CDB SEMINAR

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16:00~17:00 Auditorium C1F

An extensive HLH transcription factor network promoting longevity in response to signals from the gonad

Summary

The reproductive system is responsible for procreation but also affects life span in many species. In *C. elegans*, removal of the germline extends lifespan up to 60% (termed gonadal longevity). Several transcription factors regulate longevity arising from germline removal, yet how they work together is unknown. We have recently identified a Myc-like HLH-transcription factor network comprised of Mondo/Max-like complex (MML-1/MXL-2) required for longevity induced by germline removal, as well as by reduced TOR (Target Of Rapamycin), insulin/IGF signaling, and mitochondrial function. Germline removal triggers MML-1 nuclear localization and activity. Surprisingly MML-1 regulates nuclear localization and activity of HLH-30/TFEB, a convergent regulator of autophagy, lysosome biogenesis and longevity, by downregulating TOR signaling via LARS-1/leucyl-tRNA synthase. HLH-30 also upregulates MML-1 upon germline removal. Mammalian MondoA/B and TFEB show similar mutual regulation. MML-1/MXL-2 and HLH-30 transcriptomes show both shared and distinct outputs including MDL-1/MAD-like HLH factor required for longevity. These studies reveal how an extensive interdependent HLH transcription factor network distributes responsibility and mutually enforces states geared towards reproduction or survival.

Host:
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