

CERPI Communiqué

January 2021

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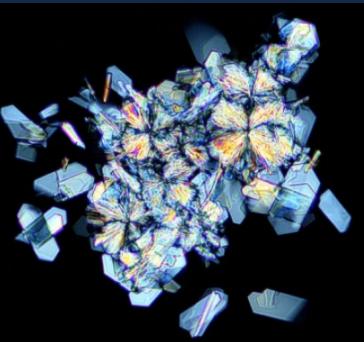
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Reminders

Do not forget to submit your progress report every 6 months, or as stipulated in your MTA. Progress reports are now required when requesting additional material or submitting an MTA amendment.

Be sure to request forms at cerp@chromadex.com when:

- Submitting an abstract, manuscript, poster, or presentation slides
- Requesting material
- Requesting an amendment to your MTA.



CERPI Spotlight



Dr. Hamity is a Research Assistant Professor in the Department of Anesthesia at the University of Iowa. Dr. Hamity received her PhD from the University of Cordoba, Argentina, where she studied peripheral mechanisms of nociception. She completed her postdoctoral training in the laboratory of CERPI Dr. Donna Hammond at the University of Iowa. Dr. Hamity recently developed her own CERP MTA, and her research involves identifying new strategies to prevent or mitigate chemotherapy-induced peripheral neuropathy (CIPN) in cancer patients. Dr. Hamity is currently a member of the Society of Neuroscience and the International Association for the Study of Pain.

Please summarize the significant findings from your two publications evaluating nicotinamide riboside (NR) and peripheral neuropathy. In our first publication, daily treatment with NR relieved tactile hypersensitivity and the aversive component of painful peripheral neuropathy induced by chemotherapy. Our second study showed that NR ameliorates tactile allodynia and prevents the loss of intraepidermal nerve fibers induced by paclitaxel. Moreover, our data showed that daily treatment with NR enhances paclitaxel's suppression of tumor growth.

What are your future NR research plans? How are you funding this research? My future plans are to extend my studies to platinum-based therapies whose mechanism of action differs from taxane-based therapies and whose sequelae can be more disabling. Given the extensive use of platinum compounds alone, and in combination with paclitaxel, I believe that the utility of NR is warranted to greater improve the quality of life in these patients. My research is currently funded by a SPIRE grant from Veterans Affairs. With the data obtained by this first study, I hope to be able to submit a proposal to obtain an RO1 from the NIH.

Do you have any recommendations for junior scientists on their pathway to independence in academia? As you are starting to establish your own path, I think it is extremely important to have a good conversation with your mentor about your research aspirations and career goals. Establishing a good network of collaborators is very important, particularly with colleagues who are going through the same process. I have been lucky to have a great research environment at the University of Iowa. It is also important to have visibility so the research community starts recognizing you as an independent investigator.

What have you enjoyed about being a ChromaDex External Research Program Investigator? I have enjoyed the good communication between ChromaDex and our team and the support and interest they provide to my project. It is my hope that we would continue collaborating for a good amount of time.

Your Partner in Scientific Discovery

Highlights from 2020's Advancements in Nicotinamide Riboside Research

Despite being a challenging year, research related to nicotinamide riboside (NR) continued to shine and make headlines. CERP investigators significantly contributed to these research advances, with 14 of 37 preclinical and 3 of 5 clinical peer-reviewed published studies from CERP. Additionally, CERP continued to provide material for ~70% of registered clinical NR studies. Below are highlights from published and peer-reviewed studies of NR from 2020.

Neurology, cognition, and brain health

- NR administration alleviated angiotensin induced cerebral small vessel disease by protecting BBB integrity, vascular remodeling, neuroinflammation, and white matter injury—associated cognitive impairment. ([1](#))
- NR supplementation slowed the axon degeneration and demyelination in facial nerves following axotomy. ([2](#))
- NR reduced alcohol-induced depression-like behaviors in a mouse model through the potential impact of the gut-brain axis. ([3](#))
- NR was shown to be beneficial in a mouse model of Gulf War Illness, by decreasing pro-inflammatory cytokines and lipid peroxidation, while increasing markers of mitochondrial bioenergetics in the brain. NR also reduced fatigue in the model. ([4](#))
- Elevating NAD through NR supplementation has a significant positive influence on circadian rhythms, improving behavior and energy in older mice resembling younger mice. ([5](#))
- NR combined with Pterostilbene delayed neuronal motor failure in amyotrophic lateral sclerosis (ALS) model. ([6](#))
- NR enhanced the proliferation and migration of neural stem cells and neuronal precursor cells in the brain of an ALS mouse model but did not extend the life of the animals. ([7](#))
- NR delayed motor neuron degeneration, decreased markers of neuroinflammation, and appeared to modify muscle metabolism in an ALS mouse model. ([8](#))
- NR levels were distinctly lower in children with Autism Spectrum Disorder, which was reversed with microbiota transfer therapy. ([9](#))
- NR supplementation reversed oxytocin deficits and improved anxiety and social behavior indicators in a mouse model of ASD. ([10](#))

Sensory health

- NR blunted the loss of intraepidermal nerve fibers induced by paclitaxel, as associated with chemotherapy-induced neuropathy, and may also delay tumor growth during taxane therapy. ([11](#))
- Short-term NR supplementation prevented the hearing loss in mouse models of Cockayne syndrome, modeling age-induced hearing loss. ([12](#))
- NR promoted oxidation resistance to protect the synapse and the inner ear morphology in a mouse model with temporary threshold-shift hearing loss. ([13](#))
- NR prevented deleterious outcomes in the retina resulting from exposure to degeneration-inducing levels of light. ([14](#))
- Intravenous NR protected against TNF-induced axon loss with possible involvement of upregulated NRK1 and SIRT1-autophagy pathway. ([15](#))

Need to Request Additional Material for Your Study?

- Please use the Material Request Form and send to cerp@chromadex.com
- Submit your request at least 6 weeks in advance to ensure on-time delivery.

Highlights from 2020's Advancements in Nicotinamide Riboside Research, continued...

Cardiovascular & circulatory health

- NR partially restored high fat diet-induced atrial fibrillation (AF) in NAMPT KO mice; NAD/NAMPT axis may be a therapeutic target for AF. ([16](#))
- NR reduced cardiometabolic risk factors and modulated cardiac oxidative stress in obese Wistar rats under caloric restriction. ([17](#))
- In a clinical pilot study, NR enhanced PBMC respiration and reduced pro-inflammatory cytokine gene expression in study participants with heart failure. ([18](#))

Liver & kidney health

- NR prevented ischemia-reperfusion injury in multiple animal models of chronic kidney disease but was not effective in preventing chronic kidney disease progression. ([19](#))
- First in-human study demonstrated depressed a NADome in individuals undergoing liver transplantation for alcohol-related liver disease and was correlated to disease severity. ([20](#))

Muscle, obesity, exercise, & energy

- NR supplementation in suckling (male) mice may help attenuate adult high fat diet-induced obesity through epigenetic programming of white adipose tissue. ([21](#))
- In a clinical study, protein levels of NAMPT decreased by 14% following twice-daily supplementation of NR for 12 weeks in obese and insulin-resistant men. Neither skeletal muscle mitochondria nor abundance of mitochondrial associated proteins were affected by NR. ([22](#))
- Healthy overweight or obese men and women receiving 6 weeks of NR or placebo in a randomized, double-blinded, placebo-controlled, crossover clinical study demonstrated increased NAD⁺ synthesis in skeletal muscle after NR compared to placebo. NR increased body fat-free mass (> in women), increased skeletal muscle acetylcarnitine concentrations, and improved sleeping metabolic rate. ([23](#))

Other exciting research

- In a study evaluating animal tissues, cell culture, and human samples exposed to coronaviruses, there was an upregulation of MARylating PARPs. Additionally, the expression of genes associated with the NAD⁺ salvage pathway were upregulated, while downregulating other NAD biosynthetic pathways. ([24](#))
- In-ovo injection of NR improved broiler chick pectoral major muscle development; the observed effect was more effective than published results for amino acids, creatine, IGF-1. ([25](#))

With multiple publications in the pipeline, it is anticipated that CERPs will continue to have a great impact on NR and NAD⁺ research advances in 2021. As a reminder, per your MTA, make sure you send your publications (manuscripts, abstracts, posters, and presentation slides) to ChromaDex prior to submission. The timeline required for this submission is typically 30-60 days and is specified in your agreement with ChromaDex. Submit all publications or questions to cerp@chromadex.com.

SCIENCE
COMMUNICATIONS
OPPORTUNITY
For Your Junior
Scientists

We are looking for junior scientists (graduate students and postdocs) to write an article for the website AboutNAD.com featuring the research conducted in your lab. The goal is to translate recently published research for a general public audience. These types of experiences are great on resumes and CVs.

Once your research is nearing publication, please have your junior scientist(s) write a 1-2 page summary of the study for the general public. Submit the summary to CERP and include a headshot and 1-2 line bio to include on the website.

Making an Impact at Nutrition 2020

The American Society for Nutrition (ASN) attracted over 30,000 registrants from all over the world for the Nutrition 2020 Meeting. The online meeting was the largest ASN meeting to date, with attendees from academia, government, the private sector, media, medicine, and the general public.

As 2020 Sustaining Partners, ChromaDex sponsored a satellite symposium, “Nicotinamide adenine dinucleotide (NAD) in human health and disease: The state of the science on nutrition interventions.” Over 750 watched the symposium when it was aired with over 4700 views. The session was co-hosted by Yasmeen Nkrumah-Elie, PhD, Director of CERP, and by CERPI Rong Tian, MD, PhD, Director of Mitochondria and Metabolism Center and Professor of University of Washington, Seattle. The following was presented during the symposium:

- *Framing the Issue: Why Should We Care about NAD+?*
 - Rong Tian, MD, PhD, University of Washington, Seattle, Washington
- *Recent Findings on NAD+ in Human Health and Disease*
 - Charles Brenner, PhD, formerly of University of Iowa, Iowa City, Iowa
- *Comparing and Contrasting NAD Precursors: A Review of Mechanisms*
 - Carles Canto, PhD, Nestlé Institute of Health Sciences, Lausanne, Switzerland
- *Emerging Effects of NAD Precursors in Humans: The Current State of Clinical Research*
 - Kevin Maki, PhD, CLS, FNLA, FTOS, FACN, Midwest Biomedical Research, Addison, IL; MB Clinical Research, Boca Raton, FL; Department of Applied Health Science, School of Public Health, Indiana University, Bloomington, IN, Addison, Illinois

Recordings of each of the sessions are available [here](#).

Additionally, there were four abstracts and two posters presented by the CERPI community and ChromaDex.

We would also like to congratulate, Dr. Charles Brenner, ChromaDex Chief Scientific Advisor and CERPI, for receiving the Mary Swartz Rose Senior Investigator Award. This award, presented by ASN and its Foundation, with support from the Council for Responsible Nutrition (CRN), recognizes an investigator who has contributed outstanding research in the field of bioactive compounds for human health.

We would like to encourage you to submit abstracts and attend the meetings listed below. It is our goal to have a significant ChromaDex and CERPI presence at each of these meetings.

- [Experimental Biology](#), April 27 – 30, 2021
- [American College of Sports Medicine](#), June 1 – 5, 2021
- [Nutrition 2021 Meeting](#), June 7-10, 2021
- [FASEB NAD+ Metabolism and Signaling Conference](#), June 15 – 16, 2021

Please let us know in advance which conferences you will be attending in 2021 so we can promote your research presentations. Please also let us know if there are any conferences you would like to see a ChromaDex presence in the future. cerp@chromadex.com



SPREAD THE NEWS

The [CERP Webpage](#) has been updated and includes new research priorities, updated CERP applications, and more. Feel free to share with your colleagues.

Requests for Proposals Coming Soon

Interested In Staying Up-To-Date on the Latest NAD+, NR, and ChromaDex Press Releases and Headlines?

[Subscribe Here](#)

Investor Email Notifications

Congratulations to our CERPI Community for 18 publications (for all ingredients) in 2020!!!

1. [Doig, C.L., et al., Induction of the nicotinamide riboside kinase NAD\(+\) salvage pathway in a model of sarcoplasmic reticulum dysfunction. *Skelet Muscle*, 2020. 10\(1\): p. 5.](#)
2. [Gerasimenko, M., et al., Nicotinamide riboside supplementation corrects deficits in oxytocin, sociability and anxiety of CD157 mutants in a mouse model of autism spectrum disorder. *Scientific Reports*, 2020. 10: p. 10035.](#)
3. [Gomez-Zorita, S., et al., Comparative Effects of Pterostilbene and Its Parent Compound Resveratrol on Oxidative stress and Inflammation in Steatohepatitis Induced by High-Fat High-Fructose Feeding. *Antioxidants*, 2020. 9, 1042.](#)
4. [Gonzalez, J.M. and A.R. Jackson, In ovo feeding of nicotinamide riboside affects broiler pectoralis major muscle development. *Translational Animal Science*, 2020.](#)
5. [Hamity, M.V., et al., Nicotinamide riboside relieves paclitaxel-induced peripheral neuropathy and enhances suppression of tumor growth in tumor-bearing rats. *Pain*, 2020.](#)
6. [Heer, C.D., et al., Coronavirus infection and PARP expression dysregulate the NAD Metabolome: an actionable component of innate immunity. *J Biol Chem*, 2020.](#)
7. [Ko, K.W., et al., SARM1 acts downstream of neuroinflammatory and necroptotic signaling to induce axon degeneration. *J Cell Biol*, 2020. 219\(8\).](#)
8. [Levine, D.C., et al., NAD\(+\) Controls Circadian Reprogramming through PER2 Nuclear Translocation to Counter Aging. *Mol Cell*, 2020.](#)
9. [Matasic, D.S., et al., Modulation of the cardiac sodium channel NaV1.5 peak and late currents by NAD\(+\) precursors. *J Mol Cell Cardiol*, 2020. 141: p. 70-81.](#)
10. [Mateuszuk, L., et al., Reversal of endothelial dysfunction by nicotinamide mononucleotide via extracellular conversion to nicotinamide riboside. *Biochem Pharmacol*, 2020: p. 114019.](#)
11. [Okur, M.N., et al., Short-term NAD\(+\) supplementation prevents hearing loss in mouse models of Cockayne syndrome. *NPJ Aging Mech Dis*, 2020. 6: p. 1.](#)
12. [Remie, C.M.E., et al., Nicotinamide riboside supplementation alters body composition and skeletal muscle acetylcarnitine concentrations in healthy obese humans. *Am J Clin Nutr*, 2020.](#)
13. [Shats, I., et al., Bacteria Boost Mammalian Host NAD Metabolism by Engaging the Deamidated Biosynthesis Pathway. *Cell Metab*, 2020. 31\(3\): p. 564-579 e7.](#)
14. [Spaulding, H.R., et al., Nutraceutical and pharmaceutical cocktails did not preserve diaphragm muscle function or reduce muscle damage in D2-mdx mice. *Exp Physiol*, 2020.](#)
15. [Sun, C., et al., Re-equilibration of imbalanced NAD metabolism ameliorates the impact of telomere dysfunction. *EMBO J*, 2020: p. e103420.](#)
16. [Zhang, C., et al., The acute effect of metabolic cofactor supplementation: a potential therapeutic strategy against non-alcoholic fatty liver disease. *Mol Syst Biol*, 2020. 16\(4\): p. e9495.](#)
17. [Zhang, X., et al., Systemic Treatment with Nicotinamide Riboside is Protective in Four Mouse Models of Retinal Degeneration. *Investigative Ophthalmology & Visual Science*, 2020. 61: p. 2753.](#)
18. [Zhou, B., et al., Boosting NAD Level Suppresses Inflammatory Activation of PBMC in Heart Failure. *The Journal of Clinical Investigation*, 2020.](#)

Announcements

We are planning to discontinue the 75 mg clinical capsules in 2021 due to a lack of requests.

Please let us know if this will significantly impact your research. We will continue with the 250 mg clinical capsules.

New Journal!

The first issue of [Nature Aging](#) is now available. We recommend considering this journal for your future publications.

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

Yasmeen Nkrumah-Elie,
Rebecca Idoine, Yusrah Ishtiaq, Aron Erickson, Marta Hamity, Jennifer L. Brown, Andrew Shao, Peter Park, Virley Laquindanum, and Heather Van Blarcom

CERPI Communiqué, January 2021



CERP

ChromaDex External Research Program

ChromaDex, Inc.
10900 Wilshire Boulevard, Suite 600
Los Angeles, California, USA 90024
+1 (310) 388-6706
cerp@chromadex.com
<http://www.chromadex.com/cerp>

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