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COLUMBIA UNIVERSITY
IRVING MEDICAL CENTER

Healthy Aging Initiative

I.   INTRODUCTION | Charge for the All-CUIMC Healthy Aging Initiative

1) Create a vision for next generation science to propel developing healthy longevity for all—spanning basic molecular, cellular, and organismal, clinical, mental health, social sciences, and public health approaches to population health
2) Identify initiatives to catapult CUIMC's leadership on science and solutions that meet health needs and optimize the opportunities of longevity
3) Identify CUIMC's strengths and gaps and our collective transformative goals that will strengthen basic science, clinical medicine, social science, and population health science, and position CUIMC as a transformative leader on aging, longevity and health
4) Create a basis for synergies among all these disciplines towards transformative goals
5) Propel collaboration among the medical center's four schools and the Irving Institute towards a shared and highly aspirational vision

II.   RECOMMENDATIONS | Input from CUIMC researchers on aging

On the charge of Anil K. Rustgi, MD, Director of the Herbert Irving Comprehensive Cancer Center and then interim Chief Executive Officer of the Columbia University Irving Medical Center and Dean of the Faculties of Health Sciences and the Vagelos College of Physicians and Surgeons, Linda P. Fried, MD, MPH, dean and DeLamar Professor of Public Health and director of the Robert N. Butler Columbia Aging Center, with the partnership of Gérard Karsenty, MD, PhD, Paul A. Marks M.D., Professor and Chair of the Department of Genetics and Development, implemented a survey, met with faculty, and led a series of convenings of all programs at CUIMC working on issues of health and aging to develop a transformative vision of research goals for the coming decade. More than 120 faculty across CUIMC participated. Group convenings included faculty from:

- Behavioral Medicine
- Biology of Aging
- CTSA Irving Institute
- Medicine
- Neurology and Sergievsky and Taub Centers
- Nursing and Dental Medicine
- Psychiatry
- Public Health
- Social Work

This outreach culminated in an October 2021 convening of all CUIMC researchers working on aging to develop recommendations (below) to strengthen an all CUIMC-wide vision and agenda on healthy aging research and to integrate existing work across many strong units toward shared goals over the coming decade. The recommendations are to:

1) Lengthen the health span for all by establishing the full science of mechanisms for understanding and influencing achievement of healthy longevity at individual and population levels, with increased health and wellbeing into the oldest ages. This endeavor would engage with global and national priorities to delay aging; prevent chronic diseases, cognitive decline, frailty and disability; and extend health span and wellbeing. From these, we will create shared goals for science and solutions to prevent diseases and other adverse outcomes of aging and to increase length of health span and positive capabilities, through understanding the dynamics, mechanisms and modifiers of the aging process and its modifiers and resolution of disparities across the life course.
   a) Determine pre-clinical and clinical and population-based geroscience approaches to delay aging plus age-related chronic diseases. Develop the new pipeline of health promoting/disease and frailty preventive interventions in the nonpharmacologic and pharmacologic spaces.
   b) Create health equity geroscience, with its focus on determining population-based approaches to identify human geroprotectors and gerotherapeutics (including nonpharmacologic technology-based/enhanced and environmental, pharmacologic and procedural/surgical) that create population health and resilience across the life course for all, resolve health disparities and lengthening health span for all, and prevent or mitigate cognitive decline, frailty and mobility and other disabilities with aging. CUIMC would have the opportunity to partner with programs in the community on this aim.
   c) Expand research on positive human development with aging and opportunities for health and wellbeing in aging: a new science of health, capabilities, reserves and resilience that capitalizes on the assets and capabilities of older age.
   d) Characterize the goals and needs of people as they age and establish effective, person-centered strategies to assist in the achievement of those goals.
   e) Identify gaps and opportunities for developing evidence-based policies to facilitate achievement of these goals at a population level, both nationally and globally.

2) Utilize CUIMC strengths in basic and translational science from T1, 2, and 3 into T4 action to achieve the goals outlined above:
   a) Identify bold targets for life course interventions that could be most effective in extending health span and wellbeing into oldest ages for individuals, community, intergenerational wellbeing, population and planetary health. Identify the needed interventions that maintain health, preserve and protect wellbeing and function, prevent disease, modify trajectories to healthy longevity, resolve disparities, lengthen health span, and build the positive assets and capabilities, social capital and contributions of older age. Criteria should be:
      i) Conditions/targets that are common and unquestionably important to older adults and will energize the community, and where CUIMC has a differential advantage. Prioritize frailty and cognition, functional outcomes, and synergies across disciplines towards these targets.
      ii) Target both positive outcomes and adverse outcomes
      iii) Prioritize prevention and resilience and enhancing capabilities of aging.

iv) Consider how emerging large scale societal-, policy-, technology- and climate-related factors may modify how aging is experienced.

3) Deploy shared tools and metrics
   a) Translate science into promising sustainable interventions for:
      i) Individuals
      ii) Communities and populations
      iii) Health systems: transformative shift from reactive medicine to whole-self health and wellbeing; innovate models of prevention and care that can meet people where they are.
         (1) Public health
         (2) Medical, dental/oral health care for the continuum of needs – within a coordinated continuum of care, integrated within and across settings, including into the home,
         (3) Long-term care
         (4) Social care
         (5) And our planet
      iv) Society: identify the policies and other bases for transitioning to successful societies for longer lives, with healthy longevity, valuing and enabling roles and responsibilities of older adults in communities that bring impact and enhance health, and enabling the social capital of older adults, intergenerational wellbeing, cohesion and connection, and creating a Third Demographic Dividend. Research should provide guidance for both global south and global north.

III. IMPLEMENTATION | Initial Steps

1) The Robert N. Butler Columbia Aging Center (CAC), a university-wide center based at the Mailman School of Public Health, will:
   a) Implement and host a CUIMC-wide Steering Committee of 8–10 diverse interdisciplinary CUIMC faculty to lead finalization of report and recommendations.
   b) Organize partnership among CUIMC Steering Committee, the Irving Institute and other Columbia schools and components.
   c) The Steering Committee will form working groups to refine scientific goals, design research, and conceptualize complex and novel interventions on thematic visionary objectives.
   d) Organize 'Think Tanks' for the development of a Columbia Cohort for the Study Successful Aging (CCSSA) with dual goals: (1) To describe the natural history of successful aging as it develops from early midlife; and (2) To identify environmental drivers of successful aging in an urban environment. The vision for the cohort is to become a foundation for the characterization of person-level healthy-aging benchmarks that can become targets in clinical practice and the identification of neighborhood-, community-, and family- and individual-level physical and social environmental features

that can become targets for programs and policies to promote healthy aging. A census of all cohorts in existence is underway so that CCSSA is positioned to build upon them. The think tanks will:

i)   Refine the goals and vision for the cohort

ii) Establish a strategy for recruitment of a diverse, place-based, multi-generational longitudinal study, including determining the scope of the geographic catchment (e.g., Upper Manhattan only vs. NYC region)

iii) Identify the targets for the first round of data collection; number of families and individuals

iv) Scope of data types to be acquired (surveys, in-person functional testing, blood samples, eco-sensing, health record data, etc.)

v) Recruit a core team of principal investigators to initiate the cohort study

2) Opportunities to consider and design for:

a) Build on pan-NYC Silver Study (ICAP); a random sample of older New Yorkers to understand impact of COVID-19 in community-dwelling older adults. Two waves of data collection to date. Could be easily adapted to other health and aging goals locally, or in phone surveys globally (link: https://icap.columbia.edu/tools_resources/silver-survey-summary-sheet/)

b) Consider natural longitudinal clinical cohort study of older adults receiving medical care at CUIMC, with data bank of biological, clinical, social, functional and bioenergetic data. Extend clinical cohort to include participants from community and other settings.

c) Strategic directions of other major funding sources, such as the Centers for Medicare and Medicaid Innovations (https://innovation.cms.gov/strategic-direction-whitepaper), a significant source for national demonstration projects

d) Build on other CUIMC existing cohorts

3) CUIMC Geroscience Biomarker Core: The biomarker core will curate the best science available to develop and maintain a Columbia Aging Biomarker Battery (CABB) to represent the state of the art in quantification of aging and health at cellular-, tissue-, and whole-organism levels of analysis. The CABB will integrate ongoing science from around the world with innovation of novel methods here at CUIMC. To complement the CABB, the Biomarker Core will establish:

a) A battery of assays that can be performed on-site using specimens collected by CUIMC researchers

b) A network of relationships with core facilities around the country to ship CUIMC samples out to generate high-throughput "omics" datasets at competitive pricing

c) A computational "back end" that will process the datasets generated from in-house and out-sourced assays to prepare analysis-ready datasets for investigators

d) A consulting service that can advise on best practices for analysis of the new biomarkers

4) CUIMC Geroscience Computational Core: Over time, the computing core should aim for self-sufficiency through fee-for service arrangements in which the core conducts analysis for investigators at CUIMC (and possibly outside). The computing core will consist of:
   a) A computing cluster capable of massively parallel computing to speed analysis of omics, informatics, and other "big" data
   b) A small staff tasked with overseeing the cluster and supporting investigators in using it

5) CUIMC Geroscience Data Core: The data core will serve two functions: (1) A repository of data generated by investigators at CUIMC, including data from population-based studies (including large-scale EHR- and claims-based data sets for observational studies), clinical trials, and experiments with animals and cultured cells; and (2) A consulting service versed in accessing data stored in public repositories for which barriers to access by new investigators are comparatively high, including the NIH dbGaP, the NHLBI BioLINCC and TOPMed, the NIA AgingResearch Biobank, as well as individual studies with powerful data for the study of aging.

6) CUIMC Health Services Research Core: For designing and testing new models of interdisciplinary care delivery, exploring economics and financial viability, feasibility and sustainability of new care delivery models.

7) Consider technology core with SEAS

IV. CUIMC-WIDE RESOURCES NEEDED | An Overview

CUIMC-wide resources are needed to decrease transaction costs for interdisciplinary, interunit science and translation.

1) Management of central electronic repository for interdisciplinary networking:
   a) Surveys of faculty interests and goals
   b) Summary map of interests of investigators on aging, what part of the life course they work on, and of current Center grants – including those planned
   c) Creation of a university-wide networking intranet site for faculty
   d) Communications hub to include listserv/website of ongoing research across CUIMC, quarterly description of ongoing activities on aging research, funding or collaborative opportunities
2) Convening:
   a) Butler Center to bring together researchers on aging itself and researchers on issues adjacent to aging regularly
   b) CUIMC-wide or university-wide symposium around progress and plans on grand themes (above), and supporting working groups (incorporating senior, mid-career and early-stage investigators) in different areas. Use symposia and working groups to create a network of opportunities for funding. Develop a plan for continuity of these groups and create an

assertive matchmaking effort. Fund pilots, built into the matchmaking, to prepare for NIH. Track results.

3) Data and Resource Hubs:
   a) Funding for development of local population-based cohort study, with collaborators across CUIMC. Create a curated library of effective aging-relevant preventive interventions and opportunities for interventions, and relate to critical points in life course
      i) Repository of population-based studies' data bases
   b) Pilot Funding and Training
      i) Training of fellows across the medical center in interdisciplinary aging science – so this is "baked in" early in training
      ii) Fund Butler Center Faculty fellowships in healthy longevity and CUIMC Pilot grant program to seed interdisciplinary teams, including Pilot funds for Intervention studies through Community resilience hub(s)

4) Developing funding and other resource supports
   a) CTSA resources to potentially apply: clinical programs; CU-led community programs; integration of Special Populations Resource; Precision Medicine and Implementation Science resources
   b) Leverage Health and Aging Policy Fellows and the CU development office to develop connections with foundations and policy-related organizations as potential collaborators
   c) Work with Orin Herskovitz et al. to create industry partnerships as appropriate

5) Biology of Aging investigators' resource needs which were previously identified:
   a) Administrator
   b) Shared space for a Center on Biology of Aging
   c) Aging mouse colony now to be started
   d) One year of seed funding for 2-3 projects per year, competitive
   e) Graduate course on biology of aging, then T32
   f) Monthly seminar series on biology of aging now implemented
   g) Develop systems biology and bioinformatics capabilities
   h) Yearly retreat symposia
   i) Bank of human samples from cohort study (see above), including iPSCs from human blood or fibroblasts from health young and old donors from various racial/ethnic backgrounds

V. REPORT BACKGROUND

SYNTHESIS OF NATIONAL INSTITUTE ON AGING STRATEGIC PLAN GOALS, 2021-2025

The CUIMC-wide survey and sub-group meetings were conducted with the following NIA strategic plan goals in mind:

1) Goal A: Better understand the biology of aging and its impact on the prevention, progression, and prognosis of disease and disability.

2) Goals B-F: Better understand the effects of personal, interpersonal, and societal factors on aging, including the mechanisms through which these factors exert their effects. Understand health disparities related to aging and develop strategies to improve the health status of older adults in diverse populations.

3) Goal D: Improve our understanding of the aging brain, Alzheimer's disease, related dementias, and other neurodegenerative diseases. Develop interventions to address Alzheimer's and other age-related neurological conditions.

4) Goals C-E: Develop effective interventions to maintain health, wellbeing, and function and prevent or reduce the burden of age-related diseases, disorders, and disabilities. Improve our understanding of the consequences of an aging society to inform intervention development and policy decisions.

5) Strategic goals of other NIH institutes to be considered.

BACKGROUND ON THE ROBERT N. BUTLER COLUMBIA AGING CENTER (CAC)

1) An endowed University Center since 2012 and based within the Columbia Mailman School of Public Health, the CAC was originally mandated to unite expertise across Columbia on how science, education, and translation can provide leadership and develop partnerships to transform to successfully aging societies.

2) Robert N. Butler, MD, was a geriatrician and founding director of the National Institute on Aging, and, among many other things, an alumnus of Columbia College and P&S. He wanted his organization, the International Longevity Center-USA, to be sustained at his alma mater. He elected, with the Provost, to embed the ILC-USA at Columbia in this University-wide center, with the School of Public Health be the unifying host.

3) CAC core research programs: Biosocial Aging and Health Equity; The Science of Health; Global Health and Aging; Thriving Aging Societies: Social Engagement and Societal Infrastructure; and the International Longevity Center-USA

4) Faculty:
   a) Allison E. Aiello, PhD, James S. Jackson Healthy Longevity professor of Epidemiology
   b) John Beard, MBBS, PhD, Irene Diamond professor; director, International Longevity Center-USA; professor of Epidemiology and Health Policy and Management
   c) Daniel W. Belsky, PhD, associate professor of Epidemiology
   d) Alan A. Cohen, PhD, associate professor of Environmental Health Sciences

e) Linda P. Fried, MD, MPH, director, Robert N. Butler Columbia Aging Center; dean and DeLamar Professor of Public Health; professor of Epidemiology and of Medicine
f) Maureen Henry, JD, PhD, deputy director, International Longevity Center-USA; deputy director for Programs, The Health and Aging Policy Fellows Program
g) John W. Rowe, MD, Julius Richmond professor of Health Policy and Aging, Health Policy and Management
h) Kavita Sivaramakrishnan, PhD, associate professor of Sociomedical Sciences
i) Adina Zeki Al Hazzouri, PhD, assistant professor of Epidemiology
j) Yuan Zhang, PhD, assistant professor of Sociomedical Sciences
k) Senior staff: Caitlin M. Hawke, associate director, programming; Rosine T. Moussa, MA, center administrator

5) Since its operational launch in 2013, the CAC focused initially on building a network of faculty across the university who work on aging and longevity, and using its resources to fund fellowships in aging and healthy longevity for faculty interested in building research programs in this area. In 2014, the CAC created, and continues to sponsor, a University Seminar – "The Future of Aging Research" – which engages a core faculty of 50 Columbia principal investigators and is currently co-chaired by Brandon Pearson, Jennifer Manly, and Kavita Sivaramakrishnan. The CAC presents a University-wide bimonthly seminar series on aging and healthy longevity. It has been a key partner in the International Longevity Center Global Alliance, which is spread across 16 countries, and is the home to the following programs for which it has built major international roles:
a) International Association of Gerontology and Geriatrics: President, John W. Rowe
b) Aging Society Network: John W. Rowe, chair; Linda P. Fried, member
c) ILINK (International Loneliness and Isolation Knowledge Network): Linda P. Fried, chair
d) US National Academy of Medicine Global Commission to Create a Global Roadmap for Healthy Longevity; Linda P. Fried, co-chair; John W. Rowe and John Beard, Commission members; Maureen Henry, former program officer for the NAM report

6) The CAC's mission and goals are focused on building the knowledge to create healthy longevity and developing opportunities for aging societies, towards accomplishing a Third Demographic Dividend. In the last three years the CAC has turned to building core programs on key academic areas for successfully aging societies and healthy longevity. These include a New York State-approved educational certificate in healthy aging; a University-wide umbrella course for undergraduates and graduate students, '(Y)our Longer Life;' a training program in health and aging; and the recruitment of core faculty for its four major programs.

RECAP OF SUBGROUP MEETINGS CONDUCTED FROM JUNE-OCTOBER 2021

1) Biology of Aging Subgroup Goals
   a) To elucidate the neurological, endocrine, cellular, molecular, genetic, and epigenetic underpinnings of age-related diseases, including cancer.

b) To propose, design, and test in model organisms and humans, novel and adapted therapies developed based on this knowledge.
c) To integrate basic science and clinical medicine by housing aging researchers in both fields in the same location.

2) Center for Behavioral Cardiovascular Health (CBCH) Subgroup High-Level Goals
   a) Understand the influences of climate, place, systemic racism, psychology, and behavior on health aging today and in the future.
   b) Bring the science of aging and behavior in line with the broader scientific understanding of future climate change and biodiversity loss, as well as the environmental, political, and social conditions implied by physical, atmospheric, political science models of the consequences of climate change and biodiversity loss.
   c) Identify disparate speed and magnitude of environmental/climate change impacts on health in communities who have been targeted for marginalization/remain more vulnerable due to resulting deficits in socioeconomic status.
   d) Develop interventions that simultaneously promote individual and planetary health (CDC's One Health concept) and conduct mechanistic research to identify creative approaches to aid cities', healthcare systems', communities', and individuals' efforts to adapt to changes that have already occurred/are certain to occur. Focus on communities that have been left most vulnerable due to systemic racism, disinvestment, overpolicing, and environmental racism.

3) Dentistry Subgroup High-Level Goals
   a) Understand the role of periodontitis as an exposure affecting cognitive decline as well as its effect on other co-morbidities.
   b) Elucidate the association of medical outcomes and improved access to oral health.
      i) Use of data, MEPs, EPIC to measure impact.
   c) Improve screening role of healthcare providers, especially dentists, in service of chronic disease prevention and management for healthier longevity.

4) Medicine Subgroup High-Level Goals
   a) Understand the mechanisms of healthy aging and resilience vs. those of frailty
      i) Examine predictors of cognitive and sensory-motor resilience in aging
      ii) Reframe aging-related disease   Focus on healthy aging and resilience
      iii) Examine predictors of frailty and hospitalization (cognitive, motor, metabolic, etc.)
      iv) Increase diversity in study populations to understand socio-cultural factors underlying resilience and frailty
      v) Understand encounters with healthcare system that are markers of specific trajectories and improve navigation of the system from an age-friendly standpoint
      vi) Translation of successful aging/resilience predictors, prevention and intervention strategies
         (1) Ex: Implementation of improved uptake of evidence-based fall prevention models in community.

          (2) Ex: Advocacy for reimagining built environment/public spaces at city planning level

5) Neurology Subgroup High-Level Goals
   a) Understand how normal aging affects cognitive, motor, and sensory functions.
   b) Understand how social determinants can affect cognitive, motor, and sensory functions in the elderly.
   c) Understand the genetic architecture of age-related neurodegenerative disorders.
   d) Use functional genomics to identify potential therapeutic targets that might be used to prevent or treat age-related neurodegenerative disorders.

6) Nursing Subgroup High-Level Goals
   a) Research development areas and strategies
      i) COVID-19
         (1) Design studies to evaluate infection control prevention strategies while minimizing impact of social isolation
         (2) Mental health implications
      ii) Shift from palliative care to Healthy Aging concepts
      iii) Technology
      iv) Efficacy of telehealth
         (1) Workforce
      v) Competency
      vi) Tools and resources
         (1) Data aggregation
      vii) Maximize reuse

7) Psychiatry Subgroup High-Level Goals
   a) Clarify the role of mind-body interaction with a focus on the impact of medical disorders on mental health and the impact of mental disorders on physical health in older adults.
   b) Research on interventions to improve quality of life in older adults.
   c) Understand barriers to effective care of mental disorders and improve cost-effectiveness of clinical management of older adults with mental disorders.
   d) Strengthen inter-departmental collaboration for research into common mental disorders in older adults (e.g., depression) and their impact on cognitive decline and dementia.

8) Public Health Subgroup High-Level Goals
   a) Create a health span that approximates increased life span as goal for population health.
   b) Understand how built, social, and climatic environments affect processes that drive aging-related disease, functional decline, and widening disparities – and modifiability.
   c) Establish the role of biological processes of aging in mediating social and environmental drivers of disparities and develop interventions to disrupt these processes to build aging health equity.
   d) Design and implement a roadmap for successfully aging societies, system change, and enable the social capital of older adults.