Newsletter for the ChromaDex External Research Program Investigators (CERPI)

CERPI Communiqué

Volume 5, Issue 1, March 2024

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Reminder

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**

CERPI Spotlight: Utilizing Niagen® to Support the Health of Patients with the Rare Disease, Ataxia Telangiectasia

Dr. Hilde Nilsen is currently the Head of Research in the Department of microbiology at Oslo University Hospital, and a Professor in the Institute of Clinical Medicine at the University of Oslo. Her field is DNA repair, with a particular focus on the Base Excision Repair pathway. Her area of expertise is highly relevant to human disease as it directly influences mutation accumulation, development and maturation of B-cells, it influences susceptibility to pathogens, and viral biology and virulence.

Moreover, increasing amounts of evidence also point to a role for dysregulation of Base Excision Repair in several age-related diseases. She has also been centrally involved in building up the national infrastructure for precision medicine in Norway, in particular building up precision cancer diagnostic activity at Akershus University Hospital (2017-2023) and precision medicine for rare diseases at Oslo University Hospital (2022-current).

1. **How did you learn about ChromaDex and the ChromaDex External Research Program (CERP®), and has there been anything you have particularly enjoyed about being a Chromadex External Research Program Investigator (CERPI)?** My work on NAD+-supplementation has mostly been work done in collaboration with Vilhelm Bohr (Serves on the ChromaDex Scientific Advisory Board). It was Dr. Bohr who invited me to contribute to his work, specifically contributing with the C. elegans model organism. Therefore, I can thank Dr. Bohr for introducing me into this field, and also introducing me to the possibility to join the CERP program.

   I particularly enjoyed was to study mechanisms of DNA driven aging in collaboration with Dr. Bohr and his post doc Evandro Fei Fang, and how this led to a path towards translation. I also recruited Evandro to the University of Oslo, and that has been extremely valuable for us. But most important, being a CERPI made it possible to follow up on the mechanistic research and run a clinical trial in the rare neurogenerative disease Ataxia telangiectasia. As a rare disease it is difficult to run clinical trials, but it is even harder to obtain funding to actually run them and being a CERPI was instrumental.

2. **What have been your most significant discoveries as it relates to NAD+ and supplementing with nicotinamide riboside?** It is that DNA repair deficiency can accelerate NAD+ suppression, and that this is a targetable pathway in rare disease. Probably also in other settings where there is a high demand for DNA repair. These were not my ideas originally, but Dr. Bohr´s group. My contribution was the C. elegans model and -omics analyses. I have also been able to take this groundbreaking discovery into clinical use and through a clinical trial potentially paved the way for a disease modifying

Nilsen Interview continued

3. **How would you define your research interests and areas of expertise?** My area of expertise is in DNA repair, specifically in Base Excision Repair. In time I am also quite good at interpreting omics data. I am also bridging the basic science and translation.
4. **Why is NAD important in rare diseases and/or mitochondrial diseases?** In rare DNA repair deficiency syndromes, NAD+ is overconsumed because PARP1 utilizes NAD+ to protect the DNA strand breaks. With Dr. Bohr, we contributed to show that this might lead to acquired mitochondrial dysfunction, that can drive aging.
5. **What are some of the next steps in this research and how do we help the people who have this?** Clinical studies in rare DNA repair diseases are not easy. We have learned quite a lot from our small clinical observation trial published in Movement disorders. But even though our trial was 2 years this is still quite short with respect to the lifespan of the patients. Finding good control groups are also difficult. We know pretty much what we need to do to arrange a well-controlled trial but it involves quite a lot of logistics, it involves also a need for NR. But getting funding is a challenge as it ultimately involves relatively small patient groups.
    - We need longer RCT studies to demonstrate meaningful clinical response.
    - We need longer studies to unequivocally demonstrate safety of long-term NAD+ supplementation.
    - We need to demonstrate the transferability to normal aging, and define at which levels of NAD+ interventions should start.
    - We need to develop better methods to measure NAD+ pools in relevant tissues (non-invasively preferably)

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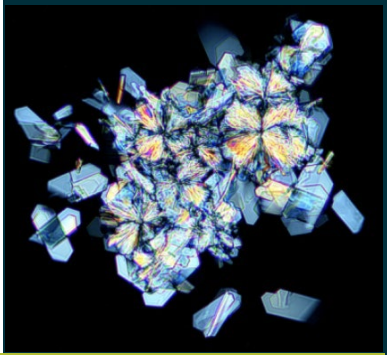
NR Year in Review

There were many impactful publications that came out last year about nicotinamide riboside (NR). We have gathered the impactful science of 2023, and you can find it using the following QR code:

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**



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 cerp@chromadex.com with the subject line: Business Development, and we will get you connected.

As a significant number of CERP clinical studies have demonstrated safety and effectiveness of Niagen® 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.**

Q1 CERP Peer-Reviewed Advances in NAD+ Science

- Differentially disrupted spinal cord and muscle energy metabolism in spinal and bulbar muscular atrophy
- The NAD+ Precursor Nicotinamide Riboside Rescues Mitochondrial Defects and Neuronal Loss in iPSC derived Cortical Organoid of Alpers' Disease
- NAD+ Precursors Reverse Experimental Diabetic Neuropathy in Mice
- WRN loss accelerates abnormal adipocyte metabolism in Werner syndrome
- A randomized placebo-controlled trial of nicotinamide riboside in older adults with mild cognitive impairment
- Contribution of nadR to the cell growth and virulence of Streptococcus suis serotype 2

Other Studies and Articles That Sparked Our Interest

- Supplementation Restores Myocardial Nicotinamide Adenine Dinucleotide Levels, Improves Survival, and Promotes Protective Environment Post Myocardial Infarction
- Chronic dietary supplementation with nicotinamide riboside reduces sleep need in the laboratory mouse
- AHA 23: Nicotinamide Riboside in PAD for Improved Walking
- Comparison of protective effects of nicotinamide mononucleotide and nicotinamide riboside on DNA damage induced by cisplatin in HeLa cells
- Nicotinamide Riboside Regulates Chemotaxis to Decrease Inflammation and Ameliorate Functional Recovery Following Spinal Cord Injury in Mice
- ChromaDex CEO calls for trust, innovation and self-policing in supplements industry
- Maternal Administration of Acetaminophen Affects Meiosis Through its Metabolite NAPQI Targeting SIRT7 in Fetal Oocytes
- Inflammation and diabetic kidney disease: Why mitochondria matter
- Nicotinamide Riboside Augments Human Macrophage Migration via SIRT3-Mediated Prostaglandin E2 Signaling
- The effectiveness of four nicotinamide adenine dinucleotide (NAD+) precursors in alleviating the high-glucose-induced damage to hepatocytes in *Megalobrama amblycephala*: Evidence in NAD+ homeostasis, sirt1/3 activation, redox defense, inflammatory response, apoptosis, and glucose metabolism
- Trigonelline is an NAD+ precursor that improves muscle function during ageing and is reduced in human sarcopenia

Come See Us at Upcoming Conferences

ACSM
2024 ANNUAL MEETING
May 28 – 31 | Boston, Massachusetts USA

Conferences Continued

We want to encourage all CERPIs, past and present, to attend FASEB's NAD Metabolism and Signaling Conference in Portugal, August 2024

ChromaDex is sponsoring a clinical trial panel on Thursday the 29th at the FASEB NAD+ Meeting. The panel will be moderated by Dr. David Katz, ChromaDex Scientific Advisory Board Member, with panelists including Dr. Eija Pirinen, Dr. Jonas Treebak, Dr. Charalampos Tzoulis, Dr. Shin-Ichiro Imai, and Dr. Michael Sack. The panel aims to gain consensus around unanswered questions regarding, what are biomarkers to measure clinical benefit of NAD+, what is the optimal level of NAD+ for clinical health outcomes, and treatment or prophylactic – how does this perspective shape considerations? Please send us all questions you would want answered during this panel. We look forward to seeing you at the meeting.

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.

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The Industry's Gold Standard for Excellence in External Research

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