The Study of MicroRNAs in Nasopharyngeal Carcinoma

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ABSTRACT

MicroRNAs (miRNAs) are small non-coding RNAs that negatively regulate gene expression by complementing to target messenger RNA (mRNA). Through studying miRNA deregulation in diseases can provide an insight on understanding the molecular mechanisms of diseases and increasing the prognostic and diagnostic potential. Nasopharyngeal Carcinoma (NPC), a squamous cell carcinoma of the nasopharynx, is frequently seen among Chinese ethnic in southern China. Growing evidence indicated that miRNAs deregulation was detected in NPC. The objectives of this thesis is to reveal the NPC-related biomarkers using miRNA profiling technique on a variety of biological and clinical samples including formalin fixed paraffin-embedded (FFPE) tissues, NPC and NP epithelial (NPE) cell lines – HK-1, C666-1, NP69, and NP460, and the corresponding conditioned medium; to evaluate the panel of miRNA candidates in the NPC patient sera; and to explore the functional characteristics of targeted miRNA.

The real-time PCR profiling data and the statistical significance were evaluated by the DataAssist™ software. The results indicated that there were 9 miRNA candidates (miR-205, miR-196a, miR-149, miR-183, miR-224, miR-210, miR-136, miR-200c and miR-141) significantly over-expressed with fold changes more than 3-fold in undifferentiated NPC patients when comparing to non-NPC controls. While only one miRNA, miR-150, was found down-regulated with the fold changes less than 3-fold in this study. Apart from this, the expression level of selected miRNA markers - miR-150, miR-200c, miR-205 and miR-196a were further evaluated in 149 human NPC patient sera and 28 non-cancerous controls. It was found that miR-150 was significantly down-regulated in the late stages NPC patients. There was about 3 and 2.5-fold decrease of miR-150 expression in T3 (p<0.01) and T4 (p<0.05) stages respectively as comparing with the non-cancerous controls. It suggests that miR-150 may serve as one of the miRNA markers for serological-based detection of NPC.

Based on these findings, miR-150 would be a potential molecular modulator in NPC tumorigenesis. Thus, the functional role of miR-150 was
studied by the gain-of-function and loss-of-function based bioassays. Data showed that miR-150 might act as tumour suppressor and mediating the epithelial-mesenchyme-transition (EMT) of NPC cells. Taken together, the current study showed miRNA deregulation in NPC clinical specimens and miRNA candidates, miR-150, seems to be highly associated with the NPC pathogenesis. Thus, it can conclude that through understanding the role of miRNAs in NPC, it could be a novel strategy for the NPC treatment.
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