about autophagy... Autophagy is a highly conserved eukaryotic pathway for sequestering and transporting bulk cytoplasm, including proteins and organelle material, to the lysosome for degradation. Upon starvation for nutrients such as carbon, nitrogen, sulfur, and various amino acids, or upon endoplasmic reticulum stress, cells initiate formation of a double-membrane vesicle, termed an autophagosome, that mediates this process. Approximately 30 autophagy-relatedproteins have been identified in S. cerevisiae, 17 of which are essential for formation of the autophagosome. Null mutations in most of these genes prevent induction of autophagy, and cells do not survive nutrient starvation; however, these mutants are viable in rich medium. Some of the Atg proteins are also involved in a constitutive biosynthetic process termed the cytoplasm-to-vacuole targetingpathway, which uses autophagosomal-like vesicles for selective transport of hydrolases aminopeptidase Iand alpha-mannosidaseto the vacuole. Autophagy proceeds via a multistep pathwaykindly provided by Dan Klionsky). First, nutrient availability is sensed by the TORC1 complex and also cooperatively by protein kinase A and Sch9p. Second, signals generated by the sensors are transmitted to the autophagosome-generating machinery comprised of the 17 Atg gene products. These 17 proteins collectively form the pre-autophagosomal structure/phagophore assembly site. The PAS generates an isolation membrane, which expands and eventually fuses along the edges to complete autophagosome formation. At the vacuole the outer membrane of the autophagosome fuses with the vacuolar membrane and autophagic bodies are released, disintegrated, and their contents degraded for reuse in biosynthesis.about the Cytoplasm-to-vacuole targetingpathway Cytoplasm-to-vacuole targetingis a constitutive and specific form of autophagy that uses autophagosomal-like vesicles for selective transport of hydrolases aminopeptidase Iand alpha-mannosidaseto the vacuole. Unlike autophagy, which is primarily a catabolic process, Cvt is a biosynthetic process. Like autophagosomes, Cvt vesicles form at a structure known as the phagophore assembly site. The PAS structure generates an isolation membrane, which expands and eventually fuses along the edges to complete vesicle formation. At the vacuole, the outer membrane of the Cvt vesicle fuses with the vacuolar membrane, the vesicle is degraded, and the cargos are released and processed into their mature forms by vacuolar peptidases. The Cvt pathway has not been observed outside of yeast, and enzymes specifically involved in this pathway are not well conserved in other organisms.about ATG9 Atg9p is required for both the bulk autophagy and Cvt pathways and is directly involved in formation of the sequestering vesicle. Atg9p is an integral membrane protein that localizes to the PAS and to smaller punctate structures throughout the cytoplasm and on the surface of mitochondria. Atg9p cycles between these locations by a process that allows it to remain associated with lipid bilayers. These findings have led to hypotheses that Atg9p may serve as a membrane carrier, and that mitochondria may be a membrane source, for the formation of the pre-autophagosome. Shuttling occurs whether the cells are maintained in conditions in which the Cvt pathway is operativeor in conditions that promote autophagy. Anterograde transport of Atg9p to the PAS is facilitated by Atg11p, Atg23p, and Atg27p; Atg23p and Atg27p also localize to punctate structures and the PAS and have been shown to form a complex with Atg9p. Atg9p is not a component of completed autophagosomes, and retrograde transport from the PAS back to its mitochondrial and cytoplasmic locations is mediated by a general process that requires the Atg1p-Atg13p complex, Atg2p, Atg18p, and phosphatidylinositol-3-phosphate kinase complex I. Atg9p homologs have been found in other organisms including plants and humans. The mammalian homolog, mAtg9, exhibits a different subcellular distribution from S. cerevisiae Atg9p: it localizes to the trans-Golgi network and to late endosomes. Starvation conditions that upregulate autophagy cause mAtg9 to redistribute to peripheral, endosomal membranes, which are autophagosomal intermediates.about autophagy nomenclature The initial identification of factors involved in autophagy was carried out by several independent labs, which led to a proliferation of nomenclature for the genes and gene products involved. The differing gene name acronyms from these groups included APG, AUT, CVT, GSA, PAG, PAZ, and PDD. A concerted effort was made in 2003 by the scientists working in the field to unify the nomenclature for these genes, and \"AuTophaGy-related\" genes are now denoted by the letters ATG. In addition to the ATG gene names that have been assigned to S. cerevisiae proteins and their orthologs, several ATG gene names, including ATG25, ATG28, and ATG30, have been used to designate proteins in other ascomycete yeast species for which there is no identifiable equivalent in S. cerevisiae.