DEPARTMENTAL SEMINAR

Molecular Genetics
UNIVERSITY OF TORONTO

From amoeba to man: an evolutionarily conserved PRP4K-CHMP4B splicing circuit regulates autophagy

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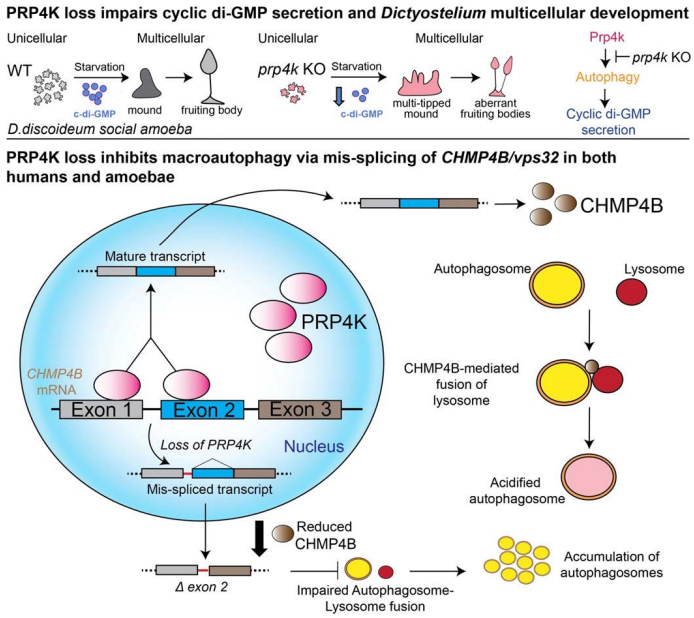
The pre-mRNA processing factor 4 kinase (PRP4K) is an essential gene in animal cells, making interrogation of its function challenging. Here, we report the first knockout model for PRP4K in the social amoeba Dictyostelium discoideum, revealing a new function in splicing events controlling autophagy. When prp4k knockout amoebae underwent multicellular development, we observed defects in differentiation linked to abnormal autophagy and aberrant secretion of stalk cell inducer c-di-GMP. Autophagosome-lysosome fusion was found to be impaired after PRP4K loss in both human cell lines and amoebae. Mechanistically, PRP4K loss results in mis-splicing and reduced expression of the ESCRT-III gene CHMP4B in human cells and its ortholog vps32 in Dictyostelium, and re-expression of CHMP4B or Vps32 cDNA (respectively) restored normal autophagosome-lysosome fusion in PRP4K-deficient cells. Thus, our work reveals a novel PRP4K-CHMP4B/vps32 splicing circuit regulating autophagy that is conserved over at least 600 million years of evolution.



Date: Tuesday, November 26th, 2024
Time: 10:00 AM
Place: MSB 3287
Host: Dr. Laurence Pelletier