

**National Institute on Aging (NIA)
National Advisory Council on Aging (NACA)
Review of the Division of Aging Biology (DAB)**

2022 DAB Review Committee Report

Rev. 4/16/2022

Review Committee Members

**current NIA Council Member at start of Review*

***former NIA Council Member*

- *Clifford Rosen, MD, Tufts University School of Medicine (Chair)
- *Margaret Goodell, PhD, Baylor College of Medicine (Co-Chair)
- *James Appleby, BSPHarm, MPH, ScD, Gerontological Society of America
- *Shalender Bhasin, MD, Harvard University
- Namandje Bumpus, PhD, Johns Hopkins Medicine
- Lynne S. Cox, PhD, University of Oxford
- Kate Creevy, DVM, MS, DACVIM, Texas A&M University
- Vishwa Deep Dixit, DVM, PhD, Yale University
- *Monica Driscoll, PhD, Rutgers University
- Stephen L. Helfand, MD, Brown University
- Carl V. Hill, PhD, MPH, Alzheimer's Association
- **Sundeep Khosla, MD, Mayo Clinic
- George A. Kuchel, MD CM, AGSF, University of Connecticut
- Laura Niedernhofer, MD, PhD, University of Minnesota
- Charlotte Peterson, PhD, University of Kentucky
- Carol Shively, PhD, Wake Forest University
- *Amy Wagers, PhD, Harvard University

Rose Maria Li, MBA, PhD, Review Administrator

Acronym Definitions

AGS	American Geriatrics Society
APB	Aging Physiology Branch
BRB	Biological Resources Branch
CALERIE	Comprehensive Assessment of Long-Term Effects of Reducing Intake of Energy Study
CITP	<i>Caenorhabditis</i> Intervention Testing Program
DAB	Division of Aging Biology
DBSR	Division of Behavioral and Social Research
DDO	Division Director's Office
DGCG	Division of Geriatrics and Clinical Gerontology
DN	Division of Neuroscience
GCBB	Genetics and Cell Biology Branch
GSIG	Geroscience Interest Group
ICs	Institutes and Centers
ITP	Interventions Testing Program
MSI	Minority Serving Institution
NACA	National Advisory Council on Aging
NHP	Nonhuman Primates
NIA	National Institute on Aging
NIDDK	National Institute of Diabetes and Digestive and Kidney Diseases
NIH	National Institutes of Health
NIMHD	National Institute on Minority Health and Health Disparities
NSC	Nathan Shock Center
RFA	Request for Applications
SDOH	Social Determinants of Health

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I. Executive Summary

The National Advisory Council on Aging (NACA) is tasked with the periodic review of each extramural Division within the National Institute on Aging (NIA) to assess whether the Division's past performance and future trajectory of supported research and training programs are appropriate for the scientific advancement of the field in the coming decade. The review is designed to assist the Division in planning and self-evaluation through expert advice and insights from the Review Committee.

The 2021-2022 NACA Division of Aging Biology (DAB) Review Committee, co-chaired by Drs. Clifford Rosen and Margaret Goodell, was charged with assessing the current state of DAB and with making recommendations about areas that merit greater emphasis in coming years. The Review Committee sought to provide a high-level perspective on DAB activities and avoid overly prescriptive guidance about processes and policies that are understood to be beyond DAB's purview. The prior review of DAB was completed in 2015.

NACA offers high praise for DAB's leadership and program officers for their knowledge, responsiveness, and accessibility to the scientific community. Additionally, the Committee appreciates Dr. Ronald Kohanski's perspectives and open-minded leadership as conducive to collaboration within NIA and the National Institutes of Health (NIH), as well as outreach to the external research community.

Recommendations

As the top priority, DAB should enable and fund the best science. The Committee identified six priority areas for the Division to address in the next five years, which are outlined below and more fully explicated in Section IV of this report. It recommends that DAB establish guidelines for prioritizing scientific directions going forward to help determine appropriate metrics of success and sunseting of prior scientific priorities as appropriate. A challenge is to balance priorities by determining which current topics most merit requests for set-aside funding and staff time, and which new topics should be introduced to the DAB portfolio as deserving greater attention. The six priority areas are:

1. Scientific Directions

- A. Hallmarks of Aging: Determine how to integrate the hallmarks of aging into a larger conceptual model of aging biology, assess whether the current hallmarks of aging should be updated, and further explore the interactions between individual hallmarks and relevant biomarkers.
- B. Cell Biology:
 - (1) Continue work on the common mechanisms of aging including senescence, sirtuin-NAD, mTOR, and other pathways. This should also include intercellular and interorgan communication, and the incorporation of disease models for senescent cell mapping.
 - (2) Support the discovery, optimization, validation, and standardization of relevant biomarkers of aging biology and generate consensus on the appropriate biomarkers based on their utility for geroscience translational research.
 - (3) Strengthen current support for bioinformatics, medical informatics, and other computational resources.

C. Integrative Physiology:

- (1) Broaden the Division's approach to systems biology.
- (2) Support work that increases the field's understanding of heterogeneity in rates of aging, including the role of circadian biology, the exposome, and lifestyle factors.
- (3) Expand the Division's emphasis on microbiomes across multiple organ systems.
- (4) Increase support toward research examining stem cell aging and resilience.

D. Impact of Early to Midlife Stressors on Later Life Health: Support studies that consider the whole life experience when examining healthy aging outcomes. Include identification of suitable laboratory and animal models for studying the strength of associations between stressors and the hallmarks of aging.

2. Biological and Data Resources

- A. Develop Metrics of Success for Resource Sharing Initiatives: Provide metrics on the effective use of the valuable animal models and biospecimens provided by DAB and evaluate whether strategies for their provision can be further optimized to accelerate research.
- B. Emerging Technologies: Integrate emerging technologies into BRB's animal model efforts and APB's systems biology approaches.
- C. Accessibility and Consistency in Methods and Models: Support efforts to standardize lab methods, assays for aging biomarkers, and models, and promote/advertise and increase accessibility to DAB resources.
- D. Data Accessibility and Curation: Determine criteria for prioritizing datasets for access and retention and establish a long-term plan to improve and sustain data accessibility and preservation.

3. Human Subjects and Health Disparities Research

Amplify DAB's unique role to bring a basic biology of aging perspective to trans-NIA and trans-NIH efforts in human subject research. Areas to emphasize are (1) identifying and addressing the impact of health disparities on biology of aging and (2) promoting biomarker discovery in broadly diverse populations.

4. Training, Education, and Outreach Programs

Leverage training and education efforts to promote DAB's unique identity and vision, particularly for geroscience and health disparities research, engage Minority Serving Institutions (MSIs) in DAB initiatives to promote the field's ability to recruit diverse new or early career researchers, and foster interdisciplinary collaborations to engage with investigators from adjacent fields.

5. Common Fund and Collaborative Activities

Provide clear guidance on how cross-cutting topics, such as emerging technologies, health disparities, hallmarks of aging, biomarkers, and geroscience, can be balanced across all three branches. Continue to leverage and expand the unique value that DAB brings to collaborative partnerships with other NIA Divisions, NIH Institutes and Centers (ICs), and international partners.

6. Staffing

Continue current plans to restructure DAB portfolios and hire staff to reduce the average and maximum number of grants/contracts per program officer, manage collaborative activities, assure the continuity of contracts for biological resources, and consider succession planning. Strongly consider adding new program officers who have additional expertise in multi-omics, modeling and bioinformatics, the peripheral nervous system, integrative and comparative physiology, data science, and clinical research (including those who can support studies that are preliminary and ancillary to clinical trials).

II. The 2021-2022 DAB Review Process

The 2022 DAB Review Committee received background material throughout the review process to assist in its deliberations, including copies of the 2015 review report, memoranda prepared by DAB program staff (e.g., future directions and responses to Committee questions), informational videos about DAB funding, and summaries of key findings from meeting discussions prepared by Rose Li and Associates, Inc. (RLA).

The Committee participated in multiple email exchanges and videoconference calls beginning in early June 2021 to complete this report. A list of materials provided to reviewers is listed in **Appendix 1**. Time was set aside for closed sessions involving only the Reviewers and RLA staff during video calls held on July 28, November 30, and January 24. Each call began with consideration of potential conflicts of interest and procedure for remediation (recusal and temporary placement in a virtual waiting room until discussion on the relevant topic conflict was concluded).¹ One or both Review Committee Co-Chairs attended each call to explain and manage this policy.

Reviewers attended a kick-off videoconference on June 2 or 8 to learn the review purpose, process, and expectations. In advance of the first progress videoconference call held on July 28, reviewers received background materials (June 30) and DAB-authored memos about proposed future directions (July 21). RLA shared all materials by email and through a secure DAB Review Committee website. The July 28 call covered DAB's primary areas of focus (e.g., hallmarks and heterogeneity of aging) and the priorities of each branch and the Division Director's Office (DDO). The call also afforded reviewers the opportunity to request additional materials from DAB to better inform their deliberations.

Committee members were assigned to subcommittees, as follows:

Subcommittee	Date	Chair	Members
Geroscience	8/24	Amy Wagers	Lynne S. Cox, George A. Kuchel, Margaret Goodell
BRB	8/25	Clifford Rosen	Kate Creevy, Monica Driscoll, Carol Shively
APB	9/9	Shalender Bhasin	Vishwa Deep Dixit, Sundeep Khosla, Charlotte Peterson
GCSB	9/30	Margaret Goodell	Monica Driscoll, Stephen L. Helfand, Laura Niedernhofer
DDO	10/8	James Appleby	Namandje Bumpus, Carl V. Hill, Clifford Rosen

¹ Dr. Driscoll recused herself during discussion of the Intervention Testing Program (ITP) and *Caenorhabditis* Intervention Testing Program (CITP) because she is one of the three Principal Investigators of the CITP. Dr. Wagers disclosed sponsored research from Sarepta Therapeutics and Elevian and consulting work with Frequency Therapeutics and Kate Therapeutics. Dr. Niedernhofer disclosed consulting work over the past two years for Merck Sharp and Dohme and ONO Pharmaceuticals, expected research support from Pfizer, and inactive service (with equity) on the scientific advisory board of Innate Biologics.

All Committee members were welcome to attend any and all subcommittee calls, which were held between late August and early October 2021.² Each subcommittee chair was involved in determining the call agenda, which included discussion about areas of accomplishment and opportunity. RLA delivered final versions of all subcommittee summaries to reviewers on November 8, after incorporating clarifications or corrections from DAB staff about the background material presented and suggested edits from reviewers about findings. These summaries were used to help inform the Committee's discussion of scientific priorities, which was the primary focus of the second progress videoconference held on November 30.

Between the subcommittee calls and the November 30 progress videoconference, the Co-Chairs met with the NIA Director and each of the three NIA extramural Division Directors to discuss interactions and collaborations between DAB and the other NIA Divisions. Highlights from these calls were shared with the Committee on the November 30 call. Themes and ideas from the November 30 call were synthesized into an early draft of this report, which included an initial set of emerging recommendations. This draft was provided to the Committee for comments and deliberation at the full Committee videoconference on January 24, which was primarily focused on prioritizing recommendations and contributing additional supporting information to the report draft. On January 25, Dr. Rosen presented a brief status update about the DAB Review to the NIA Council Working Group on Program.

The third progress videoconference held on March 8 provided the Committee an opportunity to react to an updated draft of the report that incorporated discussion from the January 24 meeting and other feedback received from reviewers via email. A penultimate version of the Report was shared on March 28 to ensure that all Committee members concurred with the Report's final recommendations, and to consider any final edit requests. The Committee members unanimously concurred with the recommendations in the Report, which will be presented by the Co-Chairs at the May 2022 NIA Council Meeting.

III. DAB Background & Accomplishments

DAB supports basic, applied, and translational research on the biology of aging, and its priorities include research on (1) mechanisms of aging, (2) hallmarks and biomarkers of aging, (3) rates of aging (including lifespan and health span), and (4) methods to alter rates of aging to improve health at older ages. These priorities are independent of which organisms are subjects of research. DAB's portfolios cover the full gamut, from humans to yeast. The objective of DAB-funded research is to elucidate the basic molecular, cellular, genetic, and physiological mechanisms underlying normal aging and age-related diseases and geriatric syndromes. This research includes investigations of the gradual or programmed alterations of structure and function that characterize normal aging. These investigations include exploring how these changes become risk factors for or accompany age-related conditions and disease states and incorporate research in different communities (e.g., human subjects research including grants on health disparities, minority health, and women's health).

DAB has a diverse portfolio that is managed by DDO and three branches: Aging Physiology (APB), Genetics and Cell Biology (GCBB), and Biological Resources (BRB). The APB supports research on the fundamental mechanisms of aging and integrative physiology. The GCBB supports research on genetic, cell biological, and metabolic changes that affect length and/or quality of life, and shares oversight of the *Caenorhabditis* Intervention Testing Program (CITP) with BRB. BRB manages biological resources to support aging research, and the Division's

² Summaries of the subcommittee calls include a list of attendees. Dr. Rosen attended all five subcommittee calls. In addition to her assigned GCBB subcommittee call, Dr. Niedernhofer attended the Geroscience, BRB, and APB subcommittee calls.

murine Interventions Testing Program (ITP), Animal Models Program, and Dog Aging Project. DDO houses the Division's geroscience work, although this topic permeates all branches. In addition to the specific areas of interest mentioned, DAB also supports interdisciplinary research and integrated studies on the mechanisms that affect aging at the organism scale, including systems biology. DAB also participates in NIA working groups, NIH Institute-and-Center joint activities, and NIH Common Fund and Special Programs in the Office of the Director and initiated and leads the NIH-wide Geroscience Interest Group (GSIG).

The NIA budget increased 350% (from \$1.1 billion to \$3.9 billion) since the last review of DAB in 2015. Most of this funding is directed toward Alzheimer's disease research, which has impacted all four extramural scientific Divisions at NIA. In FY2020, DAB awarded \$229 million (direct costs) through 723 grants across all mechanisms, of which about \$45 million was for research involving human subjects. The number (value) of new grants awarded by DAB each year has grown from around 130 (\$24 million; \$28.7 million in 2020 dollars) in 2013 to around 225 (\$62.3 million) in 2020. DAB also spends approximately \$10 million each year on contracts to develop and maintain animal colonies, tissue banks, and databases, as well as for the selection, production, characterization, and distribution of cultured cells for research on aging.

1. Division Director's Office (DDO)

Dr. Kohanski was named the DAB's Director in February 2021 after serving as Deputy Director for 13 years and as Acting Director beginning June 2020 with the departure of Dr. Felipe Sierra, DAB's former Director of 14 years. DAB's emphasis on research in geroscience and the hallmarks of aging, established under Dr. Sierra's leadership, continues under Dr. Kohanski.

Notably, Dr. Kohanski has demonstrated a long-standing commitment to understanding health disparities and has reinforced this commitment with the hiring in 2021 of Dr. Stacy Carrington-Lawrence as Deputy Director. She previously served as a Senior Scientific Advisor in the Office of AIDS Research. Dr. Carrington-Lawrence will increase DAB's contributions to research on health disparities and oversee new and ongoing research involving human subjects in the DAB portfolio.

DDO oversees the three DAB branches, as well as DAB's training programs, Nathan Shock Centers (NSCs), small business grants, and administrative and diversity supplements. DDO represents DAB to NIA leadership on policy and funding decisions and maintains two portfolios: Geroscience (overseen by Dr. Kohanski) and Health Disparities (managed by Dr. Carrington-Lawrence). DDO also actively encourages collaborations across multiple aspects of aging research through the NIA scientific retreats, monthly meetings of the NIA Division Directors, and multiple discussions of potential requests for applications (RFAs) and initiatives through the Common Fund and with other NIH ICs.

DAB plans to consolidate its training programs, NSCs, and small business grants into one portfolio. For administrative purposes, the new program officer being hired to cover training programs will be the DAB liaison to the NIA Division of Extramural Activities that oversees extramural training programs. The DDO has worked to expand the NSCs and DAB staff while stabilizing discretionary funds. This work has coincided with an increase in the number of investigators assisted through DAB and NIA discretionary funds and the promotion of high-risk/high-impact research studies.

DAB is commended for providing structure around the concepts of "geroscience" and "hallmarks of aging." DDO's focus on health disparities and promotion of diversity within the field is a welcome development. DAB can offer a unique biological perspective to trans-NIA/NIH efforts that focus on the social determinants of health (SDOH). DAB successfully collaborates with other NIA divisions and NIH ICs, and actively participates in NIH Common Fund programs.

Dr. Kohanski leads in a thoughtful and deliberate way. He sets a collegial tone that encourages interactions across branches within DAB, and across Divisions and ICs. His support for rigorous health disparities research within and outside his division, his vision for expanding and broadening the geroscience field, and his commitment to supporting liaisons across branches, divisions, and multi-stakeholder work groups, should be empowering and impactful over the next five to 10 years.

Geroscience

Geroscience is the integrated study of both the biology of aging and the biology of age-related disease. A key challenge is to identify pathways and to translate biological research into clinical applications that improve health across older ages. Collaborative work on geroscience occurs across all NIA Divisions and throughout NIH via the GSIG, which aims to understand how aging promotes disease, and exploits that knowledge to slow the onset and progression of age-related diseases and disabilities. While most collaborators within the GSIG target disease-focused aspects of aging, DAB emphasizes the core mechanisms and fundamental biology of aging itself — the root of the geroscience hypothesis. This unique DAB emphasis should continue and is useful for collaborations with other Divisions and ICs — none of which focus on basic biology of aging.

Within DAB, the Geroscience portfolio is housed under DDO, but related projects are funded by all branches. Even though DAB itself does not oversee clinical trials, DAB works closely with the Division of Geriatrics and Clinical Gerontology (DGCG) on geroscience programs that inform clinical research. One example is a recent request for a supplement to test the impact of senolytics in COVID-19 affected patients, which was overseen by two Divisions, DGCG and DAB.

DAB delivers great value from the relatively modest funding it invests in the geroscience area. DAB has performed effective outreach to share the geroscience hypothesis (i.e., the idea that interventions targeting aging will delay the onset or severity of many chronic diseases for which age is the major underlying risk factor) with key stakeholders, including in academia, government, relevant not-for-profit organizations, and private industry. This outreach helps promote the biology of aging as a useful framework for understanding and intervening in age-related diseases. Although geroscience is accepted within NIA and among investigators in aging research and has a measurable impact on the aging field, the idea should be expanded to other NIH Institutes and health care delivery systems through more outreach, meetings, and retreats.

2. Aging Physiology Branch (APB)

APB manages an extensive portfolio of research on the fundamental mechanisms of aging-related changes that alter function in different tissue and organ systems and contribute to conditions and diseases of aging. APB supports research at molecular, cellular, and higher levels of organization, including signaling between and integration across tissues and organ systems. APB also coordinates the immunology; endocrinology and stem cell; musculoskeletal and renal; urinary and digestive; pulmonary, cardiac and vascular; reproductive; and microbiome portfolios, as well as preclinical translational research for novel therapeutics and interventions to promote healthy aging.

Looking forward, APB plans to continue its focus on integrative and comparative physiology by holding workshops and requesting set-asides for projects frequently underappreciated by study sections at the NIH Center for Scientific Review, which tend to focus on individual organ systems. In addition to uncovering relationships among the hallmarks of aging and integrative physiology that impact the heterogeneity of aging, APB also aims to promote research on

metabolites produced by the microbiomes and on epigenetic mechanisms that cause stem cell aging and disrupt tissue homeostasis. APB has played an active role in research on stem cells and regenerative-focused therapies that can help the aging community.

APB's emphasis on integrative biology and how systems communicate is a strength of the branch, which is "leading the charge" to fund research on how the hallmarks of aging contribute to the heterogeneity of aging — a unique and important effort. The portfolio's emphasis on stem cell and tissue/organ/system homeostasis research is also welcome and should continue.

Translational research has been collaboratively supported through the APB's involvement in the Translational Research Group. This Group's use of the U44 funding mechanism is valuable for product development and shows great potential for burgeoning areas.

3. Biological Resources Branch (BRB)

BRB manages and maintains biological resources to support aging research via the Biological Resources Program, which includes aged rodent and nonhuman primate (NHP) colonies; rodent, NHP, and human cell and tissue banks; and the Primate Aging Database. BRB also oversees the mouse ITP and provides shared oversight of the CITP with GCBB; both Programs are leveraged to identify interventions that affect lifespan and to a lesser extent health span. BRB also oversees the Animal Models Program, which identifies, develops, and characterizes new animal models for use in aging research. Lastly, BRB supports the Dog Aging Project, a longitudinal study of aging in tens of thousands of companion dogs that aims to identify the biological and environmental factors that maximize health span and healthy aging in dogs. The Dog Aging Project is a novel and innovative approach to studying longevity and the potential impact of a socioeconomic environment shared with humans on healthy aging and is particularly relevant to genetically heterogeneous populations.

Through BRB, DAB provides valuable and cost-effective resources for researchers in the biology of aging field and supports forward-looking ideas related to heterogeneity, midlife intervention, and resilience. BRB has been highly responsive to the recommendations from the 2015 DAB Review Report and has made tremendous progress moving science forward. The rodent colony was singled out as a particularly impressive, useful, and cost-saving resource for the research community. Establishment of the Aging Cell Repository External Advisory Board has been effective in advising NIA about the current cell line collection and future growth of this resource, which helps to anticipate the needs of the field. Maintaining and managing these BRB resources is an often-underappreciated responsibility that requires constant monitoring to ensure that ongoing research needs are met.

The trans-NIA NHP Working Group has been effective in advising NIA leadership on the coordination and planning of extramural NHP-related NIA activities. BRB's K01 and other career development funding initiatives aimed at fostering early stage NHP investigators are crucial for the future of NHP research and are worthy of further support.

4. Genetics and Cell Biology Branch (GCBB)

GCBB seeks to elucidate molecular, biochemical, and cellular mechanisms underlying aging and age-related dysfunctions. Research supported by GCBB includes genetic, cell biological and metabolic changes that affect the length and/or quality of life. GCBB identified five areas of opportunity: (1) interactions and hierarchies among hallmarks of aging; (2) cellular senescence and senolytics/senomorphics (drugs that can preferentially eliminate or modify senescent cells); (3) innovative dietary interventions to promote healthy aging; (4) biomarkers of aging; and (5) emerging technologies for aging research.

GCBB effectively manages a diverse portfolio with limited staff resources, generating an impressive amount of data, and is at the forefront of geroscience research. Exciting and innovative work is being accomplished. In particular, the branch's dedication to involving grantee input in developing particular areas is a promising model for accelerating scientific progress. GCBB has elevated the biology of aging field and has attracted broader interest among members of the scientific community and the public. GCBB has also impressively leveraged Common Fund resources and collaborates effectively with other agencies to encourage research in basic biology.

IV. Committee Recommendation Findings

Overview

The Committee recommended six priority areas for DAB to address in the next five to 10 years. The Committee's deliberations began with the premise that DAB should, above all, fund the best science. Clearly defined metrics of success and methods of evaluating various aspects of the Division should help guide DAB's priorities. DAB must determine the best method for prioritizing scientific directions going forward; convening a study group to help determine appropriate metrics of success for RFAs and other initiatives could facilitate this determination. This effort should include a comparison between RFAs and investigator-initiated grants, which can guide future funding. DAB should also develop a framework for retrospective review of past initiatives to inform DAB and NIA of its successes and to maximize interest and applications for RFAs going forward. Lastly, guidelines should be established on whether or when high-profile initiatives (e.g., CITP) should be phased out based on evaluative measures of program success and utility as scientific priorities evolve.

1. Scientific Directions

A. Hallmarks of Aging

[The hallmarks of aging](#) were established nine years ago in a landmark paper that discussed "nine tentative hallmarks that represent common denominators of aging in different organisms, with special emphasis on mammalian aging."³

Promoting the hallmarks can elevate the visibility of the biology of aging field to investigators examining adjacent science topics. However, while the hallmarks of aging have been pivotal to geroscience and the biology of aging field, these hallmarks should be viewed as an initial framework for studying aging processes rather than as a definitive and rigid list of common and distinct denominators of aging. DAB should determine how to integrate these hallmarks into a larger conceptual model of aging that takes into account the scientific advances that have occurred since the hallmarks' debut in 2013; this framework would promote the idea that hallmarks are not distinct from one another. Interaction among the hallmarks must be considered, as well as new "hallmarks" not identified previously.

As DAB has noted in its own mapping of future directions, there is consensus that biomarkers are needed to study geroscience, and while there is currently no agreement on which biomarkers should be selected, the hallmarks of aging offer some promising ideas. DAB is encouraged to determine whether the current conceptual framework for the hallmarks of aging should be modified, to discuss and further explore the interactions among individual hallmarks and with relevant biomarkers, and to establish common elements of aging that have useful

³ Lopez-Otin, C., Blasco, M.A., Partridge, L., Serrano, M., & Kroemer, G. (2013). The Hallmarks of Aging. *Cell*, 153(6): p. 1194.

predictive power. Holding a workshop to discuss these topics could benefit DAB's consideration of how the hallmarks can be promoted and used going forward.

B. Cell Biology

The DAB portfolio includes exploration of the interactions and hierarchies among the hallmarks of aging. GCBB should continue its participation in the Common Fund's Cellular Senescence Network (SenNet) Initiative and continue the branch's valuable work on senescence, with emphasis on basic mechanisms of senescence, the incorporation of disease models for senescent cell mapping, and the underlying biology of senolytic agents. As knowledge in the exciting field of geroscience is evolving rapidly, DAB should continue to encourage and support research into other common mechanisms of aging and maintain balance across targets without limiting its focus to any one specific area in geroscience. DAB should continue to support funding for other biologic pathways of aging. Currently, three of the eight outcomes GCBB uses to determine funding for studies of the interactions among hallmarks involve cytosolic DNA. While cytosolic DNA shows some promise, maintaining the overall balance of research areas that contribute to DAB's outcomes is important. One area that deserves more emphasis is intercellular communication and how recent discoveries in this field might be relevant in aging. This would include both extracellular vesicles (e.g., exosomes that contain miRNAs or other genetic information), and cell-cell direct contact (e.g., exchange of signaling molecules).

DAB should support the identification, optimization, validation, and standardization of the measure of relevant biomarkers. GCBB intends to encourage innovative approaches and novel ideas aimed at discovering aging biomarkers that can capture the complex alterations during the aging process at the molecular and cellular levels. DAB's interest in supporting work to generate consensus on the appropriate biomarkers for geroscience should continue and should consider biomarkers that (1) are useful for geroscience-guided clinical trials in terms of relevant clinical outcomes and responsiveness to geroscience-guided therapies, (2) are predictive or reflective of specific age-related diseases or syndromes, and (3) may reflect the underlying biological and physiological processes of aging. Biomarkers are highly valuable, and DAB should consider how it determines which biomarkers to support, and how biomarkers will be integrated into DAB's future funding opportunities. The contexts in which biomarkers will be used are important in this selection process. DAB is encouraged to continue or possibly expand support for the NIA Predictive Biomarkers of Aging Initiative Research Centers.

Phenotype variability, biological sex, and biological versus chronological age must be considered when selecting and validating biomarkers of interest. Currently, biomarkers are not validated across various healthy or pathological states or multiple organs/tissues. Validating biomarkers against underlying pathology would offer tremendous value to biology of aging researchers and must become a priority for the field. Defining the "normal" range of values, in particular across diverse populations, will also be extremely valuable. These ranges must be determined in humans as well as in animal models. Many routine biomarkers are not currently well established in dogs, cats, or NHPs. Testing biomarkers of aging across species challenges their universality and assists with validation. Well-validated biomarkers and standardized assays for their measurements are critical for translational geroscience research.

Reference ranges must be defined for biomarkers used in animal models and in humans, and to support biomarker applications across laboratories and datasets. The definition of reference ranges could also facilitate the adaptation of aging biomarkers to adjacent, disease-focused, fields. Rigor and reproducibility of measurements between labs must be addressed, and could

be accomplished by requiring that sample aliquots be sent for assay at a central lab for external verification of accuracy.⁴

Investing in the development of reagents to help standardize the use of biomarkers would be valuable. In the early 1970s and 1980s, the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) funded the National Pituitary Agency that provided reagents for mouse and rat assays. DAB should similarly encourage biomarker research, especially in dog or cat models that better model some aspects of the human life experience than other models. Subsequent establishment of a resource to provide those reagents to investigators might be considered in the future.

DAB should invest in the computational resources needed to identify individual biomarkers of aging, identify biomarker panels, and harmonize large datasets. Further investment in bioinformatics and medical informatics would facilitate the identification, validation, and implementation of biomarkers into research studies and, ultimately, clinical medicine.

C. Integrative Physiology

DAB and APB's emphasis on integrative physiology is highly valued and the emphasis placed on scientific directions for systems biology research should continue. DAB should broaden the Division's approach to systems biology by supporting work on the interrelationships among hallmarks of aging, tissue cross talk, microbiomes, and the interface between metabolism and epigenetics in stem cell aging.

DAB should support work that increases the field's understanding of heterogeneity in rates of aging. Specific topic areas that merit added emphasis include:

- Mechanisms of communication between tissues and organ systems
- Circadian biology: encourage development of diurnal models, in addition to nocturnal models, to understand the impact on hallmarks of aging
- Mechanisms underlying the health benefits of exercise across tissues
- Nutritional aspects
- Genomic instability and clonal evolution of aging tissues
- Aging trajectories that start during midlife or before.

DAB's future directions for APB include identifying metabolites produced by the microbiomes of various tissues that are altered in aging and elucidating their role in the development and exacerbation of age-related decline in tissue function. Microbiomes clearly impact the aging process and are an exciting opportunity area for APB. While the microbiome is typically focused on the digestive system, microbiomes exist across most tissues (e.g., gut, skin, lung). APB should consider broadening its focus from metabolites to all features of microbiomes (e.g., proteomics, transcriptomics). DAB's emphasis on the microbiome should reflect the wide array of biologic interactions between the microbiome and aging,⁵ consider multisystem microbiomes, and emphasize the study of mechanisms rather than associations. A systems biology approach to integrate large datasets and the use of emerging technologies will be essential to develop a proper understanding of microbiomes and how they impact aging. The extent to which

⁴ The National Heart, Lung, and Blood Institute established lipid research clinics to address problems of unreliable measures of biomarkers.

⁵ As an example, studies have examined *Staphylococcus* bacteria driving cells into senescence.

microbiomes are interconnected is critical for a life course perspective on resilience because microbiomes can partially drive trajectories.

APB's attention to the interface between metabolism and epigenetics in stem cell aging is a novel approach. However, this interaction should not be limited to stem cells or to epigenetic regulation, but viewed in the broader context of tissue homeostasis, regenerative capacity, clonal evolution, and organ function. While BRB already funds work on resilience and tissue homeostasis, APB should place additional emphasis on defining resilience and its measure, preventing age-related diseases, and identifying interventions that can be utilized to combat age-associated decline in resilience and regenerative capacity. Targeting this topic through midlife intervention is important. DAB should also consider changes in the stem cell niche and extracellular environment, which encompasses the microbiome.

D. Impact of Early to Midlife Stressors on Later Life Health

While developmental and early influences on life are often not currently considered part of DAB's purview, these early life experiences clearly impact the aging process and must be considered. Similarly, there are likely to be juvenile protective factors that enhance resilience late in life. DAB should consider the effect of the whole life experience (e.g., stress, infection, etc. — the exposome — from in utero to midlife) on aging outcomes and determine cost-effective approaches to studying this topic.

In longitudinal studies, midlife stress appears to drive poor health later in life. BRB intends to support research that uncovers the impact of midlife stress on the hallmarks of aging, and to identify suitable laboratory animals for studying the strength of associations between stressors and the hallmarks of aging. NHPs are particularly valuable for understanding human aging because, like humans, NHPs experience a relatively long, slow degradation of motor, sensory, and cognitive function and accumulate chronic diseases of aging. A current challenge in geroscience is determining how to measure biological age or variability in rates of aging and intervene to slow aging. Preexisting (and thus cost-effective) cohorts of middle-aged NHPs could be utilized to examine biological aging and the impact of midlife stressors on hallmarks of aging and pathological processes that underlie late-life disease development.

2. Biological and Data Resources

A. Develop Metrics of Success for Resource Sharing Initiatives

BRB provides an invaluable resource to the biology of aging community. DAB must assess how well the resources are being distributed and utilized, and track resources used and publications produced from those resources. For example, BRB tracks the destination of research animals, but there is currently no measure of how those animal models are being used in research centers or what publications ultimately arise from that use. A resource tracking system could help DAB uncover the extent to which a particular animal model translates to useful scientific discoveries, as well as the interval between provision of the animals and the emanating publications. NIA mice are usually ordered as part of a grant, and hence grant tracking could facilitate the tracking of the animals. However, this may be inadequate because use of NIA mice is not called out in grant reports, and publications using the animals may post-date the final grant reports due to the typical lag in publications relative to the funding. While resource tracking is important, new tracking methods should seek to minimize the administrative burden on investigators. In addition, consideration should be given to whether investigators not funded directly by NIA should have access to these resources. To accompany these metrics of success, DAB should also conduct a comprehensive analysis of BRB's inventory of models,

requests, and distribution to better understand the benefits and drawbacks of offering various animal models.

Once an inventory has been completed, DAB should revisit which models are being developed and offered to investigators; this effort could be supported by holding a workshop or study group to examine the return on investment of biological resources and the current models being provided to investigators (e.g., different strains, ages available, sex, and species). The group should be charged to critically evaluate whether the current model of distribution is meeting research needs, and whether alternative strategies might more optimally distribute rare and precious resources. For example, provision of very limited animal numbers associated with each request may impact the statistical power of experiments, or senior investigators with multiple grants may have access to more animals than junior investigators with a single grant. Different distribution strategies might actually accelerate research. An evaluative workshop should include participants who study human aging to provide a perspective on the models' predictive value to human biology. The workshop might also include perspectives from investigators who use human biospecimens, organoids, higher order tissue engineering systems, and other preclinical models. Models and topics for possible consideration at this workshop are provided in **Appendix 2**. The outputs of this endeavor could include a prioritized list of aging models or an annotated list of the different models and their degree of suitability for different applications in aging research. The workshop could also produce a description of what makes an organism useful for preclinical or translational research on aging to provide a framework for the consideration and integration of any newly developed models into DAB and could help identify appropriate models for examining heterogenous aging trajectories that begin earlier in life.

B. Emerging Technologies

DAB should integrate emerging technologies into BRB's animal model efforts as well as APB's systems biology efforts. Developing human-relevant laboratory and animal model systems (e.g., that take into consideration the exposome) by supporting artificial intelligence and machine learning research that extracts information from existing human studies would be useful. Cell and tissue engineering approaches can be used to model aspects of tissue aging and should be considered. Modeling systems that properly reflect human biology can help researchers examine developmental, environmental, and life course influences on aging trajectories.

C. Accessibility and Consistency in Methods and Models

DAB should support efforts to standardize lab methods and models. Models such as organoids and engineered tissues are often developed in carefully designed media that are dissimilar to the human body that is exposed to an unsterile exposome. Additionally, tissue cultures for these humanized models do not use universal methods across labs. Emerging technology for microfluidics may be useful for standardizing tissue culture to enable comparison among studies. DAB should support a broadening of the models used to study aging to include animal, preclinical, and human-relevant models; this support must include the establishment of standards to be used across various models. To establish these standards, DAB should consider convening a workshop to bring external expertise into the process of developing consistency across the field.

BRB should promote and increase accessibility to resources, such as the tissue bank. Data and tissue sharing require distinct considerations, as data can be shared indefinitely while specimens cannot. The ongoing CALERIE (Comprehensive Assessment of Long-Term Effects of Reducing Intake of Energy) Study, which uses an R33 funding mechanism, operates closely with DGCG for data sharing and storage. This study can be used as a model for how NIA-funded programs can share and operate a tissue sample repository. NIA, through the NIA Biobank, has control of the samples while study investigators such as the CALERIE Committee

(Duke University) continue to evaluate individual requests from investigators and determine which merit access to the repository. This working partnership can potentially be modeled for other large and long-duration studies. The NIA's [Aging Research Biobank](#) supports biospecimen and data sharing with investigators and should be more widely promoted as a useful resource for investigators. The Tissue Mapping Centers (recently funded by the Common Fund's SenNet) are planning to apply to the NIA Biobank to provide other investigators access to the Centers' precious human tissues. BRB should also consider requiring grantees or other resource users to acknowledge BRB in publications and presentations resulting from those resources.

D. Data Accessibility and Curation

A particular challenge for NIA and DAB is determining how new technologies and massive datasets can be organized and properly annotated in a standardized manner to provide maximum accessibility for different groups of investigators. Broader community use would greatly increase the value of datasets. DAB should promote the improvement of data accessibility and curation. User accessibility is critically important to bring data sharing and analysis to a new level. However, data sharing and management can be expensive and time-consuming for institutions, and these concerns can siphon effort from new discovery. A long-term plan on how NIA and DAB intend to solve this problem must be established since institutions often do not have enough infrastructure to store and maintain data themselves, and NIA does not offer indefinite funding to maintain and store large datasets over time. Prioritization of datasets and the development of a curation system should occur to determine which data are most important for long-term preservation. These issues are particularly critical for aging studies that might require greater lengths of time to show longitudinal changes. While this is an NIH-wide problem, NIA/DAB can help improve data sharing among its grantees.

3. Human Subjects and Health Disparities Research

Understanding health inequities and how they impact the biology of aging is a high priority for DAB. The Division considers the hallmarks of aging a useful tool to identify which individuals are at greater risk for increased disease burden in old age, which can help identify those who might benefit most from interventions. Dr. Kohanski led efforts in 2015 to learn which biological determinants of health are most important to examine. With the naming of Dr. Kohanski as Director in 2020, DAB began to prioritize the study of biology of aging with human subjects — a shift from the Division's previous emphasis on preclinical research in animal models. The appointment of Dr. Carrington-Lawrence as Deputy Director in 2021 was designed to increase the Division's attention to and expertise in health disparities. Dr. Kohanski's emphasis on health disparities and human subjects is applauded and should continue. The committee is enthusiastic about the addition of Dr. Carrington-Lawrence and her expertise to the Division.

Human subjects are an important system for research on the biology of aging, and the Division should support research examining health disparities with representative human subjects and in diverse populations. Human subjects studies are best served by a team science approach that involves clinical and basic biology investigators and leverages public-private partnerships. A wide array of applicable health disparities topics should be considered as the Division develops its priorities in this area.

DAB brings a unique basic biology perspective to trans-NIA and trans-NIH efforts to identify and address health disparities. The NIA/NIH focus on health disparities includes attention to Social Determinants of Health (SDOH); DAB-funded research can explore biological aspects of health disparities in coordination with other Divisions and ICs working to understand how SDOH impact the aging process. DAB should consider aligning efforts with the Division of Neuroscience (DN) to include underrepresented populations in biomarker research. DAB's promotion of health

disparities research should be linked with trans-NIA and NIH efforts by collaborating with relevant ICs, including the National Institute on Minority Health and Health Disparities (NIMHD), and coordinating efforts with NIA's [Health Disparities Framework](#).

In future work, the Division plans to leverage the hallmarks of aging to consider how health disparities might be assessed from a biological and molecular perspective. This work requires deliberate study of which biomarkers are valid for which populations. DAB should promote research on biomarkers for diverse populations by facilitating and funding studies, including longitudinal studies, that recruit diverse populations. DAB's work on health disparities could also include attention to how interventions that target the hallmarks of aging may be able to change health trajectories, as well as consider how socioeconomic variables impact biological aging. Animal models might be a useful approach to more fully understand how hormonal influences intersect with environmental factors to impact resiliency and hallmarks of aging. Creating clear goals for health disparities research efforts would assist DAB's collaborative efforts.

4. Training, Education, and Outreach Programs

DAB has been a leader in championing “geroscience,” a term that currently has many definitions. DAB should direct a communication effort to explain the complexities of the geroscience hypothesis and concept to a wider array of target audiences. The GSIG's plan to establish an Education Program in Geroscience could facilitate this educational effort, which should aim to reach all levels of students (from secondary education through graduate/medical school), the general public, geriatricians, and others providing health care to the elderly. Education efforts could be further supported through an expanded and collaborative use of the scientific conferences (R13), research enhancement (R15), and research education (R25) funding mechanisms.

Collaborative efforts involving NIH, NIA Divisions, and the Intramural Research Program, other governmental institutions, academia across multiple disciplines, curriculum experts, and private industry could advance the production of effective geroscience training that spans the translational spectrum. Geroscience training could also be advanced by elevating the GSIG to a formal NIH Scientific Interest Group with central coordination provided by the NIH Office of Intramural Research. Moreover, continued interactions with GSIGs at the level of the Gerontological Society of America, American Geriatrics Society (AGS), and American Aging Association should be encouraged. The Division should also work with DGCG and outside professional organizations (e.g., AGS Advancing Geriatrics Academic Programs) to consider how geroscience-relevant professional competencies and geriatrics fellowship program content and length could be restructured to overcome current hurdles to recruiting physician scientists into biology of aging research.

Training and education efforts should be leveraged to promote DAB's unique identity and vision, particularly for geroscience and health disparities. Increasing the number of training grants awarded could benefit the Division given that only two additional T32 grants (which are funded at the institute level) have been supported in the past seven years.

DAB plays a critical role in shepherding researchers from diverse backgrounds into the biology of aging field. DAB should continue support for the Butler-Williams Scholars Program and consider ways to engage MSIs in DAB initiatives, such as the NSCs. DAB should encourage research-intensive MSIs to apply for an NSC and/or partner with existing NSCs, and support MSIs in building the infrastructure needed to house large DAB initiatives. This infrastructure would enable MSI investigators to easily engage with DAB in the future. An additional measure could be to require NSCs to include local MSIs in their Center network. The Resource Centers for Minority Aging Research may offer a useful model for consideration. DAB's focus on MSIs

should capture the diversity of these institutions, which span seven categorizations. To engage diverse investigators, DAB should foster interdisciplinary collaborations to engage with investigators from adjacent fields.

Packaging DAB-related content for researchers, policymakers, and the public requires intentional and careful use of descriptive language. For example, while basic biologists may frequently avoid applying to funding announcements on the “social determinants of health,” the descriptor “exposome” may be more appealing. DAB communicates with a diverse community that extends beyond biology of aging researchers and must promote materials, resources, and Funding Opportunity Announcements accordingly.

5. Common Fund and Collaborative Activities

Many topics span portfolios across the branches within DAB. DAB should provide clear guidance on how cross-cutting topics such as emerging technologies, health disparities, hallmarks of aging, biomarker discovery, and geroscience should be balanced across all three branches. While DAB currently fosters an open dialogue among branches to ensure transparency across projects, creating more specific inter-branch collaborative processes would benefit the Division and research community.

Discussion between the review Co-Chairs and the NIA Division Directors uncovered strong collaborative interests between Divisions; the Translational Research Working Group is one example of a symbiotic partnership between DAB and DGCG. DAB should leverage its unique value in collaborative partnerships with other NIA Divisions and NIH ICs and consider hiring additional staff to oversee and coordinate collaborative projects given the cross-cutting nature of geroscience and the number of RFAs and Common Fund projects in which the Division participates.

DAB is a highly collaborative Division and should continue to promote inter-Division collaborations.

- DGCG: Strong collaboration with the DGCG supports 19 clinical trials, which will be facilitated and enhanced by DAB’s plan to hire an individual with clinical research expertise. DAB is well positioned to collaborate with DGCG on translational studies focused on nutrition, stress, and resilience, as well as efforts in translational geroscience and geroscience education. Lastly, GCBB should consider collaborating with the DGCG Centenarian Consortium Project.
- Division of Behavioral and Social Research (DBSR): DAB can work with DBSR to (1) integrate research in behavioral and social topics into geroscience, (2) study mechanisms behind sociocultural influences and health disparities, (3) consider how BRB’s NHP resource may benefit DBSR’s funded studies on social stress in primates, and (4) provide DAB’s unique mechanistic and basic biology approach to DBSR’s funded research on diet.
- DN: DAB should consider aligning efforts with DN to provide a more integrated approach for aligning the aging nervous system changes with peripheral aging, and to include underrepresented populations in biomarkers research.

To promote trans-NIH collaborations, DAB should continue its efforts supporting Common Fund programs, particularly SenNet. Additionally, the following Institutes align with DAB aims and may be useful collaborators:

- The National Cancer Institute may be a valuable collaborator for the GCBB, particularly in respect to newer research developments in intercellular and intracellular communication.

- The National Institute of Arthritis and Musculoskeletal and Skin Diseases and NIDDK align well with the APB's emphasis on the musculoskeletal and renal systems.
- The National Institute of Allergy and Infectious Diseases could benefit from DAB's expertise on health conditions impacting older populations, including COVID-19, vaccine responsiveness, inflammaging, autoimmunity, and sepsis.
- NIMHD and other ICs could help support DAB's work on health disparities.

DAB should consider international collaborations with countries eager to collaborate with DAB. The United Kingdom's Medical Research Council and Biotechnology and Biological Sciences Research Council are funding the [Ageing Across the Life Course Interdisciplinary Research Network](#), which aims to increase collaboration in aging research. DAB may find utility in collaborating with such networks to engage with different perspectives on aging.

All this work requires staff effort, which cannot exclusively be measured by the number of grants and contracts managed by each program officer, given the numerous other Common Fund, trans-NIA, and other initiatives in which staff participate.

6. Staffing

Achieving the Committee's recommendations outlined in this report will require the addition of new DAB staff members. DAB must hire additional staff to reduce the burden on current program officers, manage collaborative activities, and provide DAB with the ability to bring new expertise into the Division, particularly to increase the Division's capacity to promote research on health disparities, emerging technologies, and geroscience. DAB should continue its plans to incorporate expertise on the peripheral nervous system to support research on integrated and comparative physiology, data science, and clinical research/trials that can support studies that are preliminary and ancillary to clinical trials. More expertise in multi-omics, modeling, and bioinformatics is needed; DAB should consider hiring an individual with expertise in large datasets who can participate in NIH-level activities on data sharing, develop a curation system for important datasets, and manage DAB bioinformatics practices and education.

Despite a heavy workload, program staff are highly responsive to researcher questions and requests; this responsiveness is especially noteworthy and encouraging to new investigators. Additionally, program officers spend considerable time learning about new research to remain on the cutting edge of their fields. DAB must restructure portfolios and hire staff to reduce the average and maximum number of grants/contracts per program officer, ensure the continuity of contracts for biological resources, and consider succession planning. **Appendix 3** shows the current DAB Organizational Chart.

In February 2021, DAB received approval to hire eight new program officers over a four-year period across its three branches. Six new hires were already on board by early 2022, to service new portfolios in the areas of emerging technologies, molecular epidemiology, immunology, circulatory and pulmonary systems, resilience, and stress response. Staff are also being onboarded to support Common Fund initiatives, training, and policy. DAB intends to redistribute grants and reorganize portfolios among all program officers to lower the average number of grants per portfolio.⁶ Organ system-specific titles associated with program officers should be

⁶ Over the past five years, DAB's grants workload has increased by 45% for total grants (competing and noncompeting), 39% for awards, and 110% for award direct total costs. (The percent increase was calculated for FY2020 against the average values from FY2011-FY2015.) The result of the rapid increase is that DAB has the second highest average workload for program officers among the four NIA Scientific

discouraged to help promote priority areas such as systems biology, organ communication, resilience, and biomarker discovery. The recent hire of two new program officers in APB with grant portfolios in immunology and in circulatory and pulmonary systems suggests a welcome, broadened focus.

Support staff is also needed to help the DAB leadership manage the increased workload that would result from meeting the increased demands for supporting communications and collaborations among DAB branches, across NIA Divisions, and/or throughout NIH, including Common Fund activities, tracking funding, developing workshops, managing meetings, processing travel requests and vouchers, and developing publications.

V. Note about NIA Concept Clearance Process

DAB and other NIA Divisions have limitations on the extent to which they can collaborate with external researchers before a concept reaches Council for approval. To incorporate outside perspectives, DAB holds workshops to gather information from the community. Regardless, because concepts are developed internally by DAB staff due to conflict-of-interest concerns, concepts are often “fully baked” when they arrive at Council, making it difficult at times to incorporate additional feedback. Moreover, choices for outside experts who are consulted for these concept clearances are often too narrow. Establishing approved approaches to incorporate feedback and broaden expertise well before they arrive at Council would benefit the scientific direction of these concepts. This would ensure that RFAs capture the best quality science and generate the best value for the community. Providing greater transparency in the vetting process for concepts and the reasons behind the process would help inform researchers of how divisions prioritize topics and develop funding announcements.

NIA emphasizes translating new innovations in biology of aging research to human populations. For some initiatives, there is a 10% set-aside built into grants to support collaborative efforts, encourage cross talk within the community, and bring multiple perspectives into a project. While this set-aside is beneficial in many circumstances (e.g., ensuring that biomarkers are cross-validated by a second lab) the policy can financially strain research involving human subjects that often has strict and limited budgets. Mechanisms that prioritize collaboration should be continued, but with consideration of how these policies can be designed and implemented fairly across diverse projects.

VI. Conclusion

The overarching view of the Committee is that DAB has been extremely productive and impactful given the challenging demands on staff, the change in leadership, and the recent pandemic. An example of this is the considerable investment into research on the hallmarks of aging that has led to multiple novel geroscience therapeutics and served as the foundation for dozens of clinical trials (pertinent to virtually all NIH ICs) and countless biotech companies, all in less than a decade. Since the 2015 Council review of DAB, there has been greater recognition of the compelling need to address racial and socioeconomic inequities through research to thoroughly understand the biology and heterogeneity of aging. Basic biological research is part of the foundation on which health is understood and improved. DAB has relied on a supply of

Divisions. DAB averages 80 awards per program officer while NIA averages 73 awards per program officer. This disproportionately impacts employees within the GCBB and APB, who manage 102 awards per program officer and 128 awards per program officer, respectively. The average number of applications managed by program officers are 155 and 193 for NIA and DAB respectively.

meritorious research applications from investigators, in response to trends in the field and advice from experts, while remaining nimble to react to new discoveries.

DAB clearly delivers highly valuable resources and funding opportunities. It manages an extensive and diverse portfolio under sound leadership and through the work of capable and conscientious staff. Dr. Kohanski brings to DAB and NIA leadership his institutional memory, his scientific background, and his demonstrated commitment to understanding health disparities and actively addressing them. He has also led a welcome effort to support research using human subjects — a shift from the Division's previous emphasis on preclinical research using animal models. The appointment of Dr. Carrington-Lawrence as Deputy Director in 2021, designed to increase the Division's attention to and expertise in health disparities, is exciting. Dr. Kohanski's receptive leadership is conducive to collaboration within NIA/NIH and with the external research community. Despite a disproportionately heavy workload compared to most NIA Divisions, DAB program staff are well informed and highly responsive to researcher questions and requests, and this responsiveness is especially encouraging to new investigators.

When considering scientific directions over the next five years, a clearly articulated sense of purpose and perspective, coupled with well-defined metrics of success, will help DAB bring added value to collaborative efforts and the greater research community. The Division would also benefit from the addition of more staff to relieve the burden on current program officers and allow new expertise to be brought into the Division. Emerging technologies, geroscience, diverse animal models, biomarkers, resilience, and microbiomes should all be prioritized when determining scientific directions for the coming years.

The Committee concludes this report as highly impressed with the accomplishments, direction, and service of DAB, and is confident of DAB's potential to drive innovative and impactful advances in human aging health into the next decade.

APPENDIX 1.

Background Materials Provided to Review Committee

Below is the list of DAB Review materials provided at each point in the review process.

DAB Overview Materials and Background Documents June and July 2021

- DAB Video Library on NIA and DAB Funding
- Common Fund Initiatives
- DAB Staff Biosketches
- DAB Organizational Chart
- 2015 Review of DAB
 - Major Recommendations from 2015 Review
 - 2021 DAB Narrative
- RFA Tracker
- DAB Science Advances, 2020 and 2021
- DAB Priority Setting
 - NIA Strategic Directions 2020-2025
- NIA DAB Meetings and Workshops Summary
- DAB Liaison Tracker
- DAB Workforce Overview

Kick-Off Meetings June 2 and 8

- DAB Presentation Slides

July Videoconference July 28

- Presentation on DAB Programs
- Opportunities for the APB, BRB, and GCBB
- Geroscience Future Directions
- Human Subjects and Health Disparities Research

Fall 2021 Subcommittee Calls August–October

Each subcommittee received the following documents:

- DAB Responses to Reviewer Questions
- Future Directions/Opportunities
- Programs
- DAB Liaison Tracker
- NIA DAB Meetings and Workshops Summary
- RFAs
- Table of Awards in DAB for AD

Below are other documents provided to each subcommittee

Geroscience Subcommittee

August 24

- Geroscience Summary of Activities and Proposals
- Geroscience Event and Summary Documents

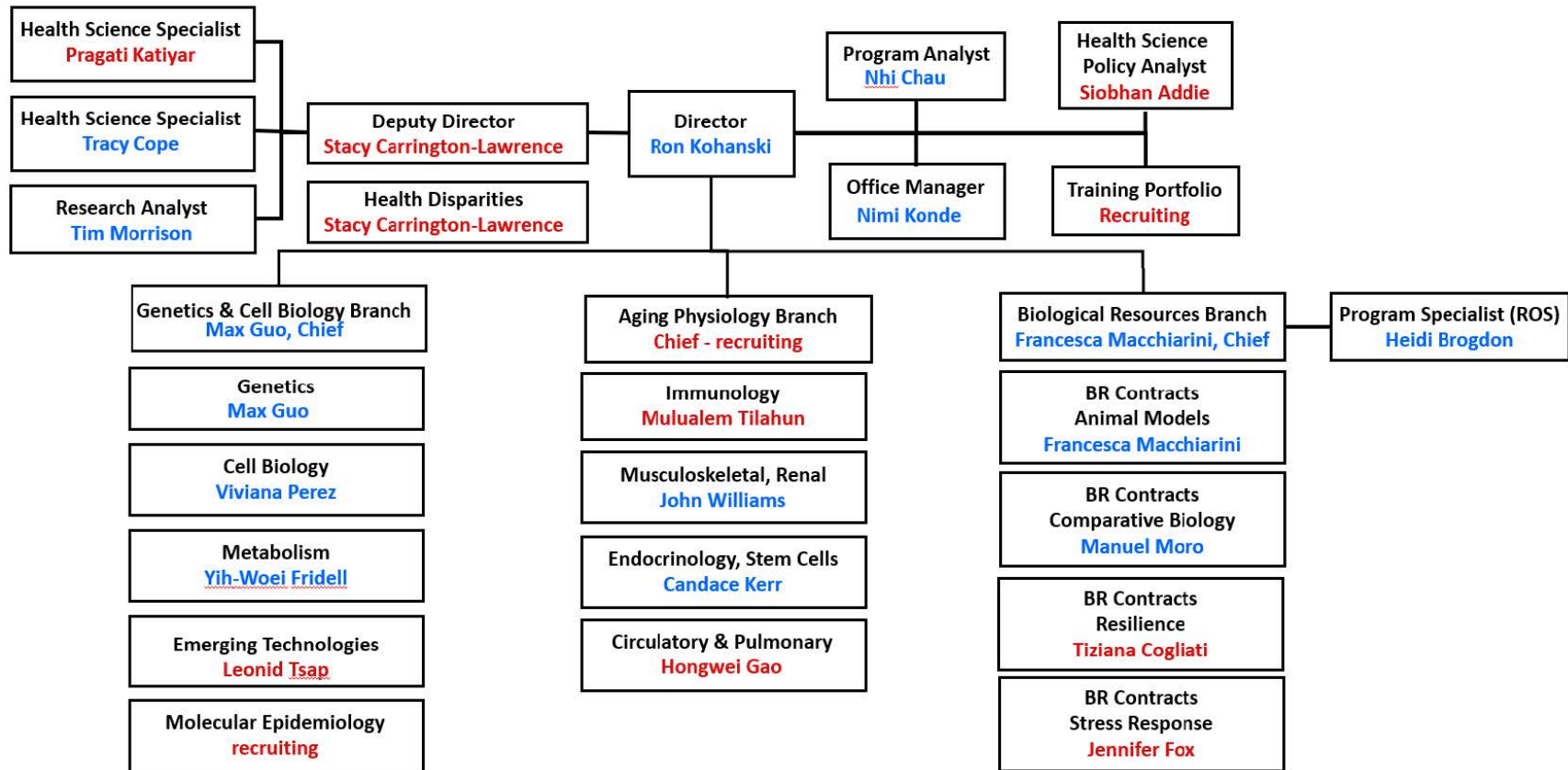
<u>Biological Resources Branch (BRB) Subcommittee</u> <ul style="list-style-type: none">• ITP Summary• BRB Portfolio Description• BRB Common Fund Initiatives	August 25
<u>Aging Physiology Branch (APB) Subcommittee</u> <ul style="list-style-type: none">• APB Portfolio Description• APB Common Fund Initiatives	September 9
<u>Genetics and Cell Biology Branch (GCBB) Subcommittee</u> <ul style="list-style-type: none">• GCBB Portfolio Description• GCBB Common Fund Initiatives	September 30
<u>Division Director's Office (DDO) Subcommittee</u> <ul style="list-style-type: none">• DAB Organizational Charts• DAB Workforce Overview• DAB Common Fund Programs• Human Subjects and Health Disparities Research• DAB Human Subjects Portfolio• Butler Williams Scholars Summary Document• 2015 Review of DAB<ul style="list-style-type: none">○ Major Recommendations from 2015 Review○ 2021 DAB Narrative• DAB Discretionary Funds and Administrative Supplements	October 8
November Videoconference <ul style="list-style-type: none">• Subcommittee Meeting Reports• DAB Organizational Charts• DAB Common Fund Programs	November 30
January Full Review Committee Virtual Meeting <ul style="list-style-type: none">• Future Directions and Opportunities Documents• Draft DAB Review Report (Rev. 2022.01.14)• DAB Staff- Expansion and Turnover• DAB Common Fund Programs and Collaborations	January 24, 2022
March Videoconference <ul style="list-style-type: none">• Draft DAB Review Report (Rev. 2022.03.04)	March 8
May Presentation to Council <ul style="list-style-type: none">• National Advisory Council on Aging Presentation Slides	May 10 and 11
Process Documents <ul style="list-style-type: none">• Review Timeline• Meeting Agendas• Subcommittee and Meeting Reports• Interim Drafts of DAB Review Report• Website for Housing Review Resources	Throughout Review

APPENDIX 2.

BRB Animal Model Future Directions: Possible Workshop Topics

- Wildtype models raised and housed in a natural environment to align the exposome of animal models more closely with the exposome of human beings.
- Balance between number of polygenic models, hybrid strains, and defined strains of mice offered.
- Four-way cross heterogeneous mice, which are frequently requested by investigators outside the ITP. Consider requiring NSCs using these models to make the tissues available to external researchers.
- Age of mice provided. While BRB provides mice at 18 months of age, many investigators would appreciate receiving mice at 24 months of age.
- Number of (H1) mice provided to investigators.
 - Should there be a requirement for investigators to provide a sample size calculation to justify the number of mice sought? Investigators currently receive a restricted number of mice at a slow rate. Instead of receiving all mice at once, currently, investigators receive a portion of these mice every month or two. Having the ability to utilize all mice at once would increase efficacy of the study and reduce the risk of mice dying mid-experiment, which is a particular concern for studies on older mice.
 - Would partnering with private companies increase inventory and ability to provide mice more quickly, and at what cost?
- Middle-aged models. Midlife is often when biological and chronological age diverge, and diseases of aging begin to accumulate, making it an important age for study.
- Stressed models. Dog models may also be useful for studying stress paradigms, possibly by utilizing animals from shelters.
- Models appropriate for geroscience research.
- Models appropriate for integrative physiology research, including the appropriate models for studying circadian biology, and which models are best for examining the heterogeneous trajectories of aging that begin at midlife.
- Diet of models. Animal models can be used to study non-pharmacological interventions. While extensive data show that diet composition drives chronic diseases of aging, little is known about diet composition effects on the biology of aging. Most laboratory animals are fed a single chow diet, which does not mimic the average human diet. Likewise, nutritional aspects must be considered in newer research studies examining pets, which have exposomes and genetic makeup more similar to humans than other models but typically eat pet-specific food. Restricted diets are a common treatment for obesity; in animal model systems, more research is needed to understand the impact of various restricted diets (calorie restricted, intermittent fasting, diet composition patterns — e.g., Mediterranean diet) on lifespan and tissue maintenance, and this research should be relevant to human interventions.
- Genetics models, which can be useful for establishing causal relationships.
- Best practices (e.g., to provide the rationale for using a certain model) for grant writing in applications that discuss the models prioritized by the workshop. The NIH Toolbox provides recommendations that are helpful for writing and reviewing grants on human subjects, and this workshop could lay the groundwork for DAB to develop a similar document.

APPENDIX 3. DAB Organizational Chart, January 2022⁷



⁷ Recently hired staff are shown in red font. The Deputy Director and APB Chief positions are replacements. DAB has expressed a preference for the new APB chief to cover microbiomes. Dr. Katiyar is supported by the Common Fund but is assigned to DAB because DAB is the major program resource for the SenNet Consortium. Her position was not among the eight new positions approved in 2021. The Health Science Policy Analyst position includes serving as the “executive secretary” for the GSIG.