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

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Yes, I am a Junior Scientist.

Primary authors: Mrs DOHME, Annika (Institute of Virology, Charité-Universitätsmedizin Berlin, Berlin, Germany); Mr EMANUEL, Jackson (Institute of Virology, Charité-Universitätsmedizin Berlin, Berlin, Germany); Mr BAJAJ, Thomas (Department of Psychiatry and Psychotherapy, University of Bonn, Medical Faculty, Bonn, Germany)

Co-authors: Dr NOMBELA DÍAZ, Iván (Institute of Virology, Charité-Universitätsmedizin Berlin, Berlin, Germany); Mrs ADLER, Julia M. (Institute of Virology, Freie Universität Berlin, Berlin, Germany); Dr DETHLOFF, Frederik (Max Planck Institute for Biology of Ageing, Cologne, Germany); Dr WYLER, Emanuel (Berlin Institute for Medical Systems Biology, Max-Delbrück-Center for Molecular Medicine in the Helmholtz Association, Berlin, Germany); Dr PAPIES, Jan (Institute of Virology, Charité-Universitätsmedizin Berlin, Berlin, Germany); Mr HEINEMANN, Nicolas (Institute of Virology, Charité-Universitätsmedizin Berlin, Berlin, Germany); Prof. LANDTHALER, Markus (Berlin Institute for Medical Systems Biology, Max-Delbrück-Center for Molecular Medicine in the Helmholtz

Association, Berlin, Germany; IRI Life Sciences, Institut für Biologie, Humboldt-Universität zu Berlin, Berlin, Germany); Dr GIAVALISCO, Patrick (Max Planck Institute for Biology of Ageing, Cologne, Germany); Prof. DROSTEN, Christian (Institute of Virology, Charité-Universitätsmedizin Berlin, Berlin, Germany; German Center for Infection Research (DZIF), partner site Charité, Berlin, Germany); Dr TRIMPERT, Jakob (Institute of Virology, Freie Universität Berlin, Berlin, Germany); Dr GASSEN, Nils C. (Department of Psychiatry and Psychotherapy, University of Bonn, Medical Faculty, Bonn, Germany); Prof. MÜLLER, Marcel A. (Institute of Virology, Charité-Universitätsmedizin Berlin, Berlin, Germany; German Center for Infection Research (DZIF), partner site Charité, Berlin, Germany)

Presenter: Mrs DOHME, Annika (Institute of Virology, Charité-Universitätsmedizin Berlin, Berlin, Germany)

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