In silico Analysis of c-Met Expression and its Correlation with Metabolic Network in Head and Neck Cancer

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Abstract

Background: Head and Neck Squamous Cell Carcinoma (HNSCC) is strongly associated with metabolic dysregulations. c-Met activation is important for high glucose induced acquisition of mesenchymal phenotype, survival under high glucose stress in HNSCC cells. Here, we utilise the *In silico* approach to analyse the c-Met expression in the head and neck cancer data extracted from The Cancer Genome Atlas (TCGA) database and its strong correlation with genes associated with cancer cell metabolism.

Methods: In the current study, our investigations were performed using different bioinformatics tools and databases, including GEPIA (a webserver which extracts data from the Cancer Genome Atlas (TCGA) data portal and the GTEx database of normal tissues. http://gepia.cancer-pku.cn), and STRING databases (functional protein association networks (https://string-db.org/).

Results: Here, we report the upregulation of c-Met in HNSCC patient cases along with a significant upregulation of major metabolic genes such as *GLUT-1, HK-II, LDH-A, MCT-1, PFK* in the HNSCC patient cases as compared to normal samples obtained from TCGA databases. Moreover, the current study revealed the c-Met overexpression across the histological and molecular subtypes of different HNSCC patient cases. We also showed the possible association of c-Met expression between the metabolic gene expression in HNSCC patient samples. We showed that patients with higher expression of c-Met had a shorter overall survival time and worse prognosis, and c-Met higher-expression levels also resulted in worse disease free survival in many cancers, confirming the association of c-Met and metabolic related genes with poor clinical outcomes in HNSCC. Furthermore, the protein-protein network analysis identifies the co-expression of metabolic associated genes with the c-Met.

Conclusions: Our analysis suggests the correlation with higher expression of c-Met with a shorter overall survival and worse prognosis of HNSCC patients. Furthermore, the protein-protein network analysis identifies the co-expression of metabolic associated genes with the c-Met expression. Those genes with moderate and very strong positive correlations with c-Met expression in cancers are involved in the glucose metabolism, lipid metabolism, cell cycle process. Considering c-Met inhibition in HNSCC would be an important strategy for therapy that may favour the sensitization of HNSCC through metabolic network.

Keywords: c-Met, HNSCC, Metabolism, In-silico, TCGA