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Analysis of the cancer genome atlas data to determine the correlation between PROX1 and TERT in hepatocellular carcinoma

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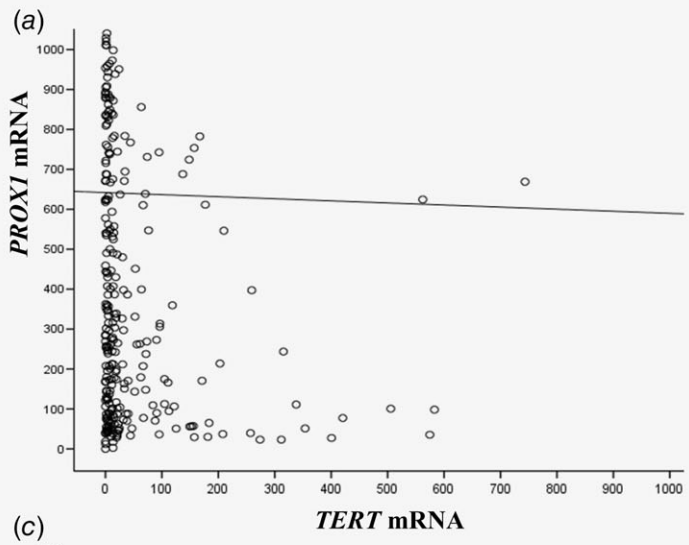
Dear Editor,

We read with great interest the article by Kim *et al.*[1] regarding the role of prospero homeobox protein 1 (PROX1) and telomerase reverse transcriptase (TERT) in hepatocellular carcinoma (HCC); their study reported that *PROX1* expression mediated *TERT* activity differently in accordance with the status of viral infection in HCC. Interestingly, *TERT* and *PROX1* mRNA expression were positively correlated in non-B



(b)

	R	P
Hepatocellular carcinoma	-0.041	0.443
B viral HCC	0.023	0.826
Non-B viral HCC	-.0.060	0.331
Breast cancer	-0.007	0.288
Bladder cancer	-0.017	0.740
Cervical cancer	-0.017	0.740
Colon cancer	0.005	0.914
Esophageal cancer	**0.187**	**0.025**
Glioblastoma	0.066	0.420
Head and neck cancer	**0.203**	**0.000**
Lung cancer (squamous)	**0.135**	**0.017**
Lung cancer (adeno)	**0.202**	**0.000**
Ovarian cancer	0.033	0.569
Pancreatic cancer	0.035	0.651
Rectal cancer	-0.148	0.064
Melanoma	**0.205**	**0.000**
Stomach cancer	-0.009	0.854
Uterine Endometrial cancer	-0.011	0.803

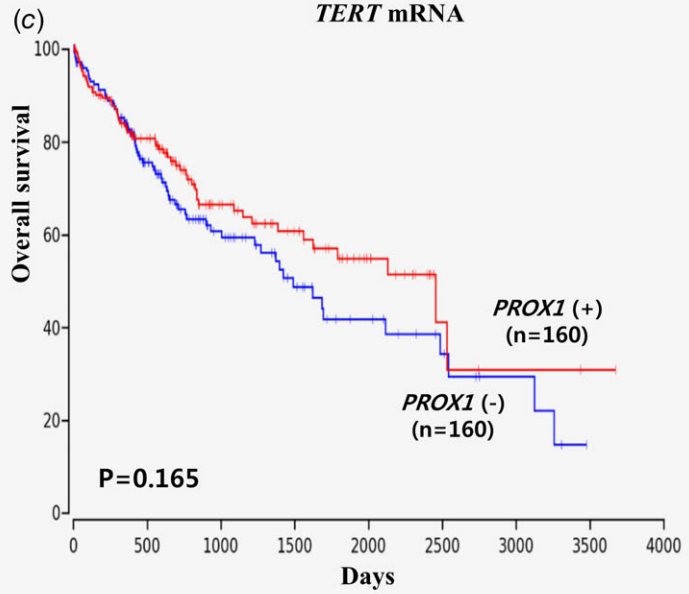


Figure 1. No correlation between *TERT* and *PROX*1 mRNA expression in hepatocellular carcinoma (HCC) (*a*). Association between *TERT* and *PROX*1 expression in various cancers based on The Cancer Genome Atlas data (*b*). Survival analysis of *PROX*1 expression in HCC (*c*). [Color figure can be viewed at wileyonlinelibrary.com]

Letter to the Editor

viral HCCs; however, this correlation was not observed in B viral HCCs. Using same approach, we analyzed the correlation between *TERT* and *PROX1* mRNA expression in various cancers including HCC, based on The Cancer Genome Atlas (TCGA) data from OncoLnc and cBioPortal.

Expression data were downloaded from TCGA's data portal (https://tcga-data.nci.nih.gov/tcga/) on July, 2018.[2] TCGA data indicated that *TERT* mRNA expression levels did not correlate with those of *PROX1* mRNA (r = -0.041, p = 0.443, Fig. 1*a*). When stratified by B viral status, there was no association between *TERT* and *PROX1* expression (Fig. 1*b*). Interestingly, the median values of TERT and *PROX1* expression in HCCs were high exclusively in TCGA data. Therefore, we investigated this association in other cancers presented on TCGA portal. Unexpectedly, *TERT* and *PROX1* mRNA expression levels were correlated in several cancer types, including melanoma, esophageal, head and neck, and lung cancers (Fig. 1*b*). Although this association was not observed previously in HCC,[1] *PROX1* may be an important activator of *TERT* in some cancers. Regarding studies on *TERT* promoter mutation, a common single nucleotide polymorphism, rs2853669, and hepatitis B virus X were not included in HCC analysis of TCGA data, thereby necessitating further comprehensive analyses.

Furthermore, the prognostic value of *PROX1* mRNA expression was analyzed in various cancers on the basis of TCGA data. In most cancers including HCC, *PROX1* did not have a prognostic value (Fig. 1*c*). However, *PROX1* downregulation indicated a poorer prognosis exclusively in melanoma (p = 0.048). The *TERT* promoter is one of the most frequent mutation sites in HCC and may be an essential modulator of *TERT* expression in cancers.[3] Moreover, *TERT* expression is a robust prognostic marker; however, the detailed mechanism underlying *TERT* regulation yet remains controversial.[4] As observed in the current and in previous studies, a positive correlation between *TERT* and *PROX1* expression in certain cancers suggested that PROX1 probably regulates TERT in an activity-dependent manner with other genetic changes.[1] The biological functions of *PROX1*- and *TERT*-associated gene alterations are of great interest for further studies in cancer.

Yours sincerely,

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