



Universiteit
Leiden

The Netherlands

Understanding and Targeting Coronaviruses: exploring advanced cell culture models and host-directed antiviral strategies

Thaler, M.

Citation

Thaler, M. (2024, July 2). *Understanding and Targeting Coronaviruses: exploring advanced cell culture models and host-directed antiviral strategies*. Retrieved from <https://hdl.handle.net/1887/3765868>

Version: Publisher's Version

License: [Licence agreement concerning inclusion of doctoral thesis in the Institutional Repository of the University of Leiden](#)

Downloaded from: <https://hdl.handle.net/1887/3765868>

Note: To cite this publication please use the final published version (if applicable).

Understanding and targeting coronaviruses

Exploring advanced cell culture models and host-directed
antiviral strategies

Melissa Thaler

PhD Thesis Melissa Thaler

The research described in this thesis was performed at Leiden University Medical Center, Department of Medical Microbiology (now LUCID), Leiden, The Netherlands

Funding The work presented in this thesis was supported in part by a COVID-19 MKMD grant from the Netherlands Organization for Health Research and Development (ZonMw), the Dutch Society for the Replacement of Animal Testing (Stichting Proefdiervrij) (grant #114025007), the Leiden University Fund (LUF), the Bontius Foundation, donations from the crowdfunding initiative “wake up to corona”, the European Union’s Horizon 2020 research and Innovation program under grant No 10100362 (the SCORE project), the RSEOH-CAG Rapid Response Research Initiative and RSEOH-CAG 2021 Extension Grant, the Deutsche Forschungsgemeinschaft (DFG) (Ta 275/7-1 and Ta 275/8-1); the coordination for the Improvement of Higher Educational Personnel (CAPES) (process no. 88881.171440/2018-01), Ministry of Education Brazil.

Layout Melissa Thaler

Cover Melissa Thaler

Print Gildeprint, www.gildeprint.nl

Copyright © 2024 Melissa Thaler, Leiden, The Netherlands. All rights reserved. The copyright of the published articles has been transferred to the respective journals or publishers. No part of this publication may be reproduced, stored in a retrieval system, or transmitted in any form or by any means without prior permission of the author, the respective journal or publisher.

Understanding and targeting coronaviruses

Exploring advanced cell culture models and host-directed
antiviral strategies

Proefschrift

ter verkrijging van

de graad van doctor aan de Universiteit Leiden,

op gezag van rector magnificus prof. dr. ir. H. Bijl,

volgens besluit van het college voor promoties

te verdedigen op dinsdag 2 juli 2024

klokke 13.45 uur

door

Melissa Thaler

Geboren te Klagenfurt am Wörthersee, Oostenrijk

in 1994

Promotor: Prof. dr. E. J. Snijder

Co-promotor: Dr. M.J. van Hemert

Leden van de promotiecommissie:

Prof. dr. P.S. Hiemstra

Dr. J.J.C. de Vries

Prof. dr. R. van Rij (Radboud Universiteit Nijmegen, Nederland)

Prof. dr. L. Delang (Katholieke Universiteit Leuven, België)

"Somewhere something incredible is waiting to be known".

(Carl Sagan)

Table of Contents

Chapter 1	1
General Introduction and Outline of the Thesis	
Chapter 2	37
Impact of changes in human airway epithelial cellular composition and differentiation on SARS-CoV-2 infection biology	
Chapter 3	83
SARS-CoV-2-infected human airway epithelial cell cultures uniquely lack interferon and immediate early gene responses caused by other coronaviruses	
Chapter 4	121
R-Propranolol has broad-spectrum anti-coronavirus activity and suppresses factors involved in pathogenic angiogenesis	
Chapter 5	141
<i>Epi</i> -cyclophellitol cyclosulphate, a mechanism-based ER α -glucosidase II inhibitor, blocks replication of SARS-CoV-2 and other coronaviruses	
Chapter 6	173
Summary and General Discussion	
Appendix	
Nederlandse Samenvatting	204
English Summary	206
List of Publications	208
Curriculum Vitae	210

