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Editorial

Measurement of COVID-19 Severity in Humanized Animal Model by ^{18}F-Fluorodeoxyglucose Positron Emission Tomography with Computed Tomography

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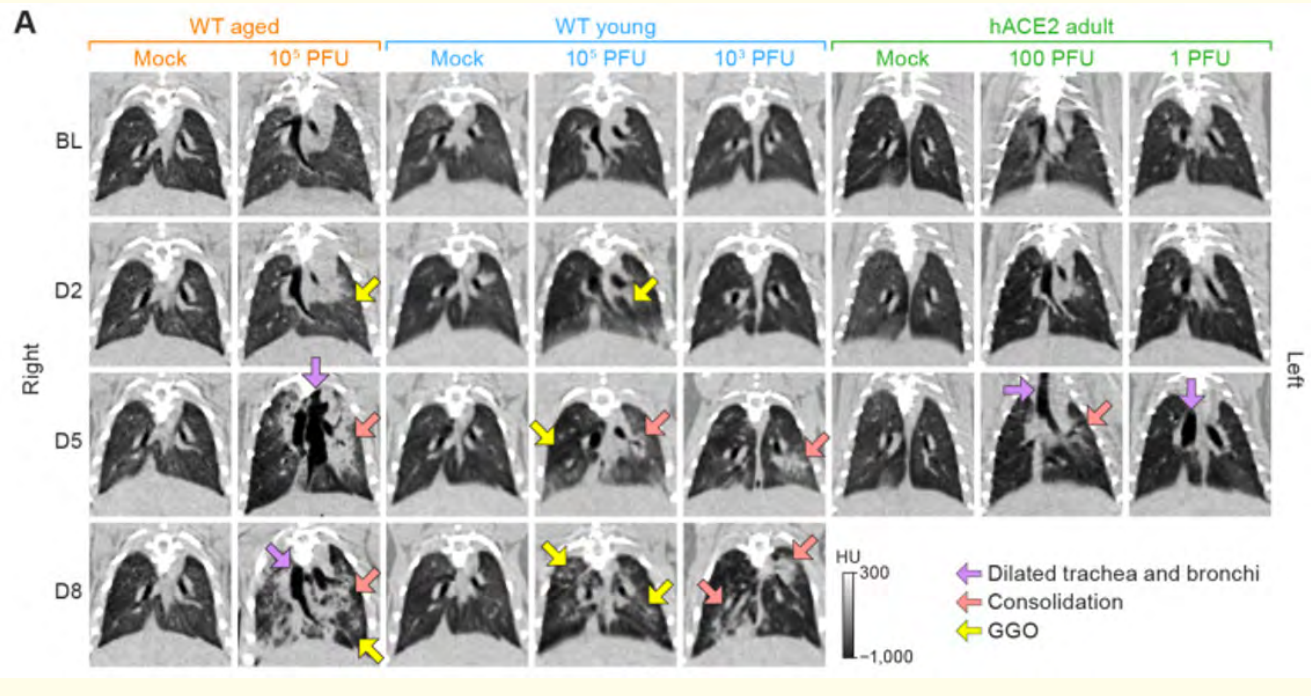
For better understanding SARS-CoV-2-infection pathophysiology for preclinical development of countermeasure, hamster model is widely used [1], whereas, diffuse pulmonary alveolar damage is frequently found in hospitalized COVID-19 patients [2-4]. Evaluation of animal models of Middle East respiratory syndrome coronavirus (MERS-CoV) have been previously used by positron emission tomography with computed tomography (CT), CT, (PET/CT), and single-photon emission computerized tomography (SPECT) [5]. In addition to being able to nasal-turbinate-damage determination, differentiation of COVID-19-lung-disease severity from mild to severe degrees was successful (Figure 1) [1]. Direct correlation between site-inflammatory-metabolic-cell activity and ^{18}F-Fluorodeoxyglucose (FDG) uptake was demonstrated [1].



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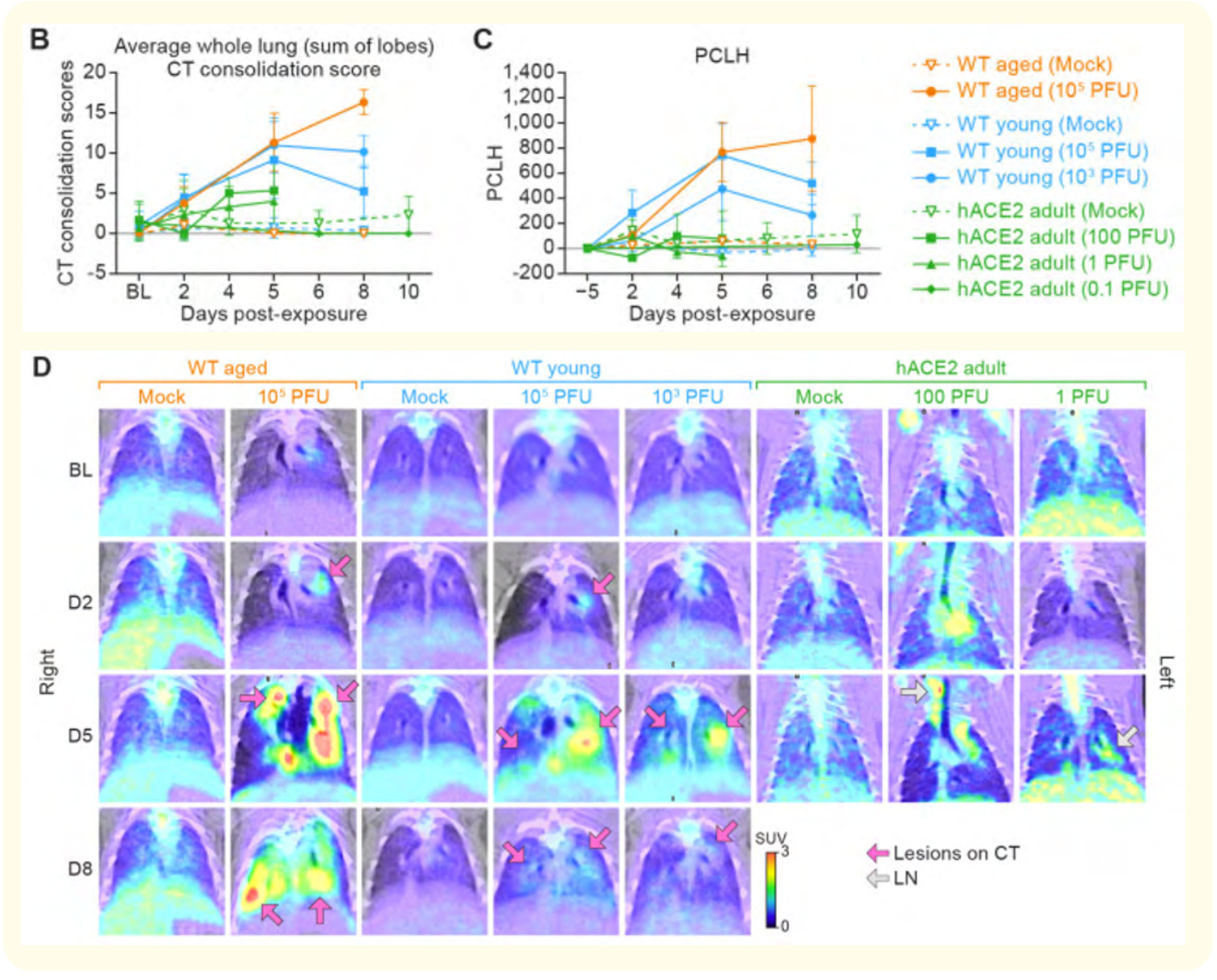
B
Average whole lung (sum of lobes) CT consolidation score
CT consolidation scores
Days post-exposure
C
PCLH
Days post-exposure
WT aged (Mock)
WT aged (10⁵ PFU)
WT young (Mock)
WT young (10⁵ PFU)
WT young (10³ PFU)
hACE2 adult (Mock)
hACE2 adult (100 PFU)
hACE2 adult (1 PFU)
hACE2 adult (0.1 PFU)
D
WT aged
WT young
hACE2 adult
Mock
10⁵ PFU
10³ PFU
100 PFU
1 PFU
BL
D2
D5
D8
Right
Left
SUV
Lesions on CT
LN

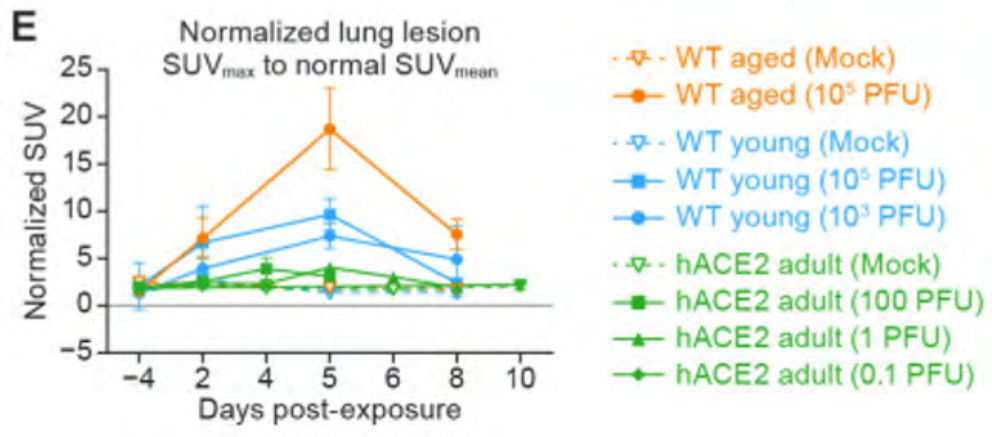

Figure 1: Demonstrating Micro-PET/CT imaging of the lungs from three models of virus-exposed hamsters over an 8–10-d period.

A. Representative chest micro-PET/CT images in the coronal plane. Columns from left to right show lung images from groups of adult hACE2 hamsters , young WT hamsters (exposed to mock inoculum, 105 PFU virus, and 103 PFU virus), and aged WT hamsters (exposed to mock inoculum and 105 PFU virus) (exposed to mock inoculum, 100 PFU virus, and 1 PFU virus), young WT hamsters (exposed to mock inoculum, 105 PFU virus, and 103 PFU virus) (exposed to mock inoculum, 100 PFU virus, and 1 PFU virus). All hamsters were exposed to mock inoculum or SARS-CoV-2 intranasally. Disease progress over time (baseline to 8 d) are shown in the images in the rows from top to bottom. Radiodensity value (in HU) is indicated in the scale bar. B. The whole lung (sum of lobes) CT consolidation score (±SD) from three hamster models is shown in semi-quantitative average. C. Average of PCLH (±SD) from three hamster models is indicated by quantitative lung CT. D. CT lung consolidation generally is correlated with 18F-FDG PET images by 18F-FDG-avid areas. (PET images show the same lungs from panels in A.) The color bar indicates SUV. E. Quantitation of 18F-FDG uptake in lungs. The longitudinal change of the 18F-FDG uptake in lungs at the different days post-exposure was reflexed by normalized SUVmax (±SD) calculation to indicate data. Two-way ANOVA with Tukey multiple comparison test was used to determine statistical significance.

Abbreviations : Micro-PET, micro-positron emission tomography; CT, computed tomography; WT, wild-type; hACE2, human angiotensin-converting enzyme 2; SARS-CoV-2, severe acute respiratory syndrome coronavirus-2; HU, Hounsfield Unit; SD, standard deviation; PCLH, percent change in lung hyperdense volume; 18F-FDG, 2-deoxy-2-[fluorine-18]fluoro-D-glucose; SUV, standardized uptake value; GGOs, ground-glass opacities; ANOVA, analysis of variance; BL, baseline; D2, day 2; D5, day 5; D8, day 8; LN, lymph node.

(Source: Cong Y, Lee JH, Perry DL, Cooper K, Wang H, Dixit S, et al. Longitudinal analyses using 18F-Fluorodeoxyglucose positron emission tomography with computed tomography as a measure of COVID-19 severity in the aged, young, and humanized ACE2 SARS-CoV-2 hamster models. Antiviral Research 2023. AVR 105605. PII : S0166-3542)23)00083-9

DOI : https://doi.org/10.1016/j.antiviral.2023.105605 [1])

In conclusion, whole-lung-CT-consolidation scores, the PCLH, a quantitative radiodensity-based parameter and the normalized-lung-SUV-max changes were well correlated in all three groups of the above recent study (60-week-old (aged) wild-type, 6-week-old (young) wild-type, and 14-22-week-old (hACE2) Golden hamsters).

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