VANIN-1 AS A PREDICTIVE MARKER OF ACUTE KIDNEY INJURY

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[Purpose] Although many medications are reported to cause acute renal tubular injury (so-called acute kidney injury [AKI]), an effective prediction approach has not been developed. To address this issue, we tried to detect a marker of AKI using primary human renal cells.

[Methods] Effects of nephrotoxic organic solvents (allyl alcohol, ethylene glycol, formaldehyde, chloroform and phenol) on gene expression profiles in primary human renal cells and human renal proximal tubule epithelial HK-2 cells were investigated using microarray and quantitative RT-PCR analyses.

[Results and Discussion] Microarray analyses revealed that organic solvents significantly increased expression of vanin-1, which is reported to antagonize PPAR-γ activity, in primary human renal cells after 24 h. Vanin-1 mRNA levels in HK-2 cells were also increased approximately 4- to 6-fold after 12-h of exposure to each solvent. In contrast, interleukin-6 (IL-6) levels in HK-2 cells showed insignificant. In addition, transcript levels of monocyte chemoattractant protein-1 (MCP-1) increased only after 48 h exposure to each solvent.

[Conclusions] Compared with the conventional inflammatory markers, vanin-1 expression was markedly elevated at earlier time during organic solvent-induced tubular cell injury in vitro. Vanin-1 might be a more useful marker to evaluate the potential risk of AKI during the development of new medications.

CIRCULATING MICRO-RNAS AS A BIOMARKER OF LIVER INJURY

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[Purpose] There are various kinds of liver injuries, including virus-related, alcoholic, non-alcoholic and drug-induced liver injuries. To diagnose each type of liver injury early and accurately, non-invasive, sensitive, and specific biomarkers need to be developed. We investigated whether blood miRNAs could be biomarkers of liver injury.

[Method] To make animal models of acute or chronic liver injury, Sprague-Dawley rats were administered acetaminophen, a-naphthylisothiocyanate and carbon tetrachloride or fed a high fat or methionine choline-deficient diet. Conventional serum markers such as ALT and AST and histopathological changes were monitored. The profiles of miRNA expression in blood was determined by TaqMan microRNA array analysis. The profiles in patients with a suspected drug-induced liver injury (DILI) were also determined and compared with the data from rat models.

[Results and Discussion] The changes in blood miRNA expressions were dramatic in rats with acute liver injury, whereas they were relatively mild in rats with chronic liver injury. It should be noted that the expression profiles were quite different between the acute vs chronic injuries as well as between the pericentral vs periportal injuries. We identified several miRNAs that could be biomarkers of each type of liver injury. The change in the miRNA expressions was more sensitive than the conventional serum markers. In patients with a suspected DILI, the expressions of multiple miRNAs were different from those in convalescence. Some of them were common with those of the rat models.

[Conclusions] We identified some miRNAs in blood that could be sensitive and specific biomarker of liver injury.