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The NO-Age and NO-AD Seminar Series 026

'Autophagy and inflammation in ageing and diseases' (tentative)

by

Prof. Alexander Clarke

The Kennedy Institute of Rheumatology, Oxford, UK

at

14:00-15:00 (CET), Friday, 15th Oct. 2021

'Mitophagy and mitochondrial dynamics in mitochondrial diseases'

by

Prof. Jo Poulton

Nuffield Department of Woment's & Reproductive healthy, Oxford, UK

at

15:00-16:00 (CET), Friday, 15th Oct. 2021

Register in advance for this webinar:

https://uio.zoom.us/webinar/register/WN_tw3Tqs5AQ0m--0et6tp2Sg

Organizers:

Evandro F. Fang (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/

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Photo: Oxford

Speaker: Alexander Clarke

Title: 'Autophagy and inflammation in ageing and diseases' (tentative)

Abstract:
To be updated

Biography:

I qualified in Medicine from UCL in 2001, and trained in Rheumatology in London. Supported by a Wellcome Trust Clinical Research Training Fellowship, I completed a PhD on the role of autophagy in lupus in 2013, supervised by Tim Vyse at King's College London.

After completing my medical specialist training, I moved to Oxford to join the group of Katja Simon at the Weatherall Institute of Molecular Medicine as a postdoctoral clinical fellow in 2014, again supported by the Wellcome Trust.

In 2018 I was awarded a Wellcome Trust Clinical Research Career Development Fellowship, establishing my own group here at the Kennedy Institute of Rheumatology.

Name: Jo Poulton
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Photo: Oxford

Speaker: Jo Poulton

Title: 'Mitophagy and mitochondrial dynamics in mitochondrial diseases'

Abstract:
To be updated

Biography:
Joanna Poulton is professor and honorary consultant in mitochondrial genetics in the University of Oxford, where she works on mitochondrial diseases. She leads research group and advises the clinical service diagnosing and managing mitochondrial diseases (the Oxford Rare Mitochondrial Disorders Service for adults and children, funded by the UK NHS Highly Specialised Services). Key areas include complex mitochondrial DNA (mtDNA) rearrangements, disorders of mtDNA maintenance, the mitochondrial bottleneck in transmission of mtDNA diseases and mitophagy (one type of mitochondrial quality control).
She developed high throughput imaging for detecting mitophagy. She also generated a mouse model for visualizing mitophagy (the RedMIT-GFP/LC3 mouse) with a view to developing drug modulators of mitophagy. However we now favour Ian Ganley's MitoQC model because it uses a more advanced system for visualizing mitophagy and is much better expressed in oocytes and early embryos than the RedMIT-GFP/LC3 mouse.

Mitophagy and mitochondrial dynamics in mitochondrial diseases
Mitochondrial function is critically important for many cellular processes and important diseases. However, mitochondrial quality control is poorly understood and the role of mitophagy is controversial. While mitophagy is widely discussed in the literature and believed to be critically important in the pathogenesis of Parkinson's disease, it is technically difficult to demonstrate. We developed IN Cell 1000 high-throughput imaging for quantifying mitophagy, being objective as well as quantitative.
Studies of control fibroblasts suggest that mitophagy declines with aging and this may make an important contribution to age-related diseases. Our method made a paradigm shift, because we are able to document dysregulated mitophagy (usually increased) in cultures from mitochondrial patients in the majority of mitochondrial DNA diseases. We believe that this is because, unlike most mitophagy groups, we study primary cultures derived from our patients rather than transformed cells, dysregulated autophagy being a feature of cancer.
We demonstrated excessive mitophagy in disordered mitochondrial dynamics including dominantly inherited optic neuropathy due to *OPA1* and also in mitochondrially inherited optic neuropathy. Mitophagy appears to contribute to mitochondrial DNA depletion syndrome.
As well as being very useful for drug development, we anticipate that our high throughput fibroblast-based assay will be useful diagnostically. In the longer term we anticipate that our assay may become useful as a biomarker for treatment efficacy.