

[PD1-54] [04/18/2003 (Fri) 13:30 - 16:30 / Hall P]

A chemical proteomic approach for in vivo evaluation of CCl₄ effect on the acute serum proteins.

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CCl₄ has been known as typical chemical which induce acute hepatitis accompanying increase in the levels of acute phase proteins in serum. In this study, after acute liver damage was induced by CCl₄ in Sprague-Dawley rats, the levels of serum acute phase proteins were examined using 2-dimensional electrophoresis and lactic dehydrogenase (LDH), alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels in blood were also examined at 1, 2, 3 days after the induction to confirm acute hepatitis. CCl₄ treated groups (CTG; n=3 for each day) were compared to the untreated group (Control; n=6) In CTG, LDH was 42 fold (1day), 2 fold (2 day) and 0.7 fold (3 day), compared to the control level. ALT and AST levels were increased by 44 fold, 46 fold (1 day) and 13 fold, 8.2 fold (2 day) and by 3.7 fold, 1.6 fold (3 day), respectively. Analysis of the acute phase proteins indicates that the levels of 19 protein spots including α 1-antitrysin, α 1-acid-glycoprotein, and haptoglobin- α were increased whereas the levels of 2 protein spots including apolipoprotein 4 were decreased. However, the time courses of proteins shows variable patterns: early maximum level followed by gradual decrease, early on set followed by plateau, gradual increase, etc., implying that a complex mechanism is involved in toxicology of a simple chemical, CCl₄. The detailed analysis is under investigation. The current investigation provides a chemical proteomic approach for in vivo evaluation of the toxic materials and the drug action screening, possibly.(supported by 00-PJ9-PG1-CO05-0002 and BK21 project, Korea)

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Identification of new ligands for RNA pseudoknot by structure-based screening of chemical database

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For many viruses, -1 ribosomal frameshifting regulate protein synthesis using an RNA pseudoknot. The integrity of pseudoknot stability and structure is the important feature for efficient frameshifting. Thus, small molecules interacting with viral RNA pseudoknots would be potential antiviral agents targeting ? frameshifting system in viruses. X-ray structure of RNA pseudoknot complexed with biotin has been reported, in which biotin is bound at the interface between the pseudoknot's stacked helices. In this study, we conducted a computational screening against RNA pseudoknot using FlexX docking program and consensus scoring function (Cscore). After screening more than 70,000 compounds from commercially available databases, about sixty high-ranked compounds were selected and their binding activities were examined by in vitro ? frameshifting assay. Some of candidate compounds affected the efficiency of ? frameshifting, and they are interesting leads for the design of novel ligands which may regulate the protein synthesis.