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Proteomic study of SET-mediated abnormal protein phosphorylation and histone modification in trichloroethylene-induced hepatic cytotoxicity

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Trichloroethylene (TCE) was widely used in industrial productions and turned into an environmental and occupational toxicant. Expression of SET protein was previously found as dose-dependent with TCE in human liver cells. It is also an important inhibitor of phosphatase 2A and histone acetyltransferase. However SET-mediated abnormal histone modification and protein phosphorylation in TCE induced hepatic cytotoxicity remain poorly understood.

SET-mediated protein phosphorylation in TCE-induced hepatic cytotoxicity was analyzed by iTRAQ labeling and IMAC enrichment based quantification proteomics study. 14 phosphopeptides from 13 proteins were found as SET-mediated (de)-phosphorylation in hepatic cytotoxicity of TCE. Furthermore, nucleolin was found self-regulating by SET-mediated phosphorylation through enhanced interaction with c-myc and inhibiting of c-myc. SET-mediated histone methylation and acetylation were analyzed by TAU-SDS-PAGE seperation combining with LC-ESI-MS based label-free quantification. The ubiquitinated and sumoylated histones were first enriched by specific antibodies then labeled with stable isotopic dimethylation reagents and analyzed by LC- ESI-MS. 12 acetylated peptides, 11 methylated peptides, 10 ubiquinated peptides and 6 sumoylation peptides were found as SET-mediated alteration in hepatic cytotoxicity of TCE. Our findings provided molecular-level evidence further supporting our previous findings that knockdown of SET attenuated TCE-induced hepatic cytotoxicity. SET-mediated self-regulating of nucleolin and abmornal histone modifications further revealed the molecular mechanism of SET-mediated hepatic cytotoxicity of TCE.

Biography

Jianjun Liu has been studying the mechanisms of TCE-induced hepatotoxicity for several years. She is a doctoral supervisor. She is the director of Key Laboratory of Modern Toxicology of Shenzhen, a division of Shenzhen Center for Disease Control and Prevention. She has published more than 60 papers in international and chinese journals and has authorized 3 patents of invention.

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