Newsletter for the ChromaDex External Research Program Investigators (CERPI)

# **CERPI Communiqué**

Volume 4, Issue 4, December 2023

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## **CERP Stats\***

10 years supporting the advancement of NAD+ Science.

#### Material Transfer Agreements (MTAs)

- 288 Total
- 81 Clinical
- 207 Preclinical only

#### Peer-Reviewed Publications

- 178 Total
- 31 Clinical
- 147 Preclinical

#### **Research Value**

- \$100 Million in estimated research costs \*\*
- Over \$4 Million in Niagen<sup>®</sup> donations (market value)

#### \*As of 12/21/2023

\*\*Based upon the average NIH grant value of \$355473.68 for nicotinamide riboside research

## 2023: A Milestone Year

As the ChromaDex External Research Program (CERP) team reflects on 2023, it has been a year of significant milestones, professional growth, and evolution. As our program continues to be more than 90% investigator-driven and third-party funded, the innovation behind many of the scientific applications of Niagen<sup>®</sup>, nicotinamide riboside chloride and other ChromaDex ingredients is coming from you, our CERP Investigators. As of December 21st, we have executed 288 material transfer agreements (MTA) to support the advancement of science of NAD+, NAD+ precursors, and other wellness ingredients.

As ChromaDex stands tall as the global leader of science-based NAD+ companies, we are grateful for Frank Jaksch's vision as company Co-Founder to start CERP ten years ago (initially as just an MTA program) to spur research and innovation. Through the years, our program has evolved as the science has developed, and continues on this natural projection. In the early years, nearly all CERP studies were preclinical. Successes in this early research inspired clinical research which primarily focused on safety, with exploratory secondary and tertiary efficacy outcomes. Now that safety has been established in 30+ clinical peer-reviewed publications with doses up to 3000 mg/day as demonstrated in the publication of the NR-SAFE study, CERPIs are now embarking on translational and efficacy studies. While this process has been exciting, there are so many more research questions to be answered, and the CERP Science Team is strategizing on how to prioritize resources and still contribute to the overall advancement of NAD+ science.

Our program model is exemplary, as most dietary supplement companies do not have the research budget to amass such an extensive R&D program, and honestly, neither do we. Based on current estimates, over \$100 million in research in has been conducted through CERP\*\*, with us donating more than \$4 million in material (market value). We are grateful that our CERPI community is determined to find their own funding which has supported over 175+ publicly trusted, peer-reviewed publications in 30+ clinical studies in this model has also helped to ensure NAD+ research advancements continue, well beyond the claim substantiation restrictions of dietary supplements.

We anticipate that 2024 will be an incredible year for ChromaDex and CERP. We looking to develop research in areas of clinical need and consumer demand. We hope that our CERPI community will be inspired to evolve with us, as we look towards having greater impact and supporting health optimization. As a science-based company, we plan to explore research in several new priority areas (see page 2) through targeted CERP campaigns. While we know that our traditional CERP model will require patience in developing the research, we hope to work closely with our current and prospective CERPIs to advance trusted research in these novel and impactful areas.

🎉 2023 CERP Milestones

## Women's Reproductive Health and NAD+ Current and Future State of the Science

A growing body of preclinical research continues to point to the link between NAD+ levels and women's reproductive health using orally administered nicotinamide riboside (NR) in mice and rat models to influence various outcomes.

Please note that while fascinating, encouraging, and inspiring, what follows is representative of early research. Further study needs to be done in humans to confirm these findings. But the potential here is certainly worthy of the scientific and research community's attention.

#### Postpartum and Infant Health and Lactation

ChromaDex Chief Scientific Advisor Dr. Charles Brenner has been quite vocal recently on this subject. On a popular science podcast, he enumerated some fascinating points from <u>a 2021</u> <u>study on NR and postpartum health</u>. The preclinical study conducted in mice and rats suggests that NR supplementation can benefit lactation, help with postpartum weight loss, and boost some of the nutritive properties of mothers' milk, most notably BDNF (brainderived neurotrophic factor).

Dr. Bruce German, also a ChromaDex scientific advisor and an expert in this field of study, continues to explore the potential benefits of NR in mothers and preterm infants.

<u>A 2023 preclinical study</u> examined showed how NR supported improved glucose metabolism and liver gluconeogenesis in hypoglycemic mouse mothers—hypoglycemia is often an issue in mothers with Type 1 diabetes. Remarkably, the NR-treated mice showed healthier fetus weights in their offspring, and maternal hypoglycemia was stabilized.

#### **Ovarian Health, Egg Quality, and Fertility Potential**

Another <u>2022 preclinical study</u> investigated the effects of NR and increased NAD+ on mouse oocytes (immature egg cells). With the premise that egg quality and NAD+ levels drop over time, the study showed (building on previous preclinical findings) that boosting NAD+ with NR can improve the ability of an early embryo to develop and grow. NR both reduced numbers of oocyte abnormalities and prevented age-related mitochondrial dysfunction. These findings could anticipate a novel strategy for improving fertility outcomes.

<u>A 2023 preclinical study</u> dives deeper into egg quality and fertility through the lens of ovarian aging. The study employed "mutant mice" — mice that were missing two critical genes for de novo NAD+ synthesis. With this synthesis pathway compromised, the mice had decreased ovarian NAD+ levels, fewer egg cells to be fertilized, irregular estrous cycles, and accelerated ovarian aging. Administration of NR increased ovarian NAD+ levels and partially restored fertility in the mice.

<u>A more recent 2023 study</u> looked at NR's impact on ovarian damage caused by gastrointestinal inflammation. The first experimental rat model to investigate the effects of NR on ovarian injury, it suggests that high-dose NR inhibited inflammatory markers and ovarian tissue damage, and increased antioxidant enzyme activity in the ovaries.



We are looking to grow our Global CERPI Community in 2024.

Please share this newsletter and/or our QR Code with interested colleagues and junior scientists. We are accepting applications on a rolling basis and are prioritizing studies in the following areas:

- Women's Health
- Aesthetics/Topical
- Animal & Pet
  Nutrition
- Novel NAD+
  Precursors
- Comparisons of NAD+ precursors
- Minimally explored routes of administration





Reminder

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Do not 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



As a significant number of CERP clinical studies have demonstrated safety and effectiveness of Niagen<sup>®</sup> at doses of 1000 mg +, ChromaDex launched our 1000 mg TruNiagen® product, and amazingly it sold out. Our consumers are paying attention to your scientific breakthroughs, and they want doses that have been effective in research clinical research. Your work is making a difference in lives all over the world.

## **Q4 CERP Advances in NAD+ Science**

- Early loss of endogenous NAD+ following rotenone treatment leads to mitochondrial dysfunction and Sarm1 induction that is ameliorated by PARP inhibition
- A novel panel of Drosophila TAFAZZIN mutants in distinct genetic backgrounds as a resource for • therapeutic testing
- Long-Term Nicotinamide Riboside Use Improves Coordination and Eye Movements in Ataxia • Telangiectasia
- Raising NAD+ Stimulates Short-Chain Dehydrogenase/Reductase Proteins to Alleviate Heart Failure Independent of Mitochondrial Protein Deacetylation
- Nicotinamide Riboside, an NAD + Precursor, Protects Against Cardiac Mitochondrial Dysfunction in Fetal Guinea Pigs Exposed to Gestational Hypoxia
- A randomized placebo-controlled trial of nicotinamide riboside in older adults with mild cognitive impairment
- NR-SAFE: a randomized, double-blind safety trial of high dose nicotinamide riboside in Parkinson's • disease
- Nicotinamide Riboside Supplementation Restores Myocardial Nicotinamide Adenine Dinucleotide Levels, Improves Survival, and Promotes Protective Environment Post Myocardial Infarction

## **Other Studies We Are Talking About**

- Anti-Aging and the Science of Nicotinamide Riboside •
- Potential Therapeutic Effects of NAMPT-Mediated NAD Biosynthesis in Depression in Vivo
- OMRF awarded \$3.1M to study diabetic heart disease
- Preclinical Characterization of Pharmacologic NAD+ boosting as a promising therapeutic approach • in rheumatoid arthritis
- Supplementation with nicotinamide riboside attenuates T cell exhaustion and improves survival in • sepsis
- National Academy of Medicine Elects 100 New Members
- Nicotinamide Riboside and Phycocyanin Oligopeptides Affect Stress Susceptibility in Chronic **Corticosterone-Exposed Rats**
- S-adenosylmethionine and nicotinamide riboside therapy in Arts syndrome: A case report and literature review
- Inflammation-induced mitochondrial and metabolic disturbances in sensory neurons control the switch from acute to chronic pain
- The potential benefic effect of nicotinamide riboside in treating a murine model of monoiodacetate-induced knee osteoarthritis
- Nicotinamide riboside modulates HIF-1 signaling to maintain and enhance odontoblastic differentiation in human dental pulp stem cells



CERP Celebrating 10 Years 🞉 of Leading NAD+ Research with CERP

In June 2023, CERP celebrated its 10<sup>th</sup> anniversary with our CERP 10 for 10. As recommended by you, our CERP Investigator (CERPI) community, we selected 10 CERPIs to honor for our celebration. We started highlighting our CERP 10 for 10 on the new ChromaDex YouTube Channel this October. Here are the links for the videos we have so far: Frank Jaksch, John Gonzalez, Paul Yen, Charles Brenner, Vilhelm "Will" Bohr, Douglas Seals, Evandro Fang, Robert Mankowski and Eija Pirinen. In 2024, we plan to share our interviews with Maria Portillo and ChromaDex's own, Philip Redpath. Make sure you like, SUBSCRIBE, and share.

## Come See Us at FASEB's NAD Metabolism and Signaling Conference in Portugal, August 2024



## NAD Metabolism and Signaling

August 25, 2024 - August 29, 2024

Lisbon, Portugal

**#NADSRC** 

A <u>Conference Summary</u> is now available.



## <u>Happy Holidays!</u>

Wishing you a Scientifically Empowered 2024



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The Industry's Gold Standard for Excellence in External Research

Interested in learning more about how to develop intellectual property that industry would want to license or how to commercialize your ideas?

If so, ChromaDex has a dynamic Business Development Team that would love to talk with you. For more information, send an email to <u>cerp@chromadex.com</u> with the subject line: Business Development, and we will get you connected.

Expand Your NAD+ Research Portfolio by including rarely studied NAD+ precursors. For more information send an email to

cerp@chromadex.com with the subject line: Novel NAD+ Precursors.

Thank you to our contributors towards this issue of the CERPI Communique:

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