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MicroRNA signature and exploration in human oral squamous cell carcinomas

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MicroRNAs (miRNAs) are small, noncoding RNAs that can influence numerous genes expression. Aberrant miRNAs expressions are often happened in cancer cells. In this study, we used a custom microarray platform to screen miRNA expression profile on 40 matched oral squamous cell carcinomas (OSCC) and normal adjacent tissue samples. Fifty-six differentially expressed miRNAs were identified with concordant fold-change by microarray analysis. Using Bayesian Binary Regression (BBR) analysis, we identified a miRNAs expression signature showed high discriminatory potential for disease prediction. Interestingly, we also found twenty down-regulation miRNAs in microarray analysis locate in DLK-MEG3 imprinted domain of chromosome 14q-arm. The array CGH data from clinical samples showed that no DLK-MEG3 region deletion among these 40 patients. Therefore, the epigenetic regulate of miRNAs may exit on this region of chromosome 14q in OSCC patients. We further analyzed these miRNAs, located around CpG islands, to identify tumor-suppressive miRNAs silenced through aberrant DNA methylation. The expression of those miRNAs was restored by treatment with DNA methyltransferase inhibitor (5'-AZA-dC) in OSCC cells lacking their expression. In addition, expression levels of these miRNAs were inversely correlated with their DNA methylation status in the OSCC cell lines. In conclusion, our study showed that (a) tumor-specific hypermethylation in OSCC was an important mechanism causing the downregulation of miRNAs; (b) a miRNAs expression signature in this study in an independent test population should be evaluated further as diagnostic biomarkers for differentiating OSCC tumor from non-diseased epithelia.

Biography

Dr. Shine-Gwo Shiah received a PhD in cell biology from the College of Medicine, National Taiwan University, Taiwan. Following post-doctoral work at National Institute of Cancer Research (NICR) in National Health Research Institutes (NHRI) for biomedical Research, Dr Shiah set up the miRNA study group at NICR. Current major research is focusing on the functional role of miRNA in oral cancer progression and cancer-related miRNA biomarker discovery.

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