Association of the miRNA146a rs2910164 C>G Polymorphism with Head and Neck Cancer Risk: A Meta-analysis

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Abstract

Objective: To investigate any association of the miRNA146a rs2910164 C>G polymorphism with head and neck cancer risk. Materials and Methods: The Medline, PubMed, PUBMED, EMBASE, Web of Science, WanFang and CNKI databases were searched and a meta-analysis was conducted using RevMan 5.2 software. Results: After searching and evaluating the literature, a total seven papers involving 2,766 patients with head and neck cancer and 6,603 healthy controls were included into this meta analysis. The results showed that there were no significant differences between patients and healthy controls overall for the miRNA rs2910164 C>G gene polymorphism (dominant model: OR=0.78, 95%CI:0.58-1.04, P=0.09; recessive model: OR=0.86, 95%CI:0.67-1.12, P=0.27;GG:CC:OR=0.75, 95%CI:0.52-1.08, P=0.12;GC:CC:OR=0.79, 95%CI:0.60-1.04, P=0.10). However, a significant association of miRNA rs2910164 C>G gene polymorphism with Chinese head and neck cancer risk was noted, limited to the dominant model (OR=0.68, 95%CI:0.50-0.95, P=0.02;GG:CC:OR=0.62, 95%CI:0.42-0.92, P=0.02;GC:CC:OR=0.72, 95%CI:0.52-0.99, P=0.04). Conclusions: miRNA146a rs2910164 C>G polymorphism is not associated with head and neck cancer risk in general, but there may be link in Chinese.

Keywords: Head and neck cancer - miRNA146a rs2910164 C>G - polymorphism - meta analysis - Chinese

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reviewed for data extraction. Discrepancies between the two reviews were resolved by discussion and consensus. The quality of all selected studies was ranked in accordance with the score of the non-randomized controlled clinical trial evaluation standard.

Statistical methods

Related-data from the comparative groups was compared using Χ² test for categorical data, a significant difference was considered when P was less than 0.05; the meta-analysis was performed using the Review Manager (RevMan) software, version 5.2. We analyzed dichotomous variables using estimation of odds ratios (OR) with a 95% confidence interval (95%CI). The quality of all selected studies was ranked in accordance with the score of the non-randomized controlled clinical trial evaluation standard.

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Results

In here, total seven papers involved 2766 patients with head and neck cancer and 6603 healthy control were included into this meta analysis. (Liu et al., 2010; Chu et al., 2012; Hung et al., 2013; Orsós et al., 2013; Huang et al., 2014; Lin et al., 2014) Among five papers involving Chinese, one was involving American and Hungarians, respectively. Two papers involving oral cancer and nasopharyngeal carcinoma and squamous cell carcinoma, respectively, one involving laryngeal cancer. More detail could be found in Table 1.

No association between miRNA rs2910164 C>G gene polymorphism and tumors

In here, there were 7 documents showed that miRNA rs2910164 C>G gene polymorphism involved in the

Table 1. Characteristics of Studies Included in the Meta-analysis

| Study | Year | Ethnicity | Tumor type | Case | Control |
|-------|------|-----------|------------|------|---------|
| Chu   | 2012 | Chinese   | Oral Cancer | 174  | 245     |
|       |      |           |            | 54   | 470     |
|       |      |           |            | 175  | 196     |
|       |      |           |            | 54   | 425     |
|       |      |           |            | 196  | 196     |
| Huang | 2014 | Chinese   | Nasopharyngeal carcinoma | 64   | 425     |
|       |      |           |            | 73   | 23      |
|       |      |           |            | 160  | 54      |
|       |      |           |            | 54   | 110     |
|       |      |           |            | 470  | 1109    |
|       |      |           |            | 1109 | 1109    |
| Hung  | 2012 | Chinese   | Laryngeal Cancer | 63   | 110     |
|       |      |           |            | 110  | 204     |
|       |      |           |            | 81   | 220     |
|       |      |           |            | 220  | 194     |
| Liu   | 2010 | American  | Squamous Cell Carcinoma | 68   | 110     |
|       |      |           |            | 630  | 1109    |
|       |      |           |            | 1109 | 70      |
|       |      |           |            | 405  | 655     |
|       |      |           |            | 1130 | 220     |
| Lung  | 2013a| Chinese   | Nasopharyngeal Carcinoma | 117  | 88      |
|       |      |           |            | 88   | 24      |
|       |      |           |            | 229  | 59      |
|       |      |           |            | 59   | 86      |
|       |      |           |            | 86   | 18      |
|       |      |           |            | 18   | 163     |
| orsos | 2013b| Hungarian | Squamous Cell Carcinoma | 9    | 136     |
|       |      |           |            | 323  | 468     |
|       |      |           |            | 468  | 16      |
|       |      |           |            | 16   | 284     |
|       |      |           |            | 284  | 468     |

* from the same study

Figure 1. Meta-analysis of the Association between miRNA146a rs2910164 Polymorphism and Susceptibility to Cancer Risk. A) Dominant model. B) Recessive model.C) GG vs CC. D) GC vs CC

Figure 2. Meta-analysis of the Association between miRNA146a rs2910164 Polymorphism and Susceptibility to Cancer Risk in Chinese. A) Dominant model. B) Recessive model.C) GG vs CC. D) GC vs CC

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| Study | Year | Ethnicity | Tumor type | Case | Control |
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|       |      |           |            | 160  | 54      |
|       |      |           |            | 54   | 110     |
|       |      |           |            | 470  | 1109    |
|       |      |           |            | 1109 | 1109    |
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|       |      |           |            | 110  | 204     |
|       |      |           |            | 81   | 220     |
|       |      |           |            | 220  | 194     |
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|       |      |           |            | 1130 | 220     |
| Lung  | 2013a| Chinese   | Nasopharyngeal Carcinoma | 117  | 88      |
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|       |      |           |            | 229  | 59      |
|       |      |           |            | 59   | 86      |
|       |      |           |            | 86   | 18      |
|       |      |           |            | 18   | 163     |
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|       |      |           |            | 323  | 468     |
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|       |      |           |            | 16   | 284     |
|       |      |           |            | 284  | 468     |

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risk of cancer in all ethnicity. The meta analysis results shown that there were no significant differences between patients and healthy control on association of miRNA rs2910164 C>G gene polymorphism involved in the risk of cancer. (Dominant model: OR=0.78, 95%CI:0.58-1.04, \(P=0.09\); Recessive model: OR=0.86, 95%CI:0.67-1.12, \(P=0.27\); GC:CC:OR=0.75, 95%CI:0.52-1.08, \(P=0.12\); GC:CC:OR=0.79, 95%CI:0.60-1.04, \(P=0.10\))(Figure 1).

Part association between miRNA rs2910164 C>G gene polymorphism and tumors in Chinese

As shown in Figure 2A, C and D, the meta analysis results in the subgroup analysis by ethnicity revealed that there were a significant differences on association of miRNAs rs2910164 C>G gene polymorphism with Chinese head and neck cancer risk between case and healthy control. (Dominant model: OR=0.68, 95%CI:0.50-0.95, \(P=0.02\); GC:CC:OR=0.62, 95%CI:0.42-0.92, \(P=0.02\); GC:CC:OR=0.72, 95%CI:0.52-0.99, \(P=0.04\) However, no differences were found in Recessive model, OR=0.75, 95%CI:0.55-1.01, \(P=0.06\) (Figure 2B)

Discussion

In here, we investigated the association of miRNA rs2910164 C>G gene polymorphism and cancer risk. The meta analysis results shown that there were no significant differences between patients and healthy control on association of miRNA rs2910164 C>G gene polymorphism involved in the cancer risk. However, there was a part association of miRNA rs2910164 C>G gene polymorphism with cancer risk in Chinese.

It is well known that individual susceptibility plays an important role in the development of most cancers. Genes polymorphisms involved in oncogenesis may have accounted for the susceptibility. Therefore, genetic susceptibility, especially single nucleotide polymorphism (SNP), to cancer has been a research focus in scientific community. Many studies have been done for figuring out the role of SNPs present in precursor and mature miRNA and their influences on susceptibility and progression of various cancers. Recent studies have identified that miRNA196 may interact with several transcription factors and involve in cancer development and progression (Li et al., 2010; Chen et al., 2011). Some findings suggest that overexpression of miRNA196 leads to more favorable prognosis and survival in leukemia (Popovic et al., 2009).

In addition, miRNA196 is associated with inflammation in specific cancers (Schetter et al., 2009). Furthermore, Christensen et al., reports a polymorphism in the mature sequence of miRNA196a2 in a case-control study (n = 1, 039) of head and neck squamous cell carcinoma (HNSCC) (Christensen et al., 2010). When the authors stratified on tumor site they did not observe a significant association between oral cancer and miRNA196a2, though the effect estimate was protective, similar to the results presented in this study. Although the reason for those discrepancies is not well-known, the different results from the report and the present study may relate to the racial/ethnic difference. In our meta analysis, there was no significant differences on the association of miRNA rs2910164 C>G gene polymorphism with cancer risk, however, no difference between Chinese patients and healthy control on the relation between miRNA rs2910164 C>G gene polymorphism and cancer risk.

The meta analysis shown a significant association between miR-146a (rs2910164) with hepatocellular carcinoma, cervical squamous cell carcinoma and prostate cancer, (Yin et al., 2013) but not with head and neck cancer risk in our result, indicating that miRNA146a rs2910164 polymorphism may play different roles in various human malignancies.

In conclusion, our meta analysis results show that miRNA 146a rs2910164 gene polymorphism more likely contribute to be associated with cancer risk in Chinese. Future well-designed and larger population studies are of great value to confirm these findings.

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