BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Chris J. Janse

eRA COMMONS USER NAME (credential, e.g., agency login): JANSECJ

POSITION TITLE: Head of the Leiden Malaria Research Group

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of Leiden, Leiden The Netherlands	DEA; University Degree in Biology	1982	Biology
University of Leiden, Leiden The Netherlands	PhD (cum laude)	1987	Biology/Malaria
Leiden University Medical Center, Leiden The Netherlands	Post-doctoral Research Scientist	1991	Molecular Biology/Malaria

A. Personal Statement

My research directly contributed to the introduction and application of advanced molecular techniques in malaria research. A major breakthrough in our laboratory, and in the field, was the implementation of technologies that permit genetic modification of rodent malaria parasites; technologies that allowed, for the first time, the generation of malaria parasites that retain stable genetic modifications. These methodologies and others that we developed opened up new avenues in malarial research worldwide and have greatly aided in the functional analysis of potential parasite drug and vaccine targets. Currently, the Leiden Malaria Research Group are leaders in the use of genetic modification as means of research into malaria. In 2005, my group was one of the first to demonstrate that it was possible to generate sterile immunity against malaria in mice after immunization with genetically attenuated parasites (GAPs). The emphasis of my research therefore is on the further development and refinements of a GAP vaccine. In addition, my research is focused on the identification and characterization of malarial vaccine candidates through the functional analysis of parasite antigens. This research combines genetic modification technologies and post-genome analyses (microarray and proteome analyses) with biochemical and biological assays.

B. Positions and Honors

Positions and employment

2008 – 2021 Head of the Leiden Malaria Research Group, Department of Parasitology Leiden University Medical Centre (LUMC).
2002-2008 Associate Professor and Co-Group leader (together with Dr. A.P. Waters) Leiden Malaria Research Group, LUMC
1991-2002 Research Scientist, Lecturer, Assistant Professor, Leiden Malaria Research Group (LUMC)
1986-1991 Post-doctoral Research Scientist, Department of Parasitology, University of Leiden Studies on the molecular biology of malaria parasites, focused on organization of chromosomes and gene expression.

1987 PhD (cum laude) Parasitology/Cell Biology. University of Utrecht, University of Leiden
Thesis title: DNA synthesis in malaria parasites during sexual and erythrocytic asexual development.
1983-1986 Research Assistant, Ph.D. Research financed by NWO (University of Leiden and University of Utrecht). Development of molecular biology and in vitro cultivation technologies for malaria parasites. Studies on the DNA replication machinery of malaria parasites.
1982 DEA; University Degree in Biology (Parasitology/Ecology), University of Leiden

Honors/awards

- Eijkman medal (Eijkman Medal) Awarded by the "Eijkman Medaille Fonds" of the Netherlands Society of Tropical Medicine and International Health (NVTG) for research on the development of in vitro culture techniques and the molecular biology of malaria parasites.
- WRO Goslings prize (W.R.O. Goslings). Awarded by the Dutch and Flanders Society for Infectious Diseases for the development of genetic modification technology for malaria parasites.

C. Contribution to Science

My research contributed to the introduction and application of advanced molecular techniques in malaria research. A major breakthrough in our laboratory was the implementation of technologies that permit genetic modification of malaria parasites; technologies that allowed, for the first time, the generation of malaria parasites that retain stable genetic modifications. These methodologies and others that we developed have opened up new avenues in malarial research worldwide and have greatly aided in the functional analysis of potential parasite drug and vaccine targets.

- Dijk, M.R. van, Waters, A.P. and Janse, C.J. (1995). Stable transfection of malaria parasite blood stages. **Science** 268, 1358-1362.
- Expression of a Plasmodium gene introduced into subtelomeric regions of Plasmodium berghei chromosomes. van Dijk MR, Janse CJ, Waters AP. **Science**. 1996 Feb 2;271(5249):662-5.
- Janse CJ, Ramesar J, Waters AP. High-efficiency transfection and drug selection of genetically transformed blood stages of the rodent malaria parasite Plasmodium berghei. **Nature Protocols**. 2006;1(1):346-56.
- Iwanaga S, Khan SM, Kaneko I, Christodoulou Z, Newbold C, Yuda M, Janse CJ, Waters AP. Functional identification of the Plasmodium centromere and generation of a Plasmodium artificial chromosome. **Cell Host and Microbe** (2010) Mar 18;7(3):245-55.
- Mogollon CM, van Pul FJ, Imai T, Ramesar J, Chevalley-Maurel S, de Roo GM, Veld SA, Kroeze H, Franke-Fayard BM, Janse CJ, Khan SM. Rapid Generation of Marker-Free P. falciparum Fluorescent Reporter Lines Using Modified CRISPR/Cas9 Constructs and Selection Protocol. **PLoS One** (2016) 20;11(12):e0168362.

My research contributed to a number of genomics and post-genomic (transcriptome, proteome) studies, revealing novel protein targets for drugs and vaccine target antigens

- Genome sequence and comparative analysis of the model rodent malaria parasite Plasmodium yoelii yoelii. Carlton JM, Angiuoli SV, Suh BB, Kooij TW, Pertea M, Silva JC, Ermolaeva MD, Allen JE, Selengut JD, Koo HL, Peterson JD, Pop M, Kosack DS, Shumway MF, Bidwell SL, Shallom SJ, van Aken SE, Riedmuller SB, Feldblyum TV, Cho JK, Quackenbush J, Sedegah M, Shoaibi A, Cummings LM, Florens L, Yates JR, Raine JD, Sinden RE, Harris MA, Cunningham DA, Preiser PR, Bergman LW, Vaidya AB, van Lin LH, Janse CJ, Waters AP, Smith HO, White OR, Salzberg SL, Venter JC, Fraser CM, Hoffman SL, Gardner MJ, Carucci DJ. **Nature**. 2002 Oct 3;419(6906):512-9
- A comprehensive survey of the Plasmodium life cycle by genomic, transcriptomic, and proteomic analyses. Hall N, Karras M, Raine JD, Carlton JM, Kooij TW, Berriman M, Florens L, Janssen CS, Pain A, Christophides GK, James K, Rutherford K, Harris B, Harris D, Churcher C, Quail MA, Ormond D, Doggett J, Trueman HE, Mendoza J, Bidwell SL, Rajandream MA, Carucci DJ, Yates JR 3rd, Kafatos FC, Janse CJ, Barrell B, Turner CM, Waters AP, Sinden RE. **Science**. 2005 Jan 7;307(5706):82-6
- Proteome analysis of separated male and female gametocytes reveals novel sex-specific Plasmodium biology.Khan SM, Franke-Fayard B, Mair GR, Lasonder E, Janse CJ, Mann M, Waters AP. **Cell**. 2005 Jun 3;121(5):675-87.

- Genome-Scale Identification of Essential Metabolic Processes for Targeting the Plasmodium Liver Stage. Stanway RR, Bushell E, Chiappino-Pepe A, Roques M, Sanderson T, Franke-Fayard B, Caldelari R, Golomingi M, Nyonda M, Pandey V, Schwach F, Chevalley S, Ramesar J, Metcalf T, Herd C, Burda PC, Rayner JC, Soldati-Favre D, Janse CJ, Hatzimanikatis V, Billker O, Heussler VT. **Cell**. 2019 Nov 14;179(5):1112-1128.e26

In 2005, my group was one of the first to demonstrate that it was possible to generate sterile immunity against malaria in mice after immunization with genetically attenuated parasites (GAPs).The current emphasis of my research is on the development and further refinements of a malaria vaccine consisting of genetically attenuated parasites (GAP). This involves testing and evaluating many GAP candidates for their attenuation and potency in rodents models after which the best candidates are then translated (i.e. the same genetic modifications) to the human malaria parasite, *P. falciparum*. These candidates P. falciparum GAPs undergo pre-clinical evaluations to establish they have an acceptable safety profile after which regulatory scrutiny. We have created a first generation GAP that has been approved for use in humans and was tested in a clinical in 2017-18. This study was the first clinical trial performed using any genetically modified parasite in Europe. In 2020 approval was gained to test in a clinical trial a second generation GAP (GA2) that was developed in my group.

- van Dijk MR, Douradinha B, Franke-Fayard B, Heussler V, van Dooren MW, van Schaijk B, van Gemert GJ, Sauerwein RW, Mota MM, Waters AP, Janse CJ. (2005). Genetically attenuated, P36p-deficient malarial sporozoites induce protective immunity and apoptosis of infected liver cells. **Proc Natl Acad Sci U S A**, 102:12194-9
- Annoura T, van Schaijk BC, Ploemen IH, Sajid M, Lin JW, Vos MW, Dinmohamed AG, Inaoka DK, Rijpma SR, van Gemert GJ, Chevalley-Maurel S, Kielbasa SM, Scheltinga F, Franke-Fayard B, Klop O, Hermsen CC, Kita K, Gego A, Franetich JF, Mazier D, Hoffman SL, Janse CJ, Sauerwein RW, Khan SM. Two Plasmodium 6-Cys family-related proteins have distinct and critical roles in liver-stage development. **FASEB J**. 2014 Feb 7.
- van Schaijk BC, Ploemen IH, Annoura T, Vos MW, Foquet L, van Gemert GJ, Chevalley-Maurel S, van de Vegte-Bolmer M, Sajid M, Franetich JF, Lorthiois A, Leroux-Roels G, Meuleman P, Hermsen CC, Mazier D, Hoffman SL, Janse CJ, Khan SM, Sauerwein RW. A genetically attenuated malaria vaccine candidate based on P. falciparum b9/slarp gene-deficient sporozoites**. Elife**. 2014 Nov 19;3.
- Genetic engineering of attenuated malaria parasites for vaccination. Khan SM, Janse CJ, Kappe SH, Mikolajczak SA. **Curr Opin Biotechnol**. 2012 Dec;23(6):908-16.
- A double-blind, placebo-controlled phase 1/2a trial of the genetically attenuated malaria vaccine PfSPZ-GA1. Roestenberg M, Walk J, van der Boor SC, Langenberg MCC, Hoogerwerf MA, Janse JJ, Manurung M, Yap XZ, García AF, Koopman JPR, Meij P, Wessels E, Teelen K, van Waardenburg YM, van de Vegte-Bolmer M, van Gemert GJ, Visser LG, van der Ven AJAM, de Mast Q, Natasha KC, Abebe Y, Murshedkar T, Billingsley PF, Richie TL, Sim BKL, Janse CJ, Hoffman SL, Khan SM, Sauerwein RW. **Sci Transl Med**. 2020 May 20;12(544):eaaz5629.

In my laboratory a large number of tools (technologies and transgenic parasite lines) have been developed to visualize *in vivo* interactions of malaria parasites with host cells and tissues in living animals. Transgenic lines expression fluorescent and luminescent reporter proteins are now used by many different labs worldwide. These transgenic parasite lines have been instrumental for the study of factors underlying malaria-related pathology. In addition transgenic parasites expressing human malaria parasite proteins/antigens have been used to evaluate/optimize subunit vaccines

- Circumsporozoite protein is required for development of malaria sporozoites in mosquitoes. Ménard R, Sultan AA, Cortes C, Altszuler R, van Dijk MR, Janse CJ, Waters AP, Nussenzweig RS, Nussenzweig V**. Nature**. 1997 Jan 23;385(6614):336-40
- Complement-like protein TEP1 is a determinant of vectorial capacity in the malaria vector Anopheles gambiae. Blandin S, Shiao SH, Moita LF, Janse CJ, Waters AP, Kafatos FC, Levashina EA. **Cell**. 2004 Mar 5;116(5):661-70
- Real-time in vivo imaging of transgenic bioluminescent blood stages of rodent malaria parasites in mice. Franke-Fayard B, Waters AP, Janse CJ. **Nat Protoc**. 2006;1(1):476-85.
- Murine malaria parasite sequestration: CD36 is the major receptor, but cerebral pathology is unlinked to sequestration. Franke-Fayard B, Janse CJ, Cunha-Rodrigues M, Ramesar J, Büscher P, Que I, Löwik C, Voshol

PJ, den Boer MA, van Duinen SG, Febbraio M, Mota MM, Waters AP. **Proc Natl Acad Sci U S A**. 2005 Aug 9;102(32):11468-73

- Reduced CD36-dependent tissue sequestration of Plasmodium-infected erythrocytes is detrimental to malaria parasite growth in vivo. Fonager J, Pasini EM, Braks JA, Klop O, Ramesar J, Remarque EJ, Vroegrijk IO, van Duinen SG, Thomas AW, Khan SM, Mann M, Kocken CH, Janse CJ, Franke-Fayard BM. **J Exp Med**. 2012 Jan 16;209(1):93-107.
- Replication of Plasmodium in reticulocytes can occur without hemozoin formation, resulting in chloroquine resistance. Lin JW, Spaccapelo R, Schwarzer E, Sajid M, Annoura T, Deroost K, Ravelli RB, Aime E, Capuccini B, Mommaas-Kienhuis AM, O'Toole T, Prins F, Franke-Fayard BM, Ramesar J, Chevalley-Maurel S, Kroeze H, Koster AJ, Tanke HJ, Crisanti A, Langhorne J, Arese P, Van den Steen PE, Janse CJ, Khan SM. **J. Exp Med**. 2015 212(6):893-903
- Common PIEZO1 Allele in African Populations Causes RBC Dehydration and Attenuates Plasmodium Infection. Ma S, Cahalan S, LaMonte G, Grubaugh ND, Zeng W, Murthy SE, Paytas E, Gamini R, Lukacs V, Whitwam T, Loud M, Lohia R, Berry L, Khan SM, Janse CJ, Bandell M, Schmedt C, Wengelnik K, Su AI, Honore E, Winzeler EA, Andersen KG, Patapoutian A. **Cell**. 2018 Apr 5;173(2):443-455.e12
- Gola A, Silman D, Walters AA, Sridhar S, Uderhardt S, Salman AM, Halbroth BR, Bellamy D, Bowyer G, Powlson J, Baker M, Venkatraman N, Poulton I, Berrie E, Roberts R, Lawrie AM, Angus B, Khan SM, Janse CJ, Ewer KJ, Germain RN, Spencer AJ, Hill AVS. Prime and target immunization protects against liver-stage malaria in mice. **Sci Transl Med**. 2018 Sep 26;10(460).

I have built and maintain a Malaria Resource Center Website, which have over 400 registered malaria scientists worldwide; it provides general information on the *Plasmodium berghei* rodent malaria model. It contains a large number of protocols on biological assays, molecular techniques and information about our standard 'in-house' plasmids necessary to create a variety of genetic modifications in malaria parasites. In addition, the website also provides databases containing information on the *Plasmodium* genomes and expression studies as well as information on individual genes (including such information as chromosome location and transcription/expression profiles etc).

I designed, maintain and curate an international web-based database and repository (**RMgmDB; www.Pberghei.eu** for all the genotype and phenotype of genetically modified rodent malaria parasite lines that have been generated worldwide. The Leiden Malaria Research Group has published on more than 400 Plasmodium mutants, including a large number of transgenic reporter/reference lines that are being extensively used by many different labs worldwide. The information in this database is shared with the 'Sanger Institute Pathogen Genome Database' (www.GeneDB.org) and 'EuPathDB Bioinformatics Resource Center for biodefense and Emerging / Re-emerging Infectious Diseases' (www.PlasmoDB.org)

- Generation of Transgenic Rodent Malaria Parasites Expressing Human Malaria Parasite Proteins. Salman AM, Mogollon CM, Lin JW, van Pul FJ, Janse CJ, Khan SM. **Methods Mol Biol**. 2015;1325:257-86. doi: 10.1007/978-1-4939-2815-6_21.
- Standardization in generating and reporting genetically modified rodent malaria parasites: the RMgmDB database. Khan SM, Kroeze H, Franke-Fayard B, Janse CJ. **Methods Mol Biol**. 2013;923:139-50.