U. of Oslo | U. of Copenhagen | Chinese U. of Hong Kong | Norwegian U. of Science and Technology | K.G. Jebsen Centre for Alzheimer's Disease | Kavli Institute for Systems Neuroscience | NO-Age | NO-AD | MIT-AD

The NO-Age and NO-AD Seminar Series 053

13:30 – 14:20: 'Enzymology and dynamics of cellular NAD metabolism' (tentative)
by **Prof. Mathias Ziegler**, Department of Biomedicine, University of Bergen, Norway

14:20 – 15:10: 'The use of isotopes to explore the mechanisms of NAD+ and its precursors' (tentative)
by **Prof. Marie Migaud**, Department of Pharmacology, University of South Alabama, USA

15:10 – 15:30: Break

15:30 – 15:55: 'A combination of NAD+ supplementation and fasting in the treatment of Alzheimer's Disease'
by **Tomás Alejandro Schmauck-Medina**, University of Oslo & Akershus University Hospital, Norway

15:55 – 16:20: 'NAD+ Repletion Rescues ApoE4-Induced Cognitive Deficits in a C. elegans Model of Alzheimer's Disease'
by **Heling Wang**, University of Oslo & Akershus University Hospital, Norway

16:20 – 17:10: 'Effects of Nicotinamide Riboside in patients with Ataxia Telangiectasia '
by **Dr. Stefanie Veenhuis**, Radboud University Medical Centre, Netherlands

17:10 – 17:35: 'Nicotinamide riboside improves hand coordination and eye movements in Ataxia Telangiectasia'
by **Rebecca Presterud**, University of Oslo, Norway

13:30-17:35 (CET), Monday, 30th May. 2022
Ahus S3: Seminarrom S305.019

Register in advance:
https://uio.zoom.us/webinar/register/WN_HZbtBEvPT52olHxXI1xKnA

Organizers: Evandro F. Fang (UiO), Jon Storm-Mathisen (UiO), Lene Juel Rasmussen (KU), W.Y. Chan (CUHK)

Name: Prof. Mathias Ziegler

Institute: Department of Biomedicine, University of Bergen, Norway

Email: Mathias.Ziegler@uib.no

Lab website: https://www.uib.no/en/persons/Mathias.Ziegler

Speaker: Prof. Mathias Ziegler

Title: 'Enzymology and dynamics of cellular NAD metabolism' (tentative)

Abstract: To be updated

Biography:

The NAD metabolome - A key determinant of cancer cell biology
Emerging roles of NAD+ and its metabolites in cell signaling

Name: **Prof. Marie Migaud**

Institute: Department of Pharmacology, University of South Alabama, USA
Email:mmigaud@health.southalabama.edu

Lab website: https://els-bib.southalabama.edu/colleges/com/departments/pharmacology/migaud.html

Speaker: Prof. Marie Migaud

Title: 'The use of isotopes to explore the mechanisms of NAD+ and its precursors' (tentative)

Abstract: To be updated

Biography:

My research interest resides in developing modular multidisciplinary strategies that seek to modulate the bioavailability of B-vitamin derived redox cofactors to interrogate biological systems while allowing the traceability of changes. Epigenetics evidence highlights the subtle orchestration of signaling and biosynthetic events controlled by the intracellular bioavailability of nicotinamide adenine dinucleotide (NAD, vitamin B3 derived, figure 1) and its phosphorylated and reduced forms (NAD(P)H), flavin adenine dinucleotide (FAD, vitamin B2 derived) and flavin mononucleotide (FMN), S-adenosyl methionine (SAM) and acyl-Co-enzyme A (Acyl-CoA, vitamin B5 derived). The availability of these coenzymes is in turn regulated by metabolic events that modulate and are modulated by the availability of other cofactors; processes we seek to examine (Figure 1). Over the past 20 years, first in the UK and since 2016 at the University of South Alabama Mitchell Cancer Institute (MCI), my laboratory has developed a robust synthetic program that tackles the chemical limitations currently encountered in accessing B-vitamin derived species designed for "task-specific biological investigations". To address the challenges of bioavailability, biodistribution, catabolism (Figure 2) and intracellularization, we develop strategies that allow for modular delivery. Key to our research efforts is the development of efficacious synthetic methodologies that allow atom-efficient scalable preparation of heteroaromatics, nucleos(t)ides and dinucleotides and give access to probes incorporating stable isotopes, fluorophores, and conjugatable containing moieties, designed to investigate the metabolic and signaling pathways regulated by B-vitamin-derived cofactors. At MCI and to complement our synthetic work, I have worked closely with biologists, nationally and internationally to manipulate and exploit the impact that these coenzymes' metabolism and bioavailability have on aging and disease.

Name: Tomás Alejandro Schmauck-Medina

Institute: University of Oslo & Akershus University Hospital, Norway

Email: tschmauck@gmail.com

Speaker: Tomás Alejandro Schmauck-Medina

Title: 'A combination of NAD+ supplementation and fasting in the treatment of Alzheimer's Disease'

Abstract

Alzheimer's disease (AD) is the most common type of dementia worldwide, and in an rapidly ageing world the growth in incidence will put a tremendous economical and social pressure in the health system. Most cases of Alzheimer's Disease are not driven by causative genes but by risk factors. Therefor developing effective treatments that reduce the risk of developing AD will not only ease the pressure but also contribute to the wellbeing of the elderly. One therapy that has shown potential is the supplementation of NAD+, which can improve the pathology of AD in multiple models. In addition, intermittent fasting, which has become widely popular around the globe for health and weight lose purposes, has also shown some preliminary benefits in AD. Both techniques can improve the autophagy machinery, which leads us to study if these two methods carry an additive or synergistic effect in the treatment of AD, which currently holds no effective treatment.

Biography:

Tomás Schmauck-Medina is a Ph.D candidate in the Evandro Fang Lab focusing on the mechanisms of aging and Alzheimer disease, as well as therapies to ameliorate both. He has a bachelor in Biomedicine and carried out a Master in Neuroscience at University College London in the lab of Linda Partridge.

Name: Heling Wang

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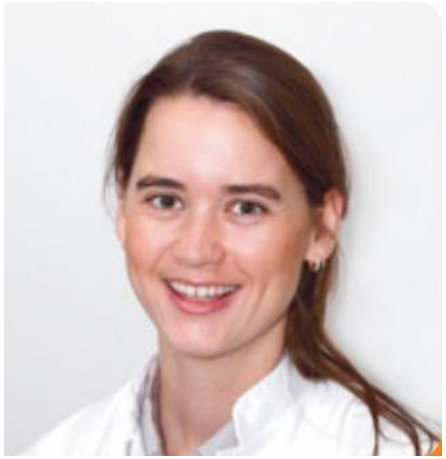
Speaker: Heling Wang

Title: NAD+ Repletion Rescues ApoE4-Induced Cognitive Deficits in a C. elegans Model of Alzheimer's Disease

Abstract:
Alzheimer's disease (AD) is a neurodegenerative disorder that is caused by a combination of genetic, lifestyle and environmental factors. The causative role of these factors in AD remains largely unknown. Extensive efforts are being made to develop AD-specific drugs; however, so far there are no medications or supplements that have been shown to decrease risk or reverse its progression.
ApoE4, one allele of human Apolipoprotein E (ApoE), is the most prevalent genetic risk factor for AD, which exacerbates amyloid-β (Aβ)- and tau-mediated neurodegeneration. Although ApoE4 has been implicated in AD development, molecular mechanisms on whether and how ApoE4 effects the initiation and progression of AD are poorly known. Our recent study showed defective mitophagy in AD patient-differentiated ApoE4 cortical neurons, while mitophagy restoration improved neuronal function in these neurons. At a younger age, sufficient cellular NAD+ maintains mitochondrial quality to preserve normal neuronal function via the NAD+ dependent regulations of mitophagy. However, as we age, increased NAD+ consumption drives NAD+ depletion, leading to impaired mitophagy and neuronal function. The reduction of NAD+ is also due to various genetic or environmental factors, including carrying ApoE4. Therefore, we propose NAD+ deficiency induces imparing mitophagy and exacerbates the initiation and progression of ApoE4-based AD.
To this end, we will utilize ApoE4 transgenic worms (Caenorhabditis elegans) and two NAD+ precusors to address this major aim.

Biography:

Heling holds a Bachelor's degree in Medicine and a Masters degree in Oral Medicine from Jilin University, China. During her Masters, she completed a one-year internship program at Okayama University, Japan, where she received training in microbiota, focusing her research mainly on microbiota related-diseases. In the Fang lab at the University of Oslo (UiO), she is focusing on the mechanistic studies of Alzheimer´s disease (AD), with focuses on ApoE4, NAD^+, and autophagy/mitophagy. She will also conduct research on microbiota and AD to address related questions.



Name: Stefanie Veenhuis

Institute: Radboud University Medical Centre, Netherlands

Email: Stefanie.Veenhuis@radboudumc.nl

Speaker: Stefanie Veenhuis

Title: 'Effects of Nicotinamide Riboside in patients with Ataxia Telangiectasia '

Abstract:
Between march and september 2019 we conducted this open-label, proof-of-concept study, to investigate the effect of Nicotinamide Riboside (NR) in patients with Ataxia Telangiectasia (A-T). During 6 consecutive months 24 patients with A-T were treated with NR. We analyzed the effects of NR on ataxia, dysarthria, quality of life, and laboratory parameters. During treatment, clinical ataxia scores improved. After NR withdrawal, these scores worsened. In immunodeficient patients, the mean serum IgG concentration increased substantially until the end of the study period. Untargeted metabolomics analysis revealed increased plasma levels of NR metabolites and purine nucleosides during treatment. Adverse effects of NR did not occur during the study period. Based on our findings we concluded that treatment with NR is tolerated well and associated with improvement in ataxia and serum immunoglobulin concentrations in patients with A-T.

Biography:
Stefanie Veenhuis is a resident in pediatrics at the Radboud University Medical Center in Nijmegen, the Netherlands.
During her recidency, she got in contact with professor dr. M.A.A.P Willemsen and started her research on Ataxia Telangiectasia under his supervision.
In 2019 she works on a research project that investigated the effects of nicotinamide riboside in patients with A-T. The results of this trial (see abstract) were published in Movement Disorders. The Dutch Association of Neurology has awarded a prize for this article as the best conducted clinical trial in the Netherlands on movements disorders.

Name: Rebecca Presterud

Institute: University of Oslo, Norway

Email: rebecca.presterud@studmed.uio.no

Speaker: Rebecca Presterud

Title: Nicotinamide riboside improves hand coordination and eye movements in Ataxia Telangiectasia

Abstract:

Background: Ataxia Telangiectasia (AT) is an autosomal recessive disorder that causes ataxia, immunodeficiency, ocular telangiectasia, and an increased susceptibility to malignancy and metabolic disorders. The ataxia progresses over the course of life, ultimately making the patients unable to walk without any assistance. Supplementation of nicotinamide riboside (NR, commercially Niagen(tm), Chromadex) increases the lifespan and ameliorates neuropathology in different AT-animal models. The aim of this pilot study is to examine the effect of supplementation in human AT-patients.
Methods: An open-label pilot study with twelve Norwegian AT-patients receiving an increasing dosage of NR (150-300-500 mg) over the course of two years. We then analyzed the effects of NR on neurological function, biochemistry and quality of life. The safety of the drug was also carefully monitored and evaluated throughout the study duration.
Results: The coordination, eye movement and total scores improved after 18 months; both in the validated International Cooperative Ataxia Rating Scale and Scale for the Assessment and Rating of Ataxia, and in the more specified but not validated the AT Neurological Examination Scale Toolkit. There were no significant changes in the biochemistry, but NADolomics indicated an increased NAD+/NADH-metabolism. None of the patients reported any adverse effects.
Conclusions: NR is a safe, well tolerated and convenient treatment option for patients with AT, that reduces neurological symptoms, increases NAD+/NADH-metabolism and stabilizes inflammation markers in the blood.

Biography:

I am a fourth year medical student who is also attending the research program at the Faculty of Medicine, University of Oslo, which is meant to encourage young upcoming doctors to pursue research and academia. The last three years I have been working in the Nilsen Group with the Niagen study with collection and analysis of patient data and blood samples, and clinical follow-ups of the patients together with our collaborators at Oslo University Hospital and Innlandet Hospital. This is my first academic work and I am excited to present it to an international audience! And who knows, maybe this is my first step towards a Ph.D.? My personal fields of interests are pediatrics, rare diseases, surgery and neurology.