Yale SCHOOL OF MEDICINE

GENETICS DEPARTMENT SEMINAR SERIES

Regulatory Mechanisms in Lysosomes and Autophagy

Autophagy is a conserved mechanism that is essential for cell survival in starvation and for cellular homeostasis. Autophagy proceeds by the engulfment of bulk cytosol and organelles by a cup-shaped double membrane sheet known as the phagophore, which matures into the autophagosome, closes, and fuses with the lysosome. The lysosome is the destination of the autophagosome and the ultimate source of the degradative power of autophagy, but it is also a signaling hub that regulates the initiation of autophagy, as well as its own biogenesis. Both autophagy and lysosomes are attracting increasing interest as targets for the treatment of neurodegenerative diseases. I will begin by describing mechanistic insights regulation of the TFEB transcription factor family by nutrients via the Rag GTPases, the FLCN-FNIP2 complex, and the amino acid transporter SLC38A9. I will then describe how the C9orf72 complex, whose expression is decreased in ALS and FTD, has a structure similar to FLCN-FNIP2 and an unexpected function as an Arf family GTPase activating protein. I will go on to describe a series of structural and reconstitution studies of mammalian autophagy initiation, which collectively connect the dots from ubiquitin chain engagement by the autophagy adaptors NDP52, OPTN, and TAX1BP1 to LC3 lipidation.

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Tuesday, October 6, 2020

11:30am - 12:30pm

Zoom Link

pw: 7852649