comment

Artificial intelligence in longevity medicine

Recent advances in deep learning enabled the development of AI systems that outperform humans in many tasks and have started to empower scientists and physicians with new tools. In this Comment, we discuss how recent applications of AI to aging research are leading to the emergence of the field of longevity medicine.

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ging is a universal feature shared by all living beings. While the rate of aging may vary among individuals and species, the time elapsed since birth is a strong predictor of health status and mortality. Targeting aging may extend the average life expectancy more substantially than prevention or treatment of individual diseases¹. However, within the established drug discovery and development framework, pharmaceutical companies are still searching for compounds and interventions for the treatment of individual chronic diseases such as cancer and cardiovascular or pulmonary diseases. Current biomedical research aims to identify the underlying mechanisms and molecular targets specific to a disease in order to modify the disease, treat its symptoms or cure it. Once a drug is approved, the medical community is obliged to follow a specific and defined protocol that is mostly targeted towards treatment of a specific disease with a specific drug or a combination. Rarely, however, do clinicians prescribe an off-label drug, even when there is evidence that it may be effective in the treatment of another disease out of concerns about possible side effects and to avoid possible malpractice claims. While evidence-based medicine has been overwhelmingly effective at reducing mortality in the past half century, it has also increased the economic burden of disease in developed countries due to the resulting extension in lifespan without a concomitant increase in healthspan. Since aging plays a key role in the onset and progression of many human diseases and affects all organs of the body, many chronic conditions manifest themselves simultaneously as comorbidities later in life. Combined with global trends in population aging, this apparent victory of modern medicine to extend our lives has led to an explosion in healthcare costs and has failed to concomitantly improve wellness and quality of life for older adults^{1,2}.

The advent of artificial intelligence in biomedical research and medicine Preventive, geroscience-based measures to treat aging at the organismal level would

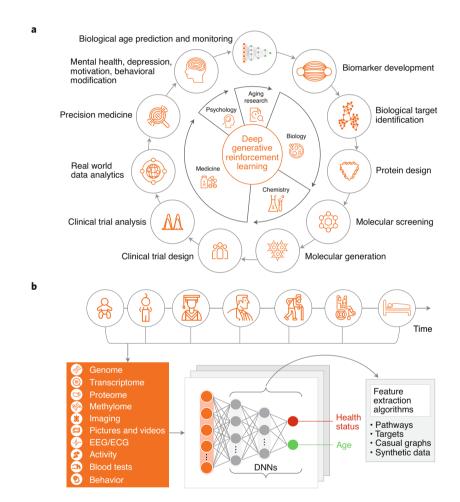


Fig. 1 | Al in longevity medicine. a, Deep generative reinforcement learning for every aspect of healthcare at every level of system organization. A multitude of DL applications in the clinical practice is represented. b, DNNs trained on longitudinal data of healthy subjects and patients with diseases learn the difference between aging and disease and have the potential to lead to applications for risk prediction and identification of optimizable factors, and positioning individuals in their optimal-performance biological age range. EEG, electroencephalogram; ECG, electrocardiogram.

provide a more substantial benefit than reactive therapeutic approaches targeted at a single disease or organ, since those do not contribute to a significant improvement in healthspan. It is often ignored that disease-focused therapeutic approaches do not remarkably extend lifespans. It has been estimated that the complete elimination of a single fatal disease such as cancer in the USA would merely lead to a 2.3-year population increase in life expectancy at birth and a 1.2-year increase at age 65, since the majority of overall mortality is due to age-related diseases and the abovementioned multimorbidy¹. Old biological age is not recommended to be reported as an official cause of death, but it remains the main reason why older adults die worldwide². Therefore, combining the prevention and elimination of chronic diseases by adding a geroscience approach to routine clinical care would yield the best outcomes in that it would promote both a long and healthy lifespan.

However, understanding the aging process requires longitudinal monitoring of millions of parameters in many different types of data sets that change very slowly during the human life course, and distinctly in genetically and socioculturally diverse populations³. While humans can be trained to accurately predict age and explain features leading to their predictions — using facial images, for instance — and even to propose corrective actions, no human doctor can do this on multiple different biological data types, such as blood tests or gene expression data4. Fortunately, the task of finding complex patterns in large volumes of longitudinal data is where modern artificial intelligence (AI) demonstrates a unique, often spectacular performance. Since 2014, AI systems have outperformed human experts in multiple areas, including image recognition, knowledge quizzes, video games, language translation and many other tasks. Most of these achievements have been made possible by various advances in deep neural networks trained on large data sets using high-performance computing. Importantly, deep generative reinforcement learning has been successfully used in a broad range of biomedical applications (Fig. 1a) ranging from drug discovery to prediction of clinical trial outcomes and personalized medicine5-7.

AI-powered tools enable longevity medicine

Deep learning (DL) was a breakthrough for AI research, allowing for the training of deep neural networks (DNNs) on massive longitudinal data sets, which were previously almost impossibly difficult to comprehensively mine and interpret in the longevity arena. There is no consensus on how to define human 'biological age', but the term usually refers to a measure that is more predictive of mortality, diseases or frailty than chronological age, and one that changes in response to geroprotective interventions and can track some of the biological hallmarks of aging, such as the promotion of cellular senescence by smoking, for instance^{8,9}. DL was instrumental in establishing Deep Aging Clocks (DAC) that generate estimates of an individual's biological age state based on data extracted from routine blood analyses (Fig. 1b)⁸. Using AI-powered tools such as DAC, clinicians

should be able to more precisely assess and monitor individual health risks and tailor appropriate interventions or changes in lifestyle for a specific person. We argue that DAC should become an essential part of the physician's tool kit, enabling AI-supported recommendations to promote long and healthy lives. Other DL-based solutions that outperform humans, such as radiological image analysis algorithms for early cancer or aneurysm detection as well as dermatological testing, can provide complementary benefits¹⁰. In this context, we define longevity medicine as a branch of precision medicine that is specifically focused on promoting healthspan and lifespan, and is powered by AI technology. AI-powered longevity medicine will facilitate the discovery of drug targets for specific individuals, the identification of tailored geroprotective interventions and aging and longevity biomarkers to enhance the study of aging and disease trajectories, and the identification of interventions that may help slow down or even reverse aging-associated biological, physiological or psychological processes¹¹. As recent advances in longevity biotechnology and AI are starting to percolate through clinical research and clinical practice, physicians will increasingly need to navigate through various AI technologies and applications, including those that may be relevant to the nascent field of longevity medicine¹².

Opportunities for longevity medicine in clinical care and the longevity industry

In order for longevity medicine to be formally seen as a branch of medicine, it needs to be practiced by physicians. Clinical practice requires clinical protocols and diagnostic and treatment guidelines with defined outcome measures, biomarkers and medications approved by national regulatory authorities, such as the Food and Drug Administration. However, to develop at least preliminary clinical recommendations for interventions in longevity medicine, aging needs to be monitored and treated as a medical condition, with designated studies performed to demonstrate both efficacy and safety of specific interventions. At present, there is a growing number of AI-based tools that give access to relevant health parameters, such as a patient's biological age, that utilize a variety of 'omics' data and present different dimensions of a patient's state of health and rate of aging to inform prognosis. In order for these tools to be adopted by clinicians and accepted by the medical community, they need to be integrated into the current framework of clinical practice, ranging from primary through to secondary prevention, treatment

and monitoring. Such integration requires the convergence of modern AI and medicine through a symbiotic collaboration between clinicians, geroscientists and AI researchers. Physicians should be encouraged and have the chance to be involved in AI-based longevity research. At the same time, AI-powered longevity biotechnology and AI-based biomarker-driven science should be promoted and seek close clinical and metaclinical collaborations. Doctors first need to have the access to tailored. validated and credible education on AI-based biogerontology sciences, such as accredited courses, that would further allow longevity physicians to build their networks and ultimately create a separate medical discipline. A basic knowledge of AI-driven geroscience is essential to bring relevant scientific discoveries to trials, and study outcomes to the clinic.

Beyond academia and regulatory authorities, industrial involvement will also be important. Like in the early days of the Internet when we witnessed the appearance of mobile technologies, instant messaging and social networks, we expect to see more venture-backed groups of expert enthusiasts starting businesses in this emerging area. These businesses will provide AI-based tools, such as DAC, to track aging, which will help build evidence-based knowledge from the data provided by and to clinicians, as well as from high-end clinics working with self-funded clientele interested in extending the period of healthy productive life.

As the field of longevity medicine develops, we must also take into consideration its potential impact on health equity. For all branches of medicine, there is a great ethical concern stemming from major inequities in health outcomes due to various factors, including socioeconomic status, geopolitical position and ethnicity. One could assume that access to longevity medicine solutions will only be available to wealthy individuals and thus deepen the health disparities. However, longevity medicine is partly equipped with a low cost and minimally-invasive arsenal, including wearable trackers and DAC, that should help address problems on a public health scale. Genetic testing already proved that a democratization of specialized precision medicine testing is possible. Similar developments are to be anticipated for other 'omics' and even imaging techniques. Nevertheless, it will be important to keep in mind the issue of health inequalities as the field of longevity medicine continues to grow.

Longevity research in academia and in the biotechnology industry should

also benefit from large pharmaceutical companies willing to employ tools for clinical trial enrollment and monitoring, and from life insurance companies interested in providing additional services to customers desiring large payouts at the end of their lives. Ultimately, such collaborations will also encourage the creation of industry groups or branches within regulatory agencies that will define and establish common clinical practice and industry standards as well as regulations required to guide the future of AI-based longevity medicine.

Conclusion

Given the rapid progression of AI-based experimental longevity medicine, it is now time to catalyse its translation to common clinical practice. This transition will bring new solutions to patients and healthy individuals. Longevity medicine is also an opportunity for multidisciplinary collaborative work of thus far often

distinctive players to transform public health into public healthy longevity.

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Author contributions

K.F.L. and A.Z. both contributed to the design and implementation of the research and to the writing of the manuscript. E.B. contributed to the rewriting and editing of the manuscript and supported the initial design.

Competing interests

K.F.L. is the founder of Sinovation Ventures, a commercial venture fund investing in AI with commercial interests in a broad range of AI companies and projects relating to longevity medicine. A.Z. is the founder and shareholder of Insilico Medicine, a drug discovery company with a focus on aging and age-related diseases, and Deep Longevity, a commercial company specializing in biomarker development and DACs. E.B. is an independent advisor to Insilico Medicine.