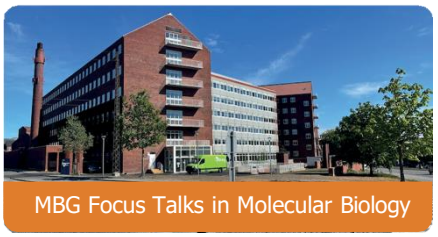
# MBG FOCUS TALK

Hosted by Tinna Stevnsner




**Monday 23 September 2024 @ 10:00-10:45**
Faculty Club (1870-816)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## Dysregulation of the NAD⁺-mitophagy axis in accelerated ageing and Alzheimer's disease


Being central to mitochondrial metabolism and bioenergetics, the cellular metabolite nicotinamide adenosine riboside (NAD⁺, oxidized form) is essential for life. Interestingly, NAD⁺ can induce mitochondrial biogenesis and mitophagy, a mitochondria-specific type of autophagy. Studying the accelerated ageing disease Werner syndrome (WS), we showed that decreased NAD⁺ led to compromised mitophagy, which drives accelerated ageing in WS. I will present how treatments with the NAD⁺ precursors nicotinamide riboside (NR) and nicotinamide mononucleotide (NMN) stimulated mitophagy and improved mitochondrial function in WS. NAD⁺-mediated induction of mitophagy enhanced mitochondrial homeostasis, inhibited senescence, and hereby slowed down ageing in WS stem cell, nematode and fruit fly models. Furthermore, we discovered compromised mitophagy leading to a severe accumulation of dysfunctional mitochondria in Alzheimer's Disease (AD). Our research established compromised mitophagy as an essential player in disease aetiology, and we demonstrated that pharmacological induction of mitophagy ameliorates both pathological hallmarks as well as cognitive deficits associated with AD. Using a new artificial intelligence approach, we identified novel mitophagy inducers and target genes, and showed how the drug-treatments ameliorate AD features *in vivo*. Combined our studies indicate the NAD⁺-mitophagy axis as druggable target with high potential as anti-AD treatment and beyond.


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