# Mitochondria-mediated caspase-independent apoptosis induced by cadmium in normal human lung cells

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## 摘要

## Abstract

Cadmium, a well-known environmental hazard, has caused serious health problems in humans and animals. Accumulating evidence suggests the cadmium toxicity is mediated by oxidative stress-induced cell death. However, the molecular signaling underlying cadmium-induced apoptosis remains unclear. In this study, we demonstrate here that cadmium induced mixed types of cell death including primary apoptosis (early apoptosis), secondary necrosis (late apoptosis), and necrosis in normal human lung cells, MRC-5, as revealed by chromatin condensation, phosphatidylserine (PS) externalization, and hypodiploid DNA content. The total apoptotic cells reached a plateau of around 40.0% after 24 h exposure of 100 microM cadmium. Pretreatment with Z-Val-Ala-Asp-fluoromethylketone (Z-VAD-fmk), a broad spectrum of caspase inhibitor, could not rescue apoptotic cells from cadmium toxicity. Coincidently, we failed to detect the activation of pro-caspase-3 and cleavage of PARP by immunoblot, which implies the apoptogenic activity of cadmium in MRC-5 cells is caspase-independent. JC-1 staining also indicated that mitochondrial depolarization is a prelude to cadmium-induced apoptosis, which was accompanied by a translocation of caspase-independent pro-apoptotic factor apoptosis-inducing factor (AIF) into the nucleus as revealed by the immunofluorescence assay. In summary, this study demonstrated for the first time that cadmium induced a caspase-independent apoptotic pathway through mitochondria-mediated AIF translocation into the nucleus. 