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Renal ischemia/reperfusion-induced mitophagy protects against renal dysfunction via Drp1-dependent-pathway

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A B S T R A C T

Autophagy is upregulated under stress conditions to degrade superfluous proteins and recycle damaged organelles including damaged mitochondria. However, the occurrence of mitochondrial autophagy and its contribution remain to be elucidated during renal ischemia/reperfusion injury (IRI). In this study, mitophagosomes and engulfed mitochondria were frequently observed by electron microscopy after renal IRI vs. control. Meanwhile, the increase of lipidated microtubule associated protein light chain 3 (LC3-II) and decrease of mitochondrial proteins were detected by western blot, suggesting the presence of mitophagy. Drp1 translocated to mitochondria and was phosphorylated at S616 in response to IRI. Interestingly, we found that inhibiting drp1 phosphorylation with mdivi-1 significantly suppressed IRI-induced mitophagy without affecting general autophagy. Furthermore, our results showed that downregulation of mitophagy significantly exacerbated cell apoptosis and markedly aggravated kidney dysfunction induced by IRI. Taken together, these data indicate that mitophagy was activated via Drp1-dependent pathway and such mitophagic clearance of damaged mitochondria protects cells from IRI-induced apoptosis.