



# **Autophagy: Chapter 4. Roles of Multiple Types of Autophagy in Neurodegenerative Diseases**

*Tomohiro Kabuta, Yuuki Fujiwara, Keiji Wada*

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To date, three forms of autophagy – macroautophagy, microautophagy, and chaperone-mediated autophagy (CMA) – have been identified. Recently, we discovered a novel type of autophagy, “RNautophagy,” in which RNA is taken up directly into lysosomes for degradation. Gain of toxic functions of accumulated misfolded proteins or abnormal RNAs in CNS participate to a considerable degree in the pathogenesis of various neurodegenerative diseases. Thus, degradation and clearance of the toxic species by autophagy systems may be important for the maintenance of neurons and prevention of neurodegenerative diseases. We showed that amyotrophic lateral sclerosis (ALS)-linked mutant SOD1 is degraded not only by the proteasome but also by macroautophagy, and that macroautophagy reduces mutant SOD1-mediated toxicity. We found that Parkinson’s disease-associated mutant UCH-L1 interacts with LAMP-2A and Hsc70, which are the components of CMA machinery, and inhibits CMA. Because RNAs containing aberrant repeats are thought to cause some of ALS or spinocerebellar ataxia (SCA), RNautophagy may also play significant roles in the pathology of neurodegenerative diseases.

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