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 ATG21 ATG18 and ATG21 are paralogous genes that, along with HSV2, encode members of a vacuolar/perivacuolar family of phosphoinositide binding proteins. Atg18p is essential for vesicle formation in both autophagy and the Cvt pathway. Atg21p is only required for vesicle formation in the Cvt pathwaybut may have some role in autophagic fidelity. Atg18p and Atg21p are WD-40 repeat proteins, expected to fold as seven bladed &#946;-propellers, that are able to bind both phosphatidylinositol-bisphosphate and phosphatidylinositol 3-phosphate. Atg21p localizes to vacuolar and perivacuolar structures at the vertices of the vacuole junctions. Loss of Atg21p activity results in decreased Atg8p-lipid conjugation as well as loss of Atg8p and Atg5p recruitment to the preautophagosomal structure. atg21 null strains are also unable to grow on media containing glycerol as the sole carbon sourceand homozygous diploid null mutants show a decrease in sporulation rate. Atg18p and Atg21p have also been shown to interact with the transcriptional activator Rtg3p, and null atg18 or atg21 mutations result in the reduced expression of RTG-regulated genes. WD-repeat proteins are conserved from yeast to man, and ATG18 and ATG21 homologs have been identified in organisms such as Drosophilaand human. Aberrant expression of human WIPI genes has been found in various cancerous tissues.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.