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Toxicometabolomics and urinary biomarkers for nephrotoxicity

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The primary objective of this study was to determine and characterize surrogate biomarkers that can predict nephrotoxicity induced by mercuric chloride (HgCl₂) using urinary proton nuclear magnetic resonance (¹H NMR) spectral data. A procedure for ¹H NMR urinalysis using pattern recognition was proposed to evaluate nephrotoxicity induced by HgCl₂ in Sprague-Dawley rats. HgCl₂ at 0.1 or 0.75 mg/kg was administered intraperitoneally (i.p.), and urine was collected every 24 h for 6 days. Animals (n = 6 per group) were sacrificed 3 or 6 days post-dosing in order to perform clinical blood chemistry tests and histopathologic examinations. Urinary ¹H NMR spectroscopy revealed apparent differential clustering between the control and HgCl₂ treatment groups as evidenced by principal component analysis (PCA) and partial least square (PLS)-discriminant analysis (DA). Time- and dose-dependent separation of HgCl₂-treated animals from controls was observed by PCA of ¹H NMR spectral data. In HgCl₂-treated rats, the concentrations of endogenous urinary metabolites of glucose, acetate, alanine, lactate, succinate, and ethanol were significantly increased, whereas the concentrations of 2-oxoglutarate, allantoin, citrate, formate, taurine, and hippurate were significantly decreased. These endogenous metabolites were selected as putative biomarkers for HgCl₂-induced nephrotoxicity. A dose response was observed in concentrations of lactate, acetate, succinate, and ethanol, where severe disruption of the concentrations of 2-oxoglutarate, citrate, formate, glucose, and taurine was observed at the higher dose (0.75 mg/kg) of HgCl₂. Correlation of urinary ¹H NMR PLS-DA data with renal histopathologic changes suggests that ¹H NMR urinalysis can be used to predict or screen for HgCl₂-induced nephrotoxicity.

AS3-2

Highlights in toxicology research in Taiwan

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Taiwan's National Science Council (NSC) is in charge of the funding policy of all basic scientific researches in Taiwan. Department of Life Science in NSC has three missions: first, to promote and support the life science research; secondly, to establish the infrastructure of life science area in Taiwan; third, to cultivate the personnel and talent for life science and biotechnology. Parts of my presentation will be introducing the funding policy as well as the trends of pharmacological/toxicological research in Taiwan.

In addition, I will also present my own research on cancer stem cell. Our recent study revealed that the histone methyltransferase G9a played a crucial role in maintaining typical characteristics of cancer stem cells such as drug resistance, self-renewal and tumorigenicity. Interestingly, some reports had been shown that the level of G9a could be up-regulated or altered by some toxicants or heavy metals. Therefore we would like to discuss the possibility of where some toxicants exposure might nurture the emergence of cancer stem cells by changing the epigenetic regulators, i.e., G9a.