

Cover Page



Universiteit Leiden



The handle <http://hdl.handle.net/1887/21624> holds various files of this Leiden University dissertation.

Author: Lin, Jingwen

Title: Generation of genetically attenuated blood-stage malaria parasites : characterizing growth and virulence in a rodent model of malaria

Issue Date: 2013-09-03

Generation of genetically attenuated blood-stage malaria parasites; characterizing growth and virulence in a rodent model of malaria

Jingwen Lin

林静雯

ISBN: 978-94-6182-322-9

Cover design: Jingwen Lin

Lay-out: Jingwen Lin

Printing: Off Page (www.offpage.nl)

© 2013 Jingwen Lin

Generation of genetically attenuated blood-stage malaria parasites; characterizing growth and virulence in a rodent model of malaria

Proefschrift

ter verkrijging van
de graad Doctor aan de Universiteit Leiden,
op gezag van de Rector Magnificus Prof.mr.dr. C.J.J.M. Stolkers,
volgens besluit van het College voor Promoties
te verdedigen op dinsdag 3 September 2013
klokke 15.00 uur

door

Jingwen Lin

Geboren te Xiamen, China
in 1982

Promotiecommissie

Promotor: Prof.Dr. A.M. Deelder

CopromotorsJune: Dr. S.M. Khan

Overige Leden: Prof.Dr. M. Yazdanbakhsh
Prof.Dr. T.H.M. Ottenhoff
Prof.Dr. H.J. Tanke
Prof.Dr. R. Sauerwein
(Radboud University Nijmegen Medical Centre,
The Netherlands)
Prof.Dr. P. Van den Steen
(Rega Institute for Medical Research, Belgium)
Dr. J. Langhorne
(MRC National Institute for Medical Research,
United Kingdom)

The research presented in this thesis was performed at the Leiden Malaria Research Group, Department of Parasitology at the Leiden University Medical Center.

Table of content

| | | |
|---|--|------------|
| Chapter 1 | Introduction | 1 |
| 1. Malaria and malaria vaccines | 2 | |
| 2. Aim of this study | 7 | |
| 3. Whole parasite based vaccine approaches against <i>Plasmodium</i> | 9 | |
| 4. Genetic modification of malaria parasites | 12 | |
| 5. Outline and structure of this thesis | 14 | |
| Chapter 2 | A novel ‘gene insertion/marker out’ (GIMO) genetic modification method for transgene expression and complementation in rodent malaria parasites | 21 |
| Chapter 3 | Screening inhibitors of <i>P. berghei</i> blood stages using bioluminescent reporter parasites | 53 |
| Chapter 4 | Loss-of-function analyses defines vital and redundant functions of the <i>Plasmodium</i> rhomboid protease family | 71 |
| Chapter 5 | Malaria parasites lacking critical proteases involved in hemoglobin degradation are viable and are less sensitive to chloroquine | 115 |
| Chapter 6 | Generation of growth and virulence attenuated blood-stage malaria parasites | 161 |
| Chapter 7 | Conclusions and discussion | 195 |
| 1. Progress in genetic modification technology for <i>Plasmodium</i> rodent malaria parasites | 196 | |
| 2. Generation of growth- and virulence-attenuated attenuated blood stage parasites (GAP _{BS}) by targeted gene deletion | 197 | |
| 3. Future research on growth- and virulence-attenuated <i>P. berghei</i> mutants | 200 | |

| | |
|----------------------------|------------|
| Summary | 207 |
| Samenvatting | 211 |
| List of publication | 217 |
| Acknowledgements | 219 |
| Curriculum Vitae | 221 |