Role of miR-10b in non-small cell lung cancer (NSCLC) cells by targeting Klotho

Jing-Yu Pan¹*, Cheng-Cao Sun¹*, Shu-Jun Li¹², Junchao Huang³, De-Jia Li¹

¹Department of Occupational and Environmental Health, School of Public Health, Wuhan University, 430071 Wuhan, P. R. China
²Wuhan Hospital for the Prevention and Treatment of Occupational Diseases, 430071 Wuhan, P. R. China
³Hubei Province Key Laboratory on Cardiovascular, Cerebrovascular, and Metabolic Disorders, School of Nuclear Technology and Chemistry & Biology, Hubei University of Science and Technology, 437100 Xianning, P.R. China

*These authors contribute equally to this work.

Correspondence: De-Jia Li
E-mail: lodjlwhu@sina.com
Received: July 29, 2015
Published online: September 17, 2015

MiR-10b was overexpressed in various cancers, including NSCLC. In early study, miR-10b was described as a carcinoma enhancer in NSCLC. Our recent study showed that silencing of miR-10b could promote NSCLC cells apoptosis and decrease proliferation, and regulation of these cell behaviors might target Klotho via miR-10b. In addition, we also explored the correlation between miR-10b and Klotho or other underlying targets. Our investigation indicated that miR-10b could play a critical role as a helpful prognosis marker and underlying target in terms of therapy of NSCLC.

Keywords: miR-10b; non-small cell lung cancer; proliferation; apoptosis; Klotho

To cite this article: Jing-Yu Pan, et al. Role of miR-10b in non-small cell lung cancer (NSCLC) cells by targeting Klotho. Can Cell Microenviron 2015; 2: e936. doi: 10.14800/ccm.936.

Lung cancer is regarded as an extremely serious and devastating cancer in the world. Every year, death of population in lung cancer exceeds the total numbers of prostate cancer, colon cancer and breast cancer, and lung cancer becomes the leading cause of cancer-related death in humans [1]. Furthermore, the proportion of NSCLC closes to 80-85 percent of all patients with lung cancer in America [2-3]. Up to now, the therapy of lung cancer hasn’t been significantly effective, which is correlated with unsatisfactory prognosis and high risk of death [4]. Although smoking is the leading cause of lung cancer, accumulating evidence has provided a significant difference in genetic factors that contribute to occurrence of lung cancer [4-5]. Accordingly, it’s crucial to explore the potential mechanisms of lung cancerization and find novel therapeutical targets that could decrease mortality of patients with lung cancer.

MicroRNAs are described as small non-coding RNAs with about 20-25 nucleotides in length, which rule gene expression in both plants and animals through targeting miRNAs in the 3’-UTR [6-8]. As a member of it, miR-10b was demonstrated to be overexpressed in numerous cancers, such as hepatic carcinoma [9], laryngeal carcinoma [10], gastric cancer [11], ovarian cancer [12] and breast cancer [13-14]. We investigated 75 patients’ NSCLC tissues and adjacent normal tissues, using statistical method to analyze the result that indicated that expression of miR-10b was significantly lower in adjacent normal tissue than in NSCLC tissues. Then we concluded that miR-10b overexpression also could be observed in NSCLC patients. Moreover, we found patients with lower miR-10b expression had much longer survival time than the higher [15].

According to some findings, miR-10b also plays a role in
plentiful cancer cells progression [16-19]. For example, the miR-10b with post-transcription regulates HOXD in gastric cancer which leads to enhance metastasis and invasion of cancer cells [11,13]. And miR-10b promotes cells invasiveness and motility in breast cancer through targeting syndecan-1 [14]. In addition, investigation of Liu et al. indicated that miR-10b plays a role as a tumor promoting factor in NSCLC cells and is also an underlying target of therapy for NSCLC [20]. However, miR-10b how to affect lung cancer cell biological behavior, including cell proliferation and apoptosis remain unknown.

The Klotho gene is considered to be a new cancer inhibiting gene that has been demonstrated recently. Klotho was reported that acted as an enhancer for the pathway of FGF and a restrainer for activating ligand-dependent the IGF-1 pathways of insulin in breast cancer [21-22]. Klotho is also identified as a suppressor gene of the insulin-like growth factor (IGF-1) pathway in human cervical carcinoma [23], which is also described as a critical target for epigenetic silencing [24]. In lung cancer cell line A549, Klotho was proved that expressed low, which was revealed as a new secreted Wnt inhibitor with inhibiting lung cancer cell tumor formation in lung cancer cells [25].

In our recent study, we found the lung cancer cells process was inhibited in the G0/G1 through silencing of miR-10b, and promoting apoptosis also could be detected by inhibition of miR-10b in NSCLC cells [15]. Liu, et al. also demonstrated miR-10b act as a role of proliferation and invasion in NSCLC cell line A549 [20]. The members of apoptosis-inducing such as Bax, caspase-3 and Fas/FasL were overexpressed and the factors of apoptosis-inhibiting like Bcl-2 and PCNA were decreased via Western blot analysis. In nude mouse, a further investigation of vivo tumor formation was also convinced, which demonstrated that suppression of miR-10b could delay the process of tumor formation in lung cancer cells [15].

Interestingly, there was a remarkable negative correlation of the level of the record between the Klotho and miR-10b, which indicated that the Klotho is a target of miR-10b in NSCLC cells [15]. Although we observed a noticeable up-regulation of Klotho by inhibiting miR-10b in lung cancer cell line 95-D and A549, the specific mechanisms remain unknown. In addition, Zhang, et al. provided evidence that inhibition of miR-10 in NSCLC cells led to E-cadherin mRNA and protein up-regulate compared with the controls, which showed that miR-10b could target E-cadherin in NSCLC [29].

Taken together, we could draw a conclusion that inhibition of miR-10b could promote cells apoptosis and decrease proliferation in NSCLC cells, and regulation of these cell behaviors might target Klotho via miR-10b. However, the exact molecular pathways of miR-10b how to target the Klotheoneed more investigation and exploration. We also believe that miR-10b could play an important role as a helpful prognosis marker and underlying target in terms of therapy of NSCLC.

**Conflicting interests**

The authors have declared that no competing interests exist.

**Acknowledgements**

This work was supported by National Natural Science Foundation of China (No. 81271943) to Dejia Li, National Natural Science Foundation of China (No. 305273570) to Junchao Huang, and the Fundamental Research Funds for the Central Universities (No. 201530502020) to Chengcao Sun.

**Abbreviations**

NSCLC: non-small cell lung cancer; miR-10b: microRNA-10b; 3’-UTR: 3’-untranslated region.

**References**


