Ssm4p and Hrd1p are ubiquitin ligasesinvolved in endoplasmic reticulum-associated degradation. Ssm4p and Hrd1p are central members of the ubiquitin ligase complexes that are responsible for recognizing and ubiquitinating misfolded proteins in the ER for degradation by the proteasome. Misfolded cytosolic proteins are ubiquitinated by Ssm4p whereas misfolded luminal and membrane proteins are ubiquitinated by Hrd1p. The Ssm4p and Hrd1p ubiquitin ligase complexes also localize to different regions along the ER-nuclear membrane system: Ssm4p localizes to the inner nuclear membrane while Hrd1p remains in the ER membrane. Despite these differences, Ssm4p and Hrd1p appear to have overlapping substrate specificities and redundant functionalities. Each ubiquitin ligase complex interacts with the Cdc48p-Npl4p-Ufd1p AAA ATPase complex via Ubx2p in order to extract ubiquitinated substrates from the ER.