Lack of consensus on an aging biology paradigm

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Abstract

At a recent symposium on the biology of aging, a debate was held as to whether or not we know what aging is. Many/most of the participants were struck not only by the lack of consensus on this core question, but also on many basic tenets of the field, and on how to ask the key questions. Together, we felt it was important to write up a summary of these cordial but important disagreements to demonstrate the work the field has before it in order to generate a clear paradigm. Accordingly, we undertook a systematic survey of participants on a number of points that were raised during the debate and symposium, and here present a summary of the conclusions. We use this to identify major directions, empirical or philosophical, that might help move the field toward a consensus paradigm. [1-2 more sentences to be added after we see survey results].

Introduction

The authors were all participants at the *Biology of Aging Symposium: Understanding Aging to Better Intervene*, held November 9-11, 2019 in Montreal, Quebec. The symposium featured 44 speakers with a diversity of expertise related to aging, including basic aging biology, translational geroscience, geriatric medicine, nutrition, immunosenescence, ecology/evolution, demography, statistics, systems biology, aging epidemiology, and complex systems theory. During the course of the symposium, a debate was held on the question, "Do we know what aging is?" with BHK ostensibly arguing the "pro" side and AAC ostensibly arguing the "con" side. There was extensive audience participation. Most participants agreed that the debate was striking in how it highlighted the lack of a clear consensus paradigm in the field, and collectively we agreed it would be important to describe this for our colleagues.

Accordingly, we designed a survey that we sent to participants of the symposium, both invited speakers and students/other participants. The survey was meant to capture the opinions on the key points of disagreement during the debate and the meeting more generally. All participants who responded to the survey are co-authors.

Methods

Survey

We used the tool SurveyMonkey to distribute a survey to the 44 invited speakers, XX students, and YY other participants at the symposium. The survey collected the following information: (1) name; (2) demographic data (sex, country of origin, career stage, domains of expertise); (3) Likert-scale and other limited response questions (see below); and (4) a single open-ended question, "In no more than two sentences or 100 words, please describe your understanding of what aging is, or is not, at a mechanistic level."

The Likert scale used was, "For each of the following statements, do you (1) Strongly disagree; (2) Moderately disagree; (3) Slightly disagree; (4) Neutral; (5) Slightly agree; (6) Moderately agree; or (7) Strongly agree?" The statements were:

- We have a relatively good understanding of the basic biological mechanisms of aging.
- Some combination of the nine hallmarks (Lopez-Otin et al. 2013) or the seven pillars (Kennedy et al. 2014) does a relatively comprehensive job of describing the mechanisms of aging.
- It is or will soon be possible to have relatively reliable metrics of the overall aging process
- Aging cannot and should not be measured by a single metric because it is multi-dimensional

- It should be possible to quantify aging well even in the absence of a clear consensus or mechanistic understanding of what aging is.
- It should be possible to intervene in aging, and evaluate interventions, even in the absence of a clear consensus or mechanistic understanding of what aging is.
- There are many species across the tree of life that do not age at a rate that is biologically relevant or appreciable
- Broadly speaking, aging mechanisms are similar in most species
- Mortality rates or survival curves are generally a reasonable proxy for aging at the organismal level
- It is important for the field to have a consensus definition of aging
- Aging is an undesirable process that should be treated, cured, or minimized

Additional questions:

- Does aging begin approximately at (1) conception; (2) birth; (3) sexual maturity; or (4) later in life?
- What percent of what we observe as aging do you think can be attributed to the following types of mechanisms (understanding that they may coexist and interact with each other): [100 points that should be distributed among the five options below]
  - Damage accumulation (DNA damage, protein aggregates, structural damage, etc.)
  - Maladaptation/antagonistic pleiotropy: mechanisms that are useful early in life (e.g. for cancer prevention) become harmful later in life.
  - Adaptation: Adjustments the organism makes to either pathological aspects of aging or to changing needs (e.g. immune repertoire) at different ages.
  - Homeostatic dysregulation: breakdown in the capacity of complex regulatory networks to maintain homeostasis
  - Other

References