MASTER'S THESIS

Cellular metabolism in in vitro toxicity and toxicology studies

Yu, Lok Chiu

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Cellular Metabolism in *In Vitro* Toxicity and Toxicology Studies

YU Lok Chiu

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Principal Supervisor: Dr. Mildred M.S. YANG

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Abstract

The aim of the present study is to clarify the role cellular metabolism plays in the course of cell death. Cellular metabolism is a study of inter-conversion of nutritional substrates to generate useful chemical molecules to maintain proper cellular function. The level of comprehensive analysis of these molecules would provide a complete picture of cellular metabolism. Because of the different variety of metabolites, the current study will concentrate on those related to energy and redox metabolism.

Using cell cultures as models, the present study aims to investigate metal induced cell death. Four objectives were set: (1) What are the energy and redox changes when cells were exposed to toxic metals? (2) Do all toxic metals affect cellular metabolism similarly? (3) Do all cells response similarly to a single toxicant? (4) What is the correlation between cellular metabolic changes and cell death?

We have studied the effect of Cd, Zn, Se and an organic hydroperoxide on the HepG2 hepatoma and the C6 glioma cells. The results demonstrated that during this initial phase of Cd and Zn administration, there was a significant increase in cellular energy state as demonstrated by an increase in ATP/TAN, and a decrease in AMP/TAN. The change was correlated to a decrease in GSH/GSSG. Se, on the other hand, caused an opposite change in cellular energy state suggesting that different toxicants act differently on cells. Upon exposure to Cd, the C6 glioma cells were more sensitive than the HepG2 hepatoma cells as demonstrated by a more sensitive decrease in GSH/GSSG. This correlated by a relatively low glutathione reductase activity in the C6 glioma cells. Finally, using Cd as a model, the dynamic change in cellular energy and redox metabolism was described over a 6-hr exposure to a 3-hr LC50 of Cd. The results correlated with the cell death through apoptosis.

Table of Contents