SKELETAL MUSCLE IN AGING, HEALTHSPAN AND DISEASE

A SYMPOSIUM ORGANIZED BY

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Dr. Joanne Bujnoski & Martin Kandes

BASIS FOR THE SYMPOSIUM

Skeletal muscle – the most abundant human tissue comprising ~40% of bodyweight and containing up to 75% of total body protein – is vital to virtually all aspects of human health extending to the management of disease. Muscle mass and function are key determinants of healthspan, morbidity, and mortality. Beyond mobility and postural stability, skeletal muscle is essential to metabolic homeostasis, thermoregulation, and inter-organ communication. As the body's primary source of amino acids, skeletal muscle is key to the management of age-related chronic diseases, acute infections, injuries, other immune system challenges, and cancer. Muscle is also increasingly recognized as a potent endocrine tissue, with active muscle producing myokines and other factors that impact cognition, mood, and visceral organ functions.

With a complex and incompletely understood interplay of biological and behavioral underpinnings, muscle mass and function decline steadily with advancing age, accompanied by physical disability, metabolic dysregulation, and a compromised immune system. The importance and efficacy of exercise training, nutrition, and other lifestyle elements (e.g., sleep, stress management) are well-recognized but gaps in both knowledge and application remain. Development of non-behavioral countermeasures (e.g., pharmacologic, technologic) has been challenging but remains an aggressive pursuit with promise.

According to the WHO, 1 in 6 people worldwide will be 60+ years of age by 2030, totaling 1.4 billion. And by 2050, the 80+ population is projected to triple, reaching 426 million. Aging muscle atrophy is thus among the most pressing but perhaps under-appreciated public health challenges of our time. The biomedical research enterprise, policy makers, regulators, and investors all have important roles in responding to this scientific and public health challenge.

Convening an interdisciplinary team of thought leaders and experienced researchers, the tripartite purpose of this symposium is to: (i) present and discuss the state of knowledge on mechanisms and countermeasures; (ii) identify remaining gaps and limitations; and (iii) chart a path toward high-impact research priorities that will ultimately benefit the world's aging population.

SUE BODINE, PHD

MuRF1, E3 Ubiquitin Ligases and the Regulation of Skeletal Muscle Mass

Dr. Bodine is a Professor in the Aging and Metabolism Research Program at the Oklahoma Medical Research Foundation and a Research Biologist at the Oklahoma City Veteran's Affairs Medical Center. Her research is focused on the study of the neuromuscular system and its response and adaptation to both positive and negative stressors, including exercise, microgravity, disuse, denervation, and aging. A major focus of her lab has been in understanding the mechanisms that regulate skeletal muscle size under growth and atrophy conditions, with specific investigation of the role of E3 ligases in the regulation of skeletal muscle mass. The lab also investigates the effect of aging on skeletal muscle mass and function, with a focus on identifying the mechanisms underlying the poor recovery of mass and function following atrophy in aged animals. Currently, her lab is a Preclinical Animal Study Site involved in the Molecular Transducers of Physical Activity Consortium (MoTrPAC). She has served as Chair and regular member of the Skeletal Muscle and Exercise Physiology review panel and as a regular member of the Aging Systems and Geriatrics review panel. She served as Editor-In-Chief of the Journal of Applied Physiology (2017-2023) and is currently an Executive Editor of Function and on the editorial board of Physiological Reviews.

AMANDA BOYCE, PHD

NIA Research Priorities in Aging Skeletal Muscle & Healthspan

Dr. Boyce is a Program Director and the Chief of the Aging Physiology Branch, Division of Aging Biology at the National Institute on Aging. She received her bachelor's degree in biology from the University of Texas at Austin and completed her Ph.D. in Cell Biology at the University of Alabama at Birmingham (UAB). During her graduate studies, Dr. Boyce conducted research on epithelial cell ion channels under the mentorship of Dr. Erik Schwiebert. As a post-doctoral fellow, she studied under Dr. Rosa Serra at UAB and then Dr. Rocky Tuan in the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS)'s Intramural Research Program working in cartilage development, osteoarthritis, and fracture healing. She left the bench and joined NIAMS as a Program Officer for Muscle Development and Physiology in 2006 and served through 2022. Dr. Boyce joined NIA in 2022 and manages a portfolio of grants focused on the basic biology of muscle and tendon.

CYNTHIA J. BROWN, PT, MD, MSPH

Hospital Associated Disability

Dr. Brown completed an undergraduate degree in physical therapy from East Carolina University and a MD from the University of North Carolina at Chapel Hill. At Yale University, Dr. Brown completed residency training in internal medicine, which included a Chief Resident year, and a three-year Geriatric Medicine fellowship. She was on faculty at the University of Alabama at Birmingham (UAB) from 2003 – 2021 where she served as the Division Director for Gerontology, Geriatrics, and Palliative Care, and Director of the UAB Center for Healthy Aging. In May 2021, Dr. Brown became Chair of the Department of Internal Medicine at Louisiana State University Health Sciences Center. Dr. Brown's research interests combine the issues of low mobility and falls in the hospitalized older adult.

KARYN ESSER, PHD

The Aging Circadian Clock in Muscle: A New Target for Therapeutics?

Dr. Esser is Professor and Chair of the Department of Physiology and Aging at the University of Florida. Dr. Esser's lab has been at the forefront in the study of circadian rhythms, circadian clocks and skeletal muscle health. In 2002, her lab made a serendipitous discovery that genes controlling the body's "biological clock" also were part of the response of muscle to high force contractions. This discovery changed the trajectory of her research program to a new focus on understanding circadian clock biology in skeletal muscle. Dr Esser's group has demonstrated that the muscle circadian clock is necessary for maintaining healthy muscle metabolism and muscle strength. In addition, her research has uncovered the importance of the muscle clock on systemic health including contributions to sleep and systemic signatures of inflammation. Her lab is actively studying 1) the role of muscle circadian clocks in the acute and trained response to exercise and 2) how the muscle clock changes with age and strategies to improve muscle clock function to support muscle and system health.

ROGER A. FIELDING, PHD

Resistance Training in Older Adults: a Function Promoting Therapy with Robust Treatment Response Heterogeneity

Dr. Fielding is a Senior Scientist with the Metabolism and Basic Biology of Aging Directive at the Jean Mayer USDA Human Nutrition Research Center on Aging at Tufts University. He is also Professor of Nutrition at the Friedman School of Nutrition Science and Policy, Professor of Medicine at Tufts University School of Medicine and Associate Director of the Boston Claude D. Pepper Older Americans Independence Center. Dr. Fielding received his Bachelor of Science in Applied Physiology from Boston University in 1983, a Master of Arts in Physical Education from Ball State University in 1985, and a PhD in Nutrition from Tufts University in 1993. Dr. Fielding is an internationally known researcher who studies the underlying mechanisms contributing to the age-associated decline in skeletal muscle mass, the resultant impact on function, and the potential role of exercise, nutrition, physical activity and other therapies on attenuating this process. He has published over 300 peer-reviewed papers (H-index 117). Dr. Fielding has a strong record of extramural funding including support from the NIH, USDA, foundations and industry. He is a Deputy Editor of the Journals of Gerontology Medical Sciences, and Calcified Tissues International and Musculoskeletal Research. He has also served as a reviewer on numerous NIH study sections and was elected to the NIH/CSR College of Reviewers. In 2015, he received the Olof Johnell Science Award from the International Osteoporosis Foundation and in 2021 he received the Herbert Fleisch Medal from the same organization. In 2024, he received the Excellence in Rehabilitation of Aging Persons Award from the Gerontological Society of America.

RUSSELL HEPPLE, PHD

Mitochondrial Involvement in Aging Skeletal Muscle

Dr. Hepple is a Professor of Muscle Biology at the University of Florida. Russ did his PhD at the University of Toronto where he did his first studies looking at the effects of resistance versus endurance exercise on skeletal muscle in elderly humans. He did his Postdoctoral studies at the University of California San Diego where he learned to use animal models and began to integrate studies of the microvasculature and mitochondria in skeletal muscle. He started his independent research career at the University of Calgary where he spent 11 years building a lab focused on the mechanisms of skeletal muscle deterioration with aging and investigating the protective effects of exercise and caloric restriction in rodent models. He then spent 6 years at McGill University where he began integrating studies of human populations with exceptional maintenance of physical function well into their later years: octogenarian track and field athletes. He joined the University of Florida in 2017 where he has continued parallel work addressing mitochondrial mechanisms of skeletal muscle impairment with aging in rodent models and human translational studies focused on understanding mechanisms that underlie extremes in physical function in advanced age (from frail elderly to competitive masters athletes). Russ is currently the MPI overseeing the skeletal muscle biology in the Study of Muscle Mobility and Aging (SOMMA), which is a large human cohort of elderly men and women 70 y and older. He is also PI and MPI on grants addressing the role of mitochondrial permeability transition in skeletal muscle dysfunction and systemic inflammation in sepsis, and the role of kynurenines in accelerating aging muscle biology in rodent models.

NATHAN LEBRASSEUR, PT, PHD

Cellular Senescence and Skeletal Muscle Aging

Dr. LeBrasseur holds the Noaber Foundation Professorship in Aging Research and has appointments in the Department of Physical Medicine and Rehabilitation and the Department of Physiology and Biomedical Engineering at Mayo Clinic. Dr. LeBrasseur is the Director of the Robert and Arlene Kogod Center on Aging and Co-Director of the Paul F. Glenn Center for Biology of Aging Research at Mayo Clinic. He is the recent chair of the NIH Cellular Mechanisms in Aging and Development Study Section. Dr. LeBrasseur's research team conducts translational "bench-to-bedside" research on strategies to improve physical function, metabolism, and resilience in the face of aging and disease. His latest work has centered on cellular senescence, a fundamental mechanism of aging, and interventions to counter this process to extend healthspan. Dr. LeBrasseur has received the Glenn Award for Research in Biological Mechanisms of Aging, the Nathan W. Shock Award Lecture from the National Institute on Aging, and the Vincent Cristofalo Rising Star Award in Aging Research from the American Federation for Aging Research. He is a Fellow of the Gerontological Society of America.

DAVID GLASS, PHD

Age-Regulated Mechanisms Affecting Skeletal Muscle Mass and Function

David J. Glass, MD, is a Vice President of Research, overseeing a group focused on Aging and Age-associated Disorders, and is the head of the Postdoctoral fellow program at Regeneron Pharmaceuticals, Inc. Dr. Glass is also a Senior Lecturer in the Department of Cell Biology at Harvard Medical School, and an Adjunct Professor in the Department of Genetics & Development at Columbia University's Vagelos School of Medicine. He holds a BS from Columbia, an MD from New York Medical College and conducted postdoctoral work at Columbia University. He's an elected fellow of AAAS and ASCI, and an elected member of the National Academy of Sciences. He is the co-author of more than 130 peer-reviewed research articles on cell signaling mechanisms in neuromuscular junction formation, skeletal muscle atrophy & hypertrophy, obesity, and mechanisms associated with aging. He's the author of "Experimental Design for Biologists," published by Cold Spring Harbor Press, which is now in its 2nd edition; and he teaches a course on the same topic at Harvard Medical School.

JAMIE JUSTICE, PHD

XPRIZE Healthspan Innovations Landscape: Global Strategies to Improve Muscle, Cognitive, and Immune Function in Aging

Dr. Justice is EVP, Health, at XPRIZE and Executive Director of XPRIZE Healthspan. At Wake Forest University School of Medicine, Jamie was Director of the Biogerontology Lab, co-leader of the Integrative Biology Core of the WF Claude D. Pepper Older Americans Independence Center (OAIC), Principal Investigator of the NIA-supported Geroscience Education and Training Network, an engaged member of the Translational Geroscience Network, Gerontological Society of America's ESPO Scientific Section Officer and Executive Committee Member from 2018-2021. She is the recipient of the Jarrahi Research Scholars Fund in Geroscience Innovation, 2022 Vincent Cristofalo Rising Star in Aging Research, and the 2022 NIA Nathan W Shock Awardee.

BENJAMIN MILLER, PHD

Changing Focus from Protein Mass to Proteostasis for Healthy Muscle Aging

Dr. Miller received a PhD from UC-Berkeley and completed a post-doc at the Muscle Research Center in Copenhagen, Denmark. In 2018, he moved from Colorado State University to the Aging and Metabolism Research Program at the Oklahoma Medical Research Foundation (OMRF). This move to OMRF was prompted by its growing reputation as a leader in aging research. At OMRF, Dr. Miller retained the title of Full Professor and in 2023 became the Department Chair of the Aging and Metabolism Research Program. Dr. Miller's expertise is in skeletal muscle, aging, mitochondria, stable isotope labeling, proteostasis and drug and lifestyle (primarily exercise) interventions. His work with tracers and in muscle aging is nationally recognized and has led to many collaborations, extensive mentoring, and leadership positions. Dr. Miller's work is almost exclusively focused on prolonging the period spent in good health (i.e., healthspan) by targeting mitochondrial energetics and proteostatic maintenance. Along with his own research, he co-directs the Multiplexing Protein Analysis Core (MPAC) within the NIA-funded Oklahoma Nathan Shock Center and is incoming Co-Director of the Center. He is also involved in leadership and activities of the Oklahoma Center for Cellular Metabolism (NIH COBRE), and the Harold Hamm Diabetes Center.

PAYEL SEN, PHD

Epigenetic Mechanisms of Skeletal Muscle Aging

Dr. Sen received her bachelor's degree in physiology and master's degree in biochemistry from the University of Calcutta, India. She received her PhD in molecular biology, microbiology and biochemistry from Southern Illinois University. Her PhD research involved dissecting the regulatory roles of the yeast SWI/SNF chromatin remodeling complex. For post-doctoral training, she joined the laboratory of Dr. Shelley Berger at the Epigenetics Institute of the University of Pennsylvania, where she identified novel epigenetic regulators of senescence and aging. She has received awards and fellowships from the American Heart Association, American Federation for Aging Research, the Paul F. Glenn Foundation, Hevolution Foundation, and the NIH. She joined the NIA in 2019 as a Stadtman Tenure-Track Investigator where she leads the Functional Epigenomics Unit. Her lab uses mouse models combined with experimental, computational, and high-throughput genome-scale approaches to identify new druggable epigenetic targets against aging.

MONICA SERRA, PHD

NIA Research Priorities in Aging Skeletal Muscle & Healthspan

Dr. Serra is a Program Officer in the Geriatrics Branch of the Division of Geriatrics and Clinical Gerontology at the NIA. She received a B.S. in Athletic Training from Duquesne University, M.S. in Nutrition from Case Western Reserve University, and Ph.D. in Exercise, Nutrition, and Preventive Health from Baylor University. She also completed a geriatrics-focused post-doctoral fellowship at the University of Maryland School of Medicine and Baltimore VA Medical Center. She has 15 years of experience designing and implementing clinical trials focusing on the application of lifestyle interventions in the prevention and treatment of obesity, chronic disease, and disability in older adults. She joined the NIA in 2024, overseeing a portfolio of clinical research in nutrition, metabolism, exercise physiology, and resilience in older adults.

DAN SONTHEIMER, MD

End of Life and Muscle Health: Proxies and Prognosis

Dr. Sontheimer is Vice President and Chief Medical Officer of Baptist Health Care (BHC). Dan joined the team at BHC in January of 2014, then left in 2018 to be a part of a BHC joint venture at Lighthouse Health Plan. He returned in 2022 as Chief Medical Officer. He oversees the medical staff credentialing, quality, patient safety and experience. Additionally, he is on the medical staff for Baptist and Gulf Breeze hospitals and assists in providing palliative care. He is a hospitalist with our partner, ApolloMD. Dan earned his medical degree at the University of Kansas. He then completed his family medicine residency in Spartanburg, S.C. He has an Master of Business Administration from Regis University in Denver, Colo. He is a member of the American Academy of Family Physicians (AAFP), and is board certified in family medicine, as well as hospice and palliative medicine.

SCOTT TRAPPE, PHD

Elite Human Performance Across the Lifespan

Dr. Trappe is the Director of the Human Performance Laboratory and John and Janice Fisher Endowed Professor of Human Bioenergetics at Ball State University. He received his undergraduate training at the University of Northern Iowa and was captain of the swim team. He worked for US Swimming at the Olympic Training Center in Colorado Springs while conducting his graduate (MS) studies at the University of Colorado. His PhD training was with Dr. David Costill at Ball State University and post-doctoral training in muscle physiology with Dr. Robert Fitts at Marquette University. For over 25 years, Dr. Trappe has been working with NASA to help optimize the exercise prescription for astronauts. Concurrent to the work with NASA, he has conducted several NIH funded exercise training studies in older adults, aging athletes, and various college and elite athletes. Dr. Trappe is currently a principal investigator for one of the human clinical centers in MoTrPAC, which is a nation-wide consortium to study the health benefits of exercise. Using a whole body to gene approach, Dr. Trappe and his colleagues have gained a better understanding of muscle plasticity and the powerful effects of exercise for health and performance. Dr. Trappe has mentored numerous trainees (post-doctoral, doctoral and master's students) over his career. Dr. Trappe is a fellow of the American College of Sports Medicine and member of the American Physiological Society and the American Association for the Advancement for Science.

REYHAN WESTBROOK, PHD

Tryptophan Metabolism: A Key Modulator of Functional Decline, Frailty and Aging

Dr. Westbrook is an Assistant Professor at Johns Hopkins University, Division of Geriatric Medicine and Gerontology. Dr. Westbrook's research is focused on determining the biological mechanisms that underlie frailty and aging using animal models and translating these findings into actionable strategies to improve health in older adults. Using metabolomics and other research tools in animal models and in humans, his work has shown that alterations in key molecular pathways can influence lifespan including the tryptophan degradation pathway and energy metabolism pathways. His current focuses include determining if genetically and pharmacologically manipulating key metabolic pathways can alter lifespan and healthspan in animal models. He also uses fluxomic techniques to understand changes in energy metabolism that occur with aging and frailty. His interests include determining the biological "signatures" of aging and frailty to boost prognostic capabilities regarding aging related declines, as well as developing therapeutic strategies to improve human health.

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