MBG FOCUS TALK

hosted by Tinna Stevnsner

MBG Focus Talks in Molecular Biology

Monday May 9, 2022 at 15.00-16.00

1875-132 (Seminar room)

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The NAD+-mitophagy axis in ageing and Alzheimer's disease and AI-based drug development

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. 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 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. 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. 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. Additionally, we are using artificial intelligence (AI) to propel drug screening and drug design targeting AD and ageing pathways.

Anyone interested is very welcome to attend