Letter to the Editor

The role and potential mechanisms of long non-coding RNA in small cell lung cancer

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Provenance: This is an invited article commissioned by Section Editor Dr. Chunlin Ou (Cancer Research Institute of Central South University, Changsha, China).

Response to: Ou C, Li G. Long non-coding RNA TUG1: a novel therapeutic target in small cell lung cancer. J Thorac Dis 2017;9:E644-E645.

Submitted Aug 19, 2017. Accepted for publication Sep 13, 2017.
doi: 10.21037/jtd.2017.09.70
View this article at: http://dx.doi.org/10.21037/jtd.2017.09.70

We thank Chunlin Ou and Guiyuan Li for their thoughtful commentary in our work (1). Small-cell lung cancer (SCLC) is a highly lethal malignancy that accounts for approximately 15% of lung cancers (2). For patients with SCLC, chemotherapy is an essential component of appropriate treatment. However, chemoresistance remains a key obstacle to improve prognosis of SCLC patients. Therefore, it is necessary to explore the potential molecular mechanisms involved in SCLC chemoresistance.

Long noncoding RNAs (lncRNAs) are defined as transcripts longer than 200 nucleotides with no protein-coding potential. Although accumulating evidence has shown that lncRNAs play an important role in cancer cell growth and chemoresistance (3,4), how do lncRNAs exert their functions remain unknown.

Previous study has demonstrated that a significant proportion of lncRNAs are physically associated with the repressive chromatin-modifying complex PRC2 (such as HOTAIR, TUG1 and XIST) (5). Similarly, a growing body of evidence suggested lncRNAs regulate genes expression by binding with PRC2 to affect the development and progression of tumor (6). Our study also found lncRNA TUG1 promotes cell growth and chemoresistance by binding with PRC2 then regulating LIMK2b expression. Together, it indicates that a shared mechanism for lncRNAs that function in tumorigenesis.

Currently, a novel regulatory mechanism between lncRNAs and miRNAs has become a hot topic. LncRNAs act as miRNA sponges to participate in the competitive endogenous RNAs (ceRNA) regulatory network and negatively regulate miRNA expression and then influence its target genes. Identically, studies have showed there was a reciprocal repression between lncRNA TUG1 and miRNA, which constitutes a ceRNA regulatory network in the progress of multiple cancer types (7). However, the regulatory mechanism between lncRNAs and miRNAs in the control of SCLC tumorigenesis has not been well documented. To examine the same biochemical mechanism in SCLC by which lncRNAs function, we drew inspiration from the study, and believe it may be a novel potential molecular mechanism in SCLC.

Of note, lncRNAs have been documented to play biological effects by Wnt/β-catenin signaling pathway in the present study. For instance, lncRNA MALAT1 modulate cell proliferation of oral squamous cell carcinoma (OSCC) through regulating Wnt/β-catenin signaling (8). Recently study also showed that lncRNA PLIN2 act as a carcinogenic factor in the progression of chronic myeloid leukemia (CML) via interacting with the GSK3 and Wnt/β-catenin signaling pathways (9). Perhaps more encouragingly, lncRNA TUG1 was also reported to promote progression of OSCC by suppressing the level of Wnt/β-catenin signaling (10), which also indicates a new research direction about the role of TUG1 in SCLC.

There are four known molecular functions of lncRNAs: signal, decoy, guide, and scaffold (3). Signaling lncRNAs are correlated with specific signaling pathways and their expression indicates an active signaling event. Decoy lncRNAs can interact with and titrate away proteins or RNAs

from binding to the target gene promoters facilitating gene activation or silencing. Guide lncRNAs may just act on neighboring or distantly located genes as guides to impart specificity to genomic locations. Scaffold lncRNAs serve as a central platform to which various protein complexes tether and get directed to specific genomic location. In the above, we summarized the various biochemical mechanism of lncRNAs function in cancer: (I) lncRNAs are associated with chromatin-modifying complexes then confer activating modifications. Our experiments also present lncRNA TUG1 mediates cell growth and chemoresistance of SCLC in this manner; (II) lncRNAs act as miRNA sponges participate in the ceRNA regulatory network then function in cancer cellular pathways; (III) lncRNAs involve in cancer cells growth, proliferation and invasion via interacting with Wnt/β-catenin signaling. However, the current study suggested lncRNAs could function in entirely different ways. It is possible provide a strategy and lead to the development of lncRNAs directed diagnostics and therapeutics against SCLC. The roles of lncRNAs and their mechanisms in SCLC clearly remains to be further explored in the future.

Acknowledgements

Funding: This work was supported by the National Natural Science Foundation of China (81172241) and Natural Science Foundation of Guangdong Province (2015A030311028).

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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Cite this article as: Niu Y, Ma F, Xue J, Huang W, Guo L. The role and potential mechanisms of long non-coding RNA in small cell lung cancer. J Thorac Dis 2017;9(10):E947-E948. doi: 10.21037/jtd.2017.09.70