Integrating sustainable malaria control solutions in the One Health sphere

Dr Dina Coertzen

One Health Symposium, 18 November 2021

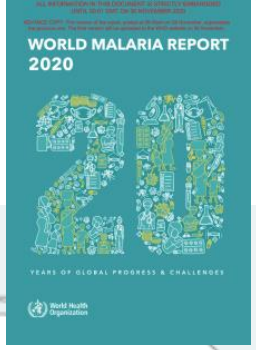
UP ISMC
UNIVERSITY OF PRETORIA
INSTITUTE FOR SUSTAINABLE MALARIA CONTROL

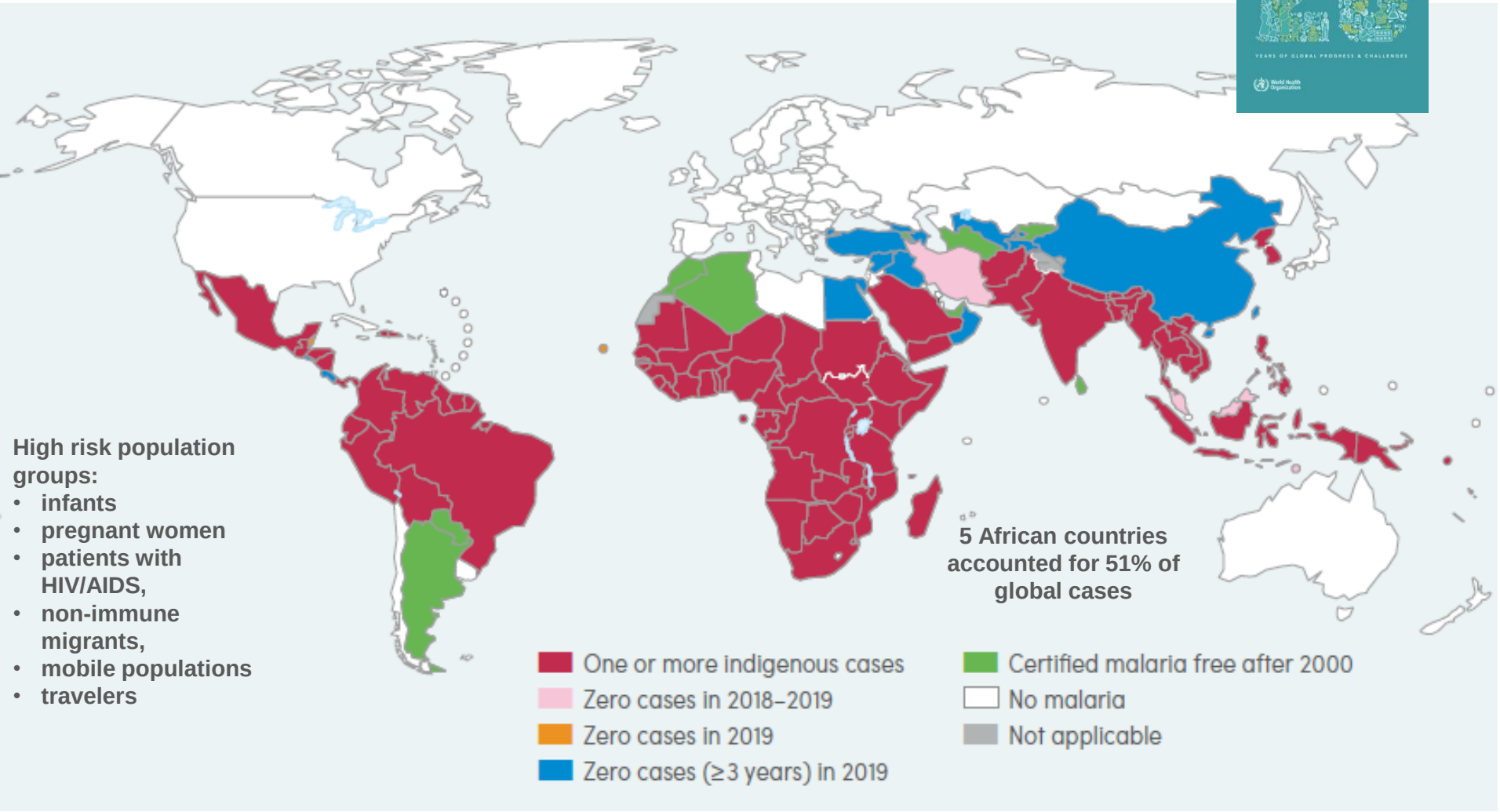
10 YEAR ANNIVERSARY

10 YEARS OF FIGHTING MALARIA
IN A TRANSDISCIPLINARY WAY

Make today matter

Global Malaria (2019)





High risk population groups:

- infants
- pregnant women
- patients with HIV/AIDS,
- non-immune migrants,
- mobile populations
- travelers

5 African countries accounted for 51% of global cases

WHO world malaria report 2020

406 malaria cases cause concern early in season

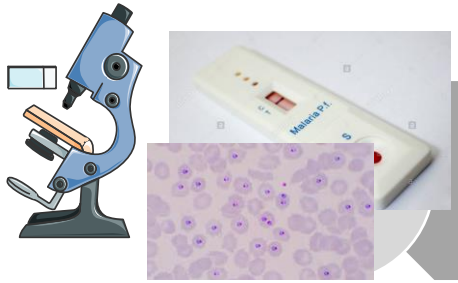
16 Nov.

Marietie Louw-Carstens

NETWERK24

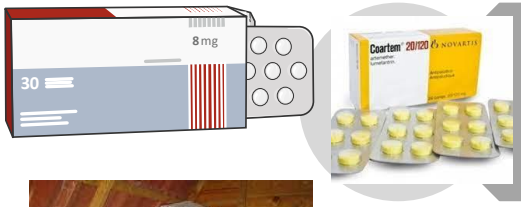
Dr. Phophi Ramathuba, MEC for health in Limpopo, himself sprayed houses in the Vhembe district with toxins in October to help prevent malaria. Photo: Facebook / Department of Health in Limpopo

Monitoring and control strategies



Diagnostics

Vaccine



Antimalarials

Vector control

Malaria is caused *Plasmodium* parasites

	% of global Cases	% of global Deaths	
	(229 million) (94% in Africa)	(409 000) (67% children < 5 years)	
Five species of *Plasmodium* genus cause malaria in humans			
P. falciparum	***~ 96.5%***	***~ 99%***	***Most lethal, most prevalent in WHO African region***
P. Vivax	***~ 3%***	***~ < 1%***	***Dormant liver stages resulting in disease relapse, prevalent in Americas***
P. ovale	***~ 0.5%***	***~ < 1%***	***Zoonotic***
P. malariae			
P. knowlesi			

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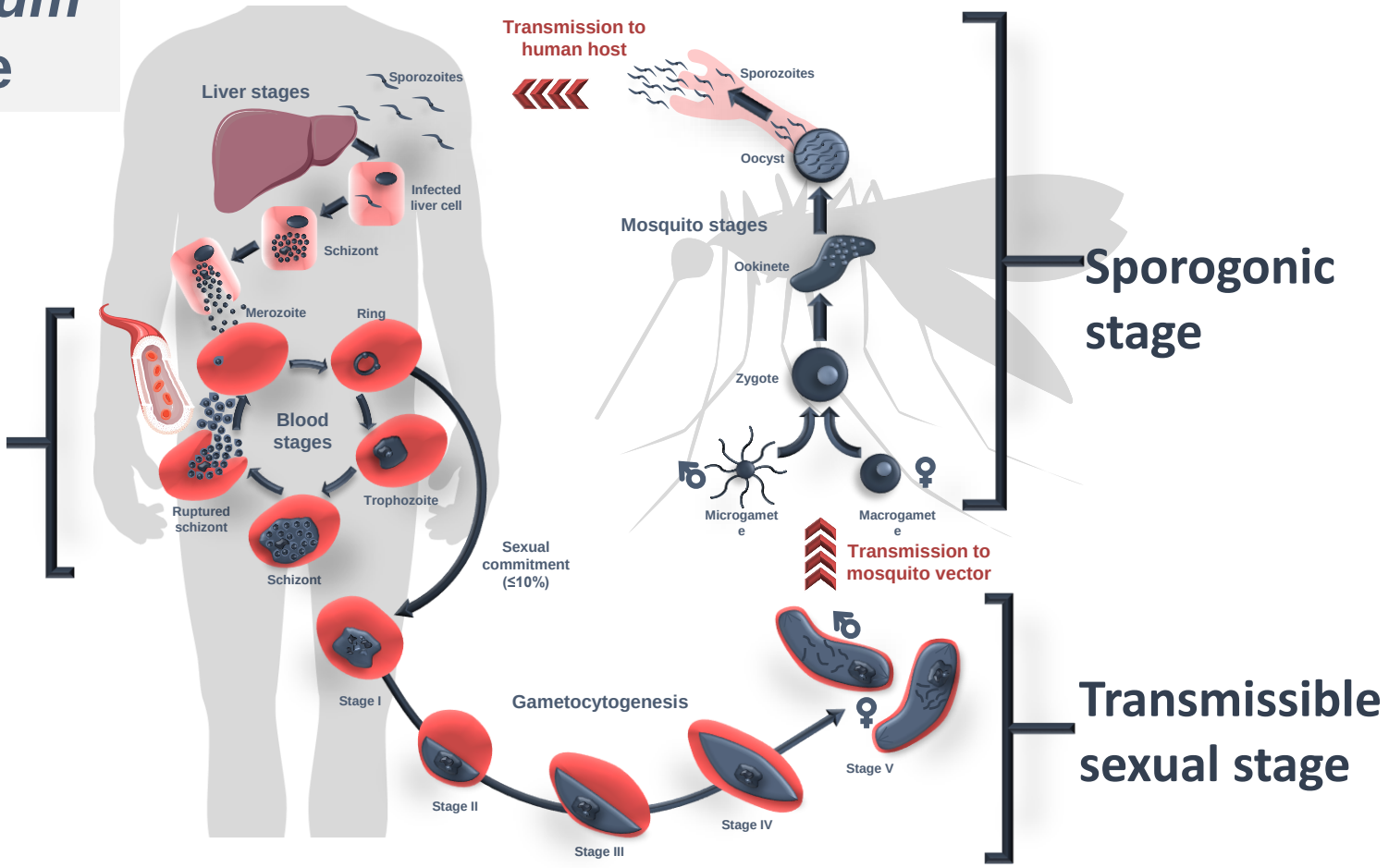
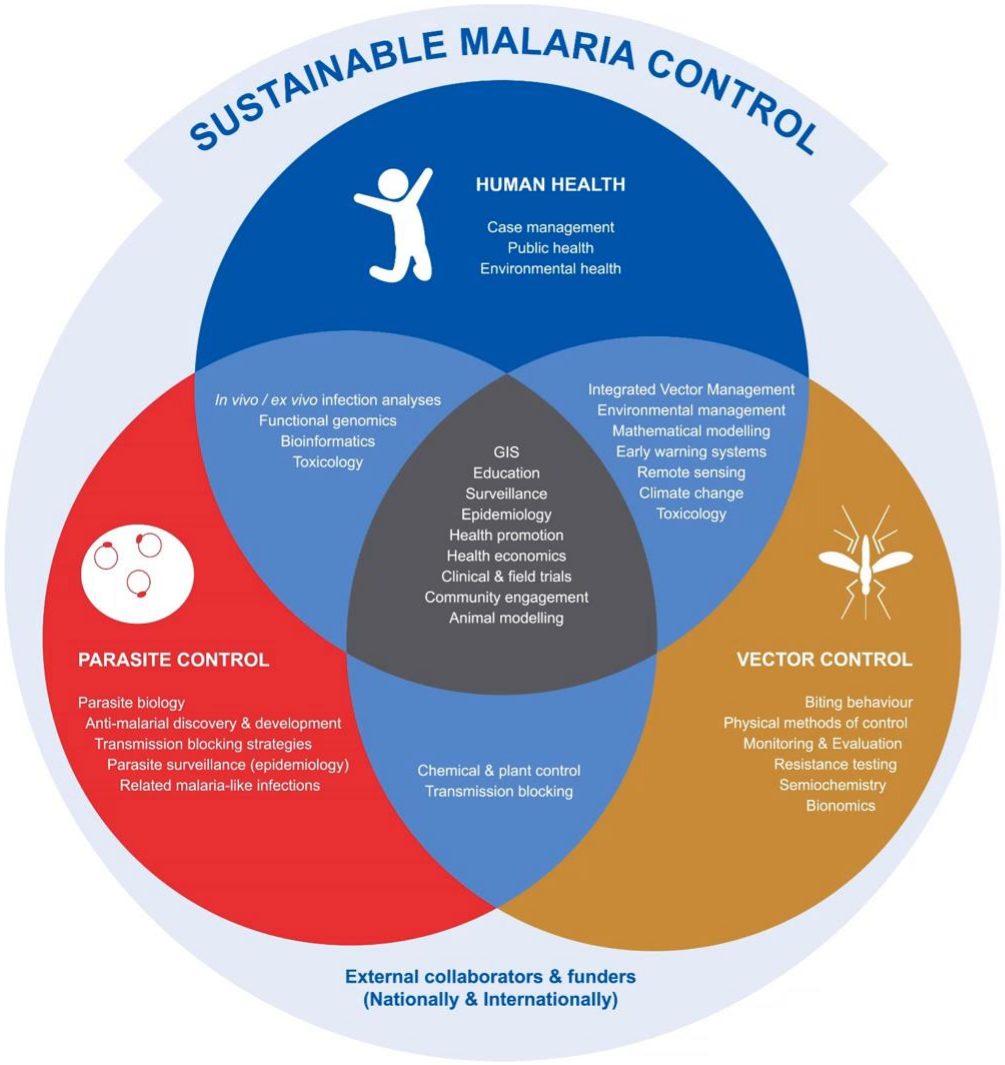
WHO world malaria report 2020

Plasmodium spp. life cycle

P. falciparum parasite

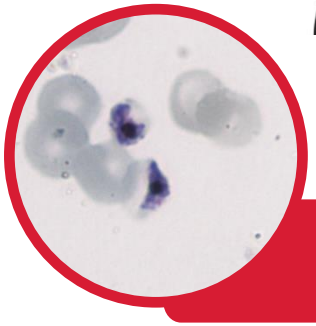


UP Institute for Sustainable Malaria Control



Malaria Parasite Molecular Laboratory (M^2PL)
Biology and Drug Discovery

Prof. Lyn-Marie Birkholtz
DSI/NRF South African Research Chair (SARChI)
Sustainable Malaria Control



Parasite Control Cluster

Human Health Cluster

Prof. Tiaan de Jager
Director of the UP ISMC
Dean of the Faculty of Health Sciences

Vector Control Cluster

Dr. Megan Riddin
Senior Researcher
Chairperson of Vector control cluster

Malaria Parasite Molecular Laboratory (M²PL)
Biology and Drug Discovery

Community of Practice on 'Evaluating malaria control interventions'.

A multisectoral transdisciplinary program working at local, national and international level to evaluate health innovations for malaria therapeutic strategies with the overall to aid in malaria elimination. Involves academia, National Department of Health, community stakeholders and industry partners.


ACS Medicinal Chemistry Letters

pubs.acs.org/acsmedchemlett

Structure–Activity Relationship Studies Reveal New Astemizole Analogues Active against *Plasmodium falciparum* In Vitro

Dickson Mambwe, Malkeet Kumar, Richard Ferger, Dale Taylor, Mathew Njoroge, Dina Coertzen, Janette Reader, Mariëtte van der Watt, Lyn-Marie Birkholtz, and Kelly Chibale*


ACS Biomaterials Science & Engineering

pubs.acs.org/journal/abseba

Facile Route to Targeted, Biodegradable Polymeric Prodrugs for t Delivery of Combination Therapy for Malaria

Lisa Fortuin, Meta Leshabane, Rueben Pfukwa,* Dina Coertzen, Lyn-Marie Birkholtz, and Bert Klumperman*


Transactions of the Royal Society of South Africa

ISSN: (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/ttrs20

Exploring the transmission-blocking activity of antiplasmodial 3,6-diarylated imidazopyridazines

Dina Coertzen, Janette Reader, Mariëtte E. van der Watt, Meta M. Leshabane, Henrico Langeveld, Peter M. Cheuka, Godwin A. Dziwornu, Kelly Chibale & Lyn-Marie Birkholtz


ACS Infectious Diseases

pubs.acs.org/journal/aidcbc

Benzimidazole Derivatives Are Potent against Multiple Life Cycle Stages of *Plasmodium falciparum* Malaria Parasites

Meta Leshabane, Godwin Akpeko Dziwornu, Dina Coertzen, Janette Reader, Phanankosi Moyo, Mariëtte van der Watt, Kelly Chisanga, Consolata Nsanzubuhoro, Richard Ferger, Erica Erlank, Nelius Venter, Lizette Koekemoer, Kelly Chibale,* and Lyn-Marie Birkholtz*


ACS Infectious Diseases

pubs.acs.org/journal/aidcbc

New Amidated 3,6-Diphenylated Imidazopyridazines with Potent Antiplasmodium Activity Are Dual Inhibitors of *Plasmodium* Phosphatidylinositol-4-kinase and cGMP-Dependent Protein Kinase

Peter Mubanga Cheuka,[‡] Luyanda Centani,[‡] Lauren B. Arendse, Stephen Fienberg, Lynn Wambua, Shoneeze S. Renga, Godwin Akpeko Dziwornu, Malkeet Kumar, Nina Lawrence, Dale Taylor, Sergio Wittlin, Dina Coertzen, Janette Reader, Mariette van der Watt, Lyn-Marie Birkholtz, and Kelly Chibale*


Journal of Medicinal Chemistry

pubs.acs.org/jmc

Antimalarial Benzimidazole Derivatives Incorporating Phenolic Mannich Base Side Chains Inhibit Microtubule and Hemozoin Formation: Structure–Activity Relationship and *In Vivo* Oral Efficacy Studies

Godwin Akpeko Dziwornu, Dina Coertzen, Meta Leshabane, Constance M. Korkor, Cleavon K. Cloete, Mathew Njoroge, Liezl Gibhard, Nina Lawrence, Janette Reader, Mariëtte van der Watt, Sergio Wittlin, Lyn-Marie Birkholtz, and Kelly Chibale*

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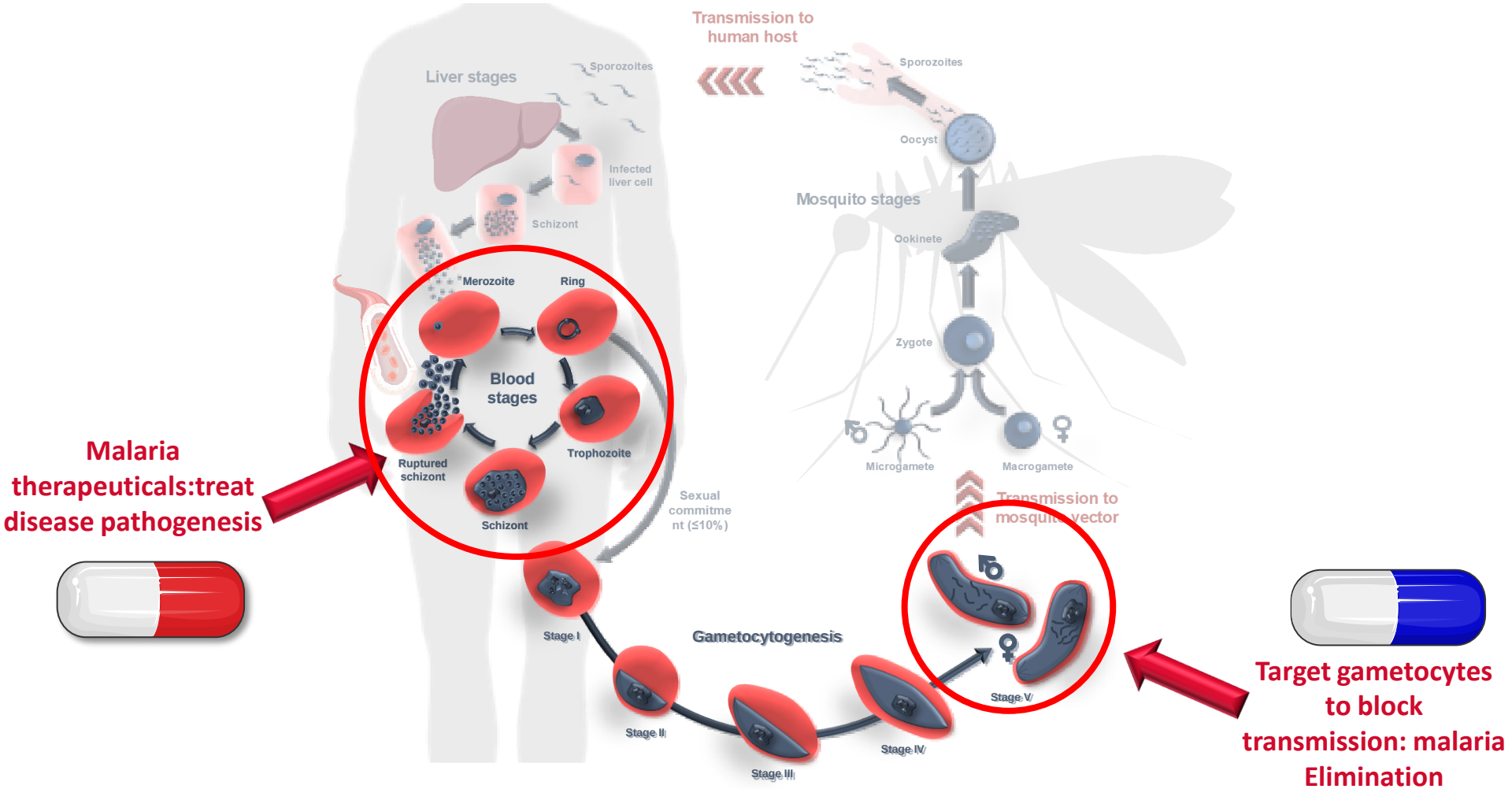
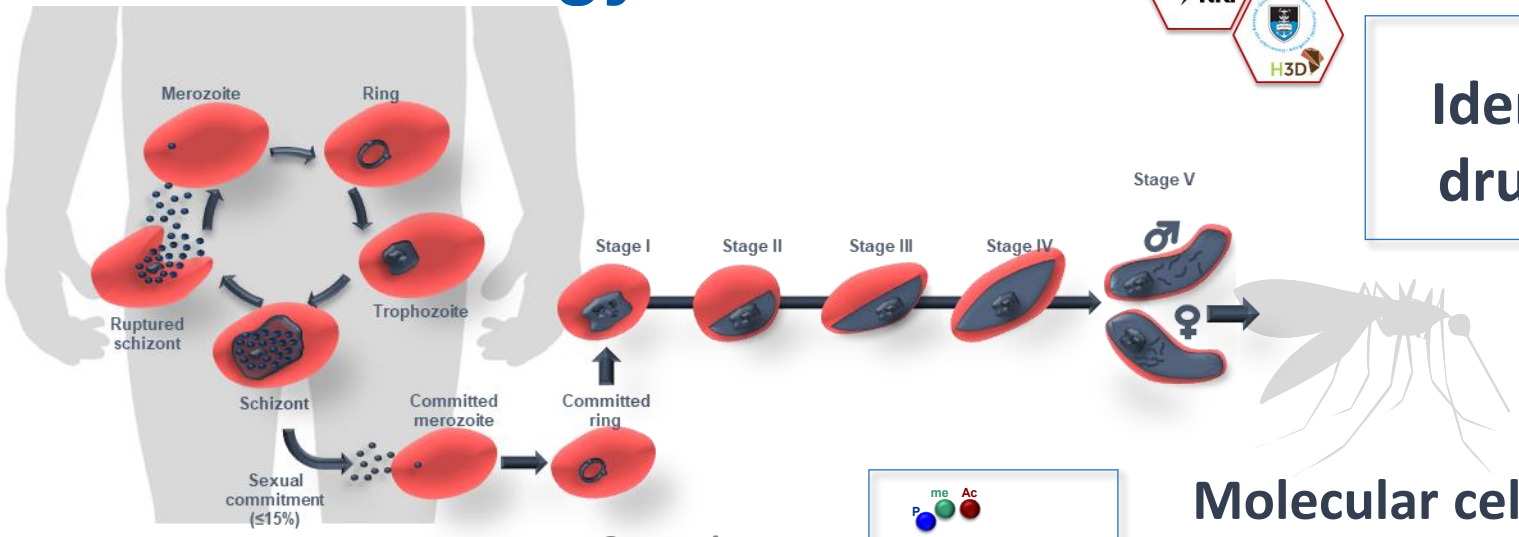
Antimalarial therapeutic strategies



Parasite biology



Identify new drug targets

Functional genomic approaches

Identify unique and essential drivers that control asexual proliferation and sexual differentiation

Genomics

Epigenomics

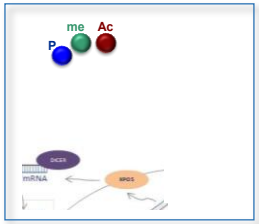
Histone PTMs

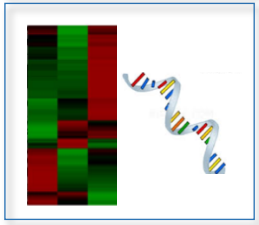
Transcriptomics

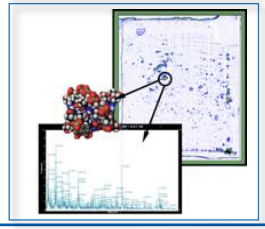
RNA

Proteomics

Proteins

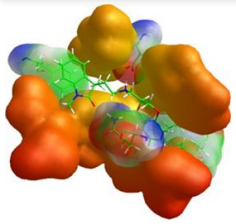






Molecular cell biology approaches

Investigate and validate novel targets and drug mechanistic actions in asexual and sexual parasites



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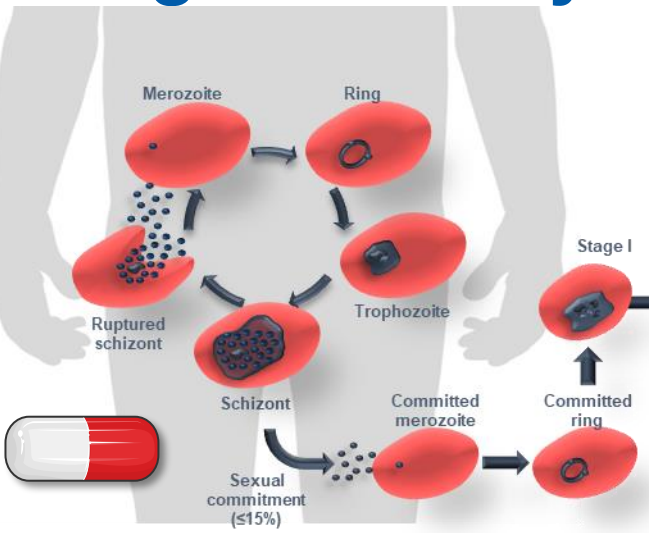
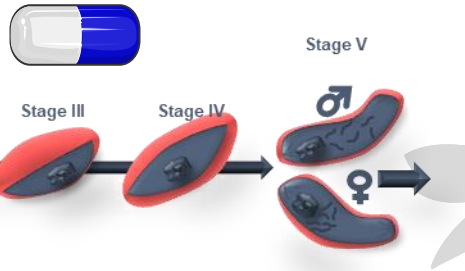
Drug discovery

Parasite Control Cluster

Identify new antimalarial compounds



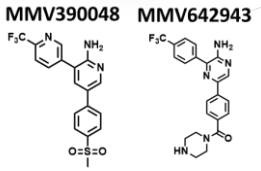


Screening of novel chemical matter and plant-based extracts

Identifying compounds that specifically target the parasite with low resistance indicators and novel mechanisms of action

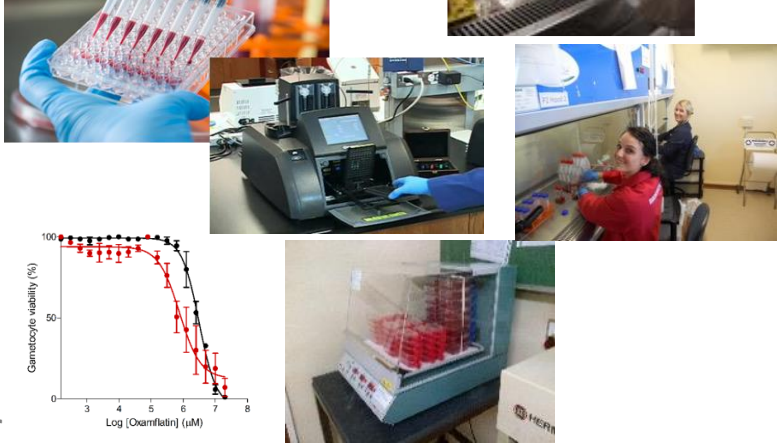
Phenotypic screens

HTS screens using assay platforms



Toxicity, specificity

Counterscreens
Kinetics, stage-specificity



Target identification

Systems and molecular evaluation

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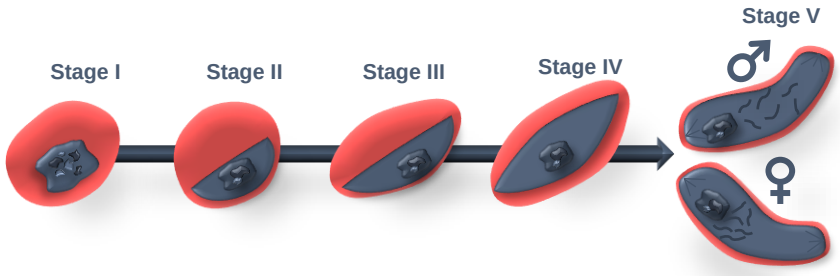
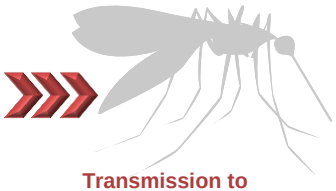
Blocking transmission

Parasite Control Cluster

Vector Control Cluster





Transmission to mosquito vector

Identify transmission blocking compounds

Screening against mosquito-borne parasitic stages

Identifying compounds that specifically target the gametocyte stages to block human to mosquito transmission for malaria elimination

Gametocyte screens

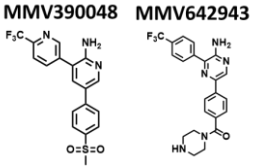
HTS screens using assay platforms

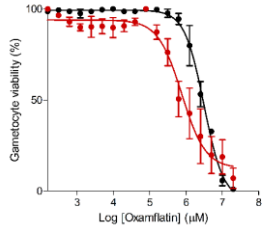
Sexual reproduction

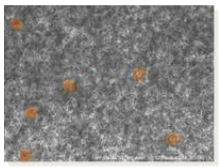
Gamete inhibition assays

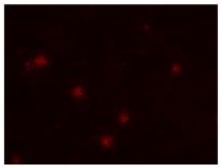
Mosquito transmission

Monitoring parasite intra-mosquito parasite development









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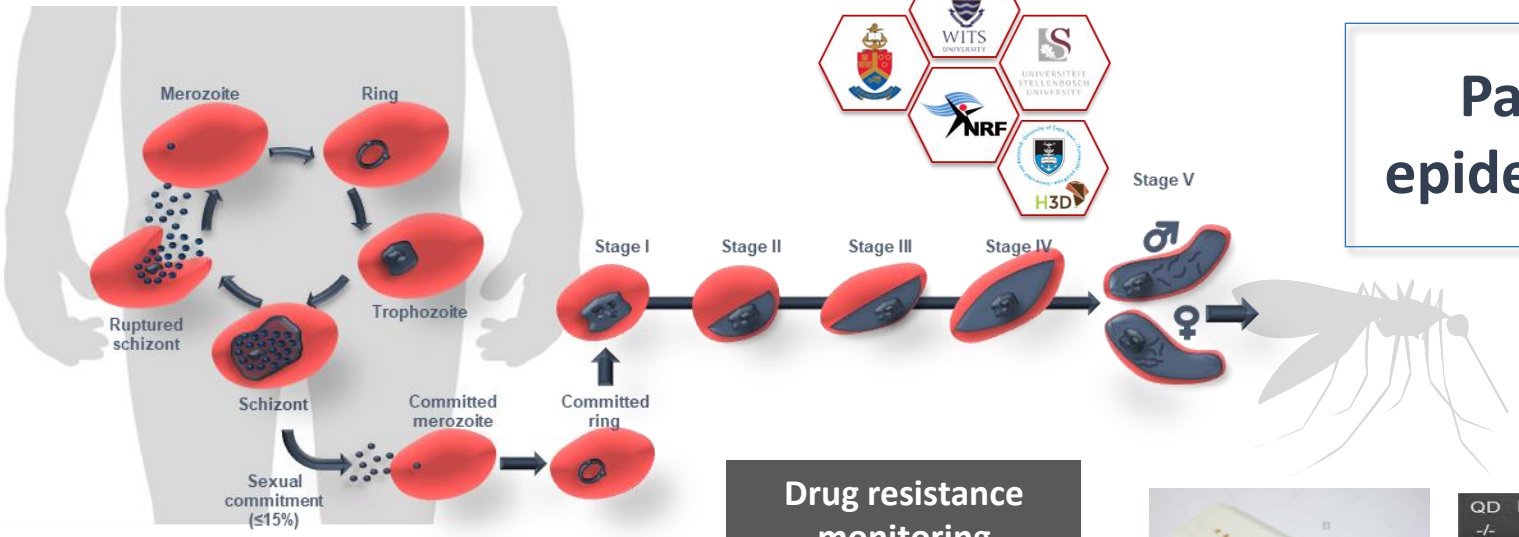
Parasite surveillance

Parasite Control Cluster

Human Health Cluster

Vector Control Cluster



Parasite epidemiology

Genotyping endemic parasite populations

Investigating genetic and resistance markers from field samples to understand parasite epidemiology and transmission dynamics

Drug resistance monitoring

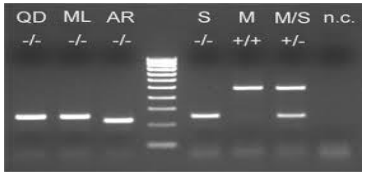
Amplification of drug resistance markers

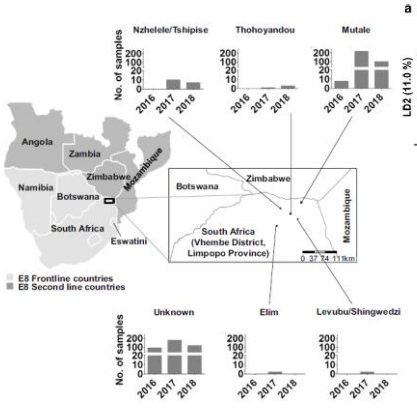
Genotyping field isolates

MOI, FwS, unique alleles, He, Multilocus LD

Transmission dynamics

Systems and molecular evaluation





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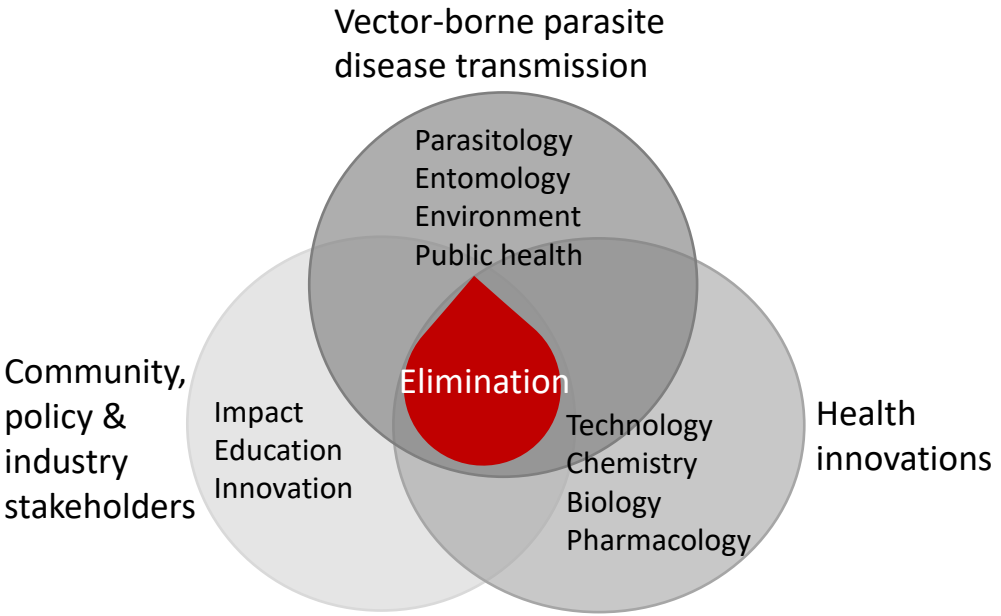
Malaria Parasite Molecular Laboratory (M²PL)
Biology and Drug Discovery

Prof L Birkholtz
SARChI Chair in Sustainable Malaria Control

Strategic focus within the One Health sphere

Transdisciplinary approach to identify health innovations that target transmission of vector-borne parasitic diseases of importance to human health



Thank You

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