Role of polymorphisms of ACE2 and Spike proteins in SARS–CoV–2 infection

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Introduction
The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has been studied worldwide due to the serious pandemic caused. COVID-19 is an infection disease caused by SARS-CoV-2 that after 4-6 incubation days leads to development of flu-like and pneumonia symptoms that can worsen and lead to fatal respiratory failure. (1) Still, many infected people have mild or no symptoms.

The SARS-CoV-2 virus needs a cell surface receptor like Angiotensin Converting Enzyme 2 (ACE2) among others, so that they can invade the host cells. (2) On the other hand, SARS coronaviruses present a coating protein – Spike – and its interaction with the ACE2 receptor triggers the fusion between virus envelope and host’s cell membrane and consequently the release of nucleocapsid into the cytoplasm. (1)

There are some ACE2 or Spike polymorphisms that modifies the affinity between these proteins and lead to an increase in the host’s resistance or susceptibility, as well as affects the SARS-CoV-2 severity and spread. (3, 4) Identifying variants on host’s ACE2 receptor or on SARS-CoV-2 Spike protein that modify the host’s response and so, the susceptibility to the virus or the severity of infection, can help in diagnosis, prognosis, and treatment. In the present work we summarize some of these variations for the understanding of their consequences either in the host or in the virus.

Methodology

PICO (Population, Intervention, Comparison and Outcome) methodology was used according COCHRANE recommendations:

<table>
<thead>
<tr>
<th>Population</th>
<th>Hotspots of ACE2 polymorphisms and SARS-CoV-2 Spike protein</th>
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<tbody>
<tr>
<td>Intervention</td>
<td>Role of ACE2 and SARS-CoV-2 polymorphisms in infection</td>
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<tr>
<td>Comparison</td>
<td>Polymorphisms that lead individuals more susceptible vs less susceptible to Infection</td>
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<tr>
<td>Outcome</td>
<td>Infection by SARS-CoV-2.</td>
</tr>
</tbody>
</table>

Results

Fig 1 - SARS-CoV-2 mutations and distribution of their occurrence in Europe

Conclusions

• Some ACE2 mutations can promote the ACE2-Spike contact conversely others reduce this interaction, leading the host differential susceptibility to a SARS-CoV-2 infection.
• There are also variations in SARS-CoV-2 proteins that modify the virus infection capacity, with the Asp614Gly and Ser943Pro being some of those that occur in Spike protein and so affect the ACE2-Spike interaction.
• While ACE2 polymorphisms can affect binding affinity to the virus and so the host’s susceptibility, SARS-CoV-2 proteins mutations are more likely to modify the pathogenicity of infection.

References

To do this research, various MeSH terms were used, like SARS-CoV-2 (D00657845), ACE2 (C413524). As result, many articles were identified from NCBI and Google Scholar and then, inclusion and exclusion criteria were applied.

Fig2 – ACE2 variations that may decrease or increase the affinity to the Spike-protein receptor binding domain and that can protect individuals or let them more susceptible to the virus.

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