Downregulation of TCF21 by EZH2 in Small Cell Lung Cancer

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Introduction

Small Cell Lung Cancer (SCLC) is a neuroendocrine carcinoma that affects around 10-15% of all lung cancers patients [1]. It originates in the center of the lung and infiltrates the bronchial submucosa [2]. Transcription Factor 21 (TCF21) is involved with mesenchymal-epithelial transition (MET) of the lung morphogenesis, which is shown to occur in metastasis [3]. The aim of our study is to determine the significance of the genetic interaction of TCF21 and EZH2 as an indicator of lung cancer.

Methods

Databases used for our study were NCBI, GeneCards, EntrezGenes, GEO, GEO2R, and string-db.org. Dataset *GSE40275,* from GEO, contained tissue samples from normal lungs, small cell (SCLC) and non-small cell lung cancer (NSCLC); we used normal (43 samples) and SCLC (20 samples). GEO2R was used to determine gene significance with a p-value cutoff of $2*10^{-20}$ and the log fold change (logFC) was set to absolute value of 2.0. We used string-db.org to determine significant genetic pathways in the top 300 differently expressed genes and further analysis was done through research of previous studies in NCBI databases.

Results

Based on the results with the above databases, we identified the genetic interaction between EZH2 and TCF21 as the focus of our study. We found that TCF21 is underexpressed in lung cancer patients (p-value 2.40E-48, log FC-4.48), and EZH2 is overexpressed (p-value 6.38E-43, log FC 3.80758885). Research into the literature showed that TCF21 was integral in the function of the transition of mesenchymal cells, which are pluripotent cells that have high cell motility, to epithelial cells which has been implicated in many cancers. EZH2 has been shown to be a silencer of TCF21 and a known transcription factor to affect other genes.

Conclusion

The overexpression of EZH2 leads to the silencing of TCF21 which causes a lack of mesenchymal-epithelial cell transition. This leads to the hypothesis that EZH2 and TCF21 can be used as an early biomarker of SCLC looking at expression levels and its effect on mesenchymal cells of the lung. Further research is recommended to look into more functions of EZH2. This will provide a way to discover genes like TCF21 involved in cell cycle processes and how they affect the physiology and function of cells. This will extend understanding of cell differentiation, and could lead to a better understanding of diagnosing lung cancer.

Keywords: TCF21, tumor suppression, lung cancer, EZH2

References

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