NANYANG TECHNOLOGICAL UNIVERSITY

School of Biological Sciences

SBS Seminar Announcement

AUTOPHAGY IN CELL DEATH SUSCEPTIBILITYPOINTS OF DEPARTURE FOR A QUANTITATIVE APPROACH

Dr Ben. Loos
Department of Physiological Sciences
Stellenbosch University, South Africa

Abstract

Impaired autophagic machinery is implicated in a number of diseases such as heart disease, neuro-degeneration and cancer. A common denominator in these pathologies is a dysregulation of autophagy, which has been linked to a change in the susceptibility to undergo cell death. Although we have progressed in understanding the molecular machinery and regulation of the autophagic pathway, many unanswered questions remain. Due to the central role of autophagy in controlling protein degradation as well as due to its fundamental position in affecting cell death susceptibility, reliable and measurable data points are needed that allow to quantify the function (and dysfunction) of organelles associated with the autophagic pathway. Currently, transmission electron microscopy (TEM) is providing the required structural detail and resolution to identify double-membraned autophagosomal structures, and hence remains the gold standard to assess these organelles. However, TEM does neither allow to distinguish between autophagosomes and lysosomes easily, nor to quantify the complete organellar pool size, as three dimensional whole cell analysis is technically challenging. Here we present some of our work which has increased our understanding of the context dependent relationship between protein degradation through autophagy and cell death susceptibility. It becomes clear that in order to understand and predict cell death and cell survival, and in order to unravel the molecular mechanisms that result in morphological overlap of cell death, we will have to take into account the metabolic status and history of the cells, as well as the matrices in which they are found. Importantly, we will have to be able to better quantify autophagic flux numerically, in order to finely control it in pathological conditions. Here, we highlight the key components that shape this cellular matrix and introduce points of departure for a novel approach to accurately quantify autophagic flux and fusion parameters between autophagosomes and lysosomes. In doing so, we highlight the strengths of structured illumination superresolution microscopy (SR-SIM) in deriving numerical data that may allow the prediction and modelling of organelle fusion behaviour and mitochondrial network function especially applicable in neurodegenerative disorders that are characterized by dysfunctional protein clearance.

Wednesday, 16 Jul 2014 2.00pm to 3.00pm SBS Classroom 3 (SBS-01n-23)

Host: Asst/Prof Esther Wong

60 Nanyang Drive, Singapore 637551
Tel: +65 6316 2800 Fax: +65 6791 3856
Email: d-sbs@ntu.edu.sg www.ntu.edu.sg/sbs