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) has shown encouraging efficacy in advanced ccRCC patients.[2] Unfortunately, TKI resistance still develops and can lead to poor progression in cancer.[3] Thus, there is an urgent need to explore more effective prognostic biomarkers and to identify novel drug targets for ccRCC therapies.

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* but not *KIF20B* expression 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; $P = 0.002$); DFS, *KIF20A* (HR, 1.470; $P = 0.063$) [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-

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Website: www.cmj.org

DOI: 10.1097/CM9.0000000000001331

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Chinese Medical Journal 2021;134(17)

Received: 10-10-2020 **Edited by:** Peng Lyu

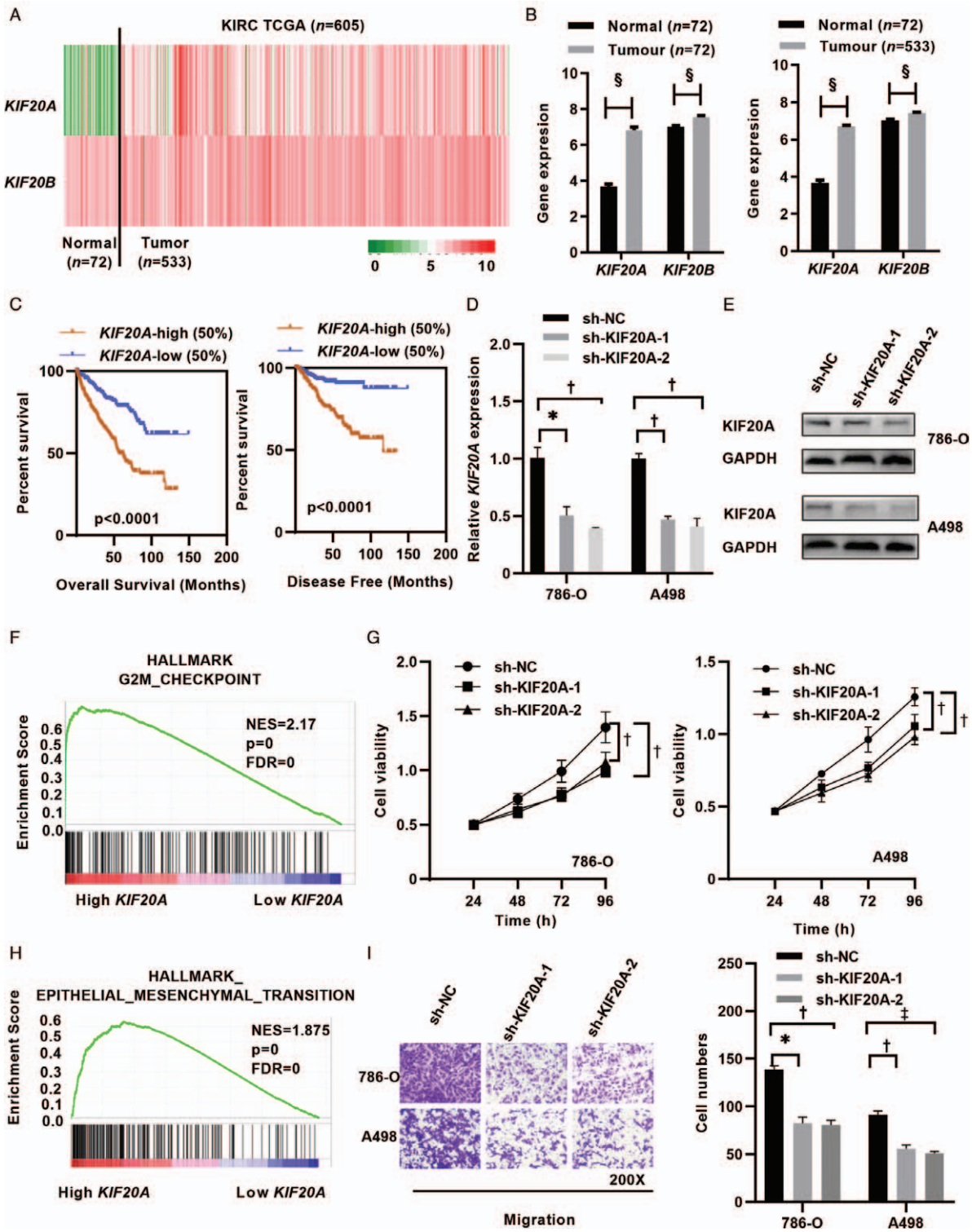

Figure 1: Kinesin family member 20A is a biomarker and promoter of renal cancer. (A) Heat map depicting *KIF20A* and *KIF20B* expression in TCGA-KIRC ($n = 605$). Red indicates high expression; white indicates medium expression; green indicates low expression. (B) Relative *KIF20A* and *KIF20B* expression 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. $^{*}P < 0.05$, $^{\dagger}P < 0.01$, $^{\ddagger}P < 0.001$, $^{\S}P < 0.0001$.

tion (EMT) signaling pathway [Figures 1F and 1H]. EMT could promote cancer progression.[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.

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.

Funding

This project was supported by grants from the National Natural Science Foundation of China (No. 81902588) and the National Key Scientific Instrument Development Project (No. 81927807).

Conflicts of interest

None.

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How to cite this article: Xiao W, Chen K, Liang HG, Zhang XP. Identification of *KIF20A* as a tumor biomarker and forwarder of clear cell renal cell carcinoma. Chin Med J 2021;134:2137–2139. doi: 10.1097/CM9.0000000000001331

Corrigendum

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

DOI: 10.1097/CM9.0000000000001765

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 Wei[1], Bing Li[1], Kok Pin Ng[2], Qing-Xi Fu[3], Sheng-Jie Dong[4], Mao-Wen Ba[1], Min Kong[5]; 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)."

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