High expression of NCF2 is associated with poor survival in patients with head and neck squamous cell carcinoma.

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Abstract

Background and aim: NCF2 expression has a significant impact on cancer development and progression. Several studies have found the increased expression of NCF2 associated with tumorigenesis and poor prognosis in patients with cancer. However, the expression and prognostic value of NCF2 remain largely unknown in HNSCC.
Objective: The present study aimed to analyze the expression and prognostic value of NCF2 in HNSCC.
Materials and methods: In the present study, we used the large TCGA (The Cancer Genome Atlas) RNA sequencing (RNAseq) dataset to explore the NCF2 expression level and its prognostic value in HNSCC. The mRNA expression level of NCF2 in various kinds of cancers, including HNSCC, was analyzed *via* the UALCAN database.
Results: We observed that the mRNA expression level of NCF2 was increased in most cancers compared with normal tissues, especially in HNSCC. Also, we also used Kaplan-Meier plotter to evaluate the prognostic value of NCF2 in HNSCC patients. It showed highly expressed NCF2 was significantly related to poor Overall Survival (OS) in HNSCC patients.
Conclusion: The NCF2 is highly expressed in HNSCC and associated with poor prognosis in HNSCC patients. Therefore, NCF2 could be a promising prognostic biomarker for HNSCC.
Keywords:
NCF2, mRNA expression, HNSCC, Prognostic value, TCGA database.

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Introduction

Head and neck cancer is the world's sixth-leading causing cancer among other types. The most common type of Head and Neck Cancer is Squamous Cell Carcinoma (HNSCC) because 90% of the head and neck cancer arises from a squamous cell they also arise from lymphomas, sarcomas, and adenocarcinomas. The lifestyle of people and use of tobacco leads to this cancer and human papilloma virus infections are risk factors for this cancer. 650,000 cases are reported every year and 300,000 patients die due to head and neck cancer. This is the sixth leading cancer worldwide based on this incidence [1,2].

While there has been an improvement in the diagnosis and HNSCC care, the prognosis of patients is low, primarily on account of the advanced stage at diagnosis and the lack of successful therapy. The changed expression of oncogenes and tumor suppressors has an association with the development and progression of HNSCC based on accumulating data. To date, however, HNSCC has not been diagnosed and treated personally as its biomarkers are highly sensitive and unique [3].

Recent studies in molecular genetics provided evidence that the majority of Head and Neck Squamous Cell Carcinomas (HNSCCs) progress within a contiguous field of preneoplastic cells [4,5]. Based on several studies shown, it can be inferred that these alterations in several cellular molecules including DNA, RNA, and proteins play an important role in tumor progression and the overall survival of the malignant cells. Our recent studies also showed that DNA, RNA, and protein alteration are associated with several diseases. [6–14]. Hence these markers can contribute to early diagnosis and prediction of prognosis. The diagnosis of carcinoma at an early stage can help to avoid extensive treatment and thus biomarkers can serve as a tool for diagnosis **[15,16]**.

The NCF2 (Neutrophil Cytosolic Factor 2) gene is located on chromosome 1q.25, consist of 16 exons and a gene length of 40kb [17,18] which also refer to p67-phox. NCF2 gene regulates cell growth, malignant differentiation, and transformation. Several recent studies revealed that NCF2 high expression is closely linked to human diseases, such as cervical cancer and inflammatory diseases [19–21].

NCF2 expression has a significant impact on angiogenesis, tumor metastasis and self-renewal, and other properties of cancer stem cells. NCF2 triggers Nf-kB signaling to induce tumor invasion [22]. Several studies are showing increased levels of NCF2 can promote tumor susceptibility and progression, or SNP/ mutations in NCF2 genes may be responsible for cancer progression. But some of the researchers also stated that decreased levels of NCF2 can also lead to

cancer progression. Hence more research in the area of NCF2 gene expression and analysis of the association between this NCF2 gene expression and tumor susceptibility progression of cancer should be promoted. This present study aimed to analyze the NCF2 gene expression in HNSCC which is an aggressive malignancy with high morbidity and mortality rates.

Materials and Methods

Gene expression analysis

The present study initially analyzed the NCF2 expression in HNSCC (n=520) and normal tissues (n=44) using data from the TCGA dataset. We used the UALCAN database to analyse the NCF2 mRNA expression in primary HNSCC and normal tissues.

Survival analysis by Kaplan-Meier plotter

In the present study, the prognostic values of NCF2 at mRNA level in HNSCC was analyzed using Kaplan-Meier Plotter is an online database containing gene expression profiles and survival information of cancer patients.

Results and Discussion

The accumulated evidence shows that the expression of NCF2 in many forms of malignancies has increased significantly. Based on these results, several human virulences have shown that NCF2 has a viable carcinogenic role [23,24]. The NCF2 expression of tumor development and unfavorable prognosis were found in previous trials to be evident and closely associated with different forms of malignancy. High NCF2 expression in colorectal cancer tissues has been seen frequently and may play an important role in colorectal cancer. In a recent study, it was found that the increased expression of NCF2 is significantly associated with the stage TNM, a recurrence that has shown that the surplus expression of NCF2 could contribute to the ESCC growth. Further, it has been shown that there have been obvious associations among the expression of increased NCF2 with short OS characteristics and poorer DFS in ESCC patients according to the Kaplan-Meier analysis and log-rank test [25].

In the present study, the NCF2 expression in HNSCC was first determined using the UALCAN database. We found that NCF2 was highly expressed in various types of cancer including HNSCC (Figure-1, p < 0. 05).

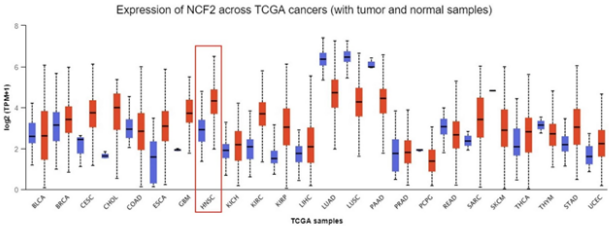

Figure 1. *NCF2 mRNA expression pattern in normal and tumor tissues (UALCAN database; P < 0.05). X-axis shows the types of tissues NCF2 were expressed and Y- axis exhibits log2 fold change values of NCF2 expression. Red boxes represent tumor tissues; blue boxes represent normal tissues.*

Besides, the UALCAN database was used to evaluate the exact NCF2 mRNA expression in HNSCC and normal tissues. We found that the mRNA level of NCF2 was significantly up-regulated in HNSCC compared to normal tissues (Figure 2, p<0.01).

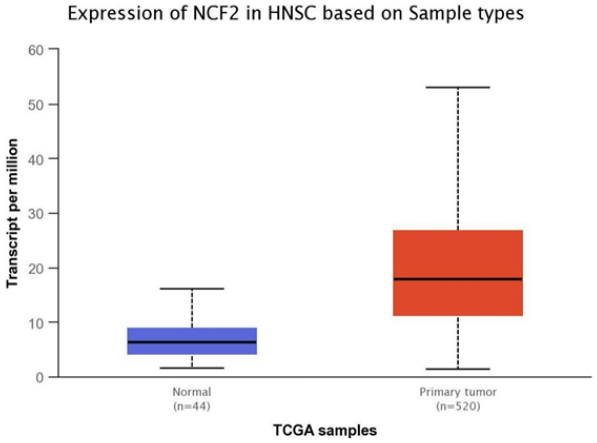

Figure 2. *Boxplot showing NCF2 expression in patients with HNSCC (primary tumor) and normal tissues (UALCAN), P<0.01. The Y axis: transcript (NCF2) per million and X axis: sample types.*

In the present study, we also found that high NCF2 expression was related to poor survival rate in HNSCC patients (Figure 3, p=04).

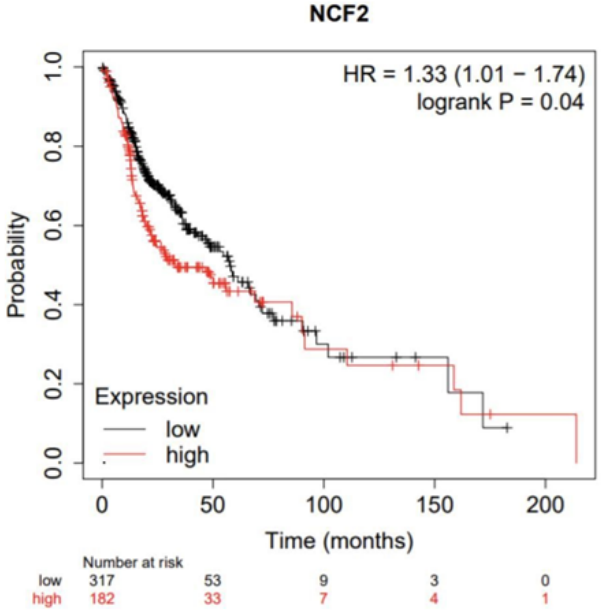

Figure 3. *Kaplan-Meier curves indicated that HNSCC patients had poorer overall survival with high expression of NCF2 mRNA (P=0.04). Red line shows the cases with highly expressed NCF2 and black line is indicated for the cases with*

lowly expressed NCF2. The y-axis is the survival probability, and the x-axis represents time (months).

Apart from HNSCC, cervical cancer, esophageal squamous cell carcinoma, and renal carcinoma also showed decreased overall survival rate associated with increased expression of the NCF2 gene [25,27]. The present study results were also under previous literature in the case of increased NCF2 expression and decreased overall survival rate of HNSCC patients. However, large-scale studies are required to substantiate the findings obtained in this study.

Conclusion

In conclusion, NCF2 was highly expressed in HNSCC and was significantly correlated to poor survival in HNSCC patients. Hence NCF2 can be used as a potential prognostic biomarker for HNSCC.

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Authors Contribution

All the authors contributed equally in concept, designing, carrying out the research and analysis of the study.

Conflict of Interest

The authors declare no conflict of interest.

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