Identification of KIF20A as a tumor biomarker and forwarder of clear cell renal cell carcinoma

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To the Editor: Renal cell carcinoma (RCC) is one of the top 10 major cancer types in adults. Current research shows that clear cell renal cell carcinoma (ccRCC) remains a deadly tumor disease and is associated with most cancer-related deaths.[1] Timely diagnosis is extremely important for the treatment of tumor patients. Adjusting the treatment plan based on the results of clinical diagnostic markers has a positive effect on patient prognosis. There is still a high risk of local recurrence or distant metastasis after nephrectomy. Tyrosine kinase inhibitor (TKI) is still a high risk of local recurrence or distant metastasis.

Kinesin family member 20A (KIF20A) or 20B (KIF20B) has been identified as an oncogene in several cancers. In the current study, we analyzed relationship between the expression profiles of KIF20A and KIF20B and patient survival and clinicopathological features in the Cancer Genome Atlas Kidney Clear Cell Carcinoma (TCGA-KIRC) and explored the biological significance of KIF20A in ccRCC. The expression levels of KIF20A and KIF20B were upregulated in total ccRCC tissues (n = 533) or paired ccRCC tissues (n = 72) with normal renal tissues (n = 72) [Figures 1A and 1B and Supplementary Figure 1, http://links.lww.com/CM9/A442]. Then, we investigated the prognostic value of KIF20A or KIF20B in ccRCC. The patients were divided into two groups by the median expression levels of KIF20A or KIF20B. Kaplan-Meier analysis results illustrated that the patients with high KIF20A had a short overall survival (OS) and disease-free survival (DFS) [Figure 1C]. Univariate and multivariate analyses showed that KIF20A was an independent risk factor for ccRCC as follows: OS, KIF20A (hazard ratio [HR], 1.741; P = 0.063) [Supplementary Figure 2, http://links.lww.com/CM9/A442].

As KIF20A had a significantly different expression between ccRCC tumor tissues and noncancerous normal tissues, receiver operating characteristic (ROC) curves were used to analyze the diagnostic efficiency of KIF20A. We found that KIF20A was significantly upregulated in RCC tissues by quantitative real-time polymerase chain reaction (Thermo, Massachusetts, USA) [Supplementary Figure 1C, http://links.lww.com/CM9/A442], and the relative expression levels of KIF20A were significantly upregulated in RCC tissues [Supplementary Figures 1D and 1E, http://links.lww.com/CM9/A442]. Kaplan-Meier analysis indicated that the patients with high KIF20A expression had shorter OS and DFS [Supplementary Figure 1F, http://links.lww.com/CM9/A442]. Immunohistochemistry results also showed that KIF20A was escalated in renal cancer tissues [Supplementary Figure 1G, http://links.lww.com/CM9/A442]. These results implicitly suggest that KIF20A might have a significant diagnostic value for patients with ccRCC. These results identified that KIF20A had a high expression level in ccRCC cancer tissues, which could be used as a diagnostic marker of ccRCC. This was consistent with previous reports,[4] but the biological role is not yet known in ccRCC.

We constructed a plasmid encoding short hairpin RNA (sh-RNA) against KIF20A (sh-KIF20A-1, sh-KIF20A-2) or negative control plasmid (sh-NC) (Addgene, Massachusetts, USA) to explore the possible role of KIF20A (Abclonal, Wuhan, China) in renal cancer cells. The plasmids were transfected into 786-O and A498 cells (which are commonly used types of kidney cancer cell lines) [Figures 1D and 1E]. Gene set enrichment analysis (GSEA) revealed that KIF20A was involved in the pathogenesis of TCGA-KIRC. The results showed that genes positively associated with KIF20A were enriched on the G2M checkpoint and epithelial-mesenchymal transi-
tion (EMT) signaling pathway [Figures 1F and 1H]. EMT could promote cancer progression.\cite{5} The silencing of KIF20A could inhibit the proliferation and migration capacities of 786-O and A498 cells [Figures 1G and 1I]. These experimental results confirmed that KIF20A can be a potential therapeutic target for renal cancer.

Figure 1: Kinesin family member 20A is a biomarker and promoter of renal cancer. (A) Heat map depicting KIF20A and KIF20B expression in TCGA-KIRC (n = 605). Red indicates high expression; white indicates medium expression; green indicates low expression. (B) Relative KIF20A and KIF20B expression in TCGA-KIRC. (C) Higher KIF20A expressers had a shorter OS and DFS than lower expressers. (D and E) KIF20A mRNA and protein expressions were successfully silenced in 786-O and A498 cells. (F) GSEA showed KIF20A was involved in the G2M checkpoint of TCGA-KIRC. (G) Silencing KIF20A restrained the proliferation of 786-O and A498 cells with cell counting kit-8 assay. (H) GSEA showed KIF20A involved in the epithelial-mesenchymal transition signaling pathway of TCGA-KIRC. (I) The silencing of KIF20A restrained the migration and invasion in 786-O and A498 cells. DFS: Disease-free survival; GAPDH: Glyceraldehyde phosphate dehydrogenase; GSEA: Gene set enrichment analysis; KIF20A: Kinesin family member 20A; KIF20B: Kinesin family member 20B; OS: Overall survival; TCGA-KIRC: The Cancer Genome Atlas kidney renal clear cell carcinoma. $^\ast P < 0.05$, $^\dagger P < 0.01$, $^\ddagger P < 0.001$, $^\S P < 0.0001$.
In conclusion, we found that KIF20A was an independent predictor for ccRCC. KIF20A expression was upregulated in database and clinical cases. Cell experiments found that suppression of KIF20A could inhibit the malignant characteristics of renal cancer cells. These results demonstrated that KIF20A could be a potential novel prognostic molecule and may become a treatment target for ccRCC. However, a large number of samples are still needed to verify its clinical value in the future.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s)/or his/her guardian has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients or his/her guardian understand that his/her/their name(s) and initials will not be published and due efforts will be made to conceal his/her/their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

None.

References


Corrigendum: Amyloid and tau positive mild cognitive impairment: clinical and biomarker characteristics of dementia progression

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In the article “Amyloid and tau positive mild cognitive impairment: clinical and biomarker characteristics of dementia progression”, which appeared in vol.134, issue14, page 1709 of Chinese Medical Journal, the following words “for Alzheimer’s disease Neuroimaging Initiative” should be added to the author section. The full authors should be corrected as “Hong-Chun Wei1, Bing Li1, Kok Pin Ng2, Qing-Xi Fu3, Sheng-Jie Dong4, Mao-Wen Ba1, Min Kong5; for Alzheimer’s disease Neuroimaging Initiative”. And in page 1717, the Funding Part shoule be corrected as “The study was supported by grants from the Shandong Provincial key research and development project (No.2018GSF118235), the Shandong Provincial Natural Science Foundation (No.ZR2016HL16) and Youth Research Start-up Fund of Yantai Yuhuangding Hospital Affiliated to Qingdao University (No.2020-25).”

Reference