macro AUTOPHAGY

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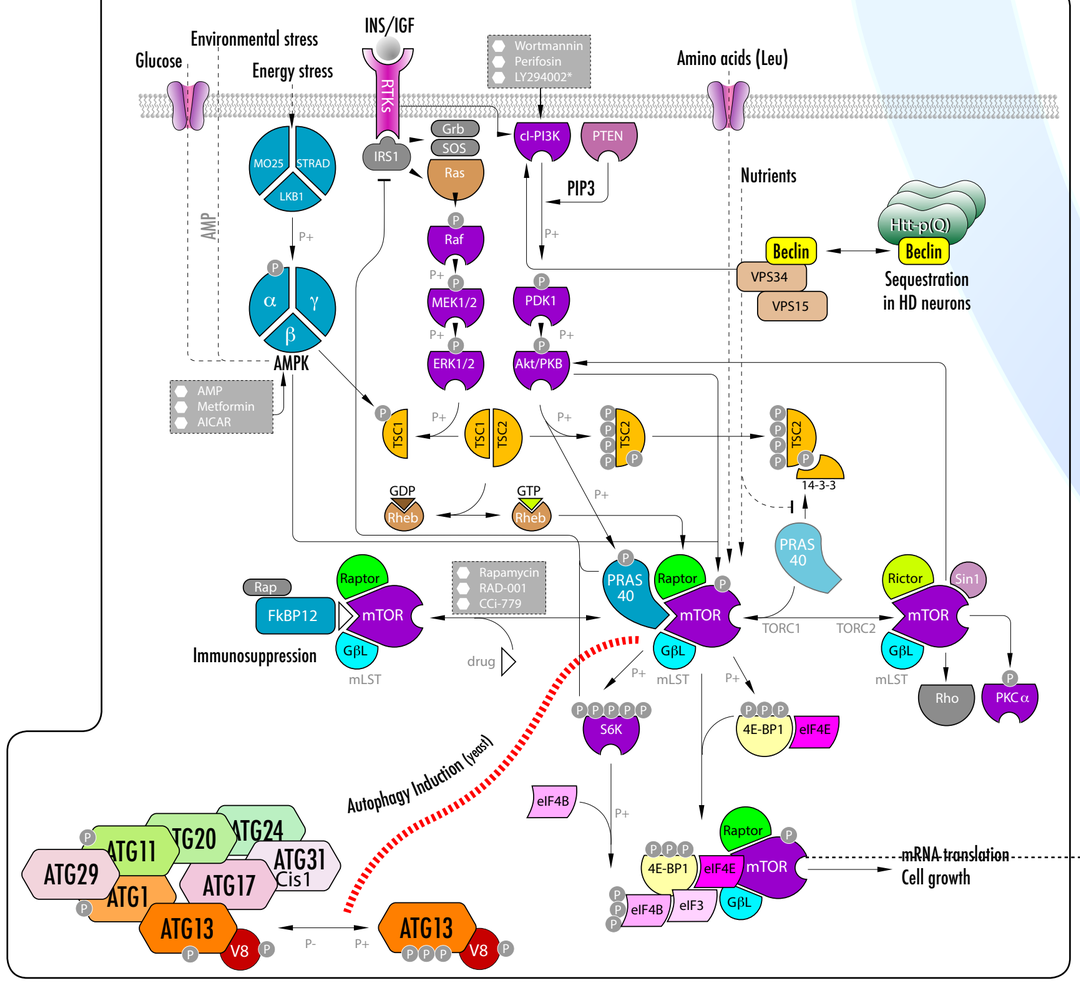
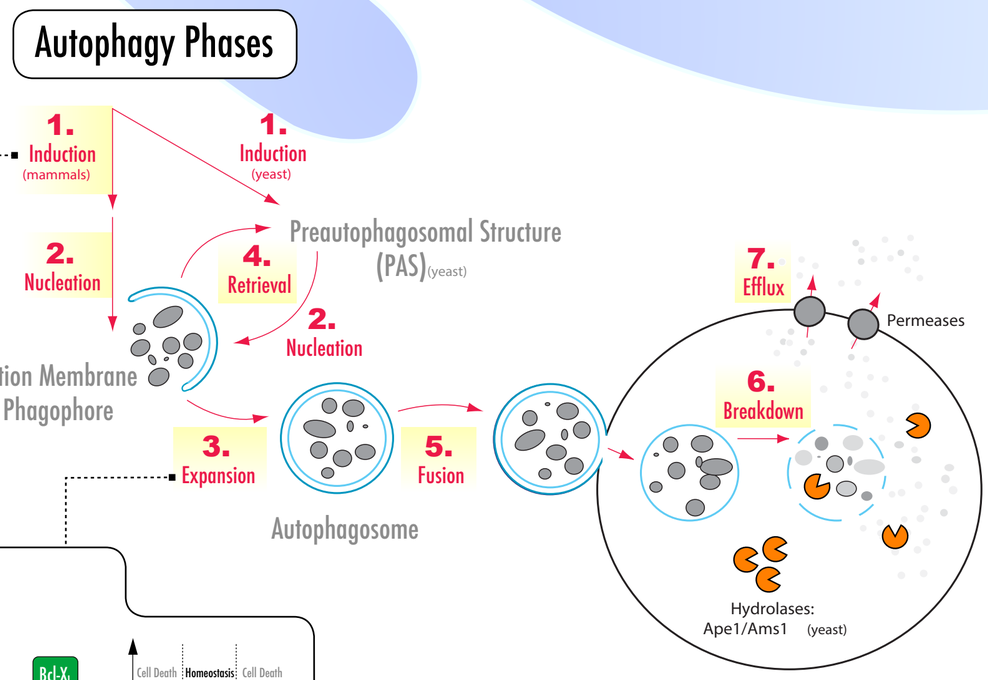
Autophagy is a major self-degradative process in eukaryotic cells, with fundamental roles in cellular and organismal homeostasis. Dysregulation of autophagy has recently been implicated in severe human pathologies such as cancer, neurodegenerative disorders, metabolic and muscular diseases, and viral infections. Structures targeted for autophagic destruction are sequestered into newly emerging double-membrane vesicles called autophagosomes, and delivered for lysosomal degradation. ATG proteins form four main multiprotein complexes: phosphatidylinositol 3-kinase (PI3K) complex, ATG13/ATG1 kinase complex, ATG9 complex, and ubiquitin-like protein conjugation systems. Current research is aimed at understanding how these complexes interact to promote autophagy.

Upstream Autophagy Events - Induction



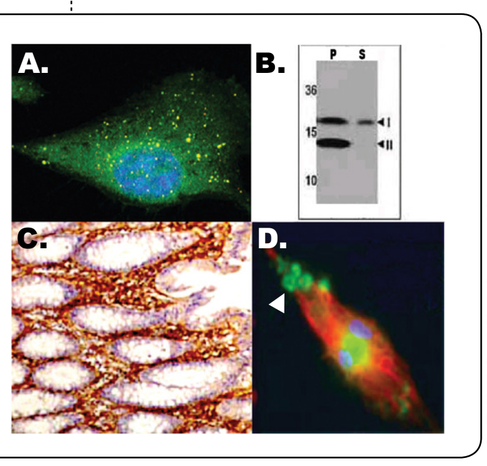
Autophagy Phases



Autophagy Antibodies

100+ additional Ab at www.abgent.com

Cat#	Target
AM1800a	LC3
AP1801a	LC3
AP1802a	LC3
AP1806a	LC3
AM1818a	Beclin
AP1818b	Beclin
AP2183b	P62
AP1813b	APG7
AP1812a	APG5
AP1812b	APG5
AP1817b	APG16
AP1816a	APG12
AP1820b	GAIP



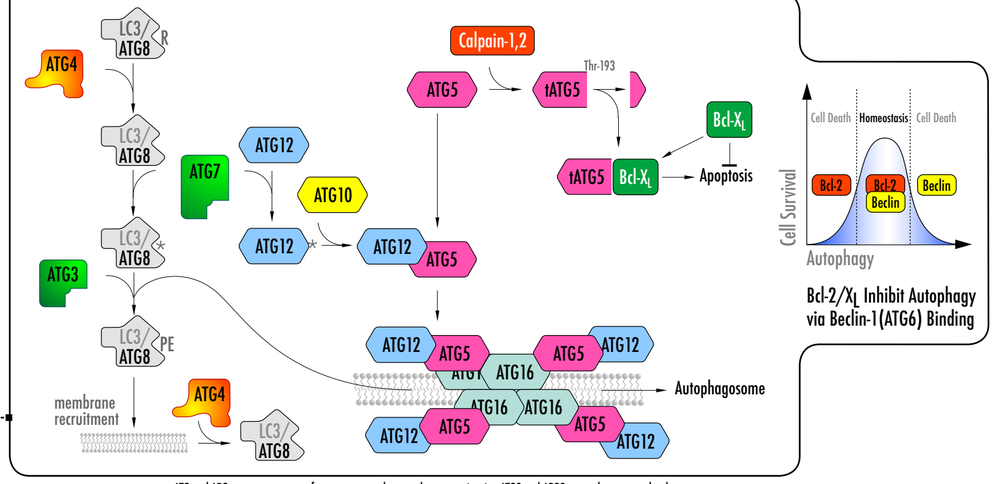
A. Mouse cerebellar cell lines stably expressing human GFP-LC3 fusion protein evaluated by immunocytochemistry using LC3 antibody (Abgent, Cat. # AM1800a). Punctuate autophagic cell vesicles, with numerous GFP-LC3 vesicles are displayed.

B. Western blot analysis of LC3 antibody (Abgent, Cat. # AP1801a) in rat brain lysate. Lipidated (arrow, II) and non-lipidated LC3 (arrow, I) detected in membrane fraction (P); only non-lipidated APG8a detected in soluble fraction (S).

C. Paraformaldehyde-fixed paraffin-embedded biopsy from patient with Crohn disease. Sections incubated with APG16L antibody (Abgent, Cat. # AP1817b).

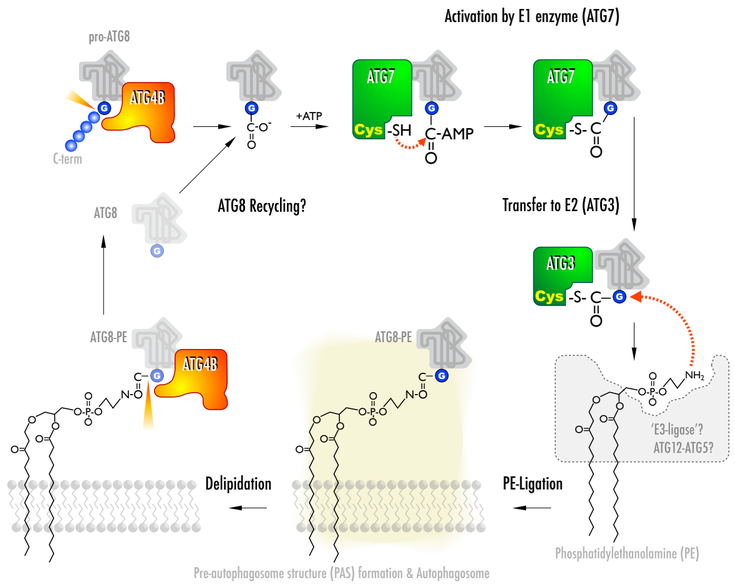
D. Mouse leukaemic monocyte macrophage cells treated with U18666A, a drug that causes cholesterol and lipid storage in cells, thereby blocking fusion between late endosomes and lysosomes. LC3 antibody (Abgent, Cat. # AP1806a) detected punctuate staining indicative of autophagic vacuole/phagosomal structures.

Autophagy Expansion & Apoptosis

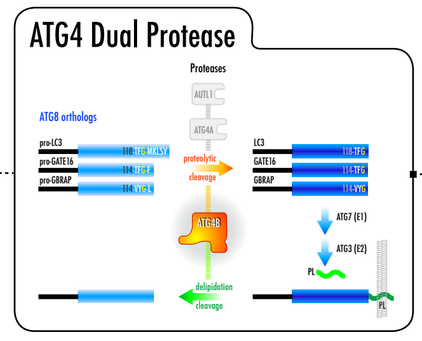


ATG and APG are synonymous references to autophagy pathway proteins; i.e. ATG8 and APG8 name the same molecule

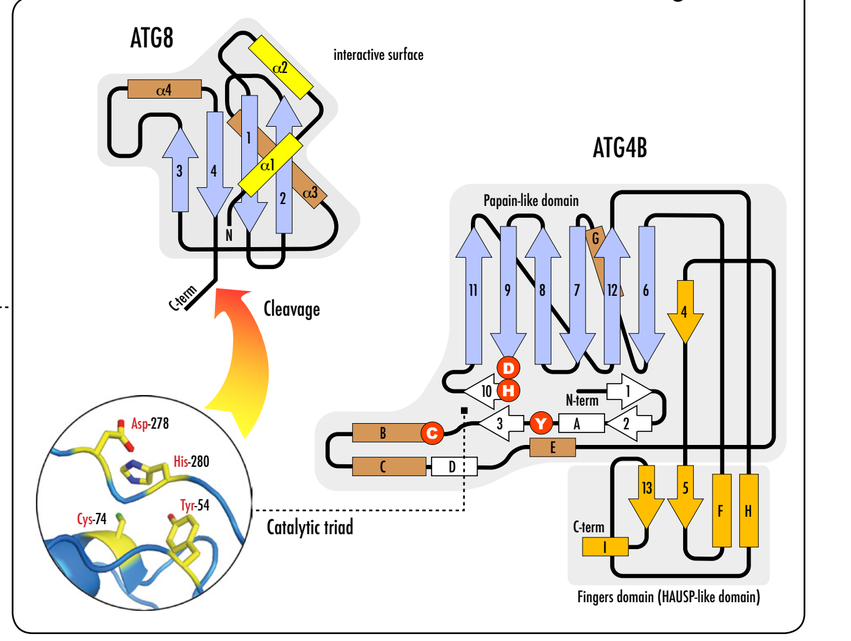
ATG8 Conjugation Cycle



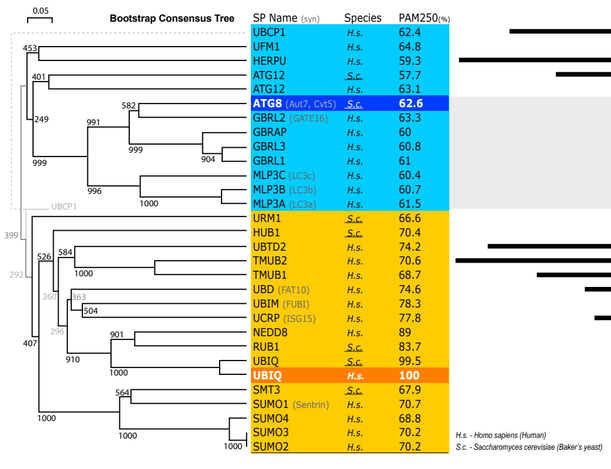
ATG4 Dual Protease



ATG4:ATG8 Cleavage Event



Ubl (Atg8) Family



PAM250 (**A**ccepted **P**oint **M**utations), Mutational matrix corresponding to a level of evolutionary change, measured by the frequency of substitutions/mutations for proteins, which have diverged 250% (250 mutations per 100 amino acids) [Ref.25].
Bootstrap, Is a statistical technique that is widely used to assess confidence limits on phylogenies. It examines the reliability of each interior branch of the phylogenetic tree. If every interior branch length is proved to be positive, the tree is regarded as reliable from a statistical point of view [Ref. 26]. The bootstrap values on each interior branch of this tree presented at the above show the number of trees matching out 1,000 possible trees.

Abbreviations (Synonyms):

AKT, RAC-alpha serine/threonine-protein kinase (C-AKT, RAC-PK-alpha, Protein kinase B, PKB); **AMP**, Adenosine monophosphate (5'-adenylic acid); **ATP**, Adenosine 5'-triphosphate (5-(6-aminopurin-9-yl)-3,4-dihydroxy-oxolan-2-yl methoxy-hydroxy-phosphoryloxy-hydroxy-phosphoryl oxyphosphonic acid)); **AMPK**, 5'-AMP-activated protein kinase catalytic subunit alpha-1 (AMPK alpha-1 chain); **ATG4B**, Cysteine protease ATG4B (Autophagin-1, hAPG4B, AUTL1); **ATG8**, Autophagy-related ubiquitin-like modifier (APG8, AUT7, CVT5); **BCL2**, Apoptosis regulator Bcl-2; **eIF4B**, Eukaryotic translation initiation factor 4B; **ERK1**, Extracellular signal-regulated kinase 1 (MAPK3, MAPK 1, p44-MAPK, ERT2, p44-ERK1, PRKM3); **FkBP12**, Immunophilin FKBP12.6 (12.6 kDa FKBP, Rotamase 1B, FK506-binding protein 1B, FKBP12.6, FKBP1L, FKBP9, OTK4); **GBRAP**, Gamma-aminobutyric acid receptor-associated protein (GABARAP, MM46); **GBRL2**, Gamma-aminobutyric acid receptor-associated protein-like 2 (GEF-2, FLC3A, GATE16); **GDP**, Guanosine diphosphate (Guanosine 5'-(trihydrogen diphosphate)); **Grb**, Growth factor receptor-bound protein; **GTP**, Guanosine 5'-triphosphate (2-amino-6-oxo-purine-5'-triphosphate); **IGF**, Insulin growth factor; **Htt**, Huntington (HD) disease protein; **MLP3C**, Microtubule-associated proteins 1A/1B light chain 3C (Autophagy-related protein LC3 C); **mTOR**, Mammalian target of rapamycin (FRAP, RAPT1); **NEDD8**, Neddylin (Ubiquitin-like protein Nedd8); **P+**, monophosphate; **PKC**, Protein kinase C; **PRAS40**, Proline-rich AKT1 substrate 1 (40 kDa AKT1S1); **PP2A**, Serine/threonine-protein phosphatase 2A; **Raf**, RAF proto-oncogene serine/threonine-protein kinase (Raf-1, cRaf); **RAPTOR**, Regulatory-associated protein of mTOR; **Rheb**, Ras homolog enriched in brain (GTP-binding protein Rheb); **S6K**, Ribosomal protein S6 kinase alpha-1 (S6K-alpha 1, p90S6K, RSK-1, p90-RSK 1); **SUMO1**, Small ubiquitin-related modifier 1 (Sentrin, Ubiquitin-like protein SMT3C, GAP-modifying protein 1, UBL1, PIC1, GMP1); **TSC1**, Hamartin (Tuberous sclerosis 1 protein); **TSC2**, Tuberin (Tuberous sclerosis 2 protein); **UBIQ**, Ubiquitin; **VPS34**, Vacuolar protein sorting-associated protein 34 (END12, PEP15, VPL7, VPT29); **VPS15**, Vacuolar protein sorting-associated protein 15 (GRD8, VAC4, VPL19).

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