

CRISPR/CAS9 genetic modification of plasmodium falciparum and transgenic parasites in malaria vaccine research

Marin Mogollon, C.Y.

Citation

Marin Mogollon, C. Y. (2018, November 28). *CRISPR/CAS9 genetic modification of plasmodium falciparum and transgenic parasites in malaria vaccine research*. Retrieved from https://hdl.handle.net/1887/67294

Version:	Not Applicable (or Unknown)
License:	<u>Licence agreement concerning inclusion of doctoral thesis in the</u> <u>Institutional Repository of the University of Leiden</u>
Downloaded from:	https://hdl.handle.net/1887/67294

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

Cover Page



Universiteit Leiden



The handle <u>http://hdl.handle.net/1887/67294</u> holds various files of this Leiden University dissertation.

Author: Marin Mogollon, C.Y. Title: CRISPR/CAS9 genetic modification of plasmodium falciparum and transgenic parasites in malaria vaccine research Issue Date: 2018-11-28

Acknowledgements

I would like to thank all the wonderful people who contributed to make my thesis possible.

I would like to express my greatest gratitude to my supervisors, **Dr. Shahid Khan** and **Dr. Chris Janse**, for their mentorship, guidance, scientific discussions and patience. I will always be grateful for your support both at the personal level and for having nurtured me to grow as a researcher. My sincerest gratitude goes also to my promoter, **Prof. Dr. Maria Yazdanbakhsh**, for her support throughout my study.

I would like to thank all the members of the Leiden Malaria Research Group (LMRG): Blandine and Séverine for their personal and scientific support; to Fiona for always being motivated to help me with the sometimes hard to love *P. falciparum* parasite. Thanks to Jai, Hans (Hansje), Takashi, Shynia, Yukiko, Surendra, Ahmed, Aurelie, Martha, Jingwen and my students Niels, Rick, and Edwin; I have learnt a lot from all of you. I would like to thank Meta and her team: Beatrice, Marijke, Heleen, Munisha, Els, Roos and Carola for the production of mosquitoes, and standardization of mosquito feedings. I also would like to thank all the collaborators who have contributed to my PhD thesis; Prof. Robert Sauerwein from the Radboud University Medical Center and his team: Marga, Geert-Jan, Annie, Sanne and Matthijs. Thanks go to Dr. Koen Dechering from TropiQ and his team: Angelika, Karin, Judith, and Martijn. I would also like to thank Prof. Kim Williamson, Dr. Jun Miao, Prof. Liwang Cui, Dr. Jose Rubio and Dr. Medhi Ghorbal for their help during my studies.

Special thanks go to my 'brother' and best friend, **Ahmad Syibli**, who taught me that differences in culture, in religion or other differences are no barrier to a sincere and pure friendship. Thank you so much bro', for making me part of your Malaysian family and for being the best confidant and friend.

I would like to thank the members of my thesis committee, for kindly making time to evaluate my PhD thesis: **Prof. Ron Hokke**, **Prof. Barend Mons**, **Dr. Milly van Dijk** and **Dr. Koen Dechering**.

I also would like to thank all my colleagues of Department of Parasitology in Leiden Abena, Alwin, Angela, Arifa, Bart, Bruno, Dian, Eric, Eunice, Hermelijn, Leonard, Maria, Mathilde, Michelle, Mikhael, Nikolas, Patrick, Suzanne, Jantien, Corrie, Ulysses, Yoanne and Yvonne for the good times during these years. To the 'other fish' in the aquarium: Frank, Miryam, Thiago, Ana, you all made aquarium a very warm and nice place to work. To my friends, **Mila, Cielo, Ana, Jenny**, **Jazz, Ayda, Roman, Andres, Ago**, thank you so much for always be there for me despite the years that have passed and the distance between us.

My deep and sincere gratitude to my lovely mother **Dennize Edith Marin Mogollon** for being a brave young single mother, thank you for all your love, for all your support, for all the sacrifices you have made in order to give me an education and for all your patience. All that I am, is because of you.

Mis más sinceros agradecimientos a mi abuelita **Edith Mogollon**, gracias por todo tu amor incondicional y por siempre estar ahí para mi. A mi soñadora hermana **Yenniffer**, gracias por tu apoyo y por haber cuidado a mi peque cuando más lo necesitaba. A mis **tías, tíos políticos y primitos**, gracias por haber sido parte de mi crecimiento como mujer, como profesional y como madre. A mi segunda familia, la **familia Alarcón Barrera**, gracias por haberme dado un lugar en su familia y tratarme como una hija más.

Finally, I would like to thank my two beloved men, who are my strength, my centre and my life. To my partner, my love and my best friend **Juan Carlos**, for all your love, patience and strength. For not giving up on me, for leaving your life behind to come to be with us, I thank you. This thesis would not have been possible without you and I am grateful for your support, for your advice and scientific discussions. To my little man and sunshine **Juan Daniel**, thank you so much for making me a better woman, thank you for teaching me what is really important in the life, you arrived and made everything worthwhile, you are my inspiration my peace and happiness. If someday you have the opportunity to read this, remember that you are the best of my life, and all my achievements are for you.

Curriculum vitae

Catherin Yizet Marin Mogollon was born on 30th December 1985, in Bogota, Colombia (South America). She completed a Bachelor's degree in Bacteriology and Clinical Laboratory Science in 2007 at Colegio Mayor University of Cundinamarca. During her Bachelor studies she performed a 12 month internship at the Department of Molecular Biology of Fundacion Instituto de Inmunologia de Colombia (FIDIC), where she gained an interest and experience in molecular biology of the parasites that cause malaria in humans, Plasmodium falciparum and P. vivax. From 2007 until 2010 she performed her Master's degree studies in Biochemistry at the Universidad Nacional de Colombia, where she completed a Master thesis entitled "Identification, expression and characterization of nicotinamide/mononucleotide adenylyltransferase of Plasmodium falciparum" under the guidance of Dr. Maria Helena Ramirez Hernandez. From 2011 until 2012 she worked as a research assistant in the Molecular Biology Laboratory of the Caucaseco Scientific Research Center in Cali, Colombia, on the production of the recombinant protein P48/45 of P. vivax as a target for transmission blocking vaccines. From 2012 until 2013 she worked in the Laboratory of Biochemistry at Colegio Mayor de Nuestra Señora del Rosario University (Bogota, Colombia) as a research assistant investigating the relationship between hypoxia and metabolism in cancer cells. In 2013 she was enrolled as a PhD student in the Leiden Malaria Research Group (LMRG) of the Department of Parasitology within the Leiden University Medical Center (LUMC, The Netherlands), with support from a Colciencias-Colfuturo PhD fellowship (Call 568 from 2012 Resolution 01218 Bogotá, Colombia). In Leiden she carried out her PhD project under supervision of Dr. Shahid Khan and Dr. Chris Janse. The results of the studies in Leiden are presented in this thesis. After finishing her PhD, Catherin Marin will continue as a post-doc in the Department of Parasitology (LUMC, Leiden) focussing on *P. falciparum* genetic modification, to both study the biology malaria parasites and to develop attenuated parasite vaccines. After this period she intends to return to Colombia and apply the knowledge that she has gained to scientific projects in her country.

List of publications

- C Marin-Mogollon, M van de Vegte-Bolmer, GJ van Gemert, FJA van Pul, J Ramesar, Othman AS, H Kroeze, J Miao, L Cui, KC Wiliamson, R Sauerwein, CJ Janse and SM Khan. The Plasmodium falciparum male gametocyte protein P230p, a paralog of P230, is vital for zygote formation and mosquito transmission. Sci Rep, 2018. 8(1): p. 14902.
- C Marin-Mogollon, FJA van Pul, S Miyazaki, T Imai, J Ramesar, AM Salman, BMF Winkel, Othman AS, H Kroeze, S Chevalley-Maurel, A Reyes-Sandoval, M Roestenberg, BM Franke-Fayard, CJ Janse and SM Khan. Chimeric Plasmodium falciparum parasites expressing Plasmodium vivax circumsporozoite protein fail to produce salivary gland sporozoites. Malar J, 2018. 17(1): p. 288.
- 3. Othman AS, JW Lin, BM Franke-Fayard, H Kroeze, FJA van Pul, S Chevalley-Maurel, J Ramesar, C Marin-Mogollon, MM Jore, MJ Morin, CA Long, R Sauerwein, A Birkett, K Miura, CJ Janse and SM Khan. Expression of full-length Plasmodium falciparum P48/45 in P berghei blood stages: A method to express and evaluate vaccine antigens. Mol Biochem Parasitol, 2018. 224: p. 44-49.
- Othman AS, BM Franke-Fayard, T Imai, ETI van der Gracht, A Redeker, AM Salman, C Marin-Mogollon, J Ramesar, S Chevalley-Maurel, CJ Janse, R Arens and SM Khan. OX40 Stimulation Enhances Protective Immune Responses Induced After Vaccination With Attenuated Malaria Parasites. Front Cell Infect Microbiol, 2018. 8: p. 247.

- LE Contreras-Rodríguez, C Marin-Mogollon, LM Sánchez-Mejía, MH Ramírez-Hernández. Structural Insights into Plasmodium falciparum nicotinamide mononucleotide adenylyltransferase: oligomeric assembly. Mem Inst Oswaldo Cruz, 2018. 113(9): p. e180073.
- Othman AS*, C Marin-Mogollon*, AM Salman, BM Franke-Fayard,CJ Janse and SM Khan. The use of transgenic parasites in malaria vaccine research. Expert Rev Vaccines, 2017. 16(7): p. 1-13.*Authors contributed equally to this study.
- CA Nieto, CY Marin, LE Contreras, MH Ramírez. Study of specific Region of Plasmodium falciparum Nicotinamide/Nicotinate Mononucleotide Adenylyl Transferase (PfNMNAT): Characterizing a Possible Therapeutic Target. J Mol Genet Med, 2017. 11(12).
- C Marin Mogollon, FJ van Pul, T Imai, J Ramesar, S Chevalley-Maurel, GM de Roo SAJ Veld, H Kroeze, BMD Franke-Fayard, CJ Janse and SM Khan, Rapid Generation of Marker-Free P. falciparum Fluorescent Reporter Lines Using Modified CRISPR/Cas9 Constructs and Selection Protocol. PLoS One, 2016. 11(12): p. e0168362.
- M Arévalo-Herrera, AF Vallejo, K Rubiano, Y Solarte, C Marin, A Castellanos, N Céspedes, S Herrera. Recombinant Pvs48/45 antigen expressed in E. coli generates antibodies that block malaria transmission in Anopheles albimanus mosquitoes. PLoS One, 2015. 10(3): p. e0119335.

- 10. M Arévalo-Herrera, Y Solarte, C Marin, M Santos, J Castellanos, JC Beier, SH Valencia. Malaria transmission blocking immunity and sexual stage vaccines for interrupting malaria transmission in Latin America. Mem Inst Oswaldo Cruz, 2011. 106 Suppl 1: p. 202-11.
- 11.AM Salman, CM Mogollon, JW Lin, FJ van Pul, CJ Janse and SM Khan.Generation of Transgenic Rodent Malaria Parasites Expressing Human Malaria Parasite Proteins. Methods Mol Biol, 2015. 1325: p. 257-86.