

## Putting brakes on Ageing

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**Some researchers argue that slowing the rate of biological ageing could be the best way to delay development of chronic diseases. Although a number of pharmacological agents targeting basic ageing pathways to extend lifespan and health-span are presently under investigation in different parts of the world, in-depth examination and comprehensive deliberations are currently ruling this space of 'anti-ageing'.**



Time and tide wait for none; ageing is the price of growth. Yet scientists today are taking bold steps towards slowing time, maybe stalling ageing or seeking to reverse it as well. However, the question that looms over us is- can a longer life really be a favourable condition for our species?

Ageing is characterised by the nine unique hallmarks: genomic instability, telomere attrition, epigenetic alterations, loss of proteostasis, deregulated nutrient-sensing, mitochondrial dysfunction, cellular senescence, stem cell exhaustion, and altered intercellular communication. Thus the goal is to impede these processes, effectively slowing the deterioration of our bodies with passage of time.

Moving in this direction is a recent announcement by a team of Japanese scientists who have developed a vaccine to delete cells that cause ageing among humans, owing to the fact that Japan is ageing fast and by 2036, people aged 65 and over will represent a third of its population.

Another interesting information that is being heard is that after his retirement and space expedition, Amazon founder Jeff Bezos is looking to invest in an anti-ageing research startup Altos Labs working on reprogramming human cells. In fact, this is not something new for Bezos. Back in 2018, he was in the limelight for backing a Silicon Valley scientist who had been working on a cure for ageing.

### Agelessness is in business

According to a recent report by Research and Markets, from \$194.4 billion in 2020, the global market size for anti-ageing is set to cross \$422.8 billion by 2030, at an 8.6 per cent CAGR between 2021 and 2030. Although the anti-ageing market was badly affected during the COVID-19 pandemic, North America stands at generating the highest revenue in this space on account of the rising volume of non-surgical cosmetic treatments, increasing skincare product awareness, and surging volume of anti-ageing treatments in Canada and the US.

Adding on, the most-significant players in the global anti-ageing market include notable names such as Procter & Gamble (P&G) Company, Hologic Inc., Nu Skin Enterprises Inc., Unilever Group, Galderma SA, Pierre Fabre S.A, Shiseido Company Limited, Home Skinovations, Candela Corporation etc.

Although there is a potential market for anti-ageing devices and aesthetic plastic surgery procedures globally, the major challenge lies in the development of anti-ageing medicines or drugs.

Very promising in this regard is rapamycin (also known as sirolimus), which is already approved by the US Food and Drug Administration (FDA) as an antibiotic and immunosuppressant drug. Similarly, metformin, the most widely prescribed oral hypoglycemic medication for type 2 diabetes worldwide, retards ageing in model organisms and reduces the incidence of ageing-related diseases such as neurodegenerative disease and cancer in humans.

“We have found the epigenetic data on ageing that is stored in the cells and seek to reverse it in our laboratory. This should mean that we can eventually reverse ageing completely. What we want to do is make ageing a preventable disease. It is not acceptable to be sick and frail at any age. The goal is to approach medicine from a different angle and get healthier in ways that we could not imagine until recently”, says Dr David A. Sinclair, Co-Director, Paul F. Glenn Center for Biology of Ageing Research, Harvard Medical School, US.

What seems remarkable is that Dr Sinclair and his team have been able to reverse ageing in mice in just a week. They are equally optimistic about the fact that these same pathways and mechanisms exist in humans.

### **How is India re-setting the clock?**

India's elderly population (aged 60 and above) is projected to touch 194 million in 2031 from 138 million in 2021, a 41 per cent increase over a decade, according to the National Statistical Office (NSO)'s Elderly in India 2021 report.

With Indian minds considered to be one of the brightest across the globe, solutions to stop the age-clock have been emerging since a very long time from Indian scientists. For example, back in 2018, Dr Keshav K Singh, a professor of genetics, pathology and environmental health at the University of Alabama at Birmingham, demonstrated how boosting the function of the mitochondria, the powerhouse of cells, makes wrinkles disappear and restores hair growth.

The quest is still ongoing in many laboratories in India with researchers developing newer targets to overcome ageing. Dr Deepak Saini's laboratory at the Indian Institute of Science (IISc), Bengaluru, is currently focusing on a class of receptors called G protein-coupled receptors (GPCRs) and their role in the event cascade leading to aged cells.

“The ongoing work is expected to impact our understanding of events which govern the aged associated inflammation, tissue injury and infection. Our work allows us to identify and characterise molecules which regulate DNA damage which leads to aging; initiation and maintenance of aged cells; which regulate age-associated inflammation and the intrinsic anti-aging mechanisms which are triggered when cellular insults occur. We study the cellular responses of aged cells using live cell imaging, pharmacological and gene inactivation and metabolomics profiling approaches”, says Dr Saini, Associate Professor, Department of Molecular Reproduction, Development and Genetics, IISc, Bengaluru.

On the other hand, Dr Swasti Raychaudhuri at Centre for Cellular and Molecular Biology (CCMB), Hyderabad, is working on a prominent hypothesis which suggests that a gradual, age-dependent decline of protein homeostasis (proteostasis) accompanied by increasing protein-aggregation is the underlying cause of many age-related loss-of-function diseases.

“Surprisingly, our current results indicate that increasing protein aggregates may not always be ‘messy’ but ‘good’ and are important to execute evolutionary conserved functions to protect from age-related degenerative phenotypes. As I say, these aggregates work as double-edged swords. Proper balance is the key as uncontrolled aggregation defeats the homeostatic purpose and invites undesired problems. Our job is to find out the balancing factors and regulate them to work for good only”, says Dr Swasti Raychaudhuri, Project Leader, Cellular Biochemistry and Proteomics, CCMB, Hyderabad.

In a recent development, Ashok Soota, former President of the Confederation of Indian Industry (CII), has established probably India's first not-for-profit entity in the private sector called SKAN, for ageing research, among others, with a fund commitment of Rs 200 crore. The strategic partner for the ‘ageing project’ is the upcoming St. John's Geriatric Centre (SJGC), to be located on the St John's Hospital campus in Bengaluru.

Another tool that is being explored by the researchers to overcome ageing is stem cell therapy or regenerative medicine. Studies have shown that stem cells, in combination with anti-ageing genes, can create a sophisticated shield, which can

prevent the effects of ageing.

Although there is not enough clinical data to be able to state whether or not stem cells may be able to cure ageing, it may be possible to slow the ageing process.

“The concept of aging that we believe is a mistake. The fountain of youth lies within us. We are talking about tapping into our own resources, namely, stem cells and growth factors within our body. They function normally to maintain homeostasis. But, with accumulating negative habits and tissue damage, these cells start struggling to maintain the balance. Thus, we age! How do we reverse this? Through functional medicine—by identifying the root cause of the problem and by adding more healthy cells to the pool. There is ongoing research on genetic changes and alternative modalities like yoga, meditation, dance and music therapies, magnetic field-based therapies, energy modulation as well, all of which aim to promote healthy aging. Functional medicine is at the forefront of anti-ageing research”, says Dr Pradeep Mahajan, Regenerative Medicine Researcher, StemRx Bioscience Solutions, Navi Mumbai.

Being the only species aware of our fate, we know that ageing is a biological certainty and yet can never be prepared to face the consequences. Science has never known boundaries and the mysteries of the body once revealed are often exploited for our benefit. Recent times have seen bashful strides been made towards understanding and combating ageing. One might believe all questions worth asking demands answers but it also makes one wonder if the quest for life extension misplaced hubris or truly worthy of research.

Time will reveal if laboratory results prove effective or not but the quest for anti-ageing drugs has definitely carved a niche for itself. But the perception that a gap is expanding between what science may offer as age-related interventions and what drug regulation can provide in response is another area that needs deeper consideration.

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