# Studies using transgenic rodent malaria parasites to improve live attenuated malaria vaccines

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## CURRICULUM VITAE

Ahmad Syibli bin Othman was born on 13th of November, 1986 in Kuala Terengganu, Malaysia. In 2010, he completed his bachelor of Medical Laboratory Technology (Honours) at the Universiti Teknologi Mara in Malaysia under a Jabatan Perkhidmatan Awam (JPA) Scholarship. He continued his Master of Science degree in Human Genetics at the Universiti Sains Malaysia from 2010 to 2013 with a scholarship from the Ministry of Higher Education in Malaysia (Skim Latihan Akademik IPTA – SLAI). His master thesis, performed under the guidance of Dr. Sarina Sulong was entitled 'Application of two techniques: fluorescence *in situ* hybridization (FISH) and quantitative real time PCR (qPCR) in detection of TERT gene amplification using cancer cell lines'. In 2014, he was enrolled as a PhD student in the Leiden Malaria Research Group in the Department of Parasitology, Leiden University Medical Center (LUMC) The Netherlands with support from the Ministry of Higher Education in Malaysia (Skim Latihan Akademik IPTA – SLAI fellowship). Here, he performed studies aiming at improving live attenuated malaria vaccines and vaccination strategies. His studies c involved the generation and characterization of genetically modified rodent malaria parasites in different rodent species. He carried out his PhD under the supervision of Dr. Shahid Khan and Dr. Chris Janse. The results of this research have been presented in this thesis. After finishing his PhD, Ahmad Syibli will bring the knowledge he has gained back to Malaysia and will work as a lecturer at Universiti Sultan Zainal Abidin, Malaysia.

# LIST OF PUBLICATIONS

**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 16(7): 1-13 (2017)
*Authors contributed equally to this study.

**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 8: 247 (2018)

**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 224: 44-49 (2018)

**Othman AS**, BM Franke-Fayard, S Chevalley-Maurel, C Marin-Mogollon, AM Mendes, H Nunes-Cabaço, H Kroeze, J Ramesar, M Prudêncio, CJ Janse and SM Khan. *Generation and protective efficacy testing of self-adjuvanting genetically attenuated rodent malaria parasites*. (Submitted)

**Othman AS**, BM Franke-Fayard, AM Mendes, SK Kolli, S Chevalley-Maurel, C Marin-Mogollon, H Nunes-Cabaço, H Kroeze, FJA van Pul, J Ramesar, M Prudêncio, CJ Janse and SM Khan. *Generation and analysis of genetically attenuated rodent malaria parasites that arrest late during liver stage development*. (Thesis chapter)

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. 17:288 (2018)

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*. (Submitted)

C Marin-Mogollon, AM Salman, KMJ Koolen, JM Bolscher, FJA van Pul, S Miyazaki, T Imai, **Othman AS**, J Ramesar, GJ van Gemert, H Kroeze, BM Franke-Fayard, S Chevalley-

Maurel, R Sauerwein, KJ Dechering, CJ Janse and SM Khan. *A P. falciparum NF54 reporter line expressing mCherry-luciferase in gametocytes, sporozoites and liver stages.* (Thesis chapter)

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