



Metabolic pathways and therapeutics to promote resilience, rehabilitation and delayed aging

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Over the past decade, research teams from major universities and other institutions have identified important metabolic pathways that link aging, disease, and function. Their work has explored the hypothesis that aging-related processes are relevant to most chronic disease and advanced the development of interventions that target the biological mechanisms of aging. The result has been some remarkable demonstrations of modulated aging in model organisms and the elucidation of a number of pathways that are conserved across species, marking them as promising targets for intervention. This research has gained impressive new momentum and, in the process, spawned a new moniker: GeroScience.

This special edition of GeroScience emerged from a State of the Science symposium focused on this field

entitled, *Metabolic Pathways and Therapeutics to Promote Resilience, Rehabilitation and Delayed Aging*. It convened at the Uniformed University of Health Sciences on October 25, 2019. That symposium and this publication highlight ongoing investigations in GeroScience conducted by researchers at fourteen major institutions. Research topics covered include the following: Time Restricted Feeding, Glycolytic Inhibition, Rapamycin, Metformin, Resveratrol, NAD boosters, Ketone Bodies, Mitochondrial Derived Peptides and PARP activators, among others.

The State of Science Symposium was sponsored by the Department of Defense, and accordingly, organizers approached it with three basic questions:

- 1) Is this field of research relevant to the core mission of the Department of Defense?
- 2) Is it currently, clinically relevant?
- 3) Can the Department of Defense play a meaningful role in the future to advance the science?

The unanimous answers to these three questions, voiced at the conclusion of the Symposium by organizers and participants alike, is yes.

Despite the fact that some view the principal goal of applied GeroScience as increased lifespan, the articles in this edition focus more on issues of resilience, performance, and health span. The titles of the articles and their authors are presented in Table 1. Effective strategies to delay loss of function and ameliorate the deficits, illness and disability promise substantial dividends to the Department of Defense (DoD) in the form of cost savings,

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improved force readiness and saved lives. First generation GeroScience-related therapeutics, including metformin and rapamycin are currently undergoing clinical trials while a number of articles in this issue reference available, or emergently available, therapeutics based on affordable metabolites or drugs. Jaime Justice PhD of Wake Forest University, for example, provides an overview of the metformin TAME trial and conference participant, Rafael de Cabo PhD, of the National Institutes of Health, highlights many of the clinical and performance benefits associated with time-restricted feeding. Research outlining the benefits of nicotinamide mononucleotide (NMN) and resveratrol in ameliorating hemorrhagic shock and traumatic brain injury and the anticatabolic effects of ketone bodies in preserving muscle mass are among the other topics that are of great relevance and potential high impact for the DoD. Given the large-scale investment and rapid pace of scientific advancement in GeroScience, additional discoveries will follow, making it as an increasingly important focus for translational and clinical

medicine, as well as an important source of an increasing number of practical strategies to improve force readiness and rehabilitation for the DoD.

A large number of outstanding partners came together to host the State of the Science symposium and produce this special edition. The editors would like to offer their thanks to, among others, the (1) Center for Rehabilitation Science Research, Department of Physical Medicine and Rehabilitation at the Uniformed Services University for the Health Sciences; (2) Department of Rehabilitation, Walter Reed National Military Medical Center; (3) University of Pittsburgh, School of Health and Rehabilitation Sciences Department of Rehabilitation Science and Technology, Human Engineering Research Laboratories; (4) University of Pittsburgh School of Medicine Center for Continuing Education in the Health Sciences; (5) Department of Veterans Affairs; and (6) National Institute on Aging at the National Institutes of Health.

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Finally, the editors would like to thank the outstanding researchers who participated in the symposium and submitted articles for this publication. We owe them a debt of gratitude, both for their contributions to this publication and for their lifetime of contributions to the field. We are grateful.

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