Title: oxidative stress, mitochondrial homeostasis, and ageing

Abstract

There were 962 million elderly (60+) people globally in 2017, and this number will rise to 2.1 billion in 2050, bringing formidable healthcare and socio-economic challenges[1, 2]. Ageing is arguably the highest risk factor for numerous human diseases, thus understanding the molecular mechanisms of human aging holds the promise of developing interventional and therapeutic strategies for many diseases simultaneously, promoting healthy longevity. Accumulation of damaged mitochondria, correlating with higher cellular ROS, is a hallmark of aging and age-related neurodegeneration, including Alzheimer's disease (AD). However, the molecular mechanisms of impaired mitochondrial homeostasis and their relationship to AD are still elusive. Mitophagy is the cellular self-clearing process of damaged and superfluous mitochondria, and therefore plays a fundamental role in maintaining neuronal function and survival[1, 3, 4]. We hypothesize that age-susceptible defective mitophagy causes accumulation of damaged mitochondria, which in combination with the two AD-defining pathologies, Aβ plaques and tau tangles, further exacerbates AD progression. Restoration of mitophagy through upregulation of cellular NAD^+, a primary molecule in human health and life, and genetic approaches, forestalls pathology and cognitive decline in *C. elegans* and three mouse models of AD and improves mitochondrial function in the AD iPSC neurons[5, 6]. We are now involved in more than 5 clinical trials on the use of NAD^+ precursors to treat AD, and premature ageing diseases, among others[7]. Additionally, we are using artificial intelligence (AI) to propel drug screening and drug design targeting AD and ageing pathways[8].

Key References

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Biography (<500 words)

Evandro F. Fang is an Associate Professor of Molecular Gerontology at the University of Oslo (UiO), Norway, and his group are working on the molecular mechanisms of human ageing and age-predisposed neurodegeneration (https://evandrofanglab.com/). More specifically, the Fang laboratory is focusing on the molecular mechanisms behind how cells clear their damaged and aged mitochondria, a process termed “mitophagy”, as well as the roles of the NAD^+-mitophagy/autophagy axis in healthy ageing and AD inhibition. NAD^+ is a fundamental molecule in life and health and decreases in ageing and AD. Dr Fang is fascinated with and actively engaged in moving his laboratory findings to translational applications and is involved in 5+ NAD^+-based clinical trials, with the overarching goal of establishing novel and safe biological approaches to promote longer and healthier human lives.

After finishing his PhD at the Chinese Universtiy of Hong Kong, he had a 6-year postdoc training with Prof. Vilhelm Bohr on molecular gerontology at the National Institute on Ageing, Baltimore. He opened his lab in Oslo in the fall of 2017.

He has published over 80 papers in international peer-reviewed journals including papers in *Cell, Cell Metabolism, Nature Reviews MCB*, *Nature Neuroscience, Nature Ageing, and Nature Biomedical Engineering*. He has received several awards including the Butler-Williams Scholar on Aging 2016 by NIA (USA) and the 'Scientific Award to Young Scientist in the Natural Sciences for 2020 by The Royal Norwegian Society of Sciences and Letters (Norway).

He is the founding (co)coordinator of the Norwegian Centre on Healthy Ageing network (**NO-Age**, www.noage100.com), the Norwegian National anti-Alzheimer’s disease Network (**NO-AD**, www.noad100.com), and the Hong Kong-Nordic Research Network.