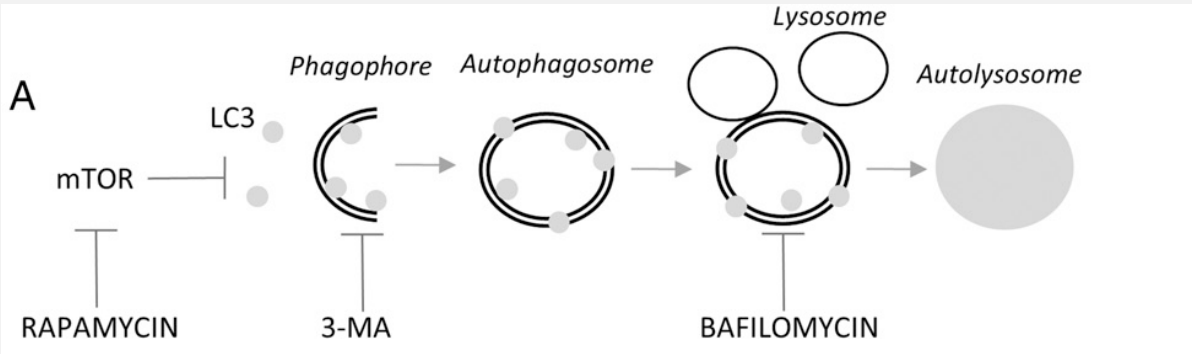
Cells under stress activate the autophagosome-lysosome system, via which redundant, damaged or misfolded proteins and organelles are degraded in lysosomes and cleared them from the cell . Within this broad category there are three distinct pathways: macroautophagy, chaperone-mediated autophagy, and microautophagy. Macroautophagy (which is commonly referred to as autophagy) involves the formation of a double membrane vesicle, with the cargo either surrounded by the elongating structure (isolation membrane/phagophore) or targeted via specialized autophagy receptor molecules to the autophagosome. Autophagy receptor molecules bind at one side to the cargo and at the other to the docking molecule LC3 via LC3 interacting region (LIR) motifs (Birgisdottir et al., 2013). Autophagosomes can fuse with endosomes, which contain ingested antigen, forming amphisomes. By fusion of autophagosomes or amphisomes with lysosomes the cargo is degraded. Digestion products (amino acids, lipids, carbohydrates) are released into the cytosol after which they can be used to produce new cell elements. In chaperone-mediated autophagy (CMA), proteins containing a KFERQ motif are bound in the cytosol by heat shock cognate and delivered to the lysosome via the lysosome-associated membrane protein (LAMP) 2A. Finally, in microautophagy, the lysosomal membrane itself deforms to engulf the target.



Activation of the autophagy pathway is controlled by multimeric protein complex that functions a nutrient sensor in cells: mammalian target of rapamycin (mTOR). Under starvation conditions mTOR dissociates, which leads to activation of a complex cascade of autophagy proteins (ATG), which leads to formation of autophagosomes (Yu et al., 2018). Frequently used activators and inhibitors in experiments are rapamycin, which induces mTOR dissociation, 3-MA, which inhibits elongation of phagophores, and bafilomycin, which prevents the fusion of autophagosomes and lysosomes.

Figure from: (Morandi et al., 2017b)