

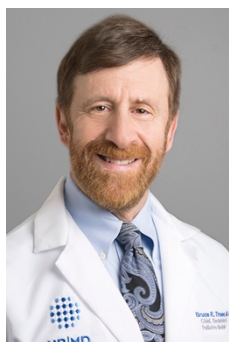
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Were your research studies delayed due to COVID-19 closures and replated impacts of the pandemic?

If you need to extend your MTA or alter your scope of work, please request the MTA Amendment Form, and we will get right on it. As a friendly reminder, per the agreement, you are only allowed to use ChromaDex's material for the activities specified in the agreement and during the duration of the agreement.

Drs. Troen & Seldeen – Taking NR Aging Research from the Bench to the Clinic



Bruce R. Troen, MD

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Drs. Bruce Troen and Kenneth Seldeen are a dynamic duo in gerontology at the University at Buffalo and the VA Western New York Healthcare System. They have developed two material transfer agreements through CERP, one for preclinical research and one for clinical research. Their most recent nicotinamide riboside (NR) publication, Seldeen et al. 2021 [“Short-term nicotinamide riboside treatment improves muscle quality and function in mice and increases cellular energetics and differentiating capacity of myogenic progenitors,”](#) contributes to the body of evidence demonstrating NR's potential benefits in support of healthy aging.

How would you define your research interests and areas of expertise?

“Bruce R. Troen, MD is an accomplished geriatrician and benchtop scientist, and Kenneth Seldeen, PhD is a gerontologist with a background in biochemistry and molecular biology. For nearly ten years, we have worked together to identify and translate possible “shortcuts” to successful aging, including maintaining physical and cognitive function, from cells to the community. Areas

of interest include minimal exercise approaches like short session high-intensity interval training, and nutritional supplementation, including the importance of maintaining vitamin D status and supplementing with novel therapeutics like NR.”

How did you learn about ChromaDex and the ChromaDex External Research Program?

“We initially set out to perform tissue culture experiments to explore the therapeutic potential of NR, and one of the sources was from ChromaDex, which we purchased online from Amazon. We first learned about the supportive resources available for investigators when we reached out to Chromadex to identify ways to buy in bulk to support an animal trial.”

What have been your most significant discoveries as it relates to NAD+ and supplementing with NR?

“We are excited by the pleiotropic potential of NR as our laboratory examines many aspects of aging, including impacts upon

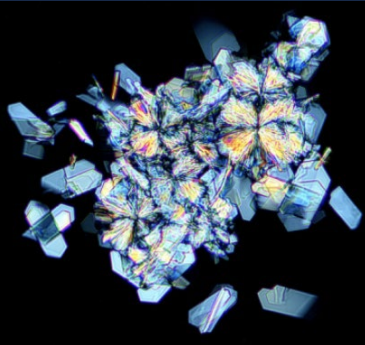


Reminder

Don't forget to submit your progress report every six (6) months or as stipulated in your MTA. An updated progress report is required when requesting additional material or submitting an MTA amendment. We will provide you with a progress report form to simplify the process.

Request forms at cerp@chromadex.com for:

- Abstract, manuscript, poster, or presentation slides submissions
- Bulk or clinical material requests
- Requesting an amendment



Troen & Seldeen, continued

bone, muscle, and brain health. Our initial work in muscle progenitor cells, which was recently published, indicates that the addition of NR increases cell fusion and fiber size and increases mitochondrial respiration. Additionally, our preliminary data support benefits from NR administration across multiple areas as we move to animal models. We recently published that just four weeks of NR supplementation in middle-aged mice was sufficient to enhance treadmill performance, maintain grip strength, and induce muscle fiber hypertrophy. Middle-aged mice (~15 months for a C57BL/6J) are generally understudied, and the work fits well in the context of the report by Zhang et al. that identified a treadmill benefit in aged mice (~24 months) but not in young mice. Our preliminary but unpublished work confirms that NR enhances treadmill performance in aged mice, increasing our confidence in its therapeutic potential for the placebo-controlled trial in older veterans (Impacts of Nicotinamide Riboside on Functional Capacity and Muscle Physiology in Older Veterans (NR-VET), [NCT04691986](#))."

What are the status and study objectives for your clinical study?

"The trial is a four-year Veterans Affairs Rehabilitation Research & Development Service (RR&D) funded study to evaluate the efficacy of NR supplementation to improve functional outcomes in older Veteran participants (65-85 years of age). Outcomes include multiple geriatric assessments such as frailty status, the short physical performance battery, gait speed, grip strength, and the six-minute walk. We also plan on examining maximal endurance (VO₂max) and changes in tissue blood oxygenation using functional near-infrared spectroscopy. Our study will look to take muscle biopsy samples before and after the 12-week treatment protocol to evaluate changes in NAD⁺ levels and other changes in the underlying biology that we observed in

our animal and tissue culture studies (i.e., changes in muscle histology and aerobic respiration). The study is currently scheduled to start recruitment before the end of 2021."

In your opinion, what are some important gaps in NAD⁺ and NR research?

"The NAD⁺ field is moving very quickly, and there are certainly many areas that could be further developed or explored (i.e., cognition, immune health, cancer)—as well as a better understanding of changes in epigenetic and metabolomic levels. Other knowledge gaps include how other similar NAD⁺ enhancing supplements such as NMN and NAD, and even exercise, may differ with regards to impacts on the underlying biology, as well as dosing, and how aging affects NAD⁺ metabolism."

What conferences are "must attend" for you for 2021?

"Our primary "go-to" conferences include annual meetings of the Gerontological Society of America (GSA), the International Conference on Frailty and Sarcopenia Research (ICFSR), the American Geriatric Society (AGS), and the American Society for Bone and Mineral Research (ASBMR). A smaller and very fun conference that we also try to get to every year (COVID willing) is the Barshop Conference on Aging in San Antonio, Texas." ■

Dr. Troen has several major foci of research: frailty, longevity/aging mechanisms, and osteoporosis, all of which result in great morbidity in older adults. He and his team have been elucidating what interventions can enhance physical performance, mobility, and cognition, particularly in those who are frail.

Dr. Seldeen's research interests include the identification of possible lifestyle strategies for successful aging, including shorter exercise regimens that can fit into busy schedules and/or nutritional supplementation to boost or maintain functional capacity (e.g., vitamin D and NR).

ChromaDex Makes an Impact at Conferences

Virtual meetings allowed ChromaDex to attend more conferences this year. For Q2 & Q3, the science teams (R&D & QA), reference standards team, and leadership spread the message of ChromaDex's commitment to advancing science and empowering the research community. June was a particularly busy month, with [Nutrition 2021](#) (shared in our previous CERPI Communique), United Mitochondrial Disease Foundation's [Mitochondrial Medicine Symposium](#), and FASEB's [NAD+ Metabolism and Signaling Conference](#). In July, we attended the [American Aging Association \(AGE\)](#) meeting both virtually and in person.

In August, members of the ChromaDex Reference Standards and Quality Assurance teams attended the [AOAC International Annual Meeting](#). They reaffirmed ChromaDex's commitment to providing reference standards to the highest level of quality for our customers. At the beginning of September, ChromaDex's co-founder and Executive Chairman of the Board presented a talk titled, "Recent Advances with Nicotinamide Riboside in Orphan Diseases and Aging," for the [Aging Research and Drug Discover Meeting](#) (ARDD). Next year, we hope to see more of the CERP community at various conferences in person. ■

Advancing the Science: Intrinsic Capacity

ChromaDex uses several categorizations to organize studies, including the nine hallmarks of aging and intrinsic capacity (IC).

The World Health Organization (WHO) defines healthy aging as the process of developing and maintaining the functional ability that enables wellbeing in older age. Functional ability is further defined as the capabilities that allow all people to be and do what they have reason to value, including the ability to meet basic needs, learn, grow, make decisions, be mobile, build and maintain relationships, and contribute to society. Functional ability is determined by both the IC of an individual and the environment in which they function. IC, in turn, is defined as the composite of all the mental and physical capacities that a person can draw on and includes their ability to walk, think, see, hear, and remember. We understand that NR represents a nutritional solution to help maintain or improve IC through maintaining optimal NAD+ levels.

IC is composed of five domains: cognition, sensory, locomotion, vitality, and psychological, all of which encompass the health of the individual. ([https://www.who.int/ageing/health-systems/clinical-consortium/JoG-intrinsic-](https://www.who.int/ageing/health-systems/clinical-consortium/JoG-intrinsic-capacity-2018.pdf)

[capacity-2018.pdf](#)). These five domains are connected to cellular health, are interrelated, and can impact all stages of lifespan. Cognitive function includes areas that focus on memory and problem-solving. Locomotion is often determined through balance, muscle strength, and gait. Sensory is often comprised of vision and hearing, among others. Psychological incorporates mood and emotional vitality, which includes social interactions. Vitality is focused on hormonal function, energy metabolism, cardio-respiratory function, and metabolic functions.

IC is tied to healthy aging and serves as an indicator of health status and the ability to respond to stress. IC from this perspective is a form of resiliency at the cellular and organismal levels, and NAD+ is a key factor in this resiliency. Nicotinamide riboside (NR), and its ability to increase NAD+, has a great potential to increase our healthy aging through enhancing IC. A significant number of studies on NR have demonstrated its benefits to various areas of IC, with most studies being categorized in the area of vitality. However, more research is needed to elucidate the full potential of NR and its ability to support healthy aging. ■

Be on the alert for a survey on planned conference attendance for you and your team in 2022. We want to be where you are to support your research and shine light on the scientific advancements made by CERPIs.

Did you know that your research may include the development of novel intellectual property (IP)?

When the CERP Science Team reviews your manuscript prior to submission, we are also checking for IP that can benefit you and your institution.

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Did we miss your publication?

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Would you like more PR around your research? We would love to promote your science more broadly. Please request the PR Form at cerp@chromadex.com

Thank you to our content contributors, editors, and reviewers:

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New CERP Publications for Q2 & Q3 2021

- Altay, O., et al. (2021). Combined Metabolic Activators Accelerates Recovery in Mild-to-Moderate COVID-19. *Adv Sci*, 2101222. [doi:10.1002/advs.202101222](https://doi.org/10.1002/advs.202101222).
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