Biogerontology (2024) 25:739–743
https://doi.org/10.1007/s10522-024-10105-x

PERSPECTIVE

Geroscience: just another name or is there more to it?

Simon Okholm

Received: 22 February 2024 / Accepted: 16 April 2024 / Published online: 15 May 2024
© The Author(s), under exclusive licence to Springer Nature B.V. 2024

Abstract The widespread use of the name 'geroscience' in the science of aging is sometimes met with a wary attitude by biogerontologists other than its inventors. Here, we provide an overview of its origin and evolution to assess what exactly it is and to discuss its theoretical and biological relationship to earlier movements of anti-aging medicine and biogerontology more generally. Geroscience posits that targeting aging may offer a cost-effective approach to improve late-life health in humans, and because aging is malleable in model organisms and what regulates this is sufficiently understood, the time is ripe for moving forward to translational and clinical research. The geroscience agenda has rebranded imagery of past traditions, yet the claim that therapies for human aging are ready or within the imminent future is contestable and on brand with tradition, even if biogerontology has made great progress in the past decades.

Keywords Geroscience · Biogerontology · Anti-aging medicine · Treatment · Demarcation · Aging · Disease · Lifespan · Healthspan

S. Okholm (✉)
CNRS, ImmunoConcEpT, UMR 5164, University of Bordeaux, Bordeaux, France
e-mail: sokholm@immuconcept.org

Introduction

'Geroscience' has become name of attraction such that many research activities today are framed in terms of it: networks, interest groups, and a journal has been rebranded in its name (Newman et al. 2019; Sierra and Kohanski 2017; Sonntag and Ungvari 2016). There are "geroscience perspectives" on organs, diseases, and mortality (e.g., Promislow 2020). There is the "geroscience hypothesis" (e.g., Kritchevsky and Justice 2020) and "geroscience trials" (Rolland et al. 2023). There is "physiological" (Seals et al. 2016), "translational" (Gill 2019; Kaeberlein et al. 2016), and even "basic geroscience" (Martin 2017), just to name a few qualifiers to it.

With such a rapid growth in the past decade, biogerontologists other than its inventors sometimes display a wary, but open-minded skepticism to the geroscience concept (e.g., Le Bourg 2022). Call this *the wary view*. This is part of a broader tradition of biogerontologists calling attention to separate the hype from the promise of biogerontology, save the field's credibility from pseudoscience, and/or warning the public against the potential harms and commercialism of so-called anti-aging medicine (e.g., Olshansky et al. 2002; de Magalhães et al. 2017; Rattan 2020). This raises what we can call the demarcation question: Is there more to geroscience warranting its merit within biogerontology, or is it the most recent avatar of anti-aging medicine,

'life-extensionism' (Stambler 2020), or the likes of it that should be separated from biogerontology?

To begin addressing this complex issue, I first provide an overview of the origin and evolution of geroscience. Second, by drawing on several theoretical and biological points of comparison with earlier movement of anti-aging medicine and biogerontology more generally, I evaluate the demarcation issue.

The emergence of a name

'Geroscience' first appeared in writing in 2007 as a name for research consortium at the Buck Institute for Aging Research, funded by National Institute of Health's (NIH) *Roadmap Initiative for Medical Research* (see also Sierra 2016). This funding program was launched to promote interdisciplinary research, address the future's health challenges, and speed up the translation from bench to bedside (Zerhouni 2003). Geroscience, as we shall see, embodies all these aspects.

In 2012, the *Trans-NIH Geroscience Interest Group* (GISG) was formed (Sierra 2016; Sierra and Kohanski 2017). Its activities were largely promotional: raising awareness, organizing workshops and summits around "the new field" (Burch et al. 2014), and forming partnerships with many of NIH's daughter institutes, promoting that aging is a malleable risk factor for their disease of interest. Importantly, this promotional work led to a position paper that identified the *Pillars of Aging* (Kennedy et al. 2014), which was an American counterpart to the *Hallmarks of Aging* (López-Otín et al. 2013).

Shortly after, *the Geroscience Network*, a communication network of more than 100 biogerontologists and clinicians, was established to facilitate a workshop series known as the R24 retreats. This led to several consensus rapports identifying roadblocks in drug development (Burd et al. 2016), in preclinical models (Huffman et al. 2016), and in traditional clinical trials (Newman et al. 2016) for translating what they called the geroscience hypothesis—i.e., that targeting aging could delay or mitigate several late-life diseases simultaneously—into clinical application. Importantly, new research protocols for proof-of-concept in geroscience trials were also designed, most notably with the Target Aging with Metformin (TAME) trial (Barzilai et al. 2016). In brief, TAME is a clinical trial to determine if repurposing metformin for non-diabetic elderly can delay the time-to-event between acquiring the first and second late-life disease, taking the rate of multimorbidity as a proxy for aging's rate (Barzilai et al. 2016).

Several other network coalitions have formed since then: One is *the Translational Geroscience Network* (TGN) that facilitates small, early-phase, clinical trials with repurposed drugs to provide auxiliary data on targeting aging to alleviate single-disease endpoints (Justice et al. 2020). Many senolytic trials currently underway (see Chaib et al. 2022) come from the TGN. Another, more recent coalition is *the Geroscience Education and Training Network* that creates curricular material, training programs, and credentialing geroscience to streamline the carrier paths for future "translational geroscientists" (Newman et al. 2019).

What's in a name?

Geroscience promotes awareness, facilitates trials, and recruiters for its research agenda all in one, but what is it, exactly? The geroscience agenda posits that targeting aging may offer a more cost-effective approach to improve late-life health in humans rather than treating each late-life disease directly, individually, and consecutively. This is because aging and its diseases are malleable in model organisms, and the mechanisms regulating this is sufficiently understood, as mapped out by the pillars/hallmarks of aging. As such, it posits that the time is ripe for translational and clinical application as part of preventive medicine.

Is geroscience part of anti-aging medicine or biogerontology?

In 2000, 'biogerontology' was coined as the "study of the biological basis for aging" (Rattan 2000). A similar case was made for a maturing science, ready to take the next step from a basic science—preoccupied with discovery, collecting data, and theory-generation—towards an applied science that would harness this basic knowledge to develop interventions for improving late-life health in humans.

Around the same time, the anti-aging movement was burgeoning, claiming that it now (or in the

foreseeable future) would be possible to target the aging process to stop, slow or reverse/rejuvenate its effects (see Mykytyn 2006 for details). In response to this, many prominent figures in the biogerontological community warned against the movement's hype, pseudoscience, harms (to the fields credibility and to individuals) and commercialism: No treatment had demonstrated to influence the rate of aging. In short, there was "no truth fountain of youth" (Olshansky et al. 2002).

The anti-aging movement of the past was promoted by a few researchers in the biogerontological community, mostly without a strong institutional grounding. By contrast, geroscience rose not only from within the quarters of the National Institute of Aging by well-respected biogerontologists, but also managed to gain substantial institutional recognition from several other branches at the National Institute of Health (i.e., the trans-NIH interest group) (Sierra and Kohanski 2017).

Moreover, geroscience takes aging to be the most important risk factor for poor late-life health, premature death, and healthcare expenditures. In contrast, several advocates of the past anti-aging movement claimed that aging needed to be recognized as a disease, ultimately in an effort to legitimize and foster research for its cure. Put differently, geroscience has apparently found a way to medicalize aging, that is reframing it as target for therapy, without pathologizing it (see Sholl 2017 for details).

The expectations for anti-aging medicine of the past were high and imaginative: Creating perpetual youth, radical life extension, and so forth. Geroscience, by contrast, modestly aims to extend healthspan, that is to improve the gap between life expectancy and the proportion of time free from debilitating late-life diseases.

For geroscientists, the last two or three decades of research in biogerontology have had a profound impact: Not only did it lead to the identification of the underlying mechanisms of aging (i.e., the hallmarks/pillars), but also demonstrating that these processes could be slowed down, at least in short-lived animal models. Seemingly, we now have the means to influence the rate of aging, contrary to previous claims. Work in caloric restriction (Masoro 2005), in genetics of aging particularly in *C. elegans* (Kenyon 2010), and in drug discovery (notably with the effects of rapamycin and senolytics in mice (Harrison et al. 2009; Baker et al. 2011)) among many other areas, together suggested that certain mechanisms exerted influence on the onset, rate, and effects of aging that were potential targets for what they now call 'geroprotection'.

It is fair to say that geroscience has cleaned up its act, but is it part of mainstream biogerontology? I believe there are two sets of reasons to resist this conclusion. The first set broadly concerns theoretical and ethical issues, and the second pertains to challenges from the biology of aging.

Concerning the theoretical reasons: First, although geroscience has explicitly refrained from considering aging as a disease, it still relies on subverting the field's traditional distinction between normal aging and late-life diseases (Blumenthal 2003; Gems 2015; Rattan 2014), thus begging the question. Second, and relatedly, the idea of extending healthspan is not without its own problems of operationalization (Kaeberlein 2018). Third, the TAME trial was designed "in consultation with the *FDA*…" (i.e., *Food and Drug Administration*) to find a solution for how and when to approve 'aging' for drug discovery and development (Kulkarni et al. 2022). Here, there is a potential ethical concern for a conflict of interest in terms of geroscientists having a lobbying influence over regulatory bodies' decision-making as to whether aging should be an indication of treatment, obviously with profound implications for the pharmaceutical industry.

Moving to the challenges pertaining to the biology of aging. First, the hallmarks/pillars approach to identify the proximate causes has been criticized for not providing an explanatory nor an evolutionary framework for understanding aging (Gems and de Magalhães 2021). Second, caloric restriction, one of the long-hailed geroprotective treatments, showed to have little effect on the lifespan of rhesus monkeys (Mattison et al. 2012), calling question to its effects in "equilibrium species" like humans with different life history features than the short-lived "opportunistic species", like mice (Demetrius 2005; Le Bourg 2016). Third, the genetic work on *C. elegans* has recently come under scrutiny as its remarkable plasticity may to some degree be a function of suppressing reproductive death, much like the pacific salmon (Kern et al. 2023), complicating yet another foundation of geroscience. Finally, our understanding of what senolytic treatments actually target, i.e.,

so-called 'senescent cells', and why they emerge, is still an open-ended question (Kowald et al. 2020; Gems and Kern 2020).

As shown in a recent editorial in *Biogerontology*, the field is still riddled with knowledge gaps pertaining to evolution, the biological limits of survival, and the heterogeneity of the aging phenotype, each with caveats for the science of aging continuous attempt to develop effective therapies for aging (Rattan 2024).

Conclusion

Geroscience is a research agenda claiming that aging is malleable in model organisms, that what regulates this is sufficiently understood as mapped out by the pillars and hallmarks of aging, and that the time is ripe for translational research to target aging and improve late-life health in humans. Geroscience may have successfully rebranded itself by changing terminology (e.g., 'gerotherapeutics' instead of 'anti-aging treatments'), adjusting its goals ('improving healthspan' instead of 'perpetual youth') among other things. The last decades of biogerontological research has made great strides towards developing promising treatments for improving human health, yet the claim of geroscience that such treatments are ready now or soon is on brand with past tradition.

Declarations

Competing interests The author declares no competing interests.

References

Baker DJ, Wijshake T, Tchkonia T, LeBrasseur N, Childs BG, van de Sluis B, Kirkland JL, van Deursen J (2011) Clearance of p16Ink4a-positive senescent cells delays ageing-associated disorders. Nature 479:232–236. https://doi.org/10.1038/nature10600

Barzilai N, Crandall JP, Kritchevsky SB, Espeland MA (2016) Metformin as a tool to target aging. Cell Metab 23:1060–1065. https://doi.org/10.1016/j.cmet.2016.05.011

Blumenthal TH (2003) The aging-disease dichotomy: true or false? J Gerontol A 58:138–145. https://doi.org/10.1093/gerona/58.2.M138

Burch JB, Augustine AD, Frieden LA, Hadley E, Howcroft KT, Ron J, Khalsa PS, Kohanski RA, Li XL, Macchiarini F, Niederehe G, Oh YS, Pawlyk AC, Rodriguez H, Rowland JH, Shen GL, Sierra F, Wise BC (2014) Advances in geroscience: impact on healthspan and chronic disease. J Gerontol A 69:S1–S3. https://doi.org/10.1093/gerona/glu041

Burd CE, Gill MS, Niedernhofer LJ, Robbins PD, Austad SN, Barzilai N, Kirkland JL (2016) Barriers to the preclinical development of therapeutics that target aging mechanisms. J Gerontol A 71:1388–1394. https://doi.org/10.1093/gerona/glw112

Chaib S, Tchkonia T, Kirkland JL (2022) Cellular senescence and senolytics: the path to the clinic. Nat Med 28:1556–1568. https://doi.org/10.1038/s41591-022-01923-y

de Magalhães JP, Stevens M, Thornton D (2017) The business of anti-aging science. Trends Biotechnol 35:1062–1073. https://doi.org/10.1016/j.tibtech.2017.07.004

Demetrius L (2005) Of mice and men. When it comes to studying ageing and the means to slow it down, mice are not just small humans. EMBO Rep 6:S39–S44. https://doi.org/10.1038/sj.embor.7400422

Gems D (2015) The aging-disease false dichotomy: understanding senescence as pathology. Front Genet. https://doi.org/10.3389/fgene.2015.00212

Gems D, de Magalhães JP (2021) The hoverfly and the wasp: a critique of the hallmarks of aging as a paradigm. Ageing Res Rev 70:101407. https://doi.org/10.1016/j.arr.2021.101407

Gems D, Kern CC (2020) Is "cellular senescence" a misnomer? Geroscience 44:2461–2469. https://doi.org/10.1007/s11357-022-00652-x

Gill TM (2019) Translational geroscience: challenges and opportunities for geriatric medicine. J Am Geriatr Soc 67:1779–1781. https://doi.org/10.1111/jgs.16056

Harrison DE, Strong R, Sharp ZD, Nelson JF, Astle CM, Flukey K, Wilkinson JE, Frenkel K, Carter CS, Pahor M, Javors MA, Fernandez E, Miller RA (2009) Rapamycin fed late in life extends lifespan in genetically heterogeneous mice. Nature 460:392–395. https://doi.org/10.1038/nature08221

Huffman DM, Justice JN, Stout MB, Kirkland JL, Barzilai N, Austad SN (2016) Evaluating health span in preclinical models of aging and disease: guidelines, challenges, and opportunities for geroscience. J Gerontol A 71:1395–1406. https://doi.org/10.1093/gerona/glw106

Justice J, Kritchevsky S, Kuchel G, Kirkland J (2020) The translational geroscience network: supporting a new paradigm to alleviate age-related chronic disease. Innov Aging 4:831–831. https://doi.org/10.1093/geroni/igaa057.3042

Kaeberlein M (2018) How healthy is the healthspan concept? Geroscience 40:361–364. https://doi.org/10.1007/s11357-018-0036-9

Kaeberlein M, Creevy KE, Promislow DEL (2016) The dog aging project: translational geroscience in companion animals. Mamm Genome 27:279–288. https://doi.org/10.1007/s00335-016-9638-7

Kennedy BK, Berger SL, Brunet A, Campisi J, Cuervo AM, Epel ES, Franceschi C, Lithgow GJ, Morimoto RI, Pessin JE, Rando TA, Richardson A, Schadt EE, Wyss-Coray T, Sierra F (2014) Geroscience: linking aging to chronic disease. Cell 159:709–713. https://doi.org/10.1016/j.cell.2014.10.039

Kenyon CJ (2010) The genetics of ageing. Nature 464:504–512. https://doi.org/10.1038/nature08980

Kern C, Srivastava S, Ezcurra M, Hsiung KC, Hui N, Townsend J, Maczik D, Zhang B, Tse V, Konstantellos V, Bähler J, Gems D (2023) *C. elegans* ageing is accelerated by a self-destructive reproductive programme. Nat Commun 14:4381. https://doi.org/10.1038/s41467-023-40088-1

Kowald A, Passos JF, Kirkwood TBL (2020) On the evolution of cellular senescence. Aging Cell 19:e13270. https://doi.org/10.1111/acel.13270

Kritchevsky SB, Justice JN (2020) Testing the geroscience hypothesis: early days. J Gerontol A 75:99–101. https://doi.org/10.1093/gerona/glz267

Kulkarni AS, Aleksic S, Berger DM, Sierra F, Kuchel GA, Barzilai N (2022) Geroscience-guided repurposing of FDA-approved drugs to target aging: a proposed process and prioritization. Aging Cell. https://doi.org/10.1111/acel.13596

Le Bourg E (2016) The somatotropic axis may not modulate ageing and longevity in humans. Biogerontology 14:421–429. https://doi.org/10.1007/s10522-015-9632-6

Le Bourg E (2022) Geroscience: the need to address some issues. Biogerontology 23:145–150. https://doi.org/10.1007/s10522-022-09951-4

López-Otín C, Blasco MA, Partridge L, Serrano M, Kroemer G (2013) The hallmarks of aging. Cell 153:1194–1217. https://doi.org/10.1016/j.cell.2013.05.039

Martin GM (2017) Geroscience: addressing the mismatch between its exciting research opportunities, its economic imperative and its current funding crisis. Exp Gerontol 94:46–51. https://doi.org/10.1016/j.exger.2016.11.008

Masoro EJ (2005) Overview of caloric restriction and ageing. Mech Ageing Dev 126:913–922. https://doi.org/10.1016/j.mad.2005.03.012

Mattison JA, Roth GS, Beasley TM, Tilmont EM, Handy AM, Herbert RL, Longo DL, Allison DB, Young JE, Bryant M, Barnard D, Ward WF, Qi W, Ingram DK, de Cabo R (2012) Impact of caloric restriction on health and survival in rhesus monkeys from the NIA study. Nature 489:318–321. https://doi.org/10.1038/nature11432

Mykytyn CE (2006) Contentious terminology and complicated cartography of anti-aging medicine. Biogerontology 7:279–285. https://doi.org/10.1007/s10522-006-9016-z

Newman JC, Milman S, Hashmi SK, Austad SN, Kirkland JL, Halter JB, Barzilai N (2016) Strategies and challenges in clinical trials targeting human aging. J Gerontol A 71:1424–1423. https://doi.org/10.1093/gerona/glw149

Newman JC, Sokoloski JL, Robbins PD, Niedernhofer LJ, Reed MJ, Wei J, Austad SN, Barzilai N, Cohen HJ, Kuchel GA, Kirkland JL, Pignolo RJ (2019) Creating the next generation of translational geroscientists. J Am Geriatr Soc 67:1934–1939. https://doi.org/10.1111/jgs.16055

Olshansky SJ, Hayflick L, Carnes BA (2002) Position statement on human aging. J Gerontol A 56:B292-297. https://doi.org/10.1093/gerona/57.8.B292

Promislow DEL (2020) A geroscience perspective on COVID-19 mortality. J Gerontol A 75:e30–e33. https://doi.org/10.1093/gerona/glaa094

Rattan SIS (2000) Biogerontology: the next step. Ann N Y Acad Sci 908:282–290. https://doi.org/10.1111/j.1749-6632.2000.tb06655.x

Rattan SIS (2014) Aging is not a disease: implications for intervention. Aging Dis 5:196–202. https://doi.org/10.14336/AD.2014.0500196

Rattan SIS (2020) Naive extrapolations, overhyped claims and empty promises in ageing research and interventions need avoidance. Biogerontology 21:415–421. https://doi.org/10.1007/s10522-019-09851-0

Rattan SIS (2024) Seven knowledge gaps in modern biogerontology. Biogerontology 25:1–8. https://doi.org/10.1007/s10522-023-10089-0

Rolland Y, Sierra F, Luigi F, Barzilai N, De Cabo R, Mannick J, Oliva A, Evans W, Angioni D, De Souto BP, Raffin J, Vellas B, Kirkland JL, the G.C.T-TF group (2023) Challenges in developing geroscience trials. Nat Commun 14:5038. https://doi.org/10.1038/s41467-023-39786-7

Seals DR, Justice JN, LaRocca TJ (2016) Physiological geroscience: targeting function to increase healthspan and achieve optimal longevity: translational physiology of ageing. J Physiol 594:2001–2024. https://doi.org/10.1113/jphysiol.2014.282665

Sierra F (2016) The emergence of geroscience as an interdisciplinary approach to the enhancement of health span and life span. Cold Spring Harb Perspect Med 6:a025163. https://doi.org/10.1101/cshperspect.a025163

Sierra F, Kohanski R (2017) Geroscience and the trans-NIH Geroscience Interest Group, GSIG. GeroScience 39:1–5. https://doi.org/10.1007/s11357-016-9954-6

Sholl J (2017) The muddle of medicalization: pathologizing or medicalizing? Theor Med Bioeth 38:265–278. https://doi.org/10.1007/s11017-017-9414-z

Sonntag WE, Ungvari Z (2016) GeroScience: understanding the interaction of processes of aging and chronic diseases. Age 38:377–378. https://doi.org/10.1007/s11357-016-9953-7

Stambler I (2020) History of life-extensionism. In: Rattan SIS, Barbagallo M, Le Bourg E (eds) Encyclopedia of biomedical gerontology, vol 2. Academic Press, London, pp 228–237

Zerhouni E (2003) The NIH roadmap. Science 302:63–72. https://doi.org/10.1126/science.1091867

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Springer Nature or its licensor (e.g. a society or other partner) holds exclusive rights to this article under a publishing agreement with the author(s) or other rightsholder(s); author self-archiving of the accepted manuscript version of this article is solely governed by the terms of such publishing agreement and applicable law.