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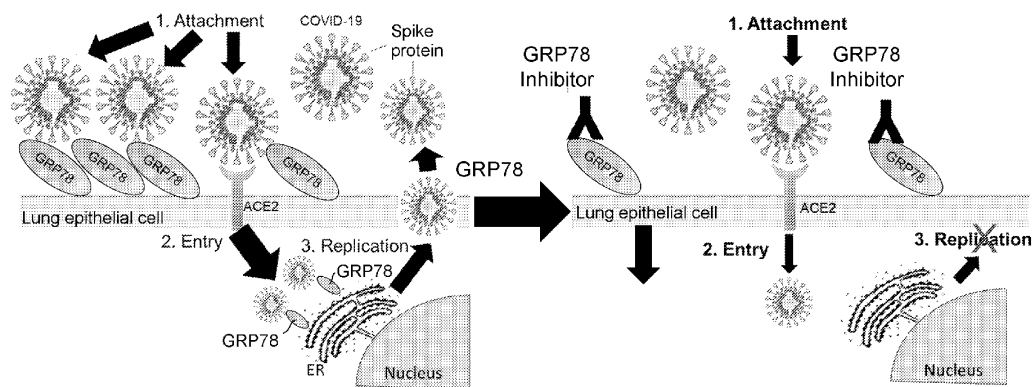


FIG. 1A

FIG. 1B

(57) Abstract: COVID-19 results from the infection of the SARS-CoV-2 virus and has spread quickly to literally infected the world. Although coronavirus spike proteins can recognize a broad range of host cell-surface proteins, inhibiting spike protein binding to a survival factor called GRP78 results in a significant reduction in SARS-CoV-2 attachment, entry and replication in lung and kidney cells. This inhibition is accomplished with a novel type of inhibitor that potently blocks the binding of SARS-CoV-2 spike protein and whole virus to surface-bound GRP78. These novel GRP78 inhibitors also down regulate cytokines (IL 10, IL6), immune co-inhibitory checkpoint proteins (PD-L1, B7H3, B7H4), and up regulate immune co-stimulatory proteins (MHC-II, CD-86) resulting in the reduction of the immune suppressive nature of infected lung alveolar epithelial cells in vitro and in vivo. Finally, these novel GRP78 inhibitors inhibit the hyperfibrinolysis of infected lung cells by reducing the activation of plasmin on cell surfaces.

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