List of Publications

1. Lin JW, Spaccapelo R, Sajid M, Annoura T, Franke-Fayard BMD, Chevalley-Maurel S, Ramesar J, Aime E, Schwarzer E, Arese P, Deroost K, Van den Steen PE, O'Toole T, Prins F, Mommaas-Kienhuis AM, Koster AJ, Tanke HJ, Ravelli RBG, Janse CJ, Khan SM (2013) Malaria parasites lacking critical proteases involved in hemoglobin degradation are viable and are less sensitive to chloroquine. (*submitted*)

2. Annoura T, van Schaijk BCL, Ploemen IHJ, Sajid M, Lin JW, Vos MW, Dinmohamed AG, van Gemert G-J, Chevalley-Maurel S, Kiełbasa S, Scheltinga F, Franke-Fayard BMD, Klop O, Hermsen CC, Gego A, Franetich J-F, Mazier D, Hoffman SL, Janse CJ, Sauerwein RW, Khan SM (2013) New members of the *Plasmodium* 6-Cys family have distinct and critical roles in liver stage development. (*submitted*)

3. Lin JW, Meireles P, Prudêncio M, Engelmann S, Annoura T, Sajid M, Chevalley-Maurel S, Ramesar J, Nahar C, Avramut CMC, Koster AJ, Matuschewski K, Waters AP, Janse CJ, Mair GR, Khan SM (2013) Loss-of-function analyses defines vital and redundant functions of the *Plasmodium* rhomboid protease family. *Molecular Microbiology*, 88(2): 318–38.

4. Deroost K, Tyberghein A, Lays N, Noppen S, Schwarzer E, Vanstreels E, Komuta M, Prato M, Lin JW, Pamplona A, Janse CJ, Arese P, Roskams T, Daelemans D, Opdenakker G, Van den Steen PE (2013) Hemozoin induces lung inflammation and correlates with malaria-associated acute respiratory distress syndrome. *Am J Respir Cell Mol Biol*, 48(5):589–600.

5. Lin JW, Sajid M, Ramesar J, Khan SM, Janse CJ, Franke-Fayard B (2013) Screening inhibitors of *P. berghei* blood stages using bioluminescent reporter parasites. *Methods Mol Biol*, 923: 507–22.

6. Lin JW, Annoura T, Sajid M, Chevalley-Maurel S, Ramesar J, Klop O, Franke-Fayard B, Janse CJ, Khan SM (2011) A novel 'gene insertion/marker out' (GIMO) method for transgene expression and gene complementation in rodent malaria parasites. *PLoS One*, 6(12): e29289.

7. Balu B, Maher SP, Pance A, Chauhan C, Naumov AV, Andrews RM, Ellis PD, Khan SM, Lin JW, Janse CJ, Rayner JC, Adams JH (2011) CCR4-associated factor 1 coordinates the expression of *Plasmodium falciparum* egress and invasion proteins. *Eukaryot Cell*, 10(9):1257–63.

8. Barker RH Jr, Urgaonkar S, Mazitschek R, Celatka C, Skerlj R, Cortese JF, Tyndall E, Liu H, Cromwell M, Sidhu AB, Guerrero-Bravo JE, Crespo-Llado KN, Serrano AE, Lin JW, Janse CJ, Khan SM, Duraisingh M, Coleman BI, Angulo-Barturen I, Jiménez-Díaz MB, Magán N, Gomez V, Ferrer S, Martínez MS, Wittlin S, Papastogiannidis P, O'Shea T, Klinger JD, Bree M, Lee E, Levine M, Wiegand RC, Munoz B, Wirth DF, Clardy J, Bathurst I, Sybertz E (2011) Aminoindoles, a novel scaffold with potent activity against *Plasmodium falciparum*. *Antimicrob Agents Chemother*, 55(6):2612–22.

9. Booker ML, Bastos CM, Kramer ML, Barker RH Jr, Skerlj R, Sidhu AB, Deng X, Celatka C, Cortese JF, Guerrero Bravo JE, Crespo Llado KN, Serrano AE, Angulo-Barturen I, Jiménez-Díaz MB, Viera S, Garuti H, Wittlin S, Papastogiannidis P, Lin JW, Janse CJ, Khan SM, Duraisingh M, Coleman B, Goldsmith EJ, Phillips MA, Munoz B, Wirth DF, Klinger JD, Wiegand R, Sybertz E (2010) Novel inhibitors of *Plasmodium falciparum* dihydroorotate dehydrogenase with anti-malarial activity in the mouse model. *J Biol Chem*, 285(43): 33054–64.

Acknowledgements

I would like to express my sincere gratitude to all the people who have helped me and made this thesis possible.

First, I want to thank my supervisors **Dr. Chris Janse** and **Dr. Shahid Khan**, who gave me the opportunity to work in Leiden Malaria Research Group. Thank you for all your kind help, your patient guidance and unyielding support. You are more than supervisors to me, you not only showed to me how to plan and carry out a research project, how to coordinate and collaborate with other groups, how to structure and write a paper, more importantly you taught me how to become a responsible scientific researcher. Thanks for always being patient in our discussions, for hearing me out and giving me chances to try out my ideas and for always being there when I needed guidance… Chris, thank you for helping me realize the value of maintaining scientific curiosity and relishing the joy of learning and discovery even in difficult times. Shahid, thanks for also being a friend to me, for being so supportive and for your countless kind help…

To everyone who worked in **Leiden Malaria Research Group**: Blandine, the master of imaging and microscopy; Jai, the master of PFG and Northern and animal work; Hans, the master of molecular cloning; Takeshi and Severine, the masters of mosquito and liver stage work; Saj, the master of protein work; Onny, the master of FACS… thank you so much for making my work much easier and enjoyable! Takeshi, thanks for your teaching and guidance and your valuable time, thanks for all the tips in molecular biology! I learned a lot from you, not only on the technical part, but also your way of thinking and your careful plan and execution of experiments. I really enjoyed our discussions, our 'Chinese-Japanese cultural exchange'. Saj, thanks for showing me around during my first day in Leiden, for making the lab such a fun place to work in, for all your kind guidance on protein work, for being a big brother to me! Blandine, thanks for all your kind guidance, help and encouragement, and for all your assistance with imaging experiments. Jai, thanks for all your invaluable help and technical support, my projects cannot be completed without your help! Hans, thanks for your countless kind help, for being the go-to person in the group and for always being so kind to me. Sev, thanks for always being there to help, to support and for being a good friend to me. Eliane, thanks for helping me fit in the new environment when I first arrived, for reminding me to enjoy life other than diving headlong into never-ending experiments. Aga and Ahmed, thanks for all our discussions. It was so fun to have fellow PhD students around. To Anneke, Jannik, Kevin and to the all students who did their internship with me: Joana, Jasper (The JJJ team!), Pascale and Tracy, thank you all!

I am very grateful for all the support I've got in LUMC: from FACS facility (Guido) and the Electron Microscopy Section (Raimond, Cristina and Prof. Abraham Koster), Department of Pathology (Frans) and Department of Infectious Diseases (Susan, Annemieke, Kees and Prof. Tom Ottenhoff).

I also really appreciate all the help I've got from all the collaborators. Thanks to the labs of Dr. Roberta Spaccapelo, Dr. Gunnar Mair, Dr. Miguel Prudêncio, Dr. Evelin Schwarzer, Dr. Photini Sinnis, Prof. John Adams, Prof. Kai Matuschewski, Prof. Gordon Langsley and Dr. Tom O'Toole. A special 'thank you' to Katrien, thanks for hosting me in Leuven and for being a friend.

I'd like to acknowledge the support from China Scholarship Council-Leiden University joint scholarship program and thank Prof. Cangsang Pan for his kind guidance during my Master training and for continuing to encourage and inspire me during my PhD.

I am very grateful to my friends in Leiden. To Xiaolei and Bo, thank you for helping me settle down in DUWO and for all the fun talks. Many thanks again to Xiaolei, and Hua, for always being there to help and for being good friends to me. To Xiaole, Sha, Bing, Qifang and Yuntao, thanks for being so nice to me. You made my second home from home a lot warmer and sweeter!

My friends in China, thank you so much for your friendship! Xiaoyu, Aya, Xuxu, Dawan, Cua and Jing, thanks for going out with me when I was back home and for the kind regards and encouragement you sent me on QQ. And Sijing, I could never thank you enough. You are a sister to me!

Lu, thanks for being in my life, for your love and understanding, for always being there to support me, comfort me and encourage me. Thank you!

In the end, I want to express my gratitude to my relatives at home, thanks so much for helping and looking after my parents. To my parents, my dearest mama and papa, thank you for unconditional love and support and for cultivating my creativity and scientific curiosity. Thanks for the understanding and encouragement you have been giving all these years. I am eternally grateful to you.

最后，感谢我的亲戚们对我父母亲的关心和帮助，谢谢！我敬爱的父母，我最最亲爱的爸爸妈妈，深深的感谢你们！感谢你们为我付出的一切！没有你们无私的爱与支持，我不可能有敢于追逐梦想的勇气。谢谢你们这些年来给的理解与鼓励，它们是我努力的动力。我永远感激你们，爱你们。

Curriculum Vitae

Jingwen Lin was born on 19th of October, 1982 in Xiamen, a coastal city in southeast China. She received her middle school and high school education in Xiamen No. 1 Middle School. She won the first prize in China High School Biology Olympia in Jujian Province in 2000 and gained the exemption from National University Entrance Examination. She entered Xiamen University in 2001 and majored in Biology.

She graduated from the School of Life Sciences in 2005, with the 'Best Bachelor's Thesis' award and 'Excellent student leadership' award. Based on her academic record during her undergraduate degree, she was granted an exemption of National Postgraduate Entrance Examination. She continued her Master's degree in Zoology (Parasitology) from 2005 to 2008 with a scholarship from Ministry of Education of China. Her master thesis was on early diagnosis and rapid detection of *Bursaphelenchus xylophilus* and differential proteome analysis of *B. xylophilus* and *B. mucronatus*, under the guidance of Prof. Cangsang Pan and Prof. Liang Chen.

In 2008, she was enrolled as a PhD student of Medicine in Leiden Malaria Research Group, Department of Parasitology, Leiden University Medical Center (LUMC, The Netherlands) with support from China Scholarship Council-Leiden University joint program. Here she performed studies on malaria using a rodent model of malaria, *Plasmodium berghei*. Under the supervision of Dr. Chris Janse and Dr. Shahid Khan, she carried out her PhD project principally focusing on screening and characterization of genetically attenuated blood-stage malaria parasites that could serve as protective immunogens, and also on improving transfection methods in rodent malaria parasites including rapid gene-insertion mutagenesis. The results of this research have been presented in this thesis. Currently she is engaged in post-doctoral research on immunological responses to virulent and non-virulent malaria infection in mouse model, in the group of Dr. Jean Langhorne, National Institute for Medical Research, London, United Kingdom.