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The NO-Age and NO-AD Seminar Series 016

14:30-17:15 (CET), Monday, 8th March 2021

14:30-15:45 'Genome Stability in Ageing and Disease: New Perspectives from C. elegans', Prof. **Björn Schumacher,** University of Cologne, Germay

16:00-17:15 'NAD+, health, and ageing' (tentative), Prof. **Shin-ichiro Imai** Washington University School of Medicine, USA

Register in advance for this webinar:
https://uio.zoom.us/webinar/register/WN_L_f-CKU6Tbq80MF_PHZ6zg

Organizers:
Evandro F. Fang (UiO), Hilde L. Nilsen (UiO), Jon Storm-Mathisen (UiO), Menno P. Witter (NTNU), Lene Juel Rasmussen (KU), W.Y. Chan (CUHK)
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Previous recorded talks are available here: https://noad100.com/videos-previous-events/

Name: Björn Schumacher
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Photo: U of Cologne

Speaker: Björn Schumacher

Title: Genome Stability in Ageing and Disease: New Perspectives from *C. elegans*

Abstract:
Ageing is an inherent property of somatic tissues. In contrast, germ cells indefinitely perpetuate the genetic information. According to the disposable soma theory, selective pressure has shaped maintenance and repair mechanisms that ensure somatic functioning early in life, while the soma may decay upon successful reproduction. We focus on three central questions: (1) How is somatic maintenance adapted to the requirements of the germline, (2) what are the underlying mechanisms for germ cell immortality, and (3) which processes determine somatic maintenance and thus control ageing?
The causal contribution of DNA damage not only to cancer development but evenly to the ageing process has been demonstrated by progeroid (premature ageing-like) syndromes that are caused by mutations in DNA repair genes. We have established the nematode *C. elegans* as metazoan model to investigate the consequences of DNA repair defects that in humans cause either cancer predisposition or developmental retardation and premature ageing.
Using this model, we identified germline DNA damage induced systemic stress resistance (GDISR) that adapts somatic maintenance to genomic impediments of germ cells. We postulate that by elevating somatic endurance, GDISR extends reproductive lifespan to allow germ cells to repair their genomes and resume offspring generation later in life.
To ensure the immortality of germ cells, genome stability in primordial germ cells (PGCs) is a prerequisite. We have determined that the DNA damage response in PGCs is regulated non-cell-autonomously through the adjacent somatic niche cells. Our data suggest that the somatic niche regulates the maintenance of heritable genomes by impacting the DDR in PGCs.
While DNA repair mechanisms counteract the accumulation of DNA damage, the organism's homeostatic processes need to be maintained during development and ageing. We identified epigenetic regulators of H3K4me2 deposition that following DNA repair reinstate protein biosynthesis and homeostasis to promote the organism's growth and longevity amid DNA damage.

Biography:
Since 2013, Björn Schumacher is full professor and director of the Institute for Genome Stability in Ageing and Diseases (IGSAD) at CECAD Research Centre of the University of Cologne. He received his PhD at the Max Planck Institute for Biochemistry in Munich and conducted his postdoctoral research as EMBO and Marie Curie fellow at the Erasmus Medical Centre in Rotterdam. B.S. received the Eva Luise Köhler Research Award, the Innovation Prize of the State of Northrhine-Westphalia, the European Research Council (ERC) starting grant, and coordinated the FP7 Marie Curie initial training network on chronic DNA damage in ageing (CodeAge). Professor Schumacher served as President of the German Society for Ageing Research (DGfA) and is currently Vice President of the German Society for DNA Repair (DGDR), co-Director of the Minerva Center of the Biological Mechanisms of Healthy Ageing at Bar-Ilan University (IL) and serves on several editorial boards. His research interest focuses on the molecular mechanisms through which DNA damage contributes to cancer development and ageing-associated diseases. Employing the *C. elegans* system and mammalian disease models, his group uncovered cell-autonomous and systemic responses through which the organism adapts to accumulating DNA damage with ageing. Through the understanding of the basic mechanisms of genome instability-driven ageing, Schumacher aims to contribute to the development of future strategies to prevent ageing-associated diseases.

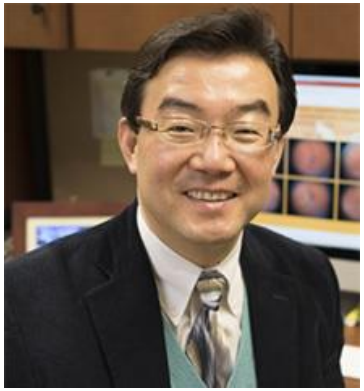

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Photo: wustl

Speaker: Shin-ichiro Imai
Title: 'NAD$^+$, health, and ageing' (tentative)

Abstract:
To be updated

Biography:
Our major interest is to understand the systemic regulation of aging and longevity in mammals and translate that knowledge into an effective anti-aging intervention that makes our later lives as healthy and productive as possible ("productive aging").

Three key tissues have been identified as basic elements in mammalian aging and longevity control: the hypothalamus as the control center, skeletal muscle as an effector and adipose tissue as a modulator.

In the dorsomedial hypothalamus (DMH), the mammalian NAD+-dependent deacetylase SIRT1 and its binding partner Nkx2-1 cooperate to counteract age-associated physiological decline and promote longevity in mice (Satoh et al., Cell Metab., 2013). Adipose tissue remotely promotes NAD+ biosynthesis, SIRT1 activity and neural activity in the hypothalamus through the secretion of nicotinamide phosphoribosyltransferase (NAMPT), a key NAD+ biosynthetic enzyme (Yoon et al., Cell Metab., 2015). Skeletal muscle secretes myokines in response to the signal from the hypothalamus, possibly affecting other tissue functions (under investigation). These findings are integrated into a comprehensive concept of mammalian aging and longevity control, named the NAD World 2.0 (Imai, npj Systems Biology and Applications, 2016).

To dissect the system dynamics of the NAD World 2.0, our lab is currently conducting the following projects: 1 The function of the hypothalamus as the "control center of aging" in mammals; 2 The function of extracellular NAMPT (eNAMPT) secreted by adipose tissue; 3 The anti-aging effect of nicotinamide mononucleotide (NMN); and 4 The function of skeletal muscle as an "effector" for aging and longevity control.

Through these projects, we aim to understand the importance of these critical inter-tissue communications among the hypothalamus, skeletal muscle and adipose tissue in mammalian aging and longevity control. The anticipated outcome of these studies will allow us to develop effective anti-aging interventions to achieve "productive aging" in the world.