EVALUATION OF THE INFLUENCE OF 17,β-ESTRADIOL AND 1,25α DIHYDROXYVITAMIN D3 ON SARS-CoV-2 INFECTION *IN VITRO*

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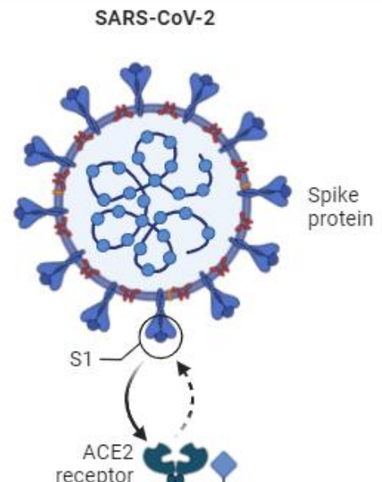
Background

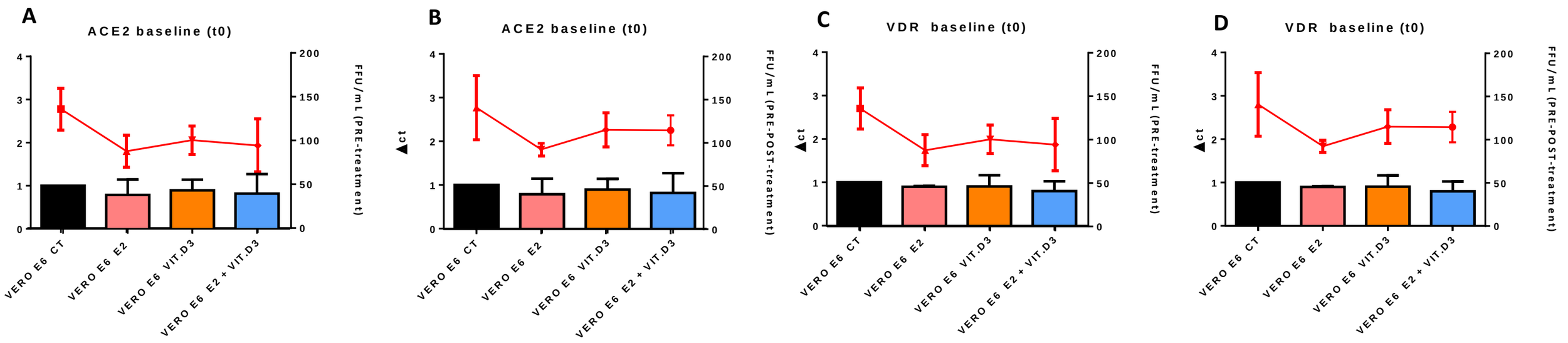
Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) is a single stranded positive virus causing Coronavirus Disease (COVID-19). Men are more prone to develop severe manifestations than women; indeed, the interaction among genetic, hormonal and environmental factors seems to influence the outcome of the disease, which may indicate a role of the sex hormone 17,β-Estradiol (E2) and 1,25 α dihydroxyvitamin D3 (vitamin D3/calcitriol) in this context. Indeed, E2 and vitamin D3 act upon key gene pathways as important immunomodulatory players and supporting molecules in several infectious respiratory diseases.



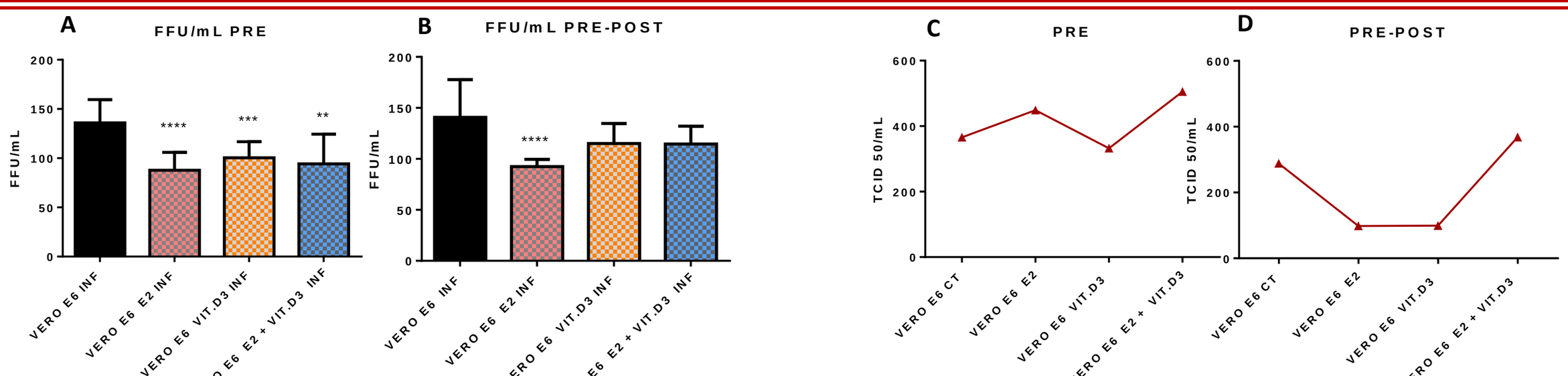
Aim of the study

We aimed to evaluate the influence of E2 and vitamin D3 on VSV-SARS-CoV-2-SΔ21 and SARS-CoV-2 infection *in vitro*.

Results



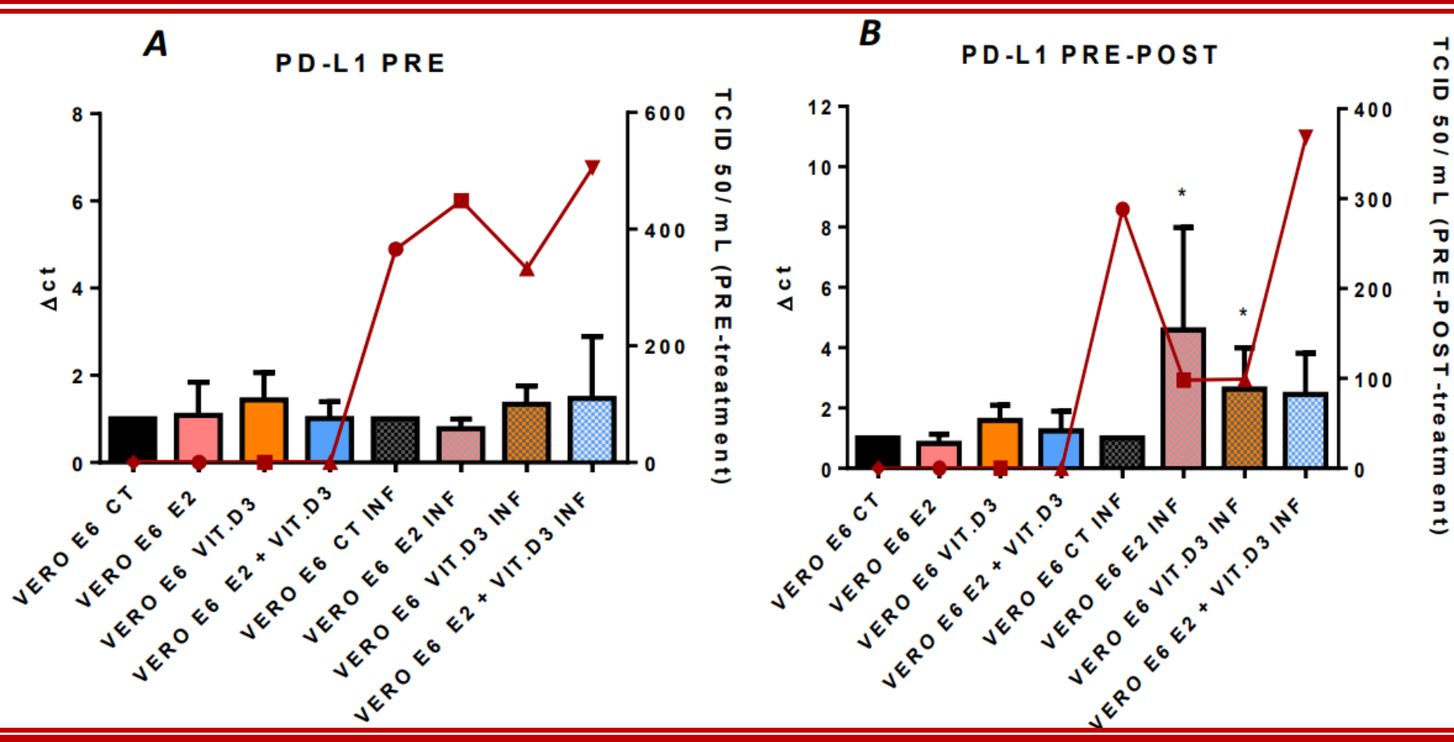
Gene expression of ACE2 (A,B) receptor located on the cellular membrane and the nuclear VDR (C,D) receptor was evaluated at baseline (t0) which correspond to the situation present when the viruses are inoculated, and no significant difference has been reported for both the receptors in the presence of the different treatments (100nM) after 12 hours of infection at 0.1 MOI.



A significant decrease in FFU count is observed in presence of E2, vitamin D3 and when the two compounds are combined in pre-treatment condition (A). On the contrary, in pre-and post- treatment set of experiment a significant decrease of FFU is obtained only in presence of E2 treatment alone (B). (after 12 hours of VSV-SARS-CoV-2-SΔ21 infection at 0.1 MOI) *p<0.05

On one side the infection with SARS-CoV-2 in pre-treatment model revealed an inhibitory effect only in presence of vitamin D3 alone (C). On the other side, in the pre-post-treatment model both E2 and vitamin D3 alone determined a reduction in the viral titre while treatment with their combination induced an increased viral production (D).

(TCID 50/mL after 24 hours of infection)



PD-L1 expression level was evaluated after SARS-CoV-2 infection in presence of the different treatments and in the two models was found that in pre-post treatment model an increase in the PD-L1 gene expression level was registered under the influence of E2, 1,25 dihydroxyvitamin D3 and their combination. *p<0.05

Conclusions

1) rVSV-SARS-CoV-2 model has not been shown comparable results to SARS-CoV-2 infection model; 2) E2 and Vitamin D3 could have a potential influence on the replication phase of SARS-CoV-2 as shown by the decrease in viral load in the pre-post treatment model; 3) E2 and Vitamin D3 in combination showed an unexpected increase in the SARS-CoV-2's viral load; 4)PD-L1 gene expression was increased after viral infection showing a crucial role of this molecule during SARS-CoV-2 infection.