



Wedne
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Nijenbo
room 51

Studying Membrane Fusion with Yeast Vacuoles: 5 Lipids, 4 SNAREs, 3 Chaperones, 2 Nucleotides, and a Rab GTPase, All Dancing in a Ring!

Wickner has developed yeast vacuoles as a paradigm of membrane fusion in endocytic and exocytic traffic. Each stage of this traffic, from yeast to humans, uses similar Rabs, effector complexes, SNAREs, and SNARE chaperones. In addition to studying vacuole fusion *in vivo* and *in vitro*, Wickner constituted proteoliposome fusion with all-purified components. This system has revealed detailed basic features of the underlying fusion mechanism, which will be discussed. In addition, several fusion catalysts have been identified that undergo regulated cycles, including HOPS and Sec17/18p, which synergistically support fusion as SNAREs cycle between cis-complexes, the uncomplexed state, and trans-complexes, and the vacuolar kinase Yck3p and unknown phosphatase(s) that regulate HOPS phosphorylation. Understanding the vacuolar HOPS complex, discovered and studied in this work, underlies studies of human arthrogryposis, renal dysfunction, and cholestasis syndromes, caused by mutations in the human VPS33 gene. Human HOPS has recently been shown to have a unique and central role in Marburg and Ebola virus invasion of human cells.