

FIGURE 6.1 Cellular quality control systems. Cells count on surveillance systems to identify prone-to-aggregate altered proteins (misfolded or damaged) and prevent their intracellular accumulation. If molecular chaperones and repairing enzymes fail to restore normal protein structure and function, the altered proteins are targeted to degradation by either proteasome or lysosomes.

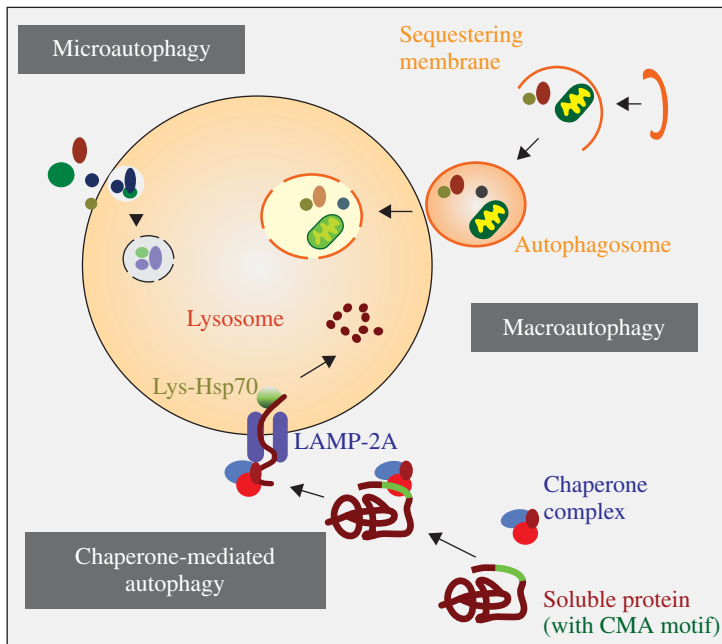


FIGURE 6.2 Types of autophagy. Schematic model of the three different autophagic pathways described in mammals: (1) Microautophagy is a constitutive nonselective sequestration of cytosolic contents directly by invaginations at the lysosomal membrane; (2) macroautophagy is an inducible form of “in bulk” degradation of cytosolic cargo sequestered inside a double-membrane vesicle (autophagosome) which acquires the necessary hydrolases by fusion with lysosomes; (3) chaperone-mediated autophagy (CMA) is a selective and inducible type of autophagy that involves a direct translocation of unfolded cytosolic protein substrates through the lysosome membrane.

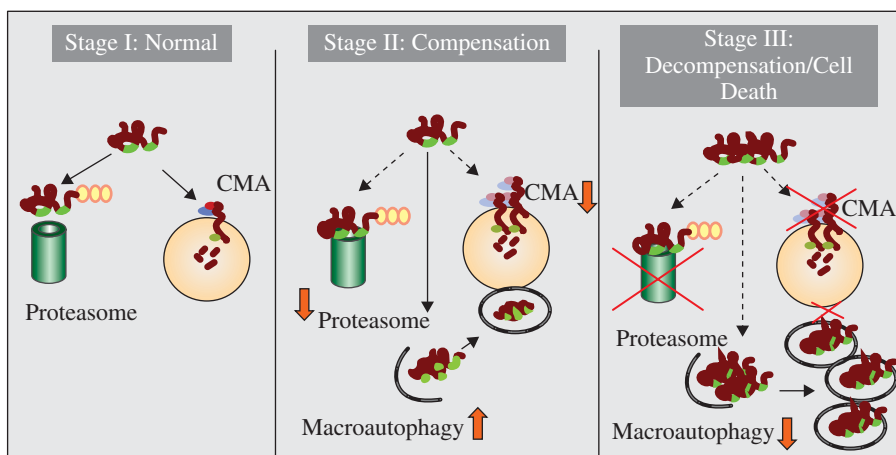


FIGURE 6.3 Autophagy and protein conformational disorders. Soluble misfolded proteins can be removed selectively by either proteasome or lysosomes via CMA (stage I). When the altered proteins interfere with the activity of other proteolytic systems, macroautophagy is up-regulated to compensate and facilitate aggregate protein removal (stage II). Eventually, different factors contribute to failure of macroautophagy, with the consequent intracellular accumulation of toxic protein products that lead to cellular decompensation and, often, cell death (stage III).