

PROJECT

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1) Project title

Study of possible hormonal implications in Sars-CoV-2 virus infection and disease progression

2) Abstract (max 500 words)

The COVID-19 pathology, caused by the infection of the Sars-Cov-2 virus, represents today a health emergency of international proportions. The development of vaccines and antiviral drugs against Sars-Cov-2 constitutes a global challenge to face the current pandemic, with the aim of returning to a world security situation. Documented epidemiological evidence regarding the severity of the prognosis of the COVID-19 disease reported a significant gender difference, highlighting worse pathological outcomes in males. In light of these considerations, attention has been focused on the study of possible hormonal implications in Sars-CoV-2 virus infection and disease progression. In the male gender, it is assumed that there's a higher expression of the TMPRSS2 protease, which is an essential component in the early stages of viral infection, being responsible for the cleavage of the spike proteins of the Coronavirus virions. TMPRSS2 is regulated by a gene that responds to androgens in the prostate, and its fusion with the oncogenic transcription factor ERG represents one of the most frequent alterations in prostate cancer: to date, the suppression of androgenic signaling through androgenic deprivation therapy (ADT) is the basis of the treatment of this tumor form. Recent studies, supported by epidemiological data, underlying that androgen deprivation therapy (ADT) may represent a determining factor in the decrease of TMPRSS2 expression in the upper respiratory tract, thus constituting a protective role in the risk of Sars-Cov-2 infection. On the other hand, in the female gender, the selective estrogen receptor modulators (SERMs) used in the treatment of breast cancer appear to be effective in countering the viral infection by Sars-Cov-2. In fact, a recent study showed that patients affected by hormonal-driven cancer receiving selective modulators/degraders or down regulators of estrogen receptors (SERMs) have a lower risk of SARS-CoV-2 infection compared with patients who receive other endocrine therapies or did not receive anti-estrogen drugs. Hormones appear to be modulators of the response to Sars-Cov-2 infection in both genders: understanding the molecular mechanisms underlying this modulation may represent an opportunity in identifying pharmacological targets for Covid-19 disease. The aim of this project is therefore to investigate the involvement of hormones receptor modulation (estrogen/androgen receptors) and relative downstream targets in viral infection and outcomes of the disease. Shedding some light on the hormone signaling pathways' role in Covid-19 disease could give hints for the development of innovative therapeutic strategies.