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Mechanism for arsenic-induced cytotoxicity in keratinocytes

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Arsenic is an ubiquitous heavy metal in various environmental media that include soil, air, and water. Numerous epidemiological studies have reported a close relationship between arsenic and skin carcinogenic effects. In addition, arsenic was also known as a blister agent in skin, and thus its derivatives have been used as a chemical weapon. However, the mechanism of blister formation, one of the most important targets for arsenic toxicity, remains poorly understood. Here we found that arsenic could induce cytotoxicity and inflammation in keratinocyte, which play key roles in the formation of blister. In this study, we used arsenic (As^{III}) and trivalent methylated metabolites of arsenic, monomethylarsonous acid (MMA^{III}), which has been found highly reactive and toxic in various cells. Treatment of As^{III} and MMA^{III} resulted in significant reduction of viability of keratinocyte (HaCaT) in a concentration- and time-dependent manner. Cell death forms, which are apoptosis and necrosis, are occurring simultaneously in As^{III} and MMA^{III} . These cell death were found to be mediated by the reactive oxygen species (ROS), depletion of glutathione by As^{III} and MMA^{III} . Consistent with these findings, mitochondrial membrane potential disruption, caspase-3 activation and DNA fragmentation were observed by treatments with As^{III} and MMA^{III} , as determined by fluorescence microscopy and flow cytometry. Exposure to arsenicals also stimulated secretion of pro-inflammatory cytokine in keratinocytes, resulting in increased levels of $TNF-\alpha$, $IL-1\alpha$, and $IL-6$. In summary, this study provides an important evidence for the role of As^{III} and MMA^{III} in arsenic-associated cytotoxicity and inflammation response in keratinocytes, suggesting a new solution to inhibit the toxicant-induced blister formation.

Biography

Jin-Ho Chung received his PhD from the Johns Hopkins University School of Public Health. He has been Professor of College of Pharmacy at Seoul National University (SNU). He manages an organization as Director at Institute of Environment Protection and Safety of SNU since June 2008. In January 2009, he served also as President of Korean Society of Toxicology. He serves in numerous advisory functions in different national organizations. He has contributed to the scientific achievements with a significant number of publications in major journals.

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