



Universiteit  
Leiden

The Netherlands

## **Dynamics and regulation of the oxidative stress response upon chemical exposure**

Bischoff, L.J.M.

### **Citation**

Bischoff, L. J. M. (2022, January 12). *Dynamics and regulation of the oxidative stress response upon chemical exposure*. Retrieved from <https://hdl.handle.net/1887/3249612>

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/1887/3249612>

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

# **Dynamics and regulation of the oxidative stress response upon chemical exposure**

Luc Bischoff

Cover design: L.J.M. Bischoff. Image based on Akiyoshi Kitaoka

Thesis lay-out: Douwe Oppewal

Printing: Ipskamp Printing, Enschede

ISBN: 978-94-6421-590-8

© Copyright, Luc Bischoff, 2021

All rights reserved. No part of this book may be reproduced in any form or by any means without permission of the author.

# **Dynamics and regulation of the oxidative stress response upon chemical exposure**

## **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 woensdag 12 januari 2022  
klokke 11:15 uur

door

Lucas Jacobus Marie Bischoff  
geboren te Boxmeer, Nederland,  
in 1984

**Promotor:**

Prof. Dr. B. van de Water (Universiteit Leiden / LACDR)

**Co-promotor:**

Dr. D. Noort (TNO, Rijswijk)

Dr. J.P. Langenberg (TNO, Rijswijk)

**Promotiecommissie:**

Prof. Dr. H. Irth (Universiteit Leiden/ LACDR) (voorzitter)

Prof. Dr. J.A. Bouwstra (Universiteit Leiden/LACDR) (secretaris)

Prof. Dr. P. Jennings (VU Amsterdam)

Prof. Dr. E.C.M. de Lange (Universiteit Leiden/LACDR)

Dr. H. Vrieling (Leids Universitair Medisch Centrum)

The research described in this thesis was performed at the division of Drug Discovery & Safety of the Leiden Academic Centre for Drug Research (LACDR), Leiden University (Leiden, The Netherlands). The research was financially supported by the Ministry of Defence of the Netherlands and the European Commission Horizon2020 EU-ToxRisk project (Grant nr 681002).

# INDEX

## **CHAPTER 1**

General introduction and aim of the thesis 7

## **CHAPTER 2**

MicroRNA patterns as biomarkers for chemical exposure and disease 21

## **CHAPTER 3**

Screening the microRNA landscape of Nrf2 pathway modulation 45  
Identifies miR-6499-3p as a novel modulator of the anti-oxidant  
response through targeting of KEAP1

## **CHAPTER 4**

A systematic analysis of Nrf2 pathway activation dynamics during 95  
repeated xenobiotic exposure

## **CHAPTER 5**

A systematic high throughput transcriptomics and phenotypic 125  
screening approach to classify the pro-oxidant mode-of-action of a  
large class of phenolic compounds

## **CHAPTER 6**

General discussion and future prospects 155

## **CHAPTER 7**

Appendices 169

