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Comparative analysis of SARS-CoV-2 receptor ACE2 expression in multiple solid tumors and matched non-diseased tissues

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ABSTRACT

The emerging severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) poses a global public health emergency. SARS-CoV-2 employs the host cell receptor ACE2 for cellular entry. Nonetheless, the differences in ACE2 expression pattern in lung versus other normal and solid tumor tissues remain incompletely characterized. Here, we analyze a large data set comprising ACE2 mRNA expression for 7592 tissue samples across 22 types of primary solid tumor and 4461 samples across matched 18 non-diseased tissues. Our results unravel eight normal tissues and 10 primary solid tumors, which might be at high risk of SARS-CoV-2 infection. These findings may provide additional insight into the prevention and treatment of SARS-CoV-2 infection, in particular for patients with these 10 vulnerable cancer types.

To the Editor,

In December 2019, a novel pneumonia disease, now termed coronavirus disease 2019 (COVID-19), emerged in Wuhan, Hubei, China (Huang et al., 2020). A previously unknown coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was identified in lower respiratory tract specimens from patients and serves as etiological agent responsible for COVID-19 (Zhu et al., 2019), which is threatening public health worldwide. As of April 4, 2020, a total of 1,051,635 laboratory-confirmed cases and 56,985 deaths caused by COVID-19 have been reported globally according to World Health Organization (https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports).

Angiotensin-converting enzyme 2 (ACE2) is known to be a host cell receptor for severe acute respiratory syndrome coronavirus (SARS-CoV) (Kuhn et al., 2004). It has been confirmed that SARS-CoV-2 like SARS-CoV utilizes ACE2 as cellular entry receptor (Hoffmann et al., 2020; Zhou et al., 2020). Notably, elevated ACE2 expression has previously promoted susceptibility to SARS-CoV spike protein-driven infection in vitro (Hofmann et al., 2004; Li et al., 2007), implying potential positive correlation between ACE2 expression level and SARS-CoV-2 infection. Although ACE2 shows a widespread distribution in various human tissues (Harmer et al., 2002), a statistically robust comparison of expression levels in lung, the main target of SARS-CoV-2 infection (Wu and McGoogan, 2020), versus other tissues based on a large sample size is still lacking.

SARS-CoV-2 infection commonly presents with fever and cough, which frequently elicits lower respiratory tract disease (Wu and McGoogan, 2020). Nonetheless, extrapulmonary clinical manifestations have been observed (Chen et al., 2020a; Guan et al., 2020; Huang et al., 2020; Wang et al., 2020), such as diarrhea, nausea or vomiting, liver abnormality, acute cardiac injury, and acute kidney injury. It is reported that cancer patients might harbor a higher risk of SARS-CoV-2 infection and inferior prognosis than those in infection without cancer (Liang et al., 2020). However, whether a heterogeneity of risk for infection exists among various cancer types remains unclear.

Here, we retrieved ACE2 mRNA expression data of 7592 tissue samples across 22 primary solid tumor types in The Cancer Genome Atlas (TCGA) and 4461 samples across 18 matched non-diseased tissues in Genotype-Tissue Expression (GTEx) from UCSC Xena (https://xena. https://doi.org/10.1016/j.meegid.2020.104428

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The vertical axis depicts the expression level shown as log2 (RSEM normalized count +1), whereas non-diseased tissues (No.) are ordered on the horizontal axis according to their median ACE2 expression values. The dashed red line represents median value (5.73) of ACE2 expression in lung. P values are calculated for comparison of expression levels in lung versus other tissues. The widths of curved shapes indicate the probability density of expression values. Box plots display the median and interquartile range, whiskers extend to 1.5 times the interquartile range, and outlier data are shown as dots. *, P < .05; **, P < .01; ***, P < .001; ns, not significant. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)
are required to validate these findings.

Declaration of Competing Interest

None.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.meegid.2020.104428.
Fig. 3. Comparison of ACE2 expression abundance in virus-positive versus virus-negative solid tumor tissues.

Cancer types (No.) are ordered on the horizontal axis according to their median ACE2 expression in normal lung tissue. Box plots display the median and interquartile range, whiskers extend to 1.5 times the interquartile range, and outlier data are shown as dots. **, P < .01; ns, not significant. CESC, cervical squamous cell carcinoma and endocervical adenocarcinoma; COAD, colon adenocarcinoma; ESCA, esophageal carcinoma; HNSC, head and neck squamous cell carcinoma; LIHC, liver hepatocellular carcinoma; READ, rectum adenocarcinoma; STAD, stomach adenocarcinoma. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

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