Cadmium-induced autophagy and apoptosis are mediated by a calium signaling pathway

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摘要

Abstract

The cytotoxicity of cadmium (Cd) induced autophagy and apoptosis in MES-13 cells was determined by flow cytometry. Autophagy was also assessed by formation of autophagosomes and processing of LC3. Pharmacological inhibition of autophagy resulted in increased of cell viability, suggesting autophagy plays a role in cell death in Cd-treated mesangial cells. Cd also induced a rapid elevation in cytosolic calcium ([Ca(2+)](i)), and modulation of [Ca(2+)](i) via treatment with IP (3)R inhibitor or knockdown of calcineurin resulted in a change in the proportion of cell death, suggesting that the release of calcium from the ER plays a crucial role in Cd-induced cell death. Inhibition of Cd-induced ERK activation by PD 98059 suppressed Cd-induced autophagy, and BAPTA-AM eliminated activation of ERK. BAPTA-AM also inhibited Cd-induced mitochondrial depolarization and activation of caspases. These findings demonstrated that Cd induces both autophagy and apoptosis through elevation of [Ca(2+)](i), followed by Ca(2+)-ERK and Ca(2+)-mitochondria-caspase signaling pathways