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MicroRNAs in biofluids as biomarker for drug-induced toxicity

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Abstract

MicroRNAs are emerging as a valuable tool in toxicological applications due to their role in regulation of gene expression in different biological pathways. Multiple studies have revealed that miRNAs are present and relatively stable in clinically accessible biofluids such as blood and urine. Thus, microRNAs in biofluids may provide a non-invasive way of detecting drug-induced toxicities. In our studies, microRNA profiling and individual miRNAs in rodent blood and urine have been evaluated for biomarkers to predict toxicities induced by several chemicals and drugs. Male B6C3F1 mice were treated with 140 mg/kg carcinogen *N*-ethyl-*N*-nitrosourea (ENU) and profiling of total miRNAs in the blood showed that a number of microRNAs associated with carcinogenesis were altered by the ENU treatment. One of these miRNAs, miR-34a, was very sensitively increased by ENU. Urine miRNA profiles were assessed from rats treated with 1250 mg/kg acetaminophen. Urinary miRNA levels were correlated with centrilobular liver necrosis and consistently elevated in the treated animals. Acute cardiotoxicity in rats was induced by a single s.c. injection of 0.5 mg/kg isoproterenol. The heart-enriched microRNAs miR-208, miR-499, and miR-1 in serum and plasma of the treated animals were evaluated. The levels of the microRNAs were increased by approximately 10-fold in serum 4 hr after treatment. The microRNA induction resulted from the release of the damaged heart cells. These results suggest that miRNA profilings and specific miRNAs in biofluids could reflect toxicities induced by chemicals and drugs and therefore have the potential to be used as noninvasive preclinical and clinical biomarkers.

Biography

Tao Chen has completed his Ph.D from University of Arkansas for Medical Sciences, diplomat of the American Board of Toxicology and postdoctoral studies from Duke University. He has been a principal investigator in National Center for Toxicological Research since 2010 and is also an adjunct professor in two universities. He has served as an editorial board member and reviewer in a number of journals, a consultant for the World Health Organization, a reviewer for research proposals for US National Science Foundation. He has published more than 200 manuscripts and abstracts in peer-reviewed journals and books, and scientific meetings.