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Editorial Article

Inhalation with ACE-2-Expressing-Lung-Exosomes for Prophylactic Protection and Treating SARS-CoV-2 Infection and Disease

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SARS-CoV-2 infectivity depends on binding its S protein with the entry-receptor " hACE-2 " a promising strategic treatment, therefore, is this interaction inhibition [1-3]. Some SARS-CoV-2 variants, such as B.1.1.7 (Alpha), B.1.617.2 (Delta), and B.1.1.529 (Omicron) variants were highly resistant to mRNA-1273 vaccine-induced humoral immunity or BNT162b2 [4-6]. A recent study demonstrated that in a female mouse model, inhalation of ACE-2-expressing-human-lung-spheroid-cells (LSC)-derived exosomes (LSC-Exo) (Figure 1) could protect the host throughout the whole lung by biodistribution and deposition against COVID-19 (SARS-CoV-2) infection by SARS-CoV-2 binding, blocking the interaction of host cells with SARS-CoV-2, and virus neutralization both in vitro and in vivo [7]. This study also revealed decrease of viral loads and protection of SARS-CoV-2-induced disease [7]. Three different types of inhalation devices are commonly used; jet, ultrasonic, and vibrating mesh (all are nebulizer) (Figure 2) [8]. In non-human primates and rats studies, when nebulized with eFlow, human immunoglobulin preparations were deposited into the airways as well as treated-lung alveoli [9]. VR942, an anti-interleukin (IL)-13 mAb is a first-in-class for dry-powder inhalers (DPIs) [10].

In conclusion, ACE-2-expressing-human-lung-spheroid-cells-derived exosomes could be a promising-broad-spectrum bioprotectant against SARS-CoV-2 variants and other emerging virus variants. By using common nebulizer inhalation, it can be administrated other therapeutic agents for treating the patients' lung and respiratory system.

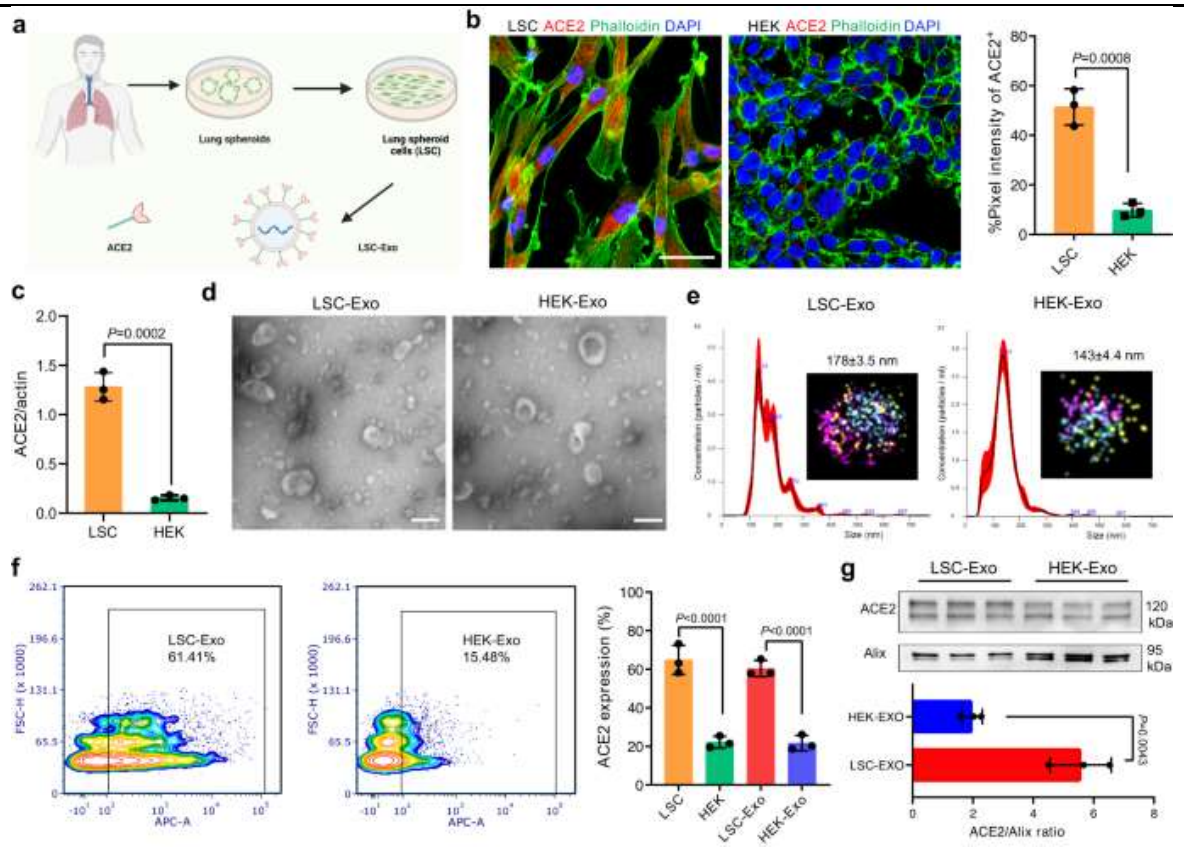

Figure 1 : A. Demonstrating extraction scheme of LSC and LSC-Exo from healthy donors, created with Biorender.com. B. Demonstrating immunofluorescence staining and quantification analysis of ACE-2 on LSC and HEK. Scale bar: 50 μm. n = 3. C. Demonstrating Western blot quantification of ACE-2 expression in LSC and HEK, which derived from the same experiments and processed in parallel. n = 3. D. Demonstrating representative TEM images of LSC-Exo and HEK-Exo from 3 independent experiments. Scale bar: 100 μm. E. Demonstrating measurements of size distribution of LSC-Exo and HEK-Exo via nanoparticle tracking analysis. Inset: 3-colar dSTORM image of CD63-Alexa Fluor®-488, PE-CD9, APC-CD81 of LSC-Exo or HEK-Exo. F. Demonstrating quantification of ACE-2 expression on LSC-Exo and HEK-Exo by flow cytometry. n = 3 [7].

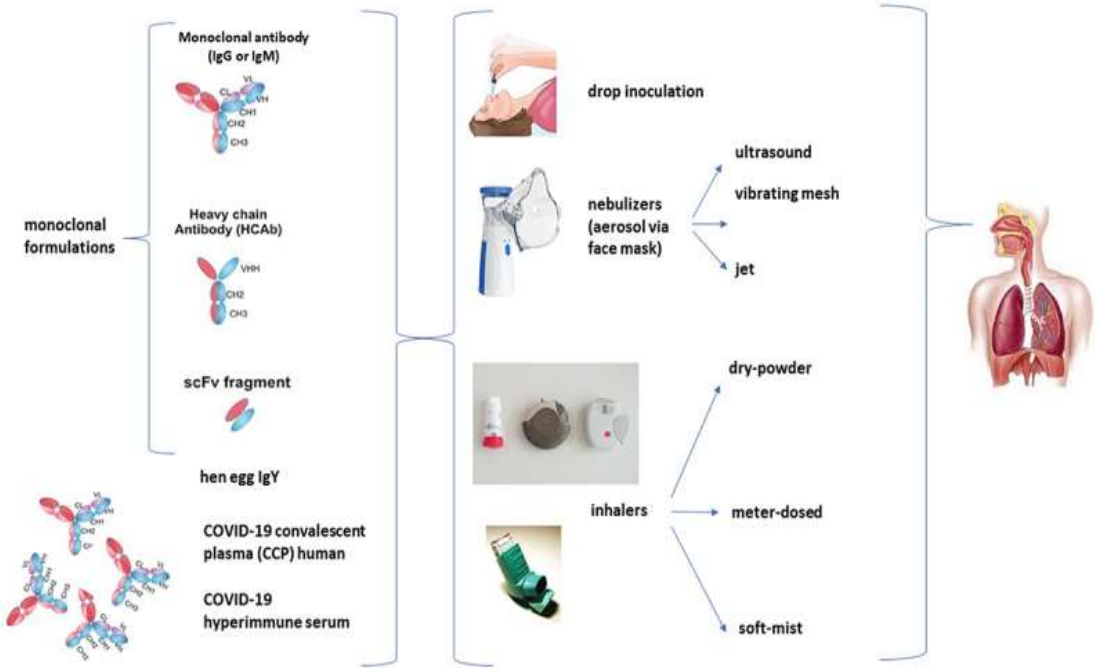

Figure 2 : Demonstrating potential therapeutic approaches for respiratory delivery of passive immunotherapeutics against SARS-CoV-2 (COVID-19) [8].

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