80909_Auto_Edited.docx

WORD COUNT 820
TIME SUBMITTED 23-DEC-2022 12:32AM
PAPER ID 94288846

Name of Journal: *World Journal of Hepatology*
Manuscript NO: 80909
Manuscript Type: LETTER TO THE EDITOR

Prognostic role of RFWD3 and immune cell infiltration in hepatocellular carcinoma

Miao YD *et al.* RFWD3 in hepatocellular carcinoma

Yan-Dong Miao, Wu-Xia Quan, Jiang-Tao Wang, Jian Gan, Xin Dong, Fang Zhang

Abstract

The expression of ring finger and WD repeat domain 3 (RFWD3) is significantly higher in unpaired and paired hepatocellular carcinoma (HCC) tissues than in normal tissues. The expression of RFWD3 has a significant correlation with the infiltration level of 14 immune cells. There is a prominent difference in overall survival, disease-specific survival, and progression-free interval between the high and low RFWD3 expression subgroups. Besides, univariate cyclooxygenase analysis indicated that RFWD3 is an independent prognostic element for HCC. RFWD3 has an ability to accurately predict the prognosis in HCC (area under curve value = 0.863). Furthermore, nomogram can predict the probabilities of 1-, 3- and 5-year OS *via* integrating the age, pathologic stage, AFP, and RFWD3 expression in HCC.

Key Words: Hepatocellular Carcinoma; RFWD3; Immune cell infiltration; Bioinformatics

Miao YD, Quan WX, Wang JT, Gan J, Dong X, Zhang F. Prognostic role of RFWD3 and immune cell infiltration in hepatocellular carcinoma. *World J Hepatol* 2022; In press

Core Tip: We discovered that ring finger and WD repeat domain 3 (RFWD3) expression is remarkable higher in tumor group than in the corresponding normal group, whether in unpaired or paired hepatocellular carcinoma (HCC) tissues. RFWD3 expression has a significant correlation with the infiltration level of 14 immune cells. Besides, univariate cyclooxygenase regression analysis indicated that RFWD3 is an independent prognostic element in HCC. RFWD3 has the ability to accurately predict the prognosis in HCC.

TO THE EDITOR

We studied with an interesting paper by Liang *et al*[1]. They assessed ring finger and WD repeat domain 3 (RFWD3) expression levels in hepatocellular carcinoma (HCC) patients. Furthermore, they found RFWD3 affects the prognosis, proliferation, invasion, and metastasis of HCC *via* regulating the Wnt/β-catenin signal pathway. We appreciate the authors' unique view in probing into the prognostic implication of RFWD3 in HCC. We also discovered the expression of RFWD3 was prominently higher in both unpaired and paired HCC tissues than in the corresponding normal tissues (Figure 1A and B). According to the current research, cancer cells, endothelial cells, stromal cells, immune cells, and cancer-associated fibroblasts cells all exist in the tumor microenvironment (TME)[3,4]. TME is also an crucial part in the development, invasion and metastasis of HCC, however, immune escape of HCC has become a hard conundrum in cancer treatment[5]. Due to the limitations of chemotherapy in the liver cancer therapy, many immunotherapy for liver cancer arises at the historic moment. Immunotherapy mainly uses immune cells inside and outside TME to specific target and attack cancer cells, which has an advantage of high specificity and low side-effect[6]. Different types of immune-related cells act diverse roles, containing inhibiting/promoting HCC and varying types that are controversial[7]. Liang *et al*[1] found RFWD3 affects the prognosis of HCC. Therefore, we tested a hypothesis that the expression of RFWD3 maybe associate with the immune cells infiltration in HCC. Detailed information are shown in Table 1.

To confirm the hypothesis, in this research, we explored the correlation between RFWD3 expression and infiltration level of 24 immune cells by spearman's analysis using ssGSEA algorithm[8]. We found that RFWD3 expression has a remarkable correlation with the infiltration level of 14 immune cells (Figure 2A), among them, RFWD3 expression is positively associated with the infiltration level of Th2 cells, T helper cells, T follicular helper (TFH) cells, T central memory (Tcm) cells, activated dendritic cell (DC), NK CD56 bright cells, Eosinophils cells (Figure 2B-H, all $P < 0.05$); and negatively associated with cytotoxic cells, DC, plasmacytoid DC (pDC), Neutrophils cells, T gamma delta cells (Tgd), Treg cells, Th17 cells (Figure 2I-O, all $P < 0.05$). These finding might encourage further detection the effection of RFWD3 in HCC immunotherapy. Detailed information is manifested in Table 2.

We agree with Liang *et al*[1], who found that higher RFWD3 expression show a worse OS in HCC. Our study found that OS, DSS, and PFI are prominently shorter in the high RFWD3 subgroup than in the low RFWD3 subgroup (Figure 3A-C, all $P < 0.05$). Besides, univariate cyclooxygenase analysis demonstrated that RFWD3 is an independent prognostic element for HCC patients (Table 3). Receiver operating characteristic curve showed that RFWD3 has the ability to accurately predict the prognosis in HCC (area under curve = 0.863). Furthermore, we utilized the nomogram to predict the probabilities of 1-, 3- and 5-year OS *via* integrating age, pathologic stage, AFP, and RFWD3 expression. Each element was assigned a score in ratio to its contribution to the survival risk (Figure 3E). Conversely, the above fingding indicated that the research performed through Liang *et al*[1] is worthy of attention and that our discover may be provide supplementary information to their study, which can make the study more significant.

80909_Auto_Edited.docx

ORIGINALITY REPORT

10%
SIMILARITY INDEX

PRIMARY SOURCES

1	peerj.com Internet	30 words —	4%
2	www.wjgnet.com Internet	29 words —	3%
3	www.ncbi.nlm.nih.gov Internet	13 words —	2%
4	assets.researchsquare.com Internet	11 words —	1%

EXCLUDE QUOTES	ON	EXCLUDE SOURCES	< 10 WORDS
EXCLUDE BIBLIOGRAPHY	ON	EXCLUDE MATCHES	< 10 WORDS