Immunotherapy: Open Access

Zhou, et al., Immunother Open Acc 2016, 2:4
DOI: 10.4172/2471-9552.1000130

Commentary Open Access

Novel Discoveries by microRNA and mRNA Expression Profiles Analysis in Non-Small-Cell Lung Cancer

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Received date: October 25, 2016, **Accepted date:** November 18, 2016, **Published date:** November 28, 2016

Commentary

Lung cancer is one of the most serious causes of cancer-related deaths all over the world, with more than 220,000 new diagnoses and nearly 158,000 deaths expected to occur in 2016 in the United States [1]. NSCLC (non-small-cell lung cancer) is the cause of 80% of all lung cancer deaths in the United States and it is composed primarily of adenocarcinoma, squamous cell carcinoma (SCC). Actually, most lung cancers are diagnosed at advanced stages with an overall five-year survival rate of 18% [1]. Consequently, there is an urgent assignment to investigate the potential molecular mechanisms of lung tumorigenesis and identify novel therapeutic targets which can enhance the survival probability of patients with lung cancer. In our study, a total of 211 differentially expressed miRNAs were found by high-throughput sequencing of non-small cell lung cancer (NSCLC) tissues and adjacent normal tissues, 171 of them were up-regulated, while 30 among them were down-regulated. In addition, we predicted 157 novel miRNAs, and identified 918 significant miRNA– mRNA pairs [2].

MicroRNAs (miRNAs), which are defined as small non-coding RNAs and have a length of about 20-25 nucleotides, play an important regulatory role through regularizing gene expression in plant and animal by pairing with target gene mRNA [3]. Ambros, Ruvkun et al. have identified the first miRNA genes *let-7* by regulating the expression of other genes at the post-transcriptional level when controlling developmental timing in nematodes [4]. Since then, the miRNA field has grown up tremendously and become an integral component of the way how the gene expression is regulated [5]. Recently, the regulation of miRNA expression was detected to play a key role on a variety of physiological and pathological processes, such as development, differentiation, cell proliferation, apoptosis, and homeostasis [6].

In recent years, thousands of differentially expressed miRNA have been screened by microarray and bioinformatics and studied in many cancers, including lung cancer. For example, the *miR-17-92* cluster (*miR-17*, *miR-18a*, *miR-19a*, *miR-19b-1*, *miR-20a* and *miR-92a-1*) has been identified to have roles in regulating cell proliferation in NSCLC [7]. Despite there are hundreds of studies and reports about mRNA/miRNA profiling and sequencing, the clear mRNA and miRNA expression patterns of NSCLC are still needed to be digged out.

Actually, we screened out 3039 potential targets of the miRNAs by using the online analytic tool DAVID (Database for Annotation, Visualization and Integrated Discovery). Furthermore, we demonstrated that the differentially expressed gene targets were related to focal adhesion, cytokine–cytokine receptor interaction and calcium-signaling pathway [2]. There are two main therapeutic strategies about the application of miRNAs: one is to reintroduce a tumour-suppressor miRNA to recover the missed function; another is to inhibit tumorigenic miRNAs directly or indirectly [8]. For example, *let-7* has been demonstrated to function as a tumor suppressor in lung cells and repress the multiple genes involved in cell-cycle and cell division directly or indirectly [9]. The other strategy was used to research neuron-specific miR-124, whose inserted target sequence restricts the expression of a transgene in a lentiviral vector to astroglial cells [10]. In fact, in our previous study, the expression level of miR-139-5p was decreased in our sequencing results and miR-139-5p repressed NSCLC cell growth, migration, invasion and colony formation, and promoted cell apoptosis by targeting 3′-UTR of c-Met [11]. Furthermore, we found these anti-expressed target genes were closely related to proliferation and variation of tumor cells through GO analysis, which also indicated that any change in cell cycle of lung cells might be essential for the progression of NSCLC [2].

The systematic study of miRNA will not only help to further reveal the molecular mechanism of lung cancer development, but also explore miRNA as a new biomarker of lung cancer or target biological therapy and provide new ideas for the diagnosis, treatment, prevention of lung cancer. Up to now, we are totally neither aware of the molecular mechanisms by which miRNAs regulating gene expression nor do we understand the complete repertoire of target mRNAs each miRNA regulates. It is our hope that we could find more about the unknown biological functions of differently expressed genes and miRNAs, and explore the roles of the novel miRNAs in tumorigenesis and development of lung cancer in the future.

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