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Profiling the glucocorticoid receptor activation during SARS-CoV-2 infection

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Background: SARS-CoV-2 infections can result in imbalanced immune responses facilitating inflammations in severe COVID-19 cases. Glucocorticoids (GCs), such as dexamethasone, have become a standard therapy for controlling the inflammatory response. The immunosuppressive features of GCs resulted in controversies about whether GC treatment should be implemented during virus infections. Glucocorticoid receptor activation (GRA) induces an immunosuppressive state but also shows induction of autophagy and enhancement of metabolism.

Goal: As SARS-CoV-2 limits autophagy and modulates metabolism, we hypothesize direct modulations of SARS-CoV-2 to GR signaling.

Results: We show that SARS-CoV-2 infection causes an accumulation of key metabolites whereas GC-treated Calu-3 human lung cells show the opposite effect. Some GR target proteins are upregulated upon SARS-CoV-2 infection. Despite endogenous GRA, we detect COVID-19 prototypic pro-inflammatory cytokine secretion upon SARS-CoV-2 infection. GC co-treatment during infection leads to a significant reduction of cytokine secretion with comparable or even enhanced viral replication in Calu-3 cells.

Conclusion: SARS-CoV-2 infection is modulating GR signaling and immunometabolism likely to promote its own propagation. Future investigations aim at characterizing the exact virus-GR signaling host protein interactions to identify specific host targets for the development of combined antiviral/anti-inflammatory therapies.

Keywords

SARS-CoV-2, Glucocorticoid Receptor, Immunity, Inflammasome, Autophagy

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Professional Status of the Speaker

PhD Student

Junior Scientist Status

Yes, I am a Junior Scientist.

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