Cancer is a risk factor for SARS-CoV-2 infection. Recent reports have shown that prostate cancer (PCA) patients who underwent androgen-deprivation therapies (ADT) were partially protected from COVID-19. The human myxovirus resistance gene 1 (MX1) is expressed in many tissues, including prostate, and its expression can indicate androgen activity in PCAs, titling the balance of endoplasmic reticulum stress towards pro-death events. Another key feature of this protein is its participation in the antiviral response. It is recognized as an IFN-stimulated gene (ISG), especially during influenza virus infection. Currently, there are several ongoing clinical trials for COVID-19 prevention or treatment using type I or III interferons. However, IFN administration could enhance a "cytokine-storm" causing a hyper-inflammatory response and contributing to multiple organ failure. In this work, we used a published case-control study (GSE152075) from SARS-CoV-2 positive (n=403) and negative patients (n=56) to analyze the response to infection assessing gene expression profiles of key host cell receptors and antagonists proteins. Additionally, given that MX1 was differentially expressed between COVID-19 and non-COVID-19 patients, we evaluated MX1 expression in A549 and Calu3 lung cell lines and ferrets infected with SARS-CoV-2. Since ADT seems to reduce SARS-CoV-2 infection incidence, we aimed to study MX1 regulation by dihydrotestosterone (DHT). We browsed publicly available HI-P-seq experiments evaluating androgen receptor (AR) binding sites in MX1 promoter and coding region in different PCa cell lines under DHT stimulation; and we treated LNCap cells with DHT to assess MX1 expression under androgen stimulation. Finally, using transcriptomics data from PCA patients under ADT, we studied how androgen ablation regulates MX1 expression.

RESULTS

1. Expression of host cell receptor genes in COVID-19 and non-COVID-19 patients


3. Principal component analysis in SARS-CoV-2 positive and negative patients

4. Association between SARS-CoV-2 viral load and gene expression

5. Analysis of MX1 expression by SARS-CoV-2 infection in lung cell lines

6. MX1 expression modulation by androgen

CONCLUSIONS

Our study shows differences in ACE2, MX1, MX2 and BSG/CD147 expression between COVID-19 and non-COVID-19 patients and point out to MX1 as a critical responder in SARS-CoV-2 infection. Furthermore, we demonstrated MX1 modulation by ADT. Taking into consideration the fact that PCA patients that underwent ADT were less prone to present the infection, we propose this gene as an alternative druggable target for COVID-19 patients, especially those with PCAs as a co-morbidity.