

## **Mechanism of axonal degeneration: from molecular signaling to the development of therapeutic applications**

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Research on the mechanism of injury-induced axonal degeneration (Wallerian degeneration) revealed that axonal degeneration is an active process involving transcriptional regulations and enzymatic reactions. Axonal degeneration is observed as part of the pathology in many neurological disorders, including neurodegenerative disorders, and causes key symptoms. Subcellular reactions regulating axonal degeneration are independent from those for apoptosis, in principle, and therefore, prevention of axonal degeneration may constitute an important therapeutic strategy against neurodegenerative disorders.

We have previously shown that ZNRF1, a ubiquitin ligase, regulates stability of microtubules constituting cytoskeletal structure in axons via regulating degradation of AKT and thereby controlling its downstream phosphorylation reaction cascade. We also found that the phosphorylation cascade also promotes autophagy in degenerating axons. In this symposium presentation, we will summarize our findings on the mechanism of ZNRF1-dependent regulation of axonal degeneration.