DANDRITE & PUMPkin Topical Seminar

by visitor Nikolai Engedal

Thursday 27th November 2014
13.15 – 14.00

Auditorium 6, building 1170
Dept. Biomedicine, Ole Worms Allé 3, 8000 Aarhus

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Deciphering how calcium and ER stress responses affect autophagy in prostate cancer cells

Prostate cancer is a frequently occurring disease that takes thousands of lives every year. As is the case with all types of cancer, a major clinical problem is the ability of advanced cancers to resist various types of therapy. Anti-cancer therapeutics often perturb intracellular calcium homeostasis and enhance ER stress as well as the resulting unfolded protein response (UPR), all of which have been linked to induction of protective autophagy. In contrast, extensive and sustained activation of calcium signals, UPR, or autophagy may instead lead to cell death. Thus, understanding the biology and how to modulate these pathways is of great interest, and a number of clinical trials involving such modulations have already been initiated on patients with various types of cancers.

We are using novel approaches to measure autophagic activity as well as to dissect the ER stress/UPR response, in order to improve our understanding of the link between calcium perturbations, ER stress and autophagy in prostate cancer cells. Surprisingly, and contrary to previous beliefs, we found that modulation of intracellular calcium levels and the UPR with either thapsigargin or calcium ionophores blocked autophagy at an early step in the pathway, and in a manner that was independent of any of the three arms of the UPR (Engedal et al., 2013, Autophagy, 9(10):1475-1490). Moreover, we have recently found that other ER stress-inducing compounds, i.e. 2-deoxyglucose and tunicamycin, differentially affect autophagy in prostate cancer cells. Taken together, our results suggest an intriguingly context-dependent influence of calcium and the UPR on autophagy.

Host: Prof. Poul Nissen, DANDRITE & PUMPkin
Prof. Jesper Vuust Møller, PUMPkin