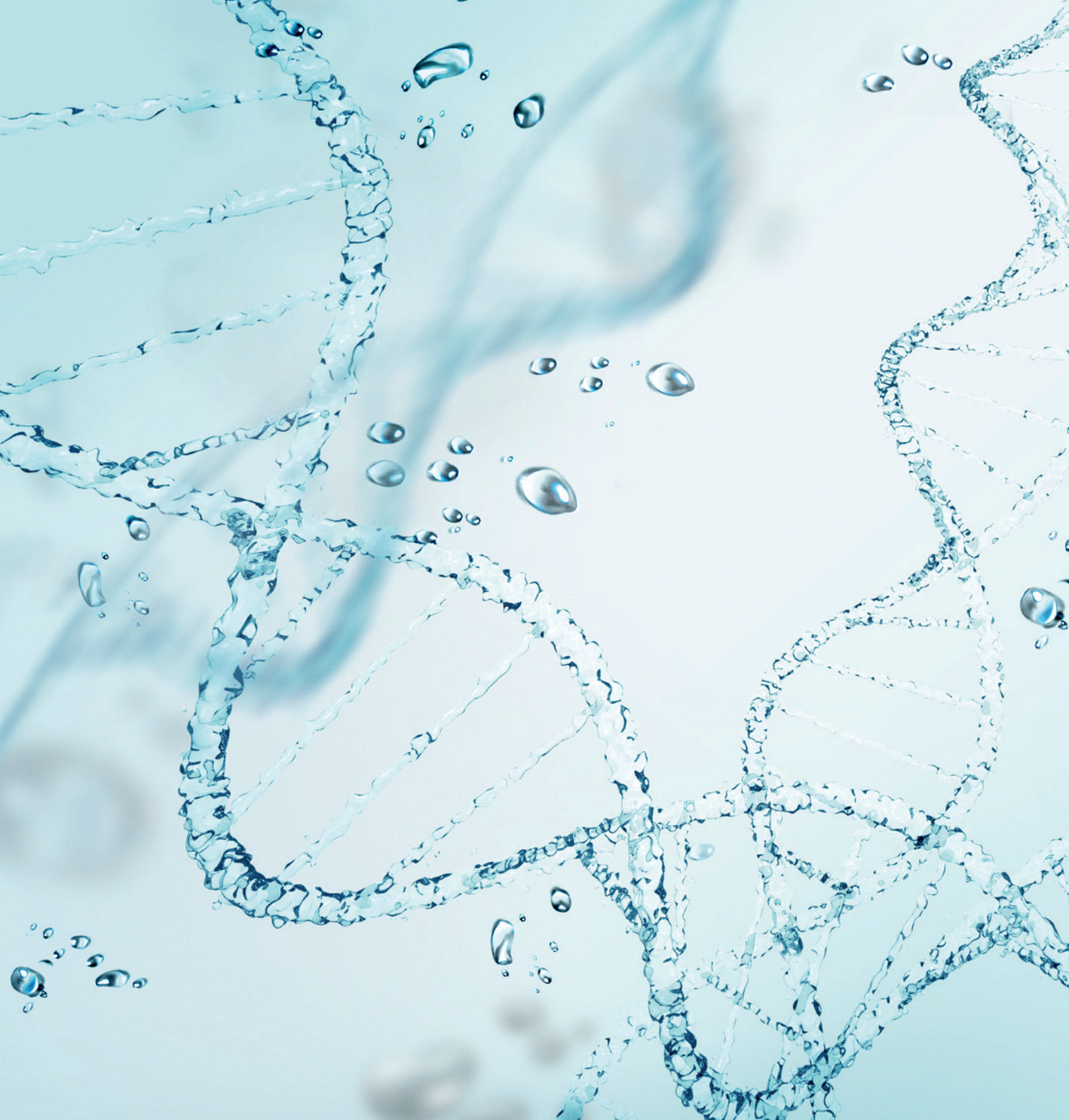
This state is associated with chronic low-grade age-related inflammation and promotes the emergence of senescent cells while decreasing their elimination by the immune system. This condition leads to an increase in senescent cells with age. Although senescent cells cannot divide, they secrete many pro-inflammatory factors, which, by contamination, contribute to

the transformation of cells in their vicinity into senescent cells. This condition favours the development of chronic diseases that impair the quality of life with age.

For more than 90 years, Clinique La Prairie's interventions and philosophy have been built on research to rebalance the immune system to reduce age-related chronic inflammation and promote cell regeneration. More recently, treatments that act on nutrient and energy-sensing cell signalling pathways and on senescent cells to reduce their emergence and facilitate their elimination have been developed. All these strategies aim to promote health maintenance with age, a condition essential for life quality, and secondarily prolong life in good conditions by slowing down the senescence and progression of chronic diseases.



*Dr Silvio Folli, Expert in pharmacology, nutrition and longevity*





ARTICLE N°2

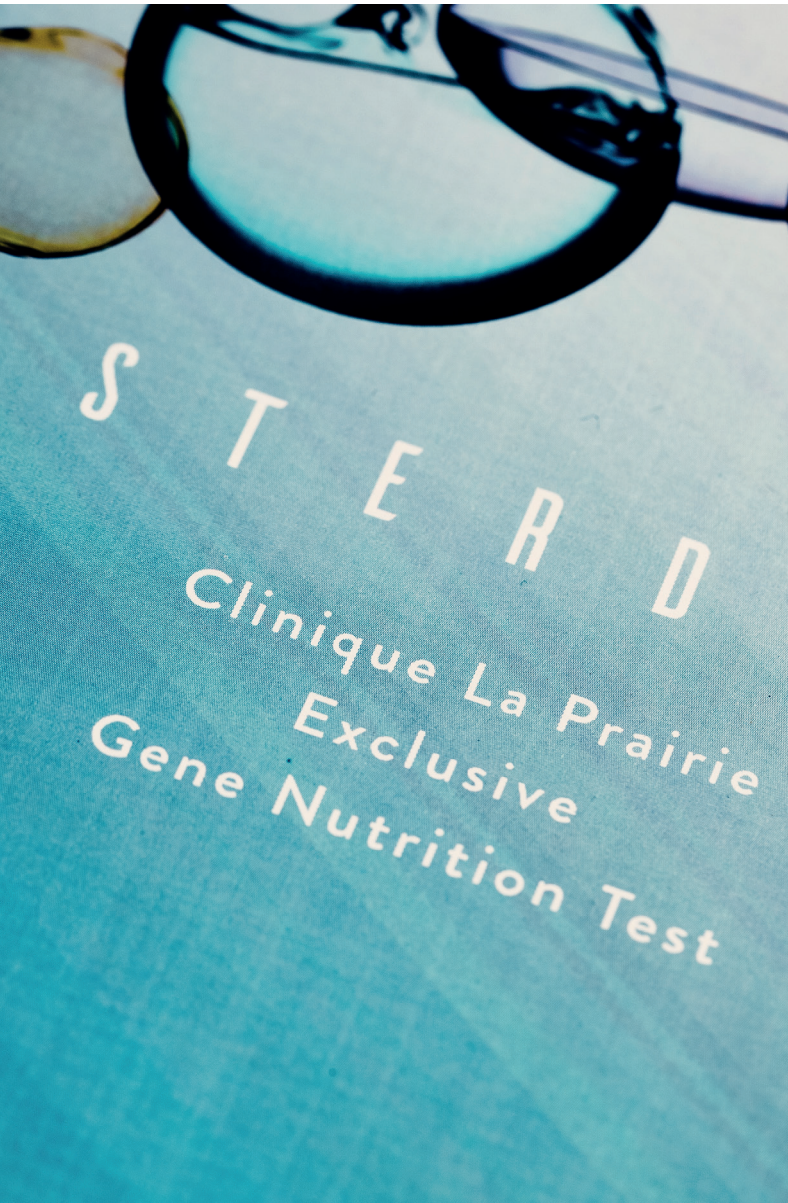
## *Knowledge of our own genetics stimulates us to adopt appropriate healthy lifestyle*

Knowledge and understanding of the human genetics have tremendously increased over the last 30 years, notably due to the technology developments such as diverse genetic arrays and next generation sequencing. The elucidation of the human genome allowed subsequently to sequence the genome of a big number of individuals and diverse human ethnicities, to compare them among each other, to establish a haplotype map of the

human genome and, to identify sequences that are related to a disease development.

*The DNA sequence of any two people is 99.9 percent identical. The variations, however, may greatly affect an individual's risk to develop a disease.*





Development of a complex disease depends on the equilibrium between the risk and the protective factors which may be genetically or environmentally determined. This postulate is the basis for actionable preventive treatments –

*one cannot change his or her genes, but can change lifestyle according to his/her genetics and thus act to decrease the risk of the disease development.*

Genetics can help to decrease oxidative stress or to predict the risk of developing deficiency in diverse nutriment, such as vitamins.

Some examples: Folate or vitamin B9 is only available through nutrition and plays an important role in the formation of red blood cells and in the healthy growth and function of cells (synthesis of DNA bases, synthesis of certain amino acids, etc); it is crucial in early pregnancy to reduce the risk of congenital malformations of the brain and spine.

Folic acid is the metabolic precursor of an important coenzyme, tetrahydrofolate; its biotransformation involves a specific enzyme (MTHFR). Genetic variant in this gene that forms this MTHFR enzyme is frequent in the general population. This variant is associated with low serum and red blood cell folate levels, as well as with elevated homocysteine levels (a risk factor for cardiovascular disease and cognitive decline). Knowledge of the existence of this variant in the genome of the person can help to decide on folate supplementation, choice of the most appropriate form of supplements (folate vs. folic acid), allow to establish a personalized surveillance of homocysteine levels to prevent development of certain diseases.

*Finally, numerous studies have shown that knowledge of our own genetics and the eventual associated risks stimulates to adopt appropriate healthy lifestyle that significantly contributes to an individual wellbeing and longevity.*

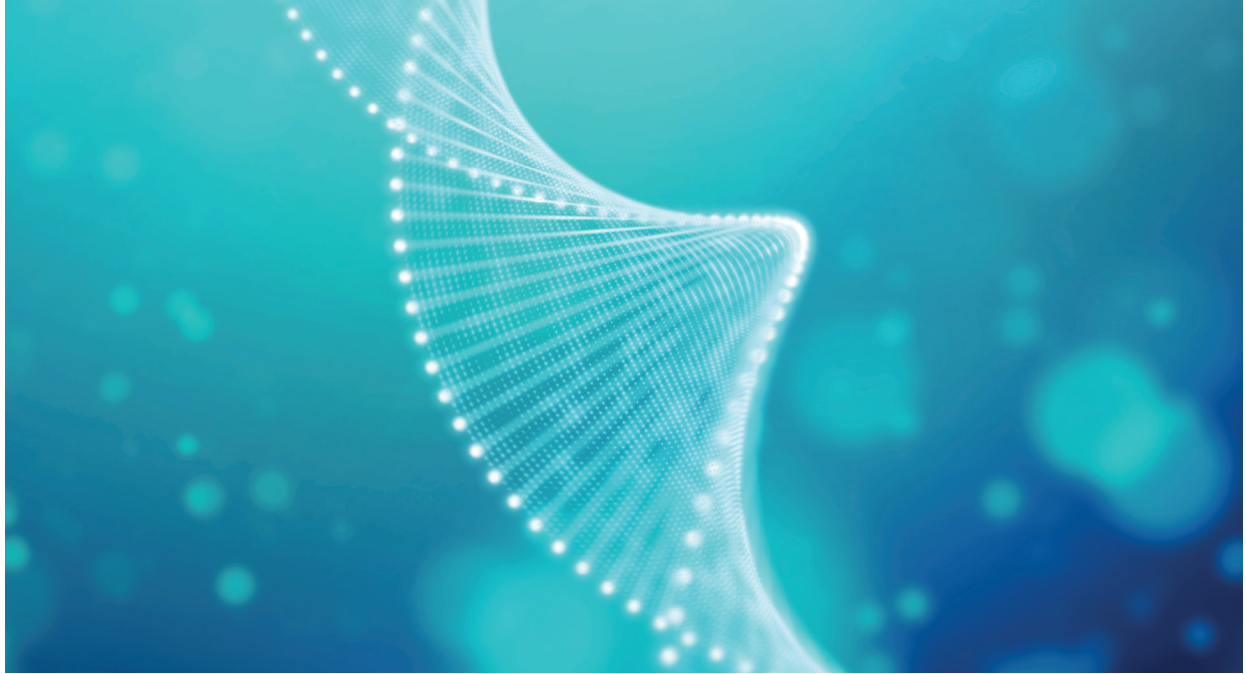
Over the last few years, Gene Predictis has developed diverse genetic tests specifically for Clinique La Prairie, allowing to the Clinic to establish a highly personalized follow-up for its

clients, as well as to propose them a highly personalized disease prevention. These tests are based upon proprietary algorithms and target complex diseases or complex traits that are determined at the same time by one or multiple genetic variants and the environment (e.g. food intolerances, diabetes, cardiovascular disease, nutrition, aging...).



*Dr. Goranka Tanackovic,  
Expert in genetics*





ARTICLE N°3

## *Longevity and epigenetics*

Aging is a natural and dynamic process that it is not in steady evolution starting at a given age, but rather a change that might be slower or faster depending on individual specificities. A question that we have all likely asked at some point in our lives might be, “is that person really 75? I thought they were 60!”

What contributes to someone moving and looking like they are 15 years younger than their actual age? Many still attribute these variations in aging speed - or accelerated aging - to genetics, but we also know that the environment and lifestyle have a tremendous impact. There is now mounting evidence that epigenetic mechanisms do mediate the effects

of these external factors on aging processes and contrary to genetics which is immutable, epigenetics is dynamic and responds – positively and negatively – to our environment.

*Your epigenetics and genetic makeup go hand-in-hand, and while we can't change our genetics, epigenetic is dynamic and modifications can actually affect how your genes are expressed along with your aging process.*

Biological age is a concept developed to study the progressive evolution the aging process. It reflects the global health state of a



person through analysis of epigenetic biomarkers and as such has been linked to the risk of developing chronic diseases as well as premature mortality. Tracking an individual's biological age over time unlocks the potential of personalized and customizable health interventions to optimize aging speed. The goal is to set up health interventions that have a real impact for you – your physiology and your habits.

Our epigenetic landscape is influenced by our environment; this includes lifestyle exposures such as tobacco or alcohol consumption, physical activity levels, nutrition, as well as depression and even our socioeconomic status as a child. Taken together, these exposures can influence our biological age. For example, smoking, excessive alcohol consumption, and a sedentary lifestyle contributes to what is termed accelerated biological aging, i.e., when your chronological age is younger than your biological age.

Fortunately, recent research suggests that it may be possible to slow down or even reverse accelerated aging by ma-

king certain lifestyle changes such as improving sleeping habits, switching to a healthier, vegetable-based diet, regularly exercising at moderate intensity, and even practicing meditation (Chaix et al., 2017, Barron-Cabrera et al., 2019, Carskadon et al., 2019, Fiorito et al., 2021).

*The field of epigenetics is constantly innovating and the technologies developed for studying its implication in health and longevity are becoming more and more precise.*

A growing number of studies links disease development to epigenetic alterations. A recent summary of published literature found evidence for an increased risk of ischemic stroke, lung and breast cancer, cardiovascular disease, and even dementia in association with accelerated biological aging (Fransquet et al., 2019). Moreover, 9 of the 10 studies that considered risk of all-cause mortality reported a significant increase in risk in association with accelerated biological aging. For example, one study observed that a 5-year increase in accelerated aging was associated with a 35% higher risk of mortality. Although the results were not unanimous across studies, this was somewhat dependent on how biological age was measured.

The plasticity and actionability of epigenetics offers a promising target of action for future age related therapeutics. Using medicines to rewire the epigenome is the science of tomorrow, and the technology is already in the works. Recent advances in molecular biology published in the journal Cell showed that the action of bioengineered molecules can modify the epigenome in the long term, paving the way for new innovative treatments (Nuñez et al., 2021, Xu et al., 2019). And while maintaining a young biological age is not a panacea to all age related issues, it is important to act where it matters and maintain a healthy lifestyle. Keeping in good shape, eating healthy, getting sufficient sleep and avoiding stress are important. Measurement of the biological age can help you keep track of your progress in combination with regular check-ups and tailored health interventions at Clinique La Prairie.



Sébastien Nusslé,  
Scientist and founder at  
GenKnowMe



Dr Semira Gonseth  
Nusslé Co-founder,  
Chief Medical Officer





ARTICLE N°4

## *Why lifestyle adjustments are beneficial already in young age to support brain health*

Most recent socio-demographical analyses predict that every fourth girl born in Switzerland after 2010 will reach the age of 100 years with men also approaching similar levels of longevity. Along the same lines, aging associated brain disorders – e.g. cardio-vascular disease or dementia, become an increasing burden on individuals and the society that cares for them. After the age of 65 years the proportion of demented people doubles every five years and at age 90+ half of the population will suffer from dementia.



On the contrary, there are also individuals resilient to the deleterious aging effects who maintain high level of cognitive and physical performance – the so called “super-agers”.

*Our focus is to track and understand the life-time factors determining “successful” aging.*

The advanced research armament includes the study of specific (epi)genetic, environmental and lifestyle modulators identifiable through laboratory work-up, behavioural testing, socio-epidemiological research and brain imaging. Cumulating scientific evidence summarised in the Lancet Commission on dementia prevention acknowledges twelve lifetime factors explaining 40% of the risk for cognitive decline over a lifetime - less education, hypertension, smoking, excessive alcohol consumption, obesity, hearing impairment, depression, physical inactivity, diabetes, low social contact, traumatic brain injury, and air pollution.

The acquired knowledge prepares the grounds for the current concept of interceptive medicine – preventing diseases before they emerge. Given the fact that the twelve lifetime factors from above impact differentially brain health across the lifespan, it becomes clear that

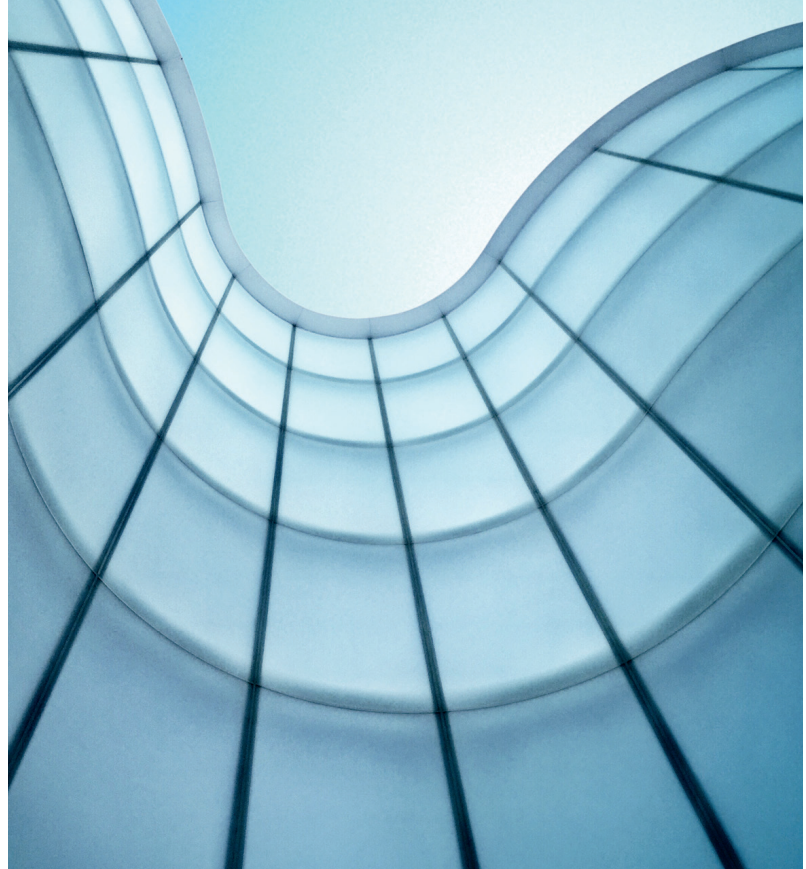
lifestyle adjustments are beneficial already in young age. I am truly convinced that avoiding the harmful effects of toxins, investing in physical activity and fighting for clean air will bring the expected benefits sooner and in a more efficient way than a range of currently proposed treatments.



*Dr. Bogdan Draganski,  
Neuroscientist*

ARTICLE N°5

## *Influence of COVID-19 pandemic on longevity*



The world life expectancy increases consistently since the early years of the 20th century and between the years 2000 and 2019 the expectancy has increased by almost 7 years. In 2019, the COVID-19 pandemic busted and changed things around. The obvious direct effect of the virus is the increase in annual mortality around the world. But the virus has a second and indirect effect that might influence the world expectancy on the long term. This effect isn't caused only by the virus infection but from the measures that were taken for the protection from it in the general population. Islam et al. showed in their research that the life expectancy decreased in about 0.03 to 2.3 years in 31

from 37 investigated countries in the year 2020 alone. In their work they took in consideration the social and economic health effect including the neglect and delay in health treatments.

*The gravity of the COVID-19 influence  
was revealed to be directly related to age.*

Here we want to point out some reflections about the indirectly COVID-19 source of risk to the (not only) elderly population that can be reduced and with some awareness and actions in these directions might minimize the life expectancy decreasing.



First of all, during the pandemic, there was a lack in diseases diagnostic and treatments. This omission has a direct influence on the aging process as we emphasized in “The Jerusalem Longitudinal Study” and now it’s the time to make sure that no prevention, treatment or diagnostic is continuing to be postponed.

Secondly, we should reduce the distance that the pandemic forced on us. Social support from family and friend is very important for aging but during the pandemic we kept our distance from our loved one for their own protection.

Finally, staying at home, if because governmental instruction or self-initiatives because of the fear of the virus, led to a decreasing in physical and social activities. The avoidance of leaving home influences in addition, on the mood and increases depression. Those factors were proved to be tightly connected to survival.

*But as presented in our 30 years longitudinal research, even inactive peoples who started exercising at a later age, showed a significant improvement in longevity.*

Thus confirming that it is never too late to make a change (or too early as we should start thinking about longevity and its consequences as from the age of thirty)! It's time to restate the importance of regular movement at any age, and to also encourage the elderly people to go out from home for a ballad in the park, take a sip of fresh air and come back to their physical activities, preferable with a friend or a family member. All together will improve the mood as well, as everything is connected.



*Dr Armand Aaron Cohen,  
Internist and Geriatrician.*

*The author would like to acknowledge  
Dr Orit Cohen contribution to the manuscript writing.*





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*All the writers of this report  
are members of the Scientific Committee  
of Clinique La Prairie.*

*Questions or want to know more?  
Contact us on [info@laprairie.ch](mailto:info@laprairie.ch)*

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