COVID Susceptibility and Severity Correlation with the ACE2 Gene

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Abstract

A wide spectrum of susceptibility and severity of infection has been observed among COVID-19 patients. While some individuals remain unaffected by the Sars-Cov-2 virus, others have contracted the virus multiple times with varying levels of severity. This poster reviews some of the research demonstrating a link between the susceptibility of the Sars-Cov-2 virus and the severity of infection, and a specific gene called ACE2. The ACE2 gene encodes an angiotensin-converting enzyme that acts as a functional receptor for the spike glycoprotein receptor binding domain of the coronavirus and severe acute respiratory syndrome coronaviruses. ACE2 presents numerous amino acid variants with different functions and catalytic properties. The Sars-Cov-2 virus utilizes the ACE2 gene as a host receptor to infect its human host through three amino acid (AA) residues (T20, Y83, and K353) near the interface. Recent single-cell RNA sequencing has found organ- and cell-specific expression of the converting enzyme in the lungs and alveolar tissue, explaining why infection typically includes respiratory symptoms. It is hypothesized that expression levels from the ACE2 gene may affect an individual's susceptibility to the virus and the severity of the infection. Awareness of genetic predisposition factors can contribute to evidence-based risk assessment which could allow for future individualized treatments and preventative measures.

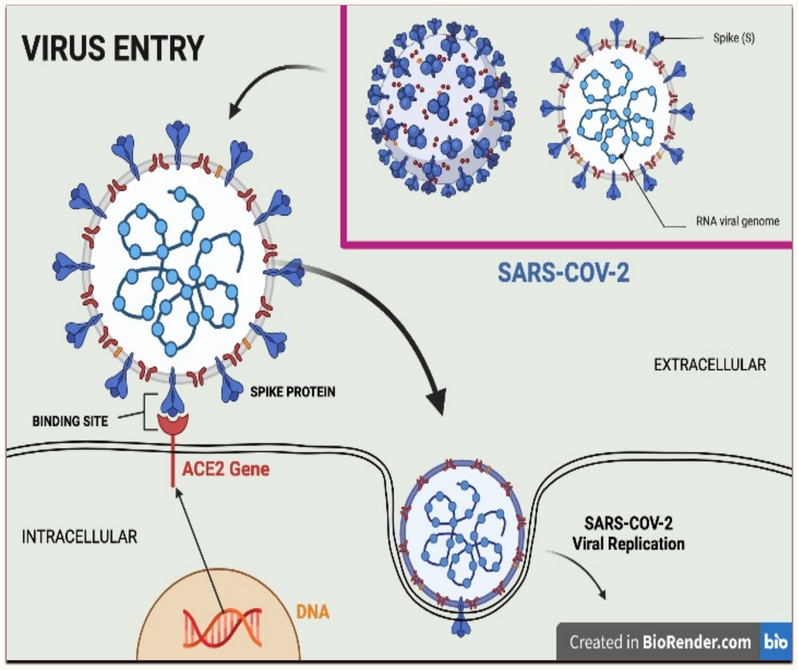

Figure 1. Mechanism of entry by Sars-Cov-2 virus into the host cell via the binding site of Sars-Cov-2 spike protein and the ACE2 receptor.

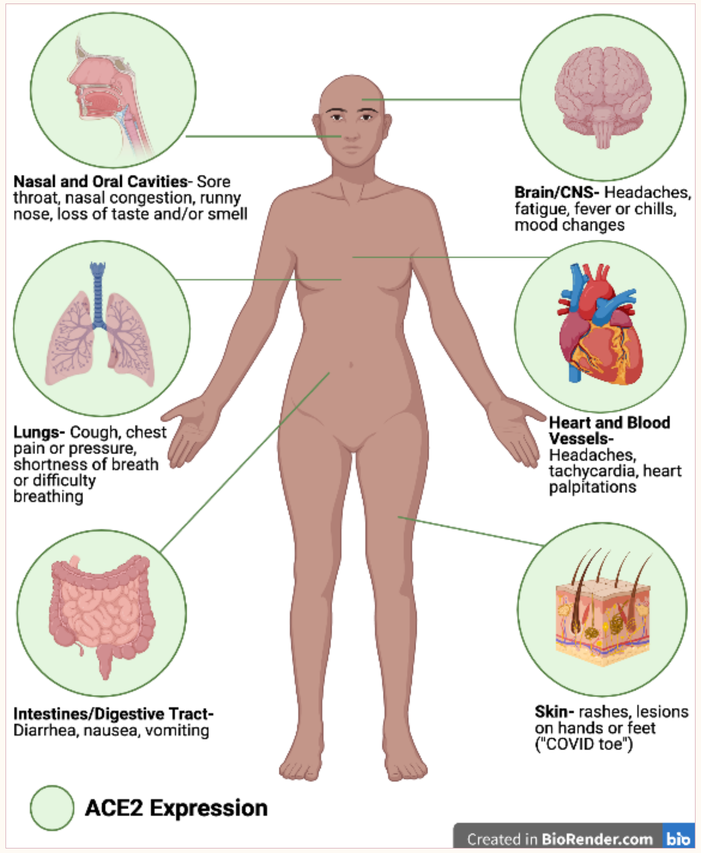

Figure 2. ACE2 expression location in organs associated with COVID symptoms. Adapted from Salamanna et al. (2020).

ACE2 Mechanism of Expression and COVID-19

The ACE2 gene encodes the host receptor that Sars-Cov-2 uses to enter a human cell. Organs and tissues where ACE2 is expressed are susceptible to the Sars-Cov-2 virus. ACE2 also encodes an enzyme that converts the angiotensin hormones Ang I and Ang II to Ang (1–9) and Ang (1–7) and plays a role in regulating the renin-angiotensin system (RAS) responsible for homeostatic regulation of vascular functioning. However, Sars-Cov-2 binds to ACE2 and blocks the ability of angiotensin to bind to ACE2, throwing the RAS out of balance. Research has revealed a correlation between low ACE2 gene expression and increased severity of COVID-19 cases. Patients with low ACE2 expression have a gene that is downregulated. When ACE2 is downregulated, it may be unable to bind to Sars-Cov-2 and maintain balance of the RAS due to a slower rate of physiological response. High expression means that the gene is upregulated and may be able to bind to Sars-Cov-2 while keeping the RAS balanced, leading to more successful coronavirus recoveries/outcomes.

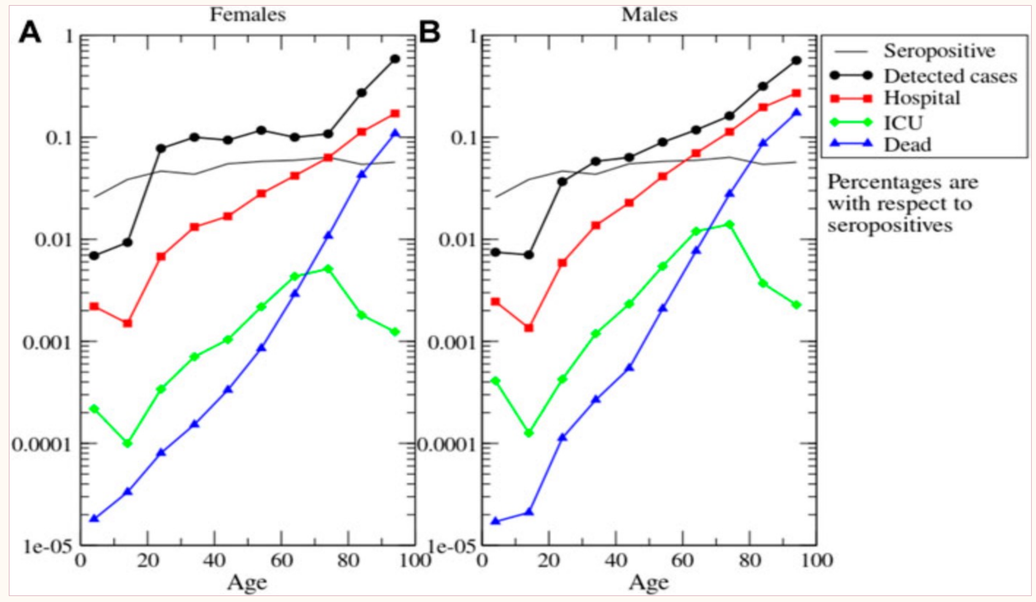

Figure 3. Percentages of positive COVID-19 cases with respect to age. Severity levels and their trends based on age are shown by the blue, green, red, and black lines. The thin black line reports the fraction of seropositive for each age class, which is used as the normalization for the fractions reported in the figures. Figure from Bastolla et al. (2022).

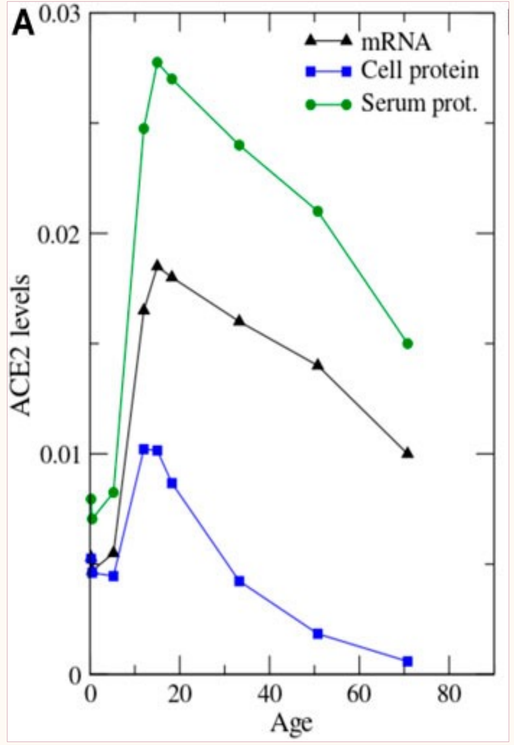

Figure 4. Model of ACE2 levels of mRNA, protein in the cellular membrane and protein in serum at different ages. Figure from Bastolla et al. (2022).

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