BOSTON PEPPER CENTER
Claude D. Pepper Older Americans Independence Center

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Program Administrator

CENTER DESCRIPTION

The Boston OAIC is unique in its thematic focus on Function Promoting Therapies (FPTs) and its positioning across the entire spectrum of translational science from mechanism elucidation, preclinical proof-of-concept studies, biomarker validation, epidemiologic investigation to randomized trials of FPTs. The Boston OAIC integrates 19 NIH-funded studies of function promoting therapies, 3 Research Education Component projects, 3 pilot projects, and 3 developmental projects into an interdisciplinary program that is supported by a Leadership and Administrative Core, a Research Education Component (REC), a Pilot and Exploratory Studies Core (PESC), and 3 resource cores (Function Assessment Core, Preclinical Discovery Core, Biostatistical and Data Analysis Core). Our REC and PESC candidates include several rising stars in Geriatrics and Gerontology, including 3 Beeson and K grant awardees. The REC will recruit the most promising stars from a vast reservoir of talent at Harvard, Tufts and BU, and train them through a didactic education and mentored research program. Integration will be achieved by the PROMOTE Program that includes a research concierge service, research meetings, annual retreats, a website and a newsletter. The Boston OAIC is well integrated with the the Harvard Geriatrics and Gerontology research community and programs, including its T32 training grant, Harvard Clinical Translational Science Institute, the Roybal Center, The New England Geriatrics Research Clinical Education Center, and the Glenn Foundation Center for Biology of Aging.

Boston OAIC's unique strengths include its focus on Function Promoting Therapies, emphasis on translation and commercialization, access to a large pool of talented young investigators, its extension across the entire spectrum of translational research, and its infrastructure for developing intellectual property and companies, and supporting several seminal randomized trials of FPTs.

CORES

Leadership and Administrative Core (LAC)

Leader 1: Shalender Bhasin, MD sbhasin@bwh.harvard.edu
Leader 2: Roger Fielding, PhD
Leader 3: Lewis A. Lipsitz, MD lipsitz@hsl.harvard.edu

The LAC is responsible for stimulating, sustaining, evaluating, and reporting OAIC's progress towards its goals and enabling integration of OAIC activities. In addition to providing administrative support, the LAC coordinates the activities of Boston OAIC's investigators, resource cores, its conferences, and career development activities.

Research Education Component (REC)

Leader 1: Lewis A. Lipsitz, MD lipsitz@hsl.harvard.edu
Leader 2: Amy Wagers, PhD
Leader 3: Edward Marcantonio, MD

The overall goal of the Research Education Component (REC) of the Boston OAIC is to train future independent research scientists who have the knowledge and the skill to translate fundamental mechanisms of disease and disability into novel interventions that can improve the health, physical function, and well-being of people as they age. The REC achieves this by selecting the most promising early career scientists from clinical and basic science disciplines and providing them with both collective and individual educational activities, research experiences, mentoring, and career guidance that will enable them to acquire future career development or research awards and ultimately become leaders in translational research devoted to the discovery of function promoting therapies (FPTs).

Pilot and Exploratory Studies Core (PESC)

Leader 1: Monty Montano, PhD MMONTANO@bwh.harvard.edu
Leader 2: Douglas P. Kiel, MD

Within the context of the OAIC's overall mission, the Pilot and Exploratory Studies Core (PESC) aims to provide catalytic support – seed funding, core support, and mentorship – for innovative pilot research projects that generate data on the mechanisms of FPT action to facilitate more definitive mechanistic studies, feasibility data to guide efficacy trials, hypothesis generating or proof-of-concept exploratory studies and retrospective analysis of existing epidemiologic data that inform FPT interventions.

Biostatistical Design and Analysis Core (BDAC)

Leader 1: Thomas Travison, PhD TGT@hsl.harvard.edu
Leader 2: Karol Pencina, PhD

The BDAC provides collaborative support in the design, execution and analysis of clinical trials and epidemiology studies conducted at the Boston OAIC. Additionally, the BDAC provides mentoring and collaborative opportunities for students and junior faculty in quantitative aspects of the study of physical function and impairments in aging. The BDAC is equipped to provide critical services on a consulting basis (e.g. in an advisory capacity in critical review of study data collection procedures) and more formally (e.g. in conducting simulation studies and power calculation).

Furthermore, the BDAC provides support for ongoing projects by providing critical review and expertise in evaluating study conduct, or more extensive, pre-specified contributions to trial objectives. Support services for study completion are also available in providing guidance and assistance in statistical analyses, as well as co-authorship of abstracts and manuscripts describing study results.

Development Projects Core

Leader 1: Shalender Bhasin, MD sbhasin@bwh.harvard.edu

The Developmental Projects core funds pilot projects chosen based on their innovation and translational value, and the need and potential of novel methods to advance OAIC projects

Functional Assessment Core (FAC)

Leader 1: Roger Fielding, PhD roger.fielding@tufts.edu
Leader 2: Kieran Reid, Ph.D. Kieran.Reid@tufts.edu

The FAC represents a strategic interdisciplinary alliance between the Muscle Mechanics and Metabolomics Laboratory, the Laboratory of Exercise Physiology and Physical Performance and the Health and Disability Research Institute at Boston University and the Nutrition, Exercise Physiology and Sarcopenia Laboratory at the Jean Mayer USDA Human Nutrition Research Center on Aging at Tufts University. The core provides standardized, state-of-the-art technologies to measure muscle performance, functional limitations, and disability in human and animal studies for OAIC's pilot and exploratory projects and for several OAIC related projects funded through other sources.

Translational Discovery Core (TDC)

Leader 1: Ravi Jasuja, PhD

The ability to genetically modify rodents has increased the need to assess reproducibly and quantifiably, the phenotype of these animals with respect to body composition and physical function. In addition to utilizing the small animal resource services, the Translational Discovery Core (TDC) provides the infrastructural and consultative support for non-invasive measurements of alterations in body composition, muscle performance, physical function and metabolic performance to facilitate longitudinal studies of FPTs during aging and metabolic stress. The PDC is also continuing its mission to spearhead innovation- development of novel 7Tesla MRI techniques to provide mechanistic insights into FPT interventions.

CAREER DEVELOPMENT

REC Scholar, Research & Grants Funded During Pepper Supported Time	Years / Publications

Sandra Shi, MD 2022-2024 /
Instructor / Harvard Medical School and Hebrew SeniorLife 9 (total)
Feasibility of a Multicomponent Frailty Intervention Adapted to the Post-Acute Nursing Setting -4 (1st/Sr)

Research focuses on improving patient centered outcomes and inform complex shared decision making in older adults with frailty requiring post-acute care at skilled nursing facilities.

- R03AG078894-01 (Aug 1, 2022 - Aug 1, 2024), NIH/NIA, Predicting and Identifying Risk Factors for Short Time at Home in Older Adults after Hospitalization

Jonathan Cunningham, MD MPH 2022-2024 /
Instructor / Harvard Medical School 25 (total)
Proteomic Profiles of Aging in Heart Failure with Preserved Ejection Fraction 3 (1st/Sr)

He seeks to leverage large-scale proteomics to identify heart failure patients with distinct physiology and more precisely target heart therapies in clinical trials.

- KL2/Catalyst Medical Research Investigator Training (CMeRIT) / Boston Claude D. Pepper Older Americans Independence Center
- American Heart Association Career Development Award 4/1/2023-3/30/2026. Title Biomarkers and Treatment of Myocardial Fibrosis in HFpEF

Heidi Kletzien, PhD 2022-2024 /
Postdoctoral Fellow / Harvard University 19 (total)
Impact of biologic sex and age on epigenetic and regenerative capacity of head and neck stem cells 5 (1st/Sr)

Characterization and quantification of stem cells in the head and neck tissues of young and aged male and female mice and in isochronic and heterochronic parabionts.

- NIA NRSA F32: In vivo screening to identify cellular and (epi) genetic mechanisms driving sex- and age-biased development of head and neck cancers
- Aramont Fellowship Fund for Emerging Science Research: Uncovering clonal mechanisms of head and neck cancer initiation and progression

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Past Scholars

Jason Sanders, MD, Harvard Medical School (2020-2021)
Hao Zhou, MD, PhD, Harvard Medical School (2020-2022)
Daniel Roh, MD, Boston University (2021-2022)
Sari Reisner, DSc., Harvard Medical School (2021-2022)
Sanjay Divakaran, MD, Harvard Medical School (2021-2022)
Timothy Anderson, MD, Harvard Medical School (2021-2022)
Clark DuMontier, MD, Harvard Medical School (2021-2022)

PILOT/EXPLORATORY PROJECTS (4 Pilot Projects Listed)

1. **Project Title:** **PES-3: Stress-driven acceleration of epigenetic age and inflammation in transgender adults.**

   Leader: **PIs: Sari Reisner, ScD and Monty Montano, PhD**

   Results from this study will establish whether there is a link between exposure to gender-related psychosocial stress and epigentic age (DNA methylation score) and inflamm-aging (e.g., elevated CRP, IL-6 levels); and whether epigentic age and inflammation are related to levels of physical function. The study outcomes will inform a followup R01 to evaluate a combined behavioral and exercise intervention to reverse accelerated aging and inflamm-aging due to life course exposure to psychosocial stressors.

2. **Project Title:** **REC-4: Skeletal Muscle Perfusion and Energetics in Patients with Symptomatic Peripheral Artery Disease. Joint Boston OAIC-Harvard Catalyst C-MERIT Awardee.**

   Leader: **Sanjay Divakaran, MD**

   Dr. Divarkaran is an Instructor in Medicine in the Division of Cardiology, BWH. His research focuses on using perfusion and metabolic positron emission tomography (PET) and magnetic resonance spectroscopy (MRS) to uncover changes in oxygen delivery and metabolism in older individuals with peripheral artery disease. Studying patients with PAD at rest and post-exercise with PET and MRS has the potential to help better phenotype patients with PAD and address critical gaps in knowledge regarding the pathophysiology of intermittent claudication. For the OAIC REC, he proposes to use PET, MRS, and omics technologies to study 10 older adults with PAD before and after endovascular revascularization procedures. He will perform novel pre- and post-exercise plasma biomarker discovery by measuring differential microRNA expression and targeted protein biomarkers. His mentors are Dr. Marcelo Di Carli, a world-expert in perfusion and metabolic PET imaging, and Dr. Mark Feinberg, Director of the Program of Cardiovascular RNA Biology at BWH. He will utilize the OAIC Functional Assessment, Preclinical Discovery, and Biostatistical Design and Analysis Cores.

3. **Project Title:** **Reversing aging-induced wound healing via androgen-estrogen modulation**

   Leader: **Devin O'Brien-Coon, MD MS**

   Dr. O’Brien-Coon had three aims for his project, which overall will be testing approaches to reverse aging-induced wound healing dysfunction via androgen-estrogen axis modulation. In Aim 1, Dr. O’Brien-Coon planned to characterize the effects of testosterone and estradiol on increased inflammation and delayed wound closure in his stented-wound model in young vs elderly mice. In Aim 2, he planned to study the differential effects of cross-sex testosterone on wound healing in elderly mice vs young controls. Towards these aims he developed and tested sustained-release estradiol implants and achieved desired levels in the wound healing group given the implants. He also developed and switched to a rat wound model due to the need for larger wounds than achievable in mice so that he could measure desired outcomes. Just prior to this progress report submission, he performed castrated rat wound healing model surgeries to finalize estradiol implant performance; if successful he will then repeat experiments with aged rats. Finally in Aim 3, he will be assessing the mechanisms and potential of sex hormone

receptor modulation as a therapeutic target to restore wound repair function in elderly mice. Progress in this aim was marked by Dr. O'Brien-Coon starting a new collaboration with Dr. Ameya Kirtane, who specializes in drug delivery, to formulate more reliable topical anti-androgen/pro-estrogen formulations for sustained wound delivery since existing topicals are for transdermal release which is the opposite goal of his project.

4. Project Title: **PHD2 modulation on muscular adaptation to exercise and functional improvement.**

Leader: **Yori Endo, MD**

Dr. Endo's project is focused on age-related elevations in PHD2 as the mechanistic link between the loss of hypoxia-dependent muscular adaptation to exercise and diminished functional gain in aged muscle. This project was based on the finding that prolyl hydroxylase domain enzyme (PHD2), an enzyme which leads to the degradation of hypoxia inducing factors and loss of hypoxia pathway signaling, was found to be elevated systemically in older adults and in skeletal muscle in old mice. In Aim 1, Dr. Endo is assessing whether increased skeletal muscle PHD2 limits response to aerobic exercise in aging mice. In specific Aim 2, Dr. Endo will evaluate whether pharmacologic inhibition of PHD2 improves muscle adaptation to aerobic exercise. Dr. Endo has made good progress so far, this first year. Using a hypoxia signaling hypomorphic mouse model, she is investigating the effect of blunted hypoxia signaling on exercise response in young and old mice. She has completed several rounds of exercise treatment and are analyzing and processing the physiological data. She will then begin to perform biochemical analyses to further characterize the effect of the loss of hypoxia signaling on muscle following exercise.

DEVELOPMENT PROJECTS (3 Development Projects Listed)

1. **Project Title:** **DP-2: Measuring intracellular NAD in skeletal muscle and brain using 7T magnetic resonance spectroscopy**

   Leader: **Alex Lin, PhD and Ravi Jasuja, PhD**

   Core(s):

   The use of 7T MR spectroscopy to measure intracellular NAD in skeletal muscle and brain is novel and will be of value to ongoing and planned studies of NAD activators.

2. **Project Title:** **DP-3: A novel statistical method to compare interventions initiated over time.**

   Leader: **Karo Pencina, PhD, Co-I: Thomas Travison, PhD.**

   Core(s):

   A novel statistical method to compare treatments initiated over time to enable epidemiological assessment of treatment disparities in older adults.

3. **Project Title:** **DP-1. Development of novel remote sensing technology to assess muscle performance in community dwelling older adults**

   Leader: **Roger A. Fielding, Tufts-HNRCA, Kieran F. Reid, Brigham and Women's Hospital and Conor J. Walsh, Harvard University**

   Core(s):

   This project will focus on the refinement of prototypes to collect data from the appropriate body segments during strength training and assessment, develop algorithms to appropriately interpret the sensor data, and refine an initial web application. Finally, we will validate and evaluate the technology with established gold-standard assessment measures of muscle strength, power, and fatigue in older adults. Aim 1. Wearable technology development. Previously, the Biodesign Lab developed a modular and wearable hardware system, which includes two Inertial Measurement Units (IMUs). Aim 2. Validation study: The prototype technology platform will be developed to capture sensor-based measures of muscle performance (muscle force, contractile velocity, power and fatigue). The reliability, reproducibility and instrumental validity of muscle performance measures will be quantitively assessed and directly compared to several gold-standard, laboratory-based assessments of muscle performance and physical function. Aim 3. Single participant longitudinal case study: One participant will train three times per week for 8 weeks in their home. Since the technology is not yet suitable for independent home use, a member of the research team will visit the participant's home.

RESEARCH (0 Projects Listed)

PUBLICATIONS

2024

2023

1. **Optimizing the Design of Clinical Trials to Evaluate the Efficacy of Function-Promoting Therapies.**
   Bhasin S, Cawthon PM, Correa-de-Araujo R, Storer TW, Volpi E, Newman AB, Dioh W, Tourette C, Evans WJ, Fielding RA
   J Gerontol A Biol Sci Med Sci, 2023 Jun 16, 78(Supplement_1): 86-93
   https://doi.org/10.1093/gerona/glad024 | PMID: 37325959 | PMCID: PMC10272979
   Citations: 1 | AltScore: NA
2. **Androgens and Selective Androgen Receptor Modulators to Treat Functional Limitations Associated With Aging and Chronic Disease.**
   Bhasin S, Krishnan V, Storer TW, Steiner M, Dobs AS
   J Gerontol A Biol Sci Med Sci, 2023 Jun 16, 78(Supplement_1): 25-31
   https://doi.org/10.1093/gerona/glad027 | PMID: 37325955 | PMCID: PMC10272983
   Citations: 1 | AltScore: 5.85
3. **Benefits and Barriers of Technology for Home Function and Mobility Assessment: Perspectives of Older Patients With Blood Cancers, Caregivers, and Clinicians.**
   Clancy DD, Revette AC, Bahl NE, Ho KT, Manor B, Testa MA, Dieli-Conwright CM, Hshieh T, Driver JA, Abel GA, DuMontier C
   JCO Clin Cancer Inform, 2023 Apr, 7: e2200171
   https://doi.org/10.1200/CCI.22.00171 | PMID: 37098230 | PMCID: PMC10281405
   Citations: NA | AltScore: NA
4. **Anorexia in Medicare Fee-for-Service Beneficiaries: A Claims-Based Analysis of Epidemiology and Mortality.**
   Dagenais S, Fielding RA, Clark S, Cantu C, Prasad S, Groarke JD
   J Nutr Health Aging, 2023, 27(3): 184-191
   https://doi.org/10.1007/s12603-023-1882-4 | PMID: 36973924 | PMCID: PMC9841141
   Citations: 1 | AltScore: 2.5
5. **Implementing 4-meter gait speed as a routine vital sign in a thoracic surgery clinic.**
   Deeb AL, Garrity M, Cooper L, Frain LN, Jaklitsch MT, DuMontier C
   J Geriatr Oncol, 2023 May, 14(4): 101481
   https://doi.org/10.1016/j.jgo.2023.101481 | PMID: 37060720 | PMCID: PMC10445274
   Citations: NA | AltScore: 4.35
6. **Novel Potential Targets for Function-Promoting Therapies: Orphan Nuclear Receptors, Anti-inflammatory Drugs, Troponin Activators, Mas Receptor Agonists, and Urolithin A.**
   Dioh W, Narkar V, Singh A, Malik F, Ferrucci L, Tourette C, Mariani J, van Maanen R, Fielding RA
   J Gerontol A Biol Sci Med Sci, 2023 Jun 16, 78(Supplement_1): 44-52
   https://doi.org/10.1093/gerona/glad072 | PMID: 37325960 | PMCID: PMC10272986
   Citations: 1 | AltScore: NA
7. **VEGFA Promotes Skeletal Muscle Regeneration in Aging.**
   Endo Y, Hwang CD, Zhang Y, Olumi S, Koh DJ, Zhu C, Neppl RL, Agarwal S, Sinha I
   Adv Biol (Weinh), 2023 Mar 29 e2200320

https://doi.org/10.1002/adbi.202200320 | PMID: 36988414 | PMCID: PMC10539483
Citations: NA | AltScore: NA

8. **Editorial: Outcomes for Regulatory Approval in Geriatrics: Embracing Loss of Mobility and Mobility Disability as Clinically Meaningful Therapeutic Indications.**
Fielding RA, LeBrasseur NK
J Nutr Health Aging, 2023, 27(7): 496-497
https://doi.org/10.1007/s12603-023-1944-7 | PMID: 37498095
Citations: NA | AltScore: 1.5
9. **Multi-modal profiling of peripheral blood cells across the human lifespan reveals distinct immune cell signatures of aging and longevity.**
Karagiannis TT, Dowrey TW, Villacorta-Martin C, Montano M, Reed E, Belkina AC, Andersen SL, Perls TT, Monti S, Murphy GJ, Sebastiani P
EBioMedicine, 2023 Apr, 90: 104514
https://doi.org/10.1016/j.ebiom.2023.104514 | PMID: 37005201 | PMCID: PMC10114155
Citations: 6 | AltScore: 749.954
10. **Geriatric Syndromes and Health-Related Quality of Life in Older Adults with Chronic Kidney Disease.**
Liu CK, Miao S, Giffuni J, Katzel LI, Fielding RA, Seliger SL, Weiner DE
Kidney360, 2023 Apr 1, 4(4): e457-e465
https://doi.org/10.34067/KID.0000000000000078 | PMID: 36790849 | PMCID: PMC10278840
Citations: NA | AltScore: 5.85
11. **Association of Proinflammatory Diet With Frailty Onset Among Adults With and Without Depressive Symptoms: Results From the Framingham Offspring Study.**
Millar CL, Dufour AB, Hebert JR, Shivappa N, Okereke OI, Kiel DP, Hannan MT, Sahni S
J Gerontol A Biol Sci Med Sci, 2023 Feb 24, 78(2): 250-257
https://doi.org/10.1093/gerona/glac140 | PMID: 35830506 | PMCID: PMC9951064
Citations: NA | AltScore: 257.06
12. **Maladaptive Immune Activation in Age-Related Decline of Muscle Function.**
Montano M, Correa-de-Araujo R
J Gerontol A Biol Sci Med Sci, 2023 Jun 16, 78(Supplement_1): 19-24
https://doi.org/10.1093/gerona/glad036 | PMID: 37325961 | PMCID: PMC10272988
Citations: 1 | AltScore: 2.5
13. **Mild Neurocognitive Disorder, Social Engagement, and Falls Among Older Primary Care Patients.**
Quach LT, Pedersen MM, Ogawa E, Ward RE, Gagnon DR, Spiro A, Burr JA, Driver JA, Gaziano M, Dhand A, Bean JF
Arch Phys Med Rehabil, 2023 Apr, 104(4): 541-546
https://doi.org/10.1016/j.apmr.2022.10.008 | PMID: 36513122 | PMCID: PMC10073260
Citations: NA | AltScore: 0.5
14. **Higher abdominal adiposity is associated with higher lean muscle mass but lower muscle quality in middle-aged and older men and women: the Framingham Heart Study.**
Raghupathy R, McLean RR, Kiel DP, Hannan MT, Sahni S
Aging Clin Exp Res, 2023 Jul, 35(7): 1477-1485
https://doi.org/10.1007/s40520-023-02427-6 | PMID: 37166563 | PMCID: PMC10450777
Citations: NA | AltScore: 1.85
15. **Association of Vascular Health Measures and Physical Function: A Prospective**

Analysis in the Framingham Heart Study.
Sahni S, Dufour AB, Wang N, Kiel DP, Hannan MT, Jacques PF, Benjamin EJ, Vasan RS, Murabito JM, Newman AB, Fielding RA, Mitchell GF, Hamburg NM
J Gerontol A Biol Sci Med Sci, 2023 May 15, 78(7): 1189-1197
pii: glad097. https://doi.org/10.1093/gerona/glad097 | PMID: 37183502 | PMCID: PMC10329234
Citations: NA | AltScore: 163.1

16. **Mortality and Heart Failure Hospitalization Among Young Adults With and Without Cardiogenic Shock After Acute Myocardial Infarction.**
Siddiqi HK, Defilippis EM, Biery DW, Singh A, Wu WY, Divakaran S, Berman AN, Rizk T, Januzzi JL, Bohula E, Stewart G, Carli MD, Bhatt DL, Blankstein R
J Card Fail, 2023 Jan, 29(1): 18-29
https://doi.org/10.1016/j.cardfail.2022.08.012 | PMID: 36130688 | PMCID: PMC10403806
Citations: 1 | AltScore: 32.6
17. **Dairy Food Intake Is Not Associated With Frailty in Adults From the Framingham Heart Study.**
Siefkas AC, Millar CL, Dufour AB, Kiel DP, Jacques PF, Hannan MT, Sahni S
J Acad Nutr Diet, 2023 May, 123(5): 729-739.e1
https://doi.org/10.1016/j.jand.2022.09.012 | PMID: 36108932
Citations: NA | AltScore: NA
18. **Biomarkers of cellular senescence and risk of death in humans.**
St Sauver JL, Weston SA, Atkinson EJ, Mc Gree ME, Mielke MM, White TA, Heeren AA, Olson JE, Rocca WA, Palmer AK, Cummings SR, Fielding RA, Bielinski SJ, LeBrasseur NK
Aging Cell, 2023 Oct 6 e14006
https://doi.org/10.1111/acel.14006 | PMID: 37803875
Citations: NA | AltScore: NA
19. **Exercise and Behavior: Adjuncts to Pro-Myogenic Compounds for Enhancing Mobility in Older Adults.**
Storer TW, Pahor M, Woodhouse LJ, Lachman ME, Fielding RA
J Gerontol A Biol Sci Med Sci, 2023 Jun 16, 78(Supplement_1): 61-66
https://doi.org/10.1093/gerona/glad041 | PMID: 37325956 | PMCID: PMC10272978
Citations: NA | AltScore: NA
20. **Testosterone replacement in prostate cancer survivors with testosterone deficiency: Study protocol of a randomized controlled trial.**
Valderr?bano RJ, Pencina K, Storer TW, Reid KF, Kibel AS, Burnett AL, Huang G, Dorff T, Privat F, Ghattas-Puylara C, Wilson L, Latham NK, Holmberg M, Bhasin S
Andrology, 2023 Jan, 11(1): 93-102
https://doi.org/10.1111/andr.13299 | PMID: 36181480 | PMCID: PMC9771994
Citations: NA | AltScore: 9.25
21. **Successful aging after elective surgery II: Study cohort description.**
Ward M, Hshieh TT, Schmitt EM, Arnold SE, Cavallari M, Dickerson BC, Dillon ST, Fong TG, Jones RN, Libermann TA, Pascual-Leone A, Shafi MM, Touroutoglou A, Weng K, Xu G, Earp BE, Kunze L, Lange J, Vlassakov K, Marcantonio ER, Inouye SK, Travison TG, SAGES II Study Team
J Am Geriatr Soc, 2023 Oct 12
https://doi.org/10.1111/jgs.18627 | PMID: 37823746
Citations: NA | AltScore: 2
22. **Association Between Systemic Vasculitis and Coronary Microvascular Dysfunction in**

the Absence of Obstructive Coronary Artery Disease.
Weber B, Wallace ZS, Parks S, Cook C, Huck DM, Garshick M, Brown JM, Divakaran S, Hainer J, Dorbala S, Blankstein R, Liao KP, Aghayev A, Choi HK, Di Carli M
Circ Cardiovasc Imaging, 2023 Jan, 16(1): e014940
https://doi.org/10.1161/CIRCIMAGING.122.014940 | PMID: 36649456 | PMCID: PMC9999265
Citations: NA | AltScore: NA

23. **Effect of Long-term Exercise Training on Physical Performance and Cardiorespiratory Function in Adults With CKD: A Randomized Controlled Trial.**
Weiner DE, Liu CK, Miao S, Fielding R, Katzel LI, Giffuni J, Well A, Seliger SL
Am J Kidney Dis, 2023 Jan, 81(1): 59-66
https://doi.org/10.1053/j.ajkd.2022.06.008 | PMID: 35944747 | PMCID: PMC9780154
Citations: 3 | AltScore: 59

EXTERNAL ADVISORY BOARD MEMBERS

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RECOGNITION AND AWARDS (2023-2024)

Amy Wagers (2023)

- Recipient of NIH Director's Pioneer Award; Member of the NIA Council

Lew Lipsitz (2023)

- Appointed Editor-in-Chief of the Journal of Gerontology Series A Medical Sciences

Monty Montano (2023)

- Appointed Editor-in-Chief, Aging Cell
- Recipient of a Merck Investigators Study Program Award

Roger Fielding (2023)

- The ESCEO-IOF Herbert Fleisch Medal, awarded annually by the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO) and the International Osteoporosis Foundation (IOF). Chair, ASG Study Section; Appointed Associate Director of the Jean Mayer USDA Human Nutrition Research Center on Aging

Shalender Bhasin (2023)

- Member of the NIA Council
- Appointed Co-Director, Center for Transgender Health, Brigham and Women's Hospital

MINORITY RESEARCH

General Brief Description of Minority Activities:
Not defined.

Minority Trainee(s):

- Rodrigo Valderrabano, MD, MSc., Assistant Professor of Medicine
  Dr. Valderrabano was recruited to Mass General Brigham from the University of Miami, Miami, FL, where he was an Assistant Professor of Medicine at the University of Miami, Miami, FL. Dr. Valderrabano received his medical degree from the Medical School in Puerto Rico and did a fellowship in Bone Health at Stanford University. Dr. Valderrabano is currently interested in muscle / bone dysfunction in people with diabetes and spinal cord injury. Integrating aging and outcomes of physical activity interventions is planned. Dr. Valderrabano is also coinvetigator on two research projects with Dr. Montano that are focused on HIV and Aging and COVID-19, respectively. Received a career development award in 2022

Minority Grant(s):

1. **Project Title:** **ROLE OF MICRORNAS ON AGE AND CONTRACTION-INDUCED SKELETAL MUSCLE GROWTH**
   Leader(s): **RIVAS, DONATO A**
   TUFTS UNIVERSITY BOSTON
   NIH K01AG047247 / (2015-2020)

DESCRIPTION (provided by applicant): The age-associated loss of skeletal muscle mass and function (sarcopenia) is associated with substantial social and economic costs. The plasticity and adaptability of skeletal muscle to contraction (i.e. resistance-exercise) is a fundamental physiological event leading to larger and more robust skeletal muscle. However, muscle growth in response to resistance exercise (RE), like other anabolic stimuli, is attenuated in older adults The cause of aberrant muscle adaptation with aging is complex. Recent work has revealed a novel role for small non-coding RNAs, called microRNAs (miRNA) in the regulation of gene expression. Using an integrated bioinformatics analysis of protein-coding gene and miRNA array data from young and older men, I identified ten specific miRNAs as important regulators of muscle plasticity (Plasticity Related miRs [PR-miRs]) leading to the transcriptional response to exercise and lean mass in young and older men. However, the precise mechanisms underlying the expression of PR-miRs on age-related changes in muscle anabolism and sarcopenia are currently unknown. Thus, the overall objective of this K01 application will be to determine the mechanistic role(s) of these PR-miRs in skeletal muscle adaptation to anabolic stimulation in 1) healthy young, 2) sarcopenic older and 3) age- and functionally-matched non-sarcopenic older males and females. This will be accomplished by determine the differences in expression of PR-miRs with aging and sarcopenia in response to anabolic stimulation (AIM 1). Mechanistically determine the extent to which manipulation of PR-miR levels in vitro, in human primary myocytes, can reverse anabolic resistance observed with age and sarcopenia (AIM 2) and the effect of altering PR-miRs levels on skeletal muscle growth and development (AIM 3). This project will improve our understanding of the molecular mechanisms that contribute to the loss of skeletal muscle and eventually leading to the

development of drug therapies for the treatment of sarcopenia in the ever growing aging population. The mentorship team includes, Dr. Roger Fielding, a leader in aging research and muscle biology, Dr. Kenneth Walsh, a cardiovascular researcher and leading molecular biologist, Dr. Laurence Parnell a computational biologist and authority in gene and miRNA expression analysis, Dr. Thomas Gustafsson a physician-scientist and clinical researcher and Dr. Thomas Travison an expert in biostatistics. The mentorship team has a variety of know-how in every facet of this project including, conducting human clinical trials and skeletal muscle biology, computational biology and genomics and molecular biology and mechanisms. The proposed career development plan includes research-oriented and didactic training at Tufts University, Boston University and the Karolinska Institute in Stockholm,Sweden. The pursuit of the specific aims of the research project, the multidisciplinary mentorship team and the career development plan will facilitate a transition to an independent research career.

2. Project Title: **THE ENRGISE STUDY**
Leader(s): **PAHOR, MARCO ; AMBROSIUS, WALTER T ;**
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Growing evidence from our group and others shows that low-grade chronic inflammation, characterized by elevations in plasma C-reactive protein, tumor necrosis factor alpha, and particularly Interleuk