International Journal of Cancer Management
Volume 17 · Issue 1 · e151012

OPEN PEER REVIEW

Expression of Five Important Biomarkers in Non-small Cell Lung Cancer: MicroRNAs-128, miR-335-5p, miR-1254, VEGF, and K-RAS

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SUBMITTED	REVISED	ACCEPTED	DOI
23 Jul 2024	7 Sep 2024	16 Sep 2024	10.5812/ijcm-151012

About this report

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1 Original submission

2 comments · 11 Aug 2024 – 21 Aug 2024

Reza Hosseini Reviewer

REJECT 11 Aug 2024

Dear Editor-in-Chief, IJCM

I would like to thank you for your invitation to referee the manuscript titled " miRNA-128, miR-335-5p, and miR-1254 in pathogenesis and tumourigenesis of Non-small cell lung cancer via KRAS and VEGF genes". The authors have examined the expression of miRNA-128, miR-335-5p, and miR-1254 in NSCLC samples and have attempted to find a mechanistic rationale for their downregulation. Considering the published literature and the following comments, this manuscript lacks enough novelty, and the conclusion is not based on the data presented.

1- The main results of this manuscript, including the downregulation of the investigated miRNAs, have already been reported in the literature. For example, a study in 2014 showed that miRNA-128 is a tumor suppressor whose downregulation could increase lung cancer invasiveness through the VEGF pathway (microRNA-128 plays a critical role in human non-small cell lung cancer tumourigenesis, angiogenesis and lymphangiogenesis by directly targeting vascular endothelial growth factor-C, DOI: 10.1016/j.ejca.2014.06.005). Similarly, several studies have demonstrated the downregulation of miRNA-128, miR-335-5p, and miR-1254 in lung cancer.

2-The authors have shown downregulation of the investigated miRNAs (previously reported) and upregulation of VEGF, while concluding that VEGF upregulation might depend on the downregulation of the three target miRNAs. However, for such a conclusion, several knock-in and knock-out models should be employed. Indeed, the upregulation of VEGF might not be due to the decrease in miRNA-128, miR-335-5p, and miR-1254, and this may be a coincidence. For instance, previous studies have shown that the downregulation of miRNA-1254 in lung cancer leads to cancer progression via the Wnt/B Catenin pathway and SFRP1, but not VEGF, etc. (miR-1254 promotes lung cancer cell proliferation by targeting SFRP1, DOI: 10.1016/j.biopha.2017.05.116).

3- Since there are no mechanistic experiments that confirm the authors' claim regarding the relationship between miRNA-128, miR-335-5p, and miR-1254 downregulation and higher expression of VEGF and KRAS, it would be better for the authors to investigate and compare the prognostic significance of miRNA-128, miR-335-5p, and miR-1254 as well as VEGF and KRAS in NSCLC.

The following articles can also be considered by the authors as references:

1- https://doi.org/10.1038/s41419-018-1262-x
2-DOI: https://doi.org/10.1166/jbt.2021.2794
3-https://doi.org/10.11748/bjmy.issn.1006-1703.2019.04.040
4-https://doi.org/10.1016/j.yexmp.2021.104738
5-DOI: 10.1186/s12931-019-1184-x
6-DOI https://doi.org/10.2147/OTT.S245136

Associate Editor

REJECT 21 Aug 2024

Dear Editor-in-chief,

This manuscript describes a study on the expression of 3 miRNAs and VEGF and KRAS in NSCLC. The authors have analyzed both cancerous tissue and peripheral blood. There are some points to consider:
1. In the title, the authors mention "miRNAs in pathogenesis and tumorigenesis in NSCLC via KRAS and VGEF". How did they show that the effect of these miRNAs in NSCLC is through VEGF and KRS?! They have just analyzed their expression in cancerous tissue. This does not show which one is the "cause" and which one is the "effect".
2. The authors have analyzed the expression of KRAS and VEGF in peripheral blood and compared it to the expression in the cancerous tissue. The expression of each gene in each tissue is different, and they should compare the expression to normal lung tissue.

2

Revision 1

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

Dear Editor-in-Chief, IJCM

Thank you for your attention, the explanation is sent as follows:

Reviewer:

With respect to the Reviewer's opinion;

1. The important point is that the expression of these three markers (miRNA-128, miR-335-5p, miR-1254) and two markers (VEGF and KRAS) have been examined together and simultaneously and can be presented as a diagnostic package, which has not been done so far. On the other hand, no study has been done on these markers in the native Iranian race. Therefore, this research was necessary according to the geography of the region.

2. The purpose of this study was only to investigate the expression of markers in tissue and blood separately as diagnostic markers, and it is obvious that many factors can play a role in the development of cancer in different ways.

3. As explained, in this study, with the help of bioinformatics and Real-time PCR methods, several important markers have been studied as diagnostic markers, and the relationship between these factors and biomarkers can be investigated in another study with a larger sample size and different markers.

Associate Editor :

With respect to the Associate Editor's opinion;

1. It should be noted that the study aimed to investigate the expression of markers as diagnostic markers in cancer and the relationship between them and cause and effect was not intended.

For this reason, the title of the manuscript has been changed according to your opinion as follows:

“Expression of five important biomarkers in non-small cell lung cancer: miRNA-128, miR-335-5p, miR-1254, VEGF and KRAS”

2. Since genes have different expressions in different tissues, in the present study, the expression of markers in cancerous tissue has been compared with normal tissue, and also the expression of markers in the blood of people with cancer has been compared with the peripheral blood of healthy people.

2 Revision 1

0 comments

No public comments in this round.