

Development of a microRNA assay for evaluating genotoxicity of agents

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MicroRNAs (miRNAs) are a class of small RNAs and play an important role in carcinogenesis. miR-34a has been suggested as a tumor suppressor miRNA and its expression is directly controlled by the p53 gene to respond to DNA damage and cell apoptosis. In this study, alternation of miR-34a expression by genotoxins was evaluated to determine whether this miRNA could be used as an indicator for genotoxic damage in vivo and in vitro. In our in vivo study, it was found that miR-34a was up-regulated by N-ethyl-N-nitrosourea (ENU), a direct acting mutagen, in mouse liver and spleen, by aristolochic acid, a human genotoxic carcinogen, in rat kidney and liver, by riddelliine and comfrey, genotoxic botanical carcinogens, in rat liver; while no such change was detected in tissues of mice treated with non-genotoxic carcinogens. In our in vitro study, miR-34a expression in TK6 human cells was significantly increased by treatment of different genotoxins, ENU, cisplatin, etoposide, mitomycin C, methyl methane sulfonate, and toxal in a dose dependent manner. In contrast, treatment of cells with usnic acid, a non-genetic toxin, did not dysregulate miR-34a. The fold-changes of miR-34a expression for the treatments over the controls generally were large, for example, 22-fold in comfrey treatment and 12-fold in AA treatment. Therefore, miR-34a expression responds sensitively and specifically to genotoxic insults of chemicals. Thus, miR-34a expression has the potential to become a biomarker for genotoxin exposure.

Biography

Dr. Chen is an expert on genetic and genomic toxicology in U.S. Food and Drug Administration. He is also an adjunct professor in two universities. Dr. Chen serves as an editor or reviewer for a number of journals in toxicology, molecular biology and bioinformatics. He has served as a consultant for the World Health Organization and as a reviewer for research proposals for US National Science Foundation. He has been invited to present a number of seminars, keynote speeches and planetary lectures in national and international scientific meetings, and to write many review papers or book chapters on carcinogenesis and mutagenesis. He has published more than 100 manuscripts and abstracts in peer-reviewed journals and books, and scientific meetings. Dr. Chen's research addresses on defining different biomarkers for carcinogenesis like gene expression, microRNA expression, DNA adducts, mutations, and tumors.