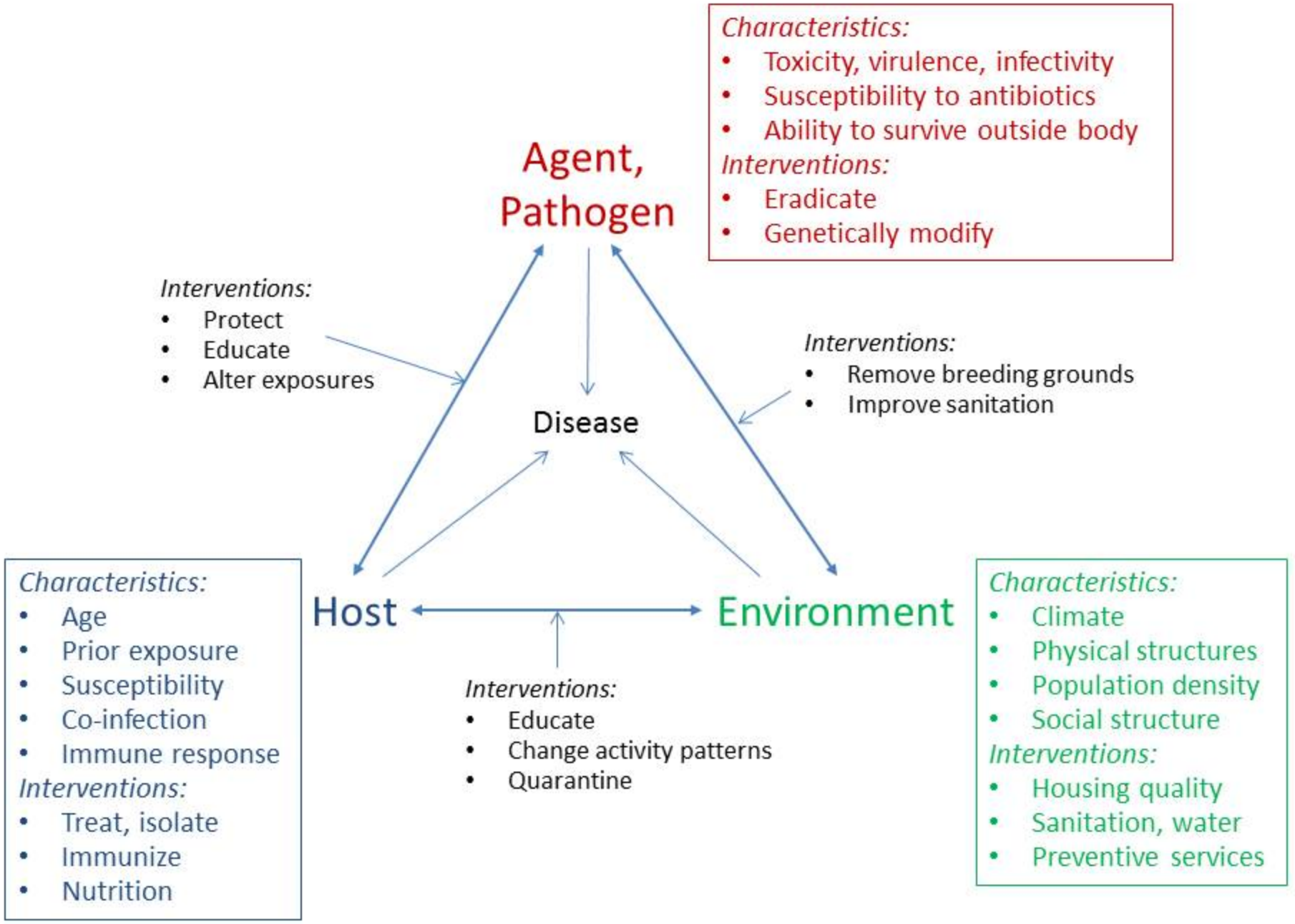
# Research Foundation in Tropical Diseases and the Environment

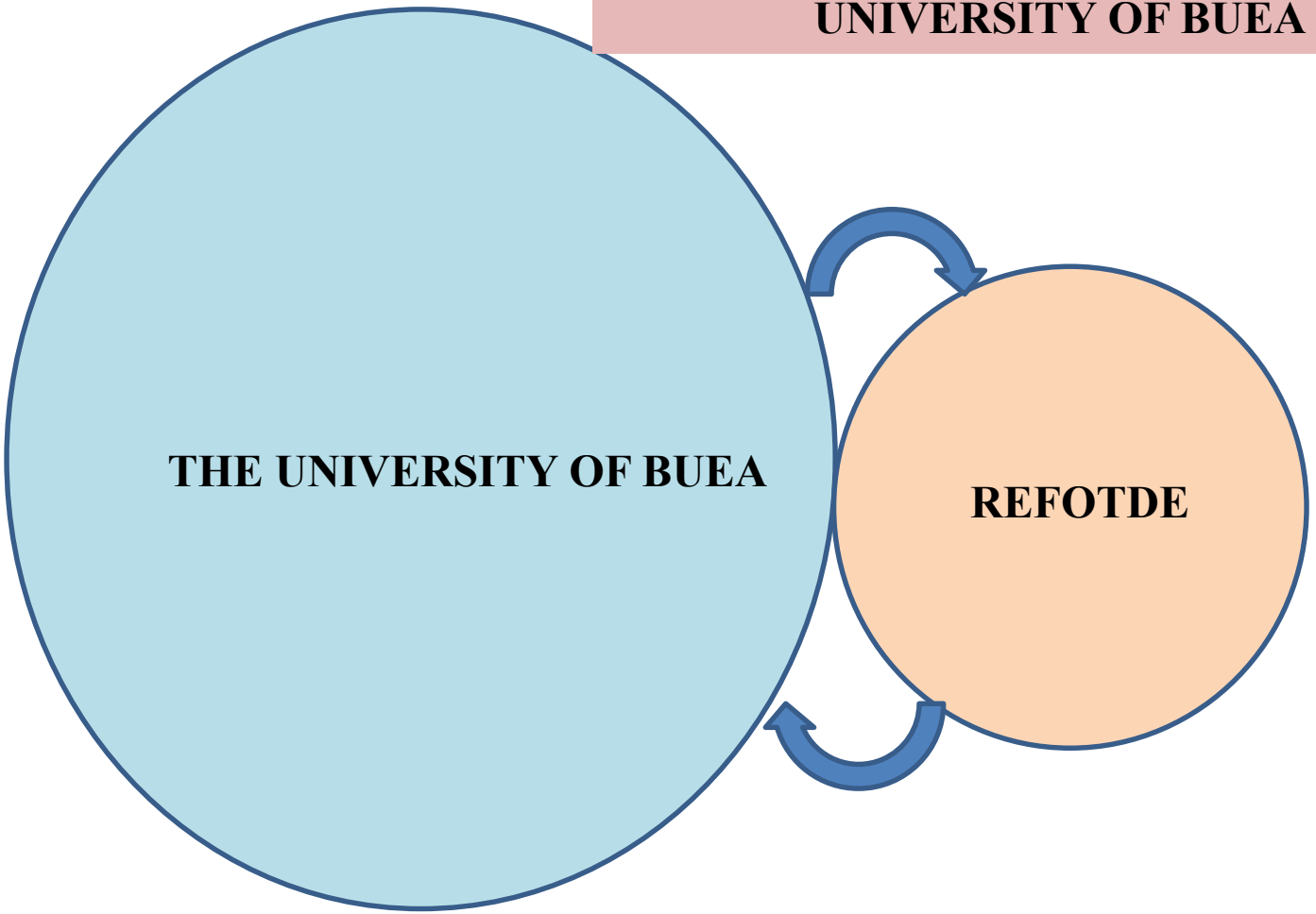

BUEA, CAMEROON

# REFOTDE MISSION

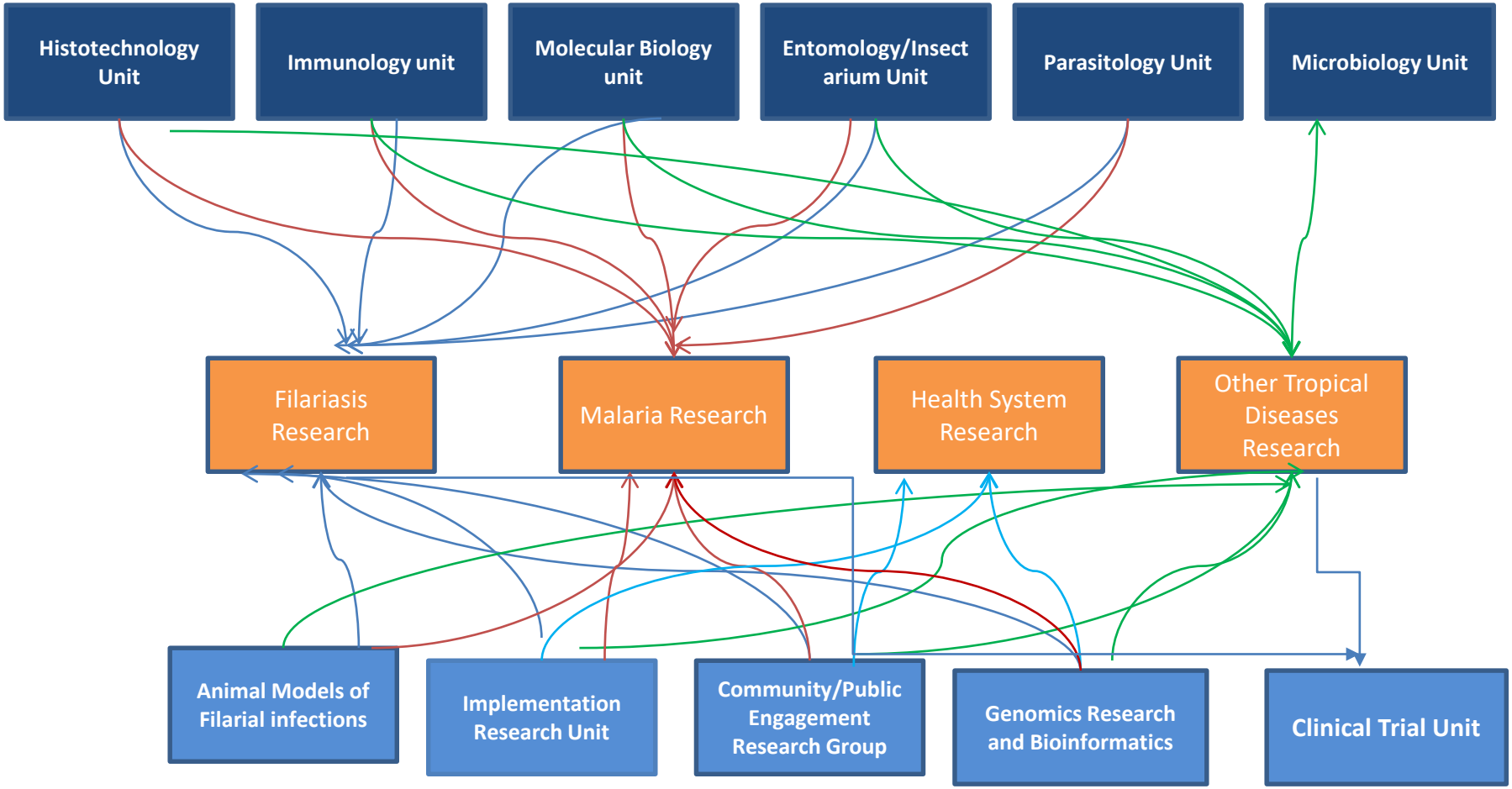
**Contribution to find solutions to problems paused by Tropical Diseases to African Populations using integrated approach that take into consideration the Human population, the Pathogens , their vectors and the Environment**


Agent, Pathogen
Characteristics:
• Toxicity, virulence, infectivity
• Susceptibility to antibiotics
• Ability to survive outside body
Interventions:
• Eradicate
• Genetically modify
Interventions:
• Protect
• Educate
• Alter exposures
Interventions:
• Remove breeding grounds
• Improve sanitation
Disease
Host
Environment
Characteristics:
• Age
• Prior exposure
• Susceptibility
• Co-infection
• Immune response
Interventions:
• Treat, isolate
• Immunize
• Nutrition
Interventions:
• Educate
• Change activity patterns
• Quarantine
Characteristics:
• Climate
• Physical structures
• Population density
• Social structure
Interventions:
• Housing quality
• Sanitation, water
• Preventive services

# THE MUTUALISTIC RELATIONSHIP BETWEEN REFOTDE AND THE UNIVERSITY OF BUEA



# RESEARCH NETWORK AT THE REFOTDE- CAMEROON



# FILARIASIS RESEARCH HIGHLIGHTS AT REFOTDE

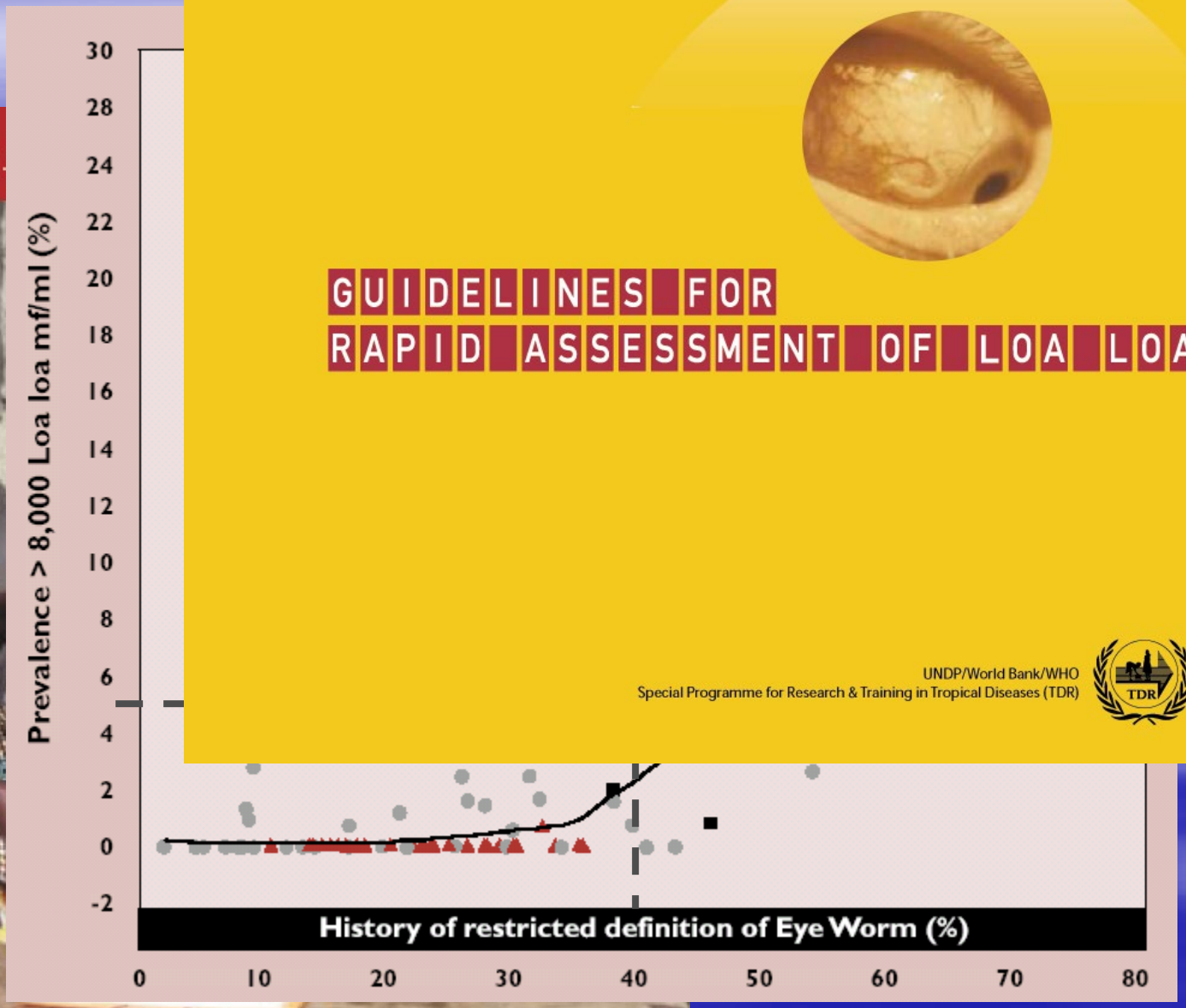
# FOCUS ON LOIASIS RESEARCH

# DEVELOPMENT OF THE RAPID ASSESSMENT PROCEDURE FOR LOAISIS

# RAPLOA Development and Validation

# RAPLOA

REPORT OF A MULTI-






## GUIDELINES FOR RAPID ASSESSMENT OF LOA LOA

UNDP/World Bank/WHO
Special Programme for Research & Training in Tropical Diseases (TDR)

# VALIDATION OF RAPLOA IN A DIFFERENT SOCIO_CULTURAL CONTEXT

Wanji et al. Parasites & Vectors 2012, 5:25
http://www.parasitesandvectors.com/content/5/1/25

Parasites & Vectors

RESEARCH Open Access

## Validation of the rapid assessment procedure for loiasis (RAPLOA) in the democratic republic of Congo

Samuel Wanji[1,2*], Dowo O Akotshi[3], Maurice N Mutro[4], Floribert Tepage[5], Tony O Ukety[6], Peter J Diggle[7] and Jan H Remme[8]

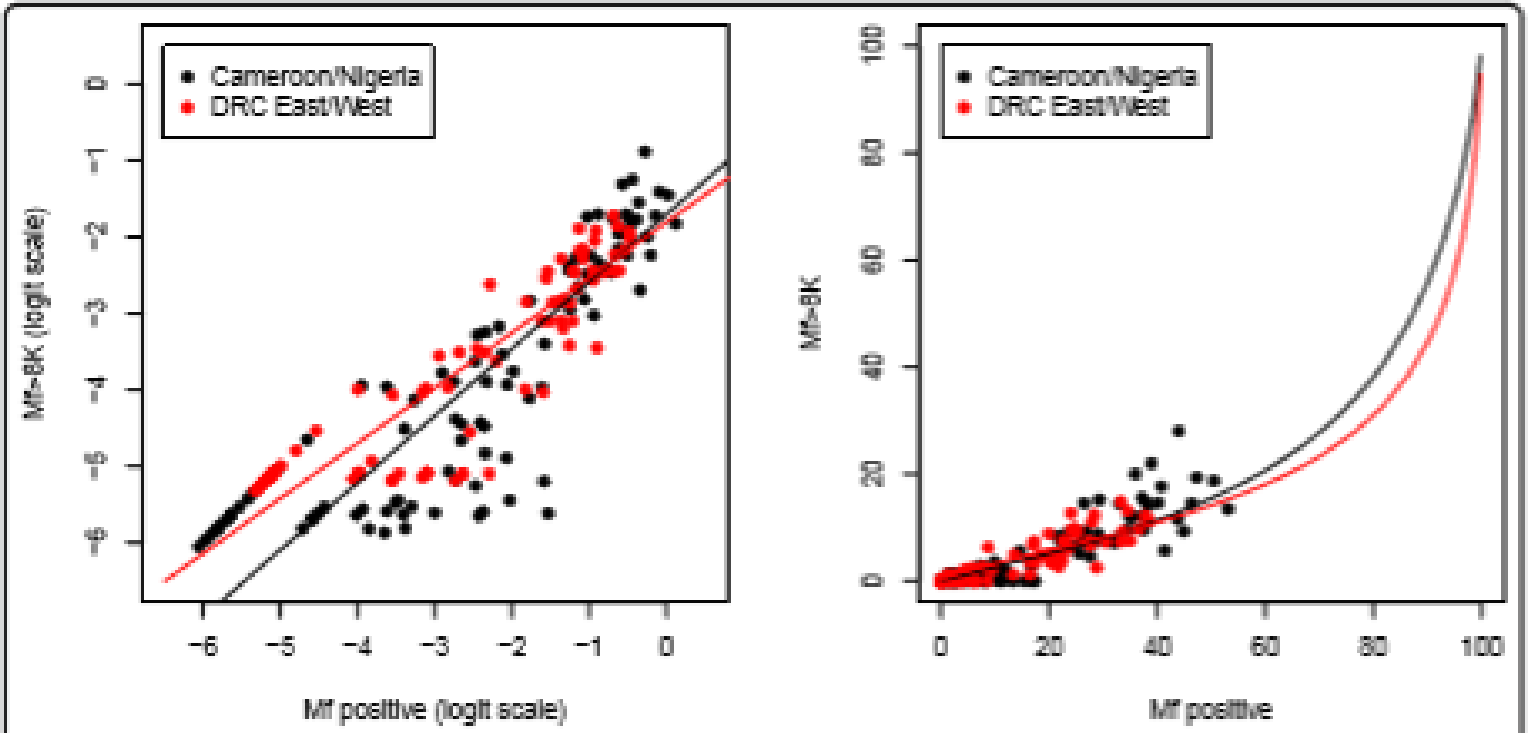



**Figure 2 Relationship between the prevalence of high microfilarial loads (> 8000 Mf/ml) and the prevalence of microfilaraemia at the community level (*original and validation data*).** The black and red lines show the calibration models fitted to the original and validation data, respectively. The left-hand panel shows the data and models on the log-odds scale, the right-hand panel on the prevalence scale. The original data are from [10].

# GENERATING THE FIRST LOA LOA MAP OF AFRICA USING GROUND DATA FROM RAPLOA

OPEN ACCESS Freely available online

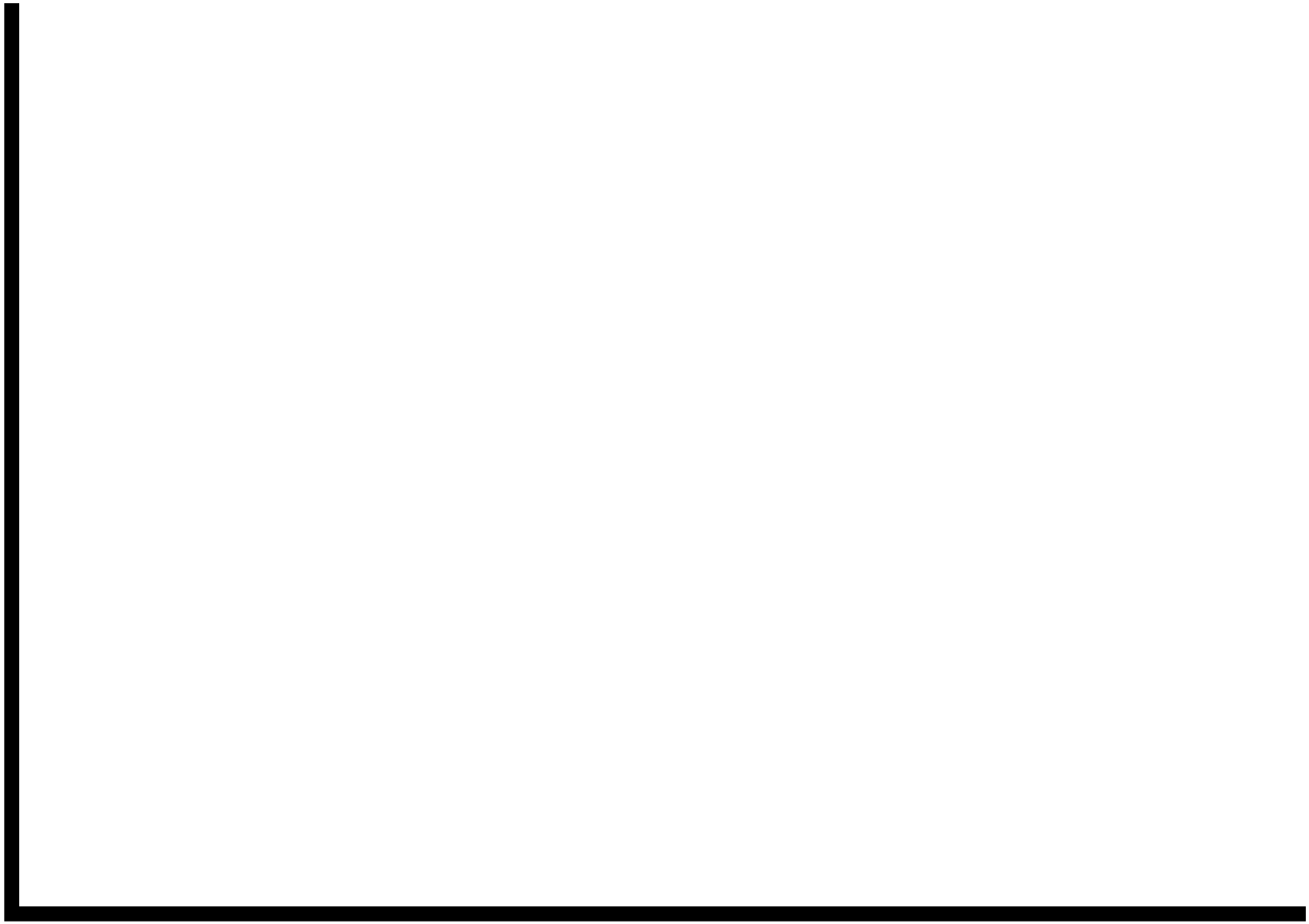
PLoS NEGLECTED TROPICAL DISEASES

## The Geographic Distribution of *Loa loa* in Africa: Results of Large-Scale Implementation of the Rapid Assessment Procedure for Loiasis (RAPLOA)

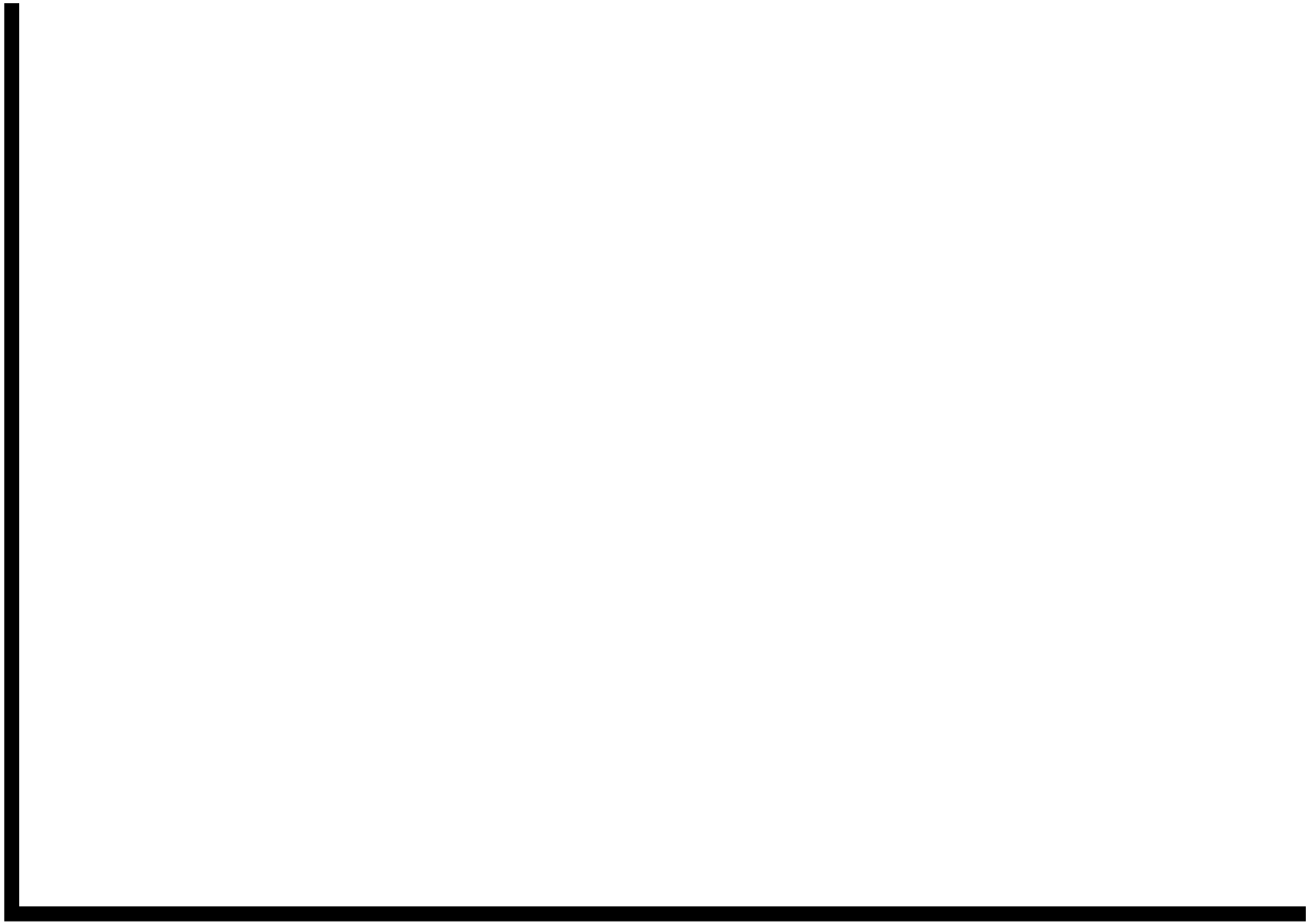
**Honorat Gustave Marie Zouré[1]*, Samuel Wanji[2,3], Mounkaïla Noma[1], Uche Veronica Amazigo[1], Peter J. Diggle[4], Afework Hailemariam Tekle[1], Jan H. F. Remme[5]**

**1** African Programme for Onchocerciasis Control, World Health Organization, Ouagadougou, Burkina Faso, **2** Research Foundation for Tropical Diseases and Environment, Buea, Cameroon, **3** Department of Biochemistry and Microbiology, University of Buea, Buea, Cameroon, **4** Institute of Infection and Global Health, University of Liverpool, Liverpool, United Kingdom, **5** Consultant, Ornex, France

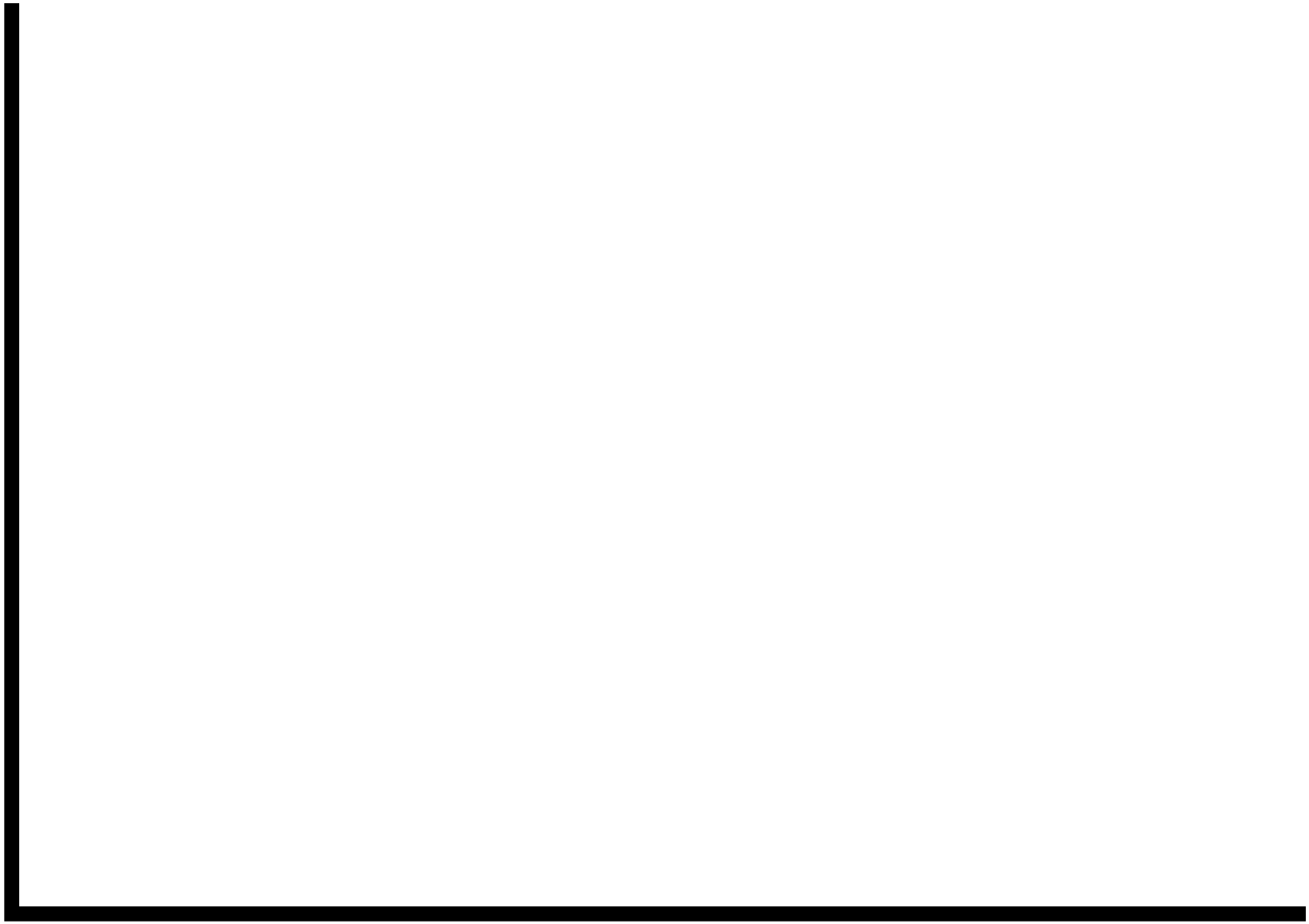
Map of the estimated prevalence of eye worm history in Africa



Map of the predictive probability that the prevalence of eye worm $\geq$ 40%



ArcGIS probability kriging: probability that prevalence of eye worm $\geq 40\%$



# Assessment of the Impact of CDTI on L. loa Parasitological indicators

PLOS | NEGLECTED TROPICAL DISEASES

RESEARCH ARTICLE

# Impact of repeated annual community directed treatment with ivermectin on loiasis parasitological indicators in Cameroon: Implications for onchocerciasis and lymphatic filariasis elimination in areas co-endemic with *Loa loa* in Africa

**Samuel Wanji[1,2]*, Winston Patrick Chounna Ndongmo[1,2], Fanny Fri Fombad[1,2], Jonas Arnaud Kengne-Ouafo[1,2], Abdel Jelil Njouendou[1,2], Yolande Flore Longang Tchounkeu[2], Benjamin Koudou[3], Moses Bockarie[3], Grace Fobi[4], Jean Baptiste Roungou[4], Peter A. Enyong[1,2]**

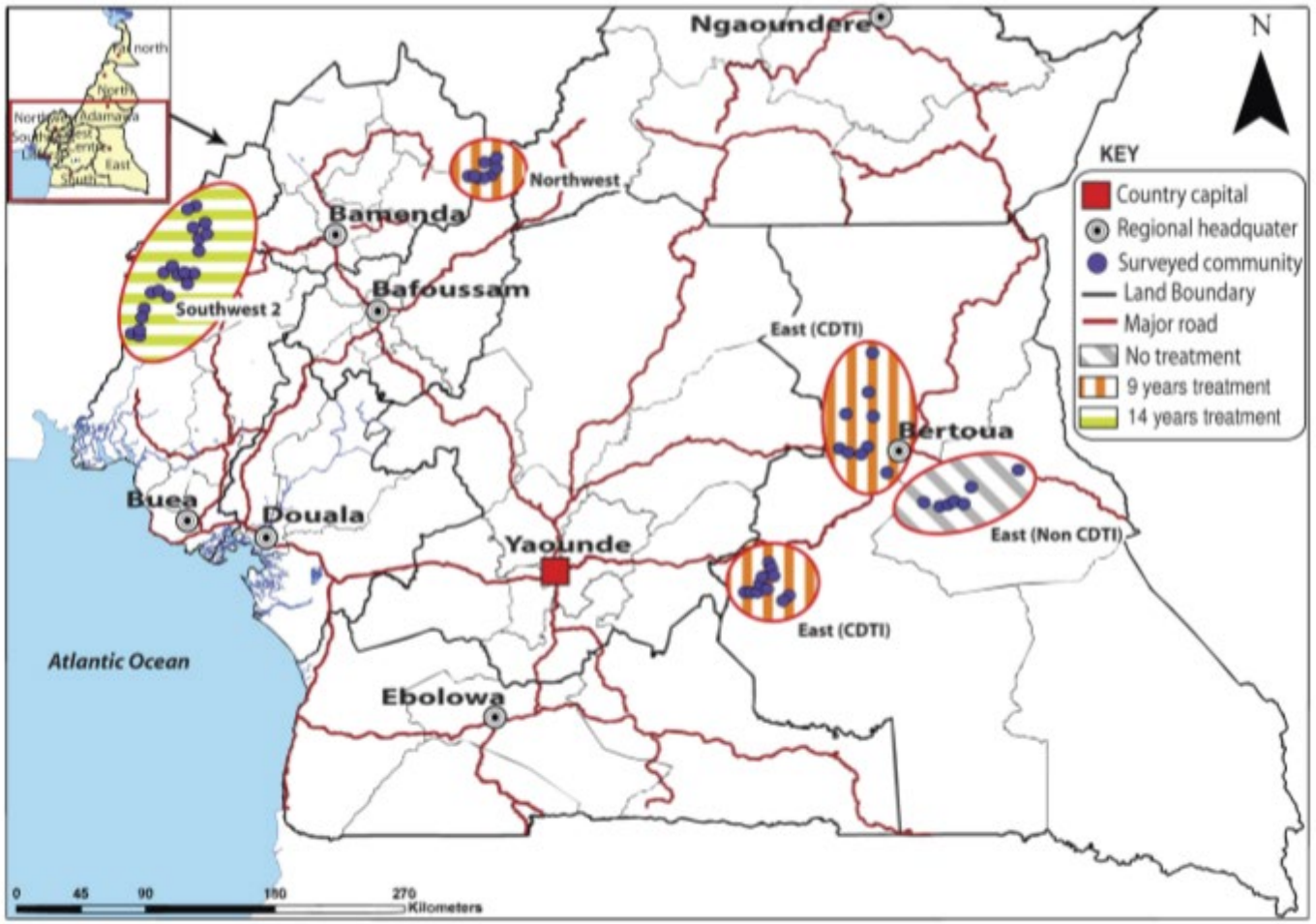



**Fig 1. Map showing the locations of the study sites (QGIS software version 2.0.1).**

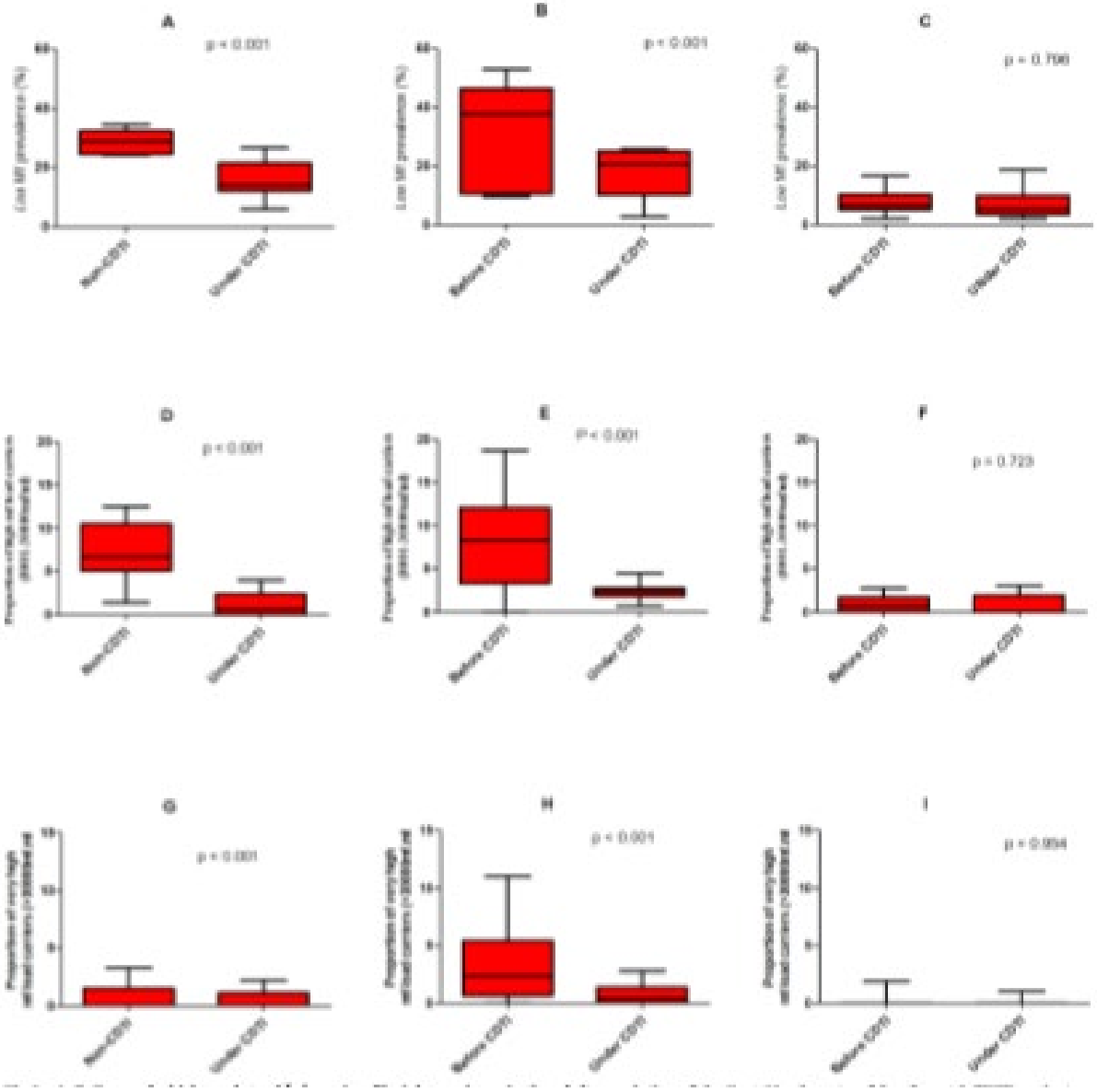
https://doi.org/10.1371/journal.pntd.0006750.g001

# Impact of CDTI on L. Loa Prevalence and Intensity

East

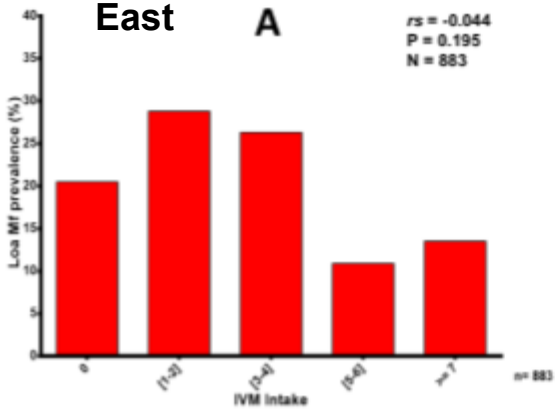
North West

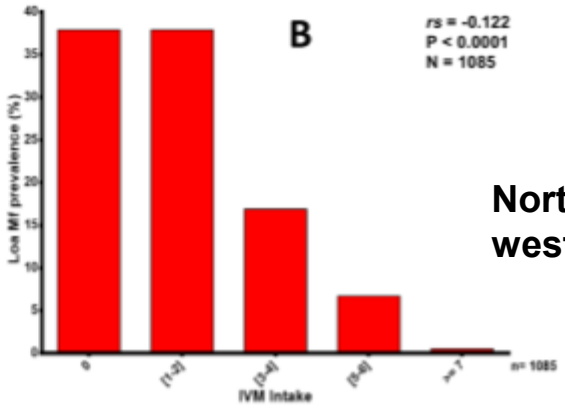
South west



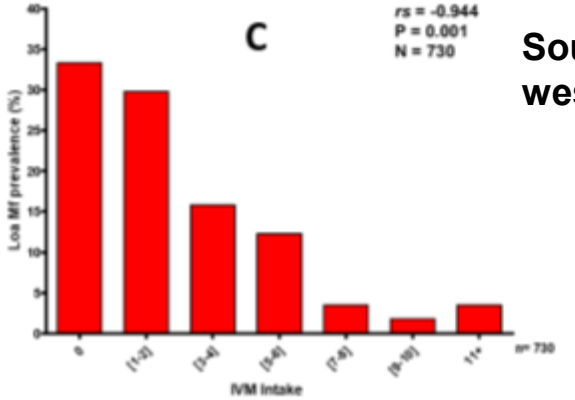
**Significant Reduction in L. loa Prevalence and Intensity in CDTi Areas**

# Relationship Between L. loa Microfilarial Prevalence and Ivermectin Intake



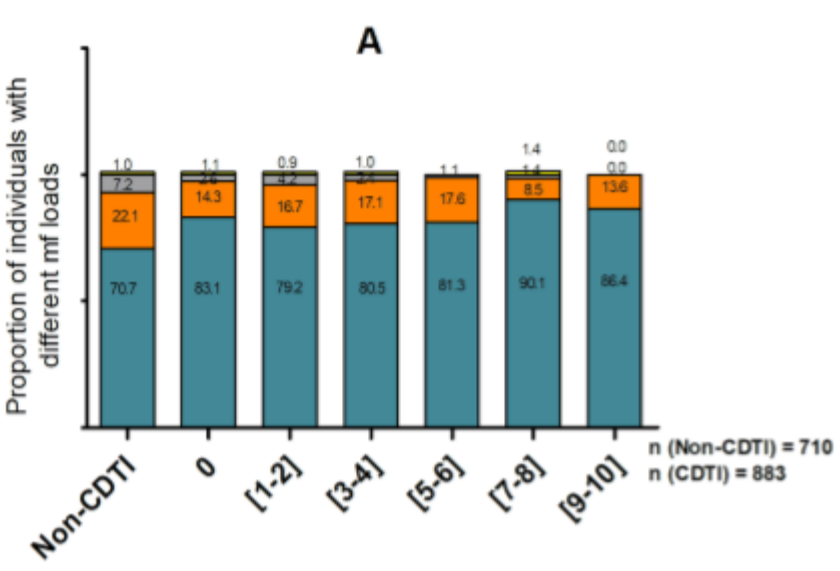

North west

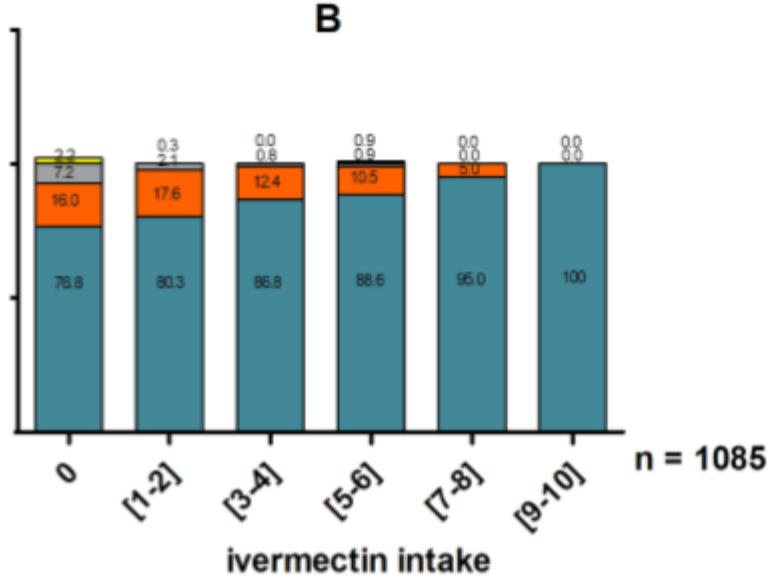


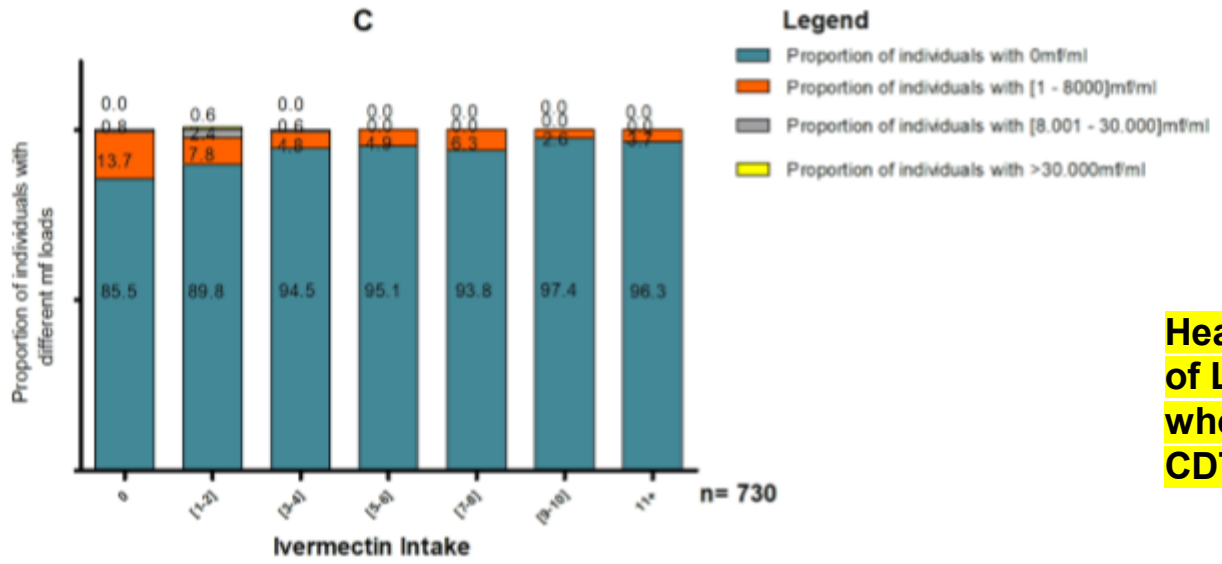

South west

The Reduction in L. loa Prevalence is Ivermectin Adherence Dependent

# Relationship Between the proportions of individuals in different L. loa microfilarial load classes and Ivermectin Intake




**Heavy Microfilarial Load of L. loa is rare in people who comply better to CDTi**

# It may be very difficult to eliminate L. loa with Ivermectin

This will also have negative implications on the Elimination of Onchocerciasis and Lymphatic Filariasis in areas of co-endemicity with L. loa

# Development of the Animal model of Loa Encephalopathy following Ivermectin Treatment in non human primate

LOA/BABOON

PLOS | NEGLECTED TROPICAL DISEASES

RESEARCH ARTICLE

# Parasitological, Hematological and Biochemical Characteristics of a Model of Hyper-microfilariaemic Loiasis (*Loa loa*) in the Baboon (*Papio anubis*)

**Samuel Wanji[1,2]*, Ebanga-Echi Eyong[2,3,4], Nicholas Tendongfor[1,2], Che Ngwa[2], Elive Esuka[2], Arnaud Kengne-Ouafo[1,2], Fabrice Datchoua-Poutcheu[1,2], Peter Enyong[1,2], Adrian Hopkins[5], Charles D. Mackenzie[6]**

**1** Parasites and Vectors Research Unit, Department of Microbiology and Parasitology, Faculty of Science, University of Buea, South West Region, Cameroon, **2** Research Foundation for Tropical Diseases and Environment (REFOTDE), South West Region, Cameroon, **3** Department of Biological Sciences, Faculty of Science, University of Bamenda, North West Region, Cameroon, **4** Department of Zoology and Animal Physiology, Faculty of Science, University of Buea, South West Region, Cameroon, **5** Mectizan Donation Programme, Decatur, Georgia, United States of America, **6** Department of Pathobiology and Diagnostic Investigation, Michigan State University, East Lansing, Michigan, United States of America

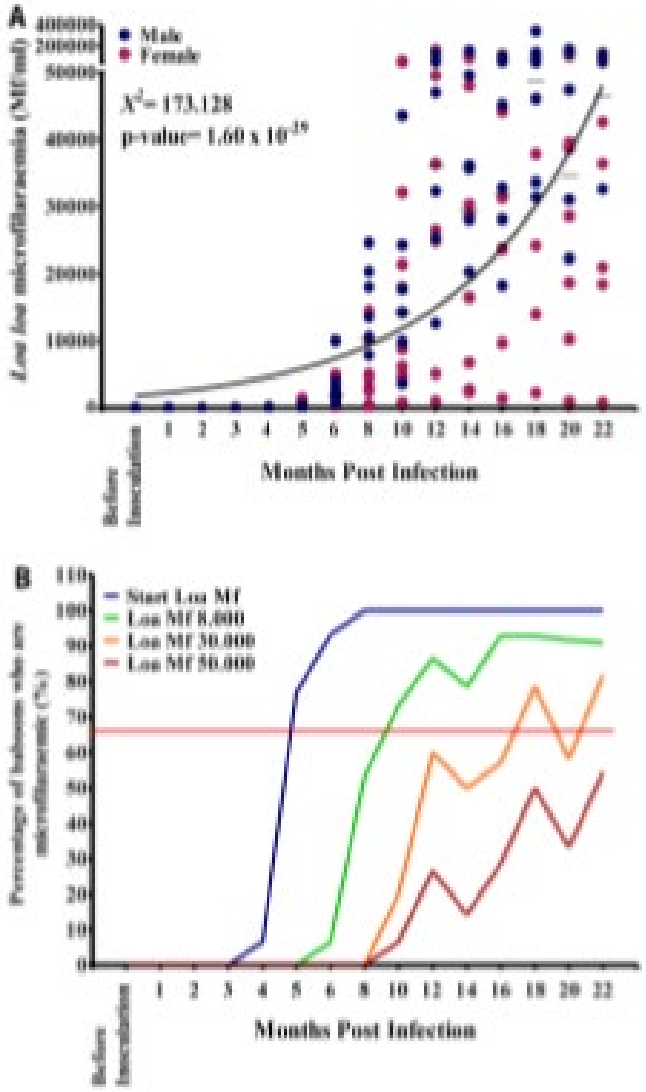



**Fig 2. Microfilariaemia in splenectomised baboons.** A. Time course of microfilariaemia in 15 baboons experimentally infected with human *Loa loa*. B. Proportions of baboons who are *Loa loa* microfilariaemic at various times during infection.

doi:10.1371/journal.pntd.0004202.g002

**Splecnotomised can harbor up to 400,000 Mf L. loa per ml of Blood**

**Up to 40% of infected Baboon can develop up to 50,000 Mf/ml of blood**

PLOS | NEGLECTED TROPICAL DISEASES

RESEARCH ARTICLE

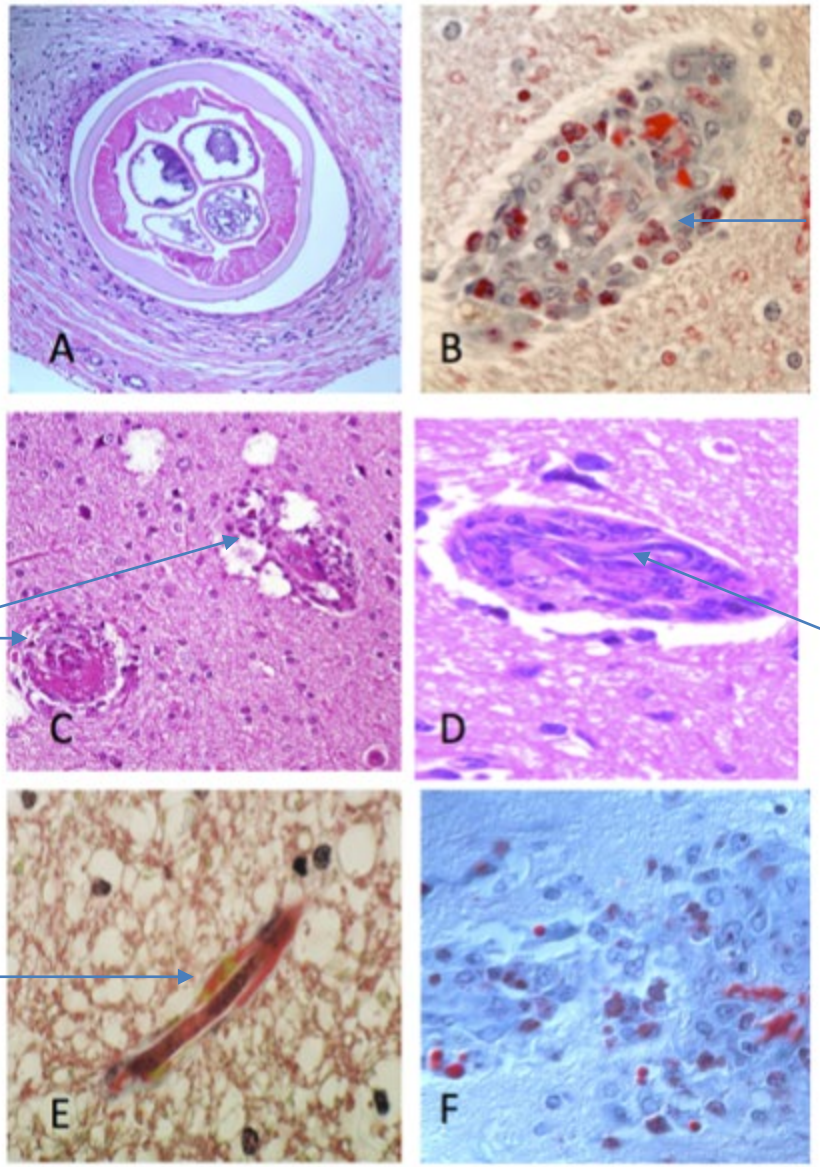
# Ivermectin treatment of *Loa loa* hyper-microfilaraemic baboons (*Papio anubis*): Assessment of microfilarial load reduction, haematological and biochemical parameters and histopathological changes following treatment

**Samuel Wanji[1,2]*, Ebanga-Echi J. Eyong[2,3,4], Nicholas Tendongfor[2], Che J. Ngwa[2], Elive N. Esuka[2], Arnaud J. Kengne-Ouafo[1,2], Fabrice R. Datchoua-Poutcheu[1,2], Peter Enyong[1,2], Dalen Agnew[5], Rob R. Eversole[6], Adrian Hopkins[7], Charles D. Mackenzie[8]**

# Baboon showing a  Typical Behavioral Response after Ivermectin Treatment: Depression and Reluctance to participate in normal activities

**Fig 5. The typical behavioral response after treatment: Depression and reluctance to participate in normal activities.**

https://doi.org/10.1371/journal.pntd.0005576.g005




**Blocked CNS vessel with eosinophils, Fibrin, Macrophages and L. loa Mf debris**

**Blocked CNS vessel with damage (Vacuolation of the Parenchyma)**

**Intact *L. loa* Mf caught in a cellular intravascular Mass in the CNS**

**A degenerated *L. loa* Mf in a Capillary of the CNS surrounded by Fibrin**

**Fig 10. Microscopic lesions present in the treated animals more than 72 hours after treatment.** A. Adult L. loa worm in connective tissue beneath the skin. B. Blocked CNS vessel comprised of eosinophils, fibrin, macrophages and parasite debris. C. Blocked CNS vessels with associated damage (vacuolation of the parenchyma). D. Intact microfilariae caught in a cellular intravascular mass in the CNS, E. A degenerating mf in a capillary of the CNS and surrounded by fibrin. F. Area of vascular and parenchymal damage in the CNS predominately filled with macrophages and eosinophils.

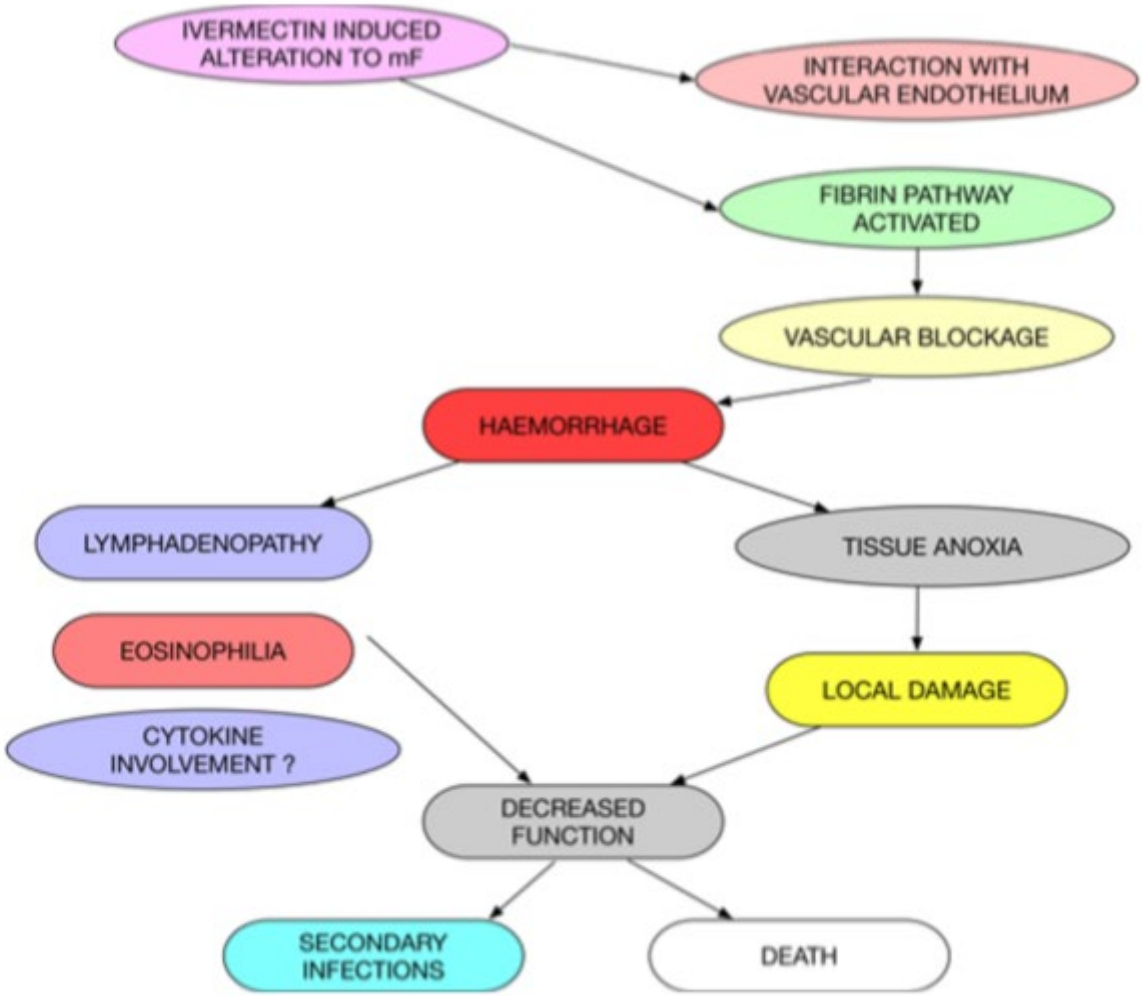



**Fig 11. Potential pathogenesis of Loa encephalopathy following the ivermectin treatment of Loa hyper-microfilaraemic individuals.**

https://doi.org/10.1371/journal.pntd.0005576.g011

# Development and Validation of In vitro Models of Loa loa

## With Implications for Drug Screening for Loaisis

Zofou et al. Parasites & Vectors (2018) 11:275
https://doi.org/10.1186/s13071-018-2852-2

Parasites & Vectors

RESEARCH Open Access

# Evaluation of *in vitro* culture systems for the maintenance of microfilariae and infective larvae of *Loa loa*

Denis Zofou[1,2†], Fanny Fri Fombad[1,3†], Narcisse V. T. Gandjui[1,3†], Abdel Jelil Njouendou[1,3†], Arnaud Jonas Kengne-Ouafo[1,3], Patrick W. Chounna Ndongmo[1,3], Fabrice R. Datchoua-Poutcheu[1], Peter A. Enyong[1], Dizzle Tayong Bita[1,3], Mark J. Taylor[4], Joseph D. Turner[4] and Samuel Wanji[1,3*†]

# Main Effects of different Factors on the Predicted Loa loa microfilariae and L3 Motility



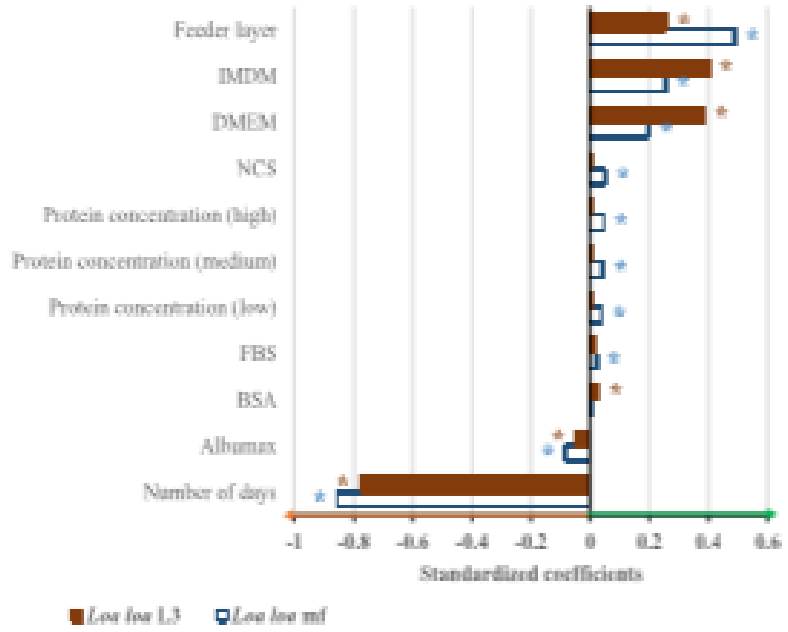



**Fig. 10** Graphical representation of the standardized coefficients of the main effects of different factors on the predicted *Loa loa* microfilariae and L3 motility. Adjusted $R^2$: *L. loa* mf = 0.709; *L. loa* L3 = 0.716

Njouendou et al. Parasites & Vectors (2018) 11:223
https://doi.org/10.1186/s13071-018-2799-3

Parasites & Vectors

RESEARCH Open Access

# Heterogeneity in the in vitro susceptibility of *Loa loa* microfilariae to drugs commonly used in parasitological infections

Abdel J. Njouendou[1†], Fanny F. Fombad[1†], Maeghan O'Neill[2], Denis Zofou[3], Chuck Nutting[4], Patrick C. Ndongmo[1], Arnaud J. Kengne-Ouafo[1], Timothy G. Geary[2], Charles D. Mackenzie[5,6†] and Samuel Wanji[1*†]

## Mortality of *L. loa* Microfilariae Exposed to different Concentrations of the active drugs

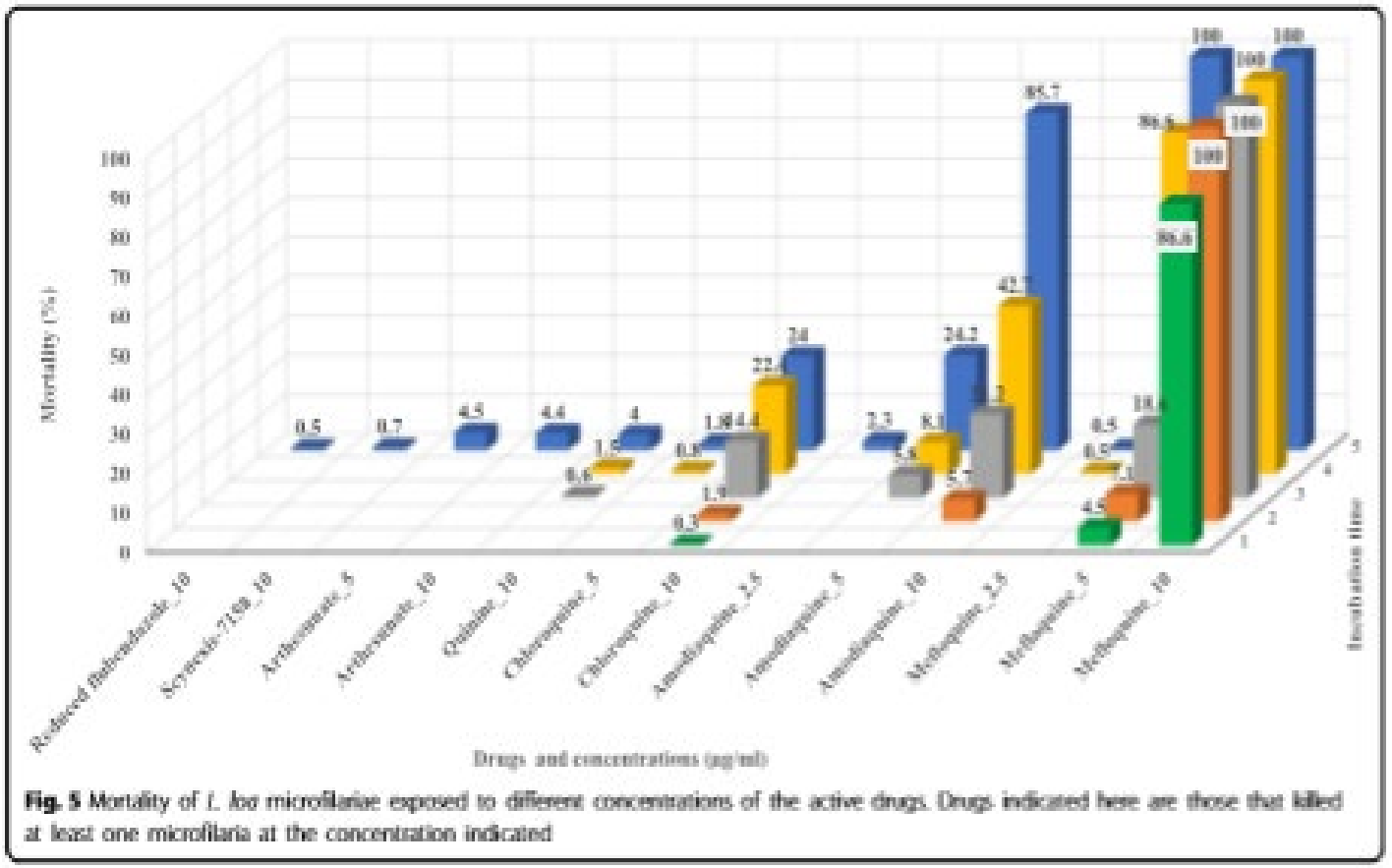



**Fig. 5** Mortality of *L. loa* microfilariae exposed to different concentrations of the active drugs. Drugs indicated here are those that killed at least one microfilaria at the concentration indicated

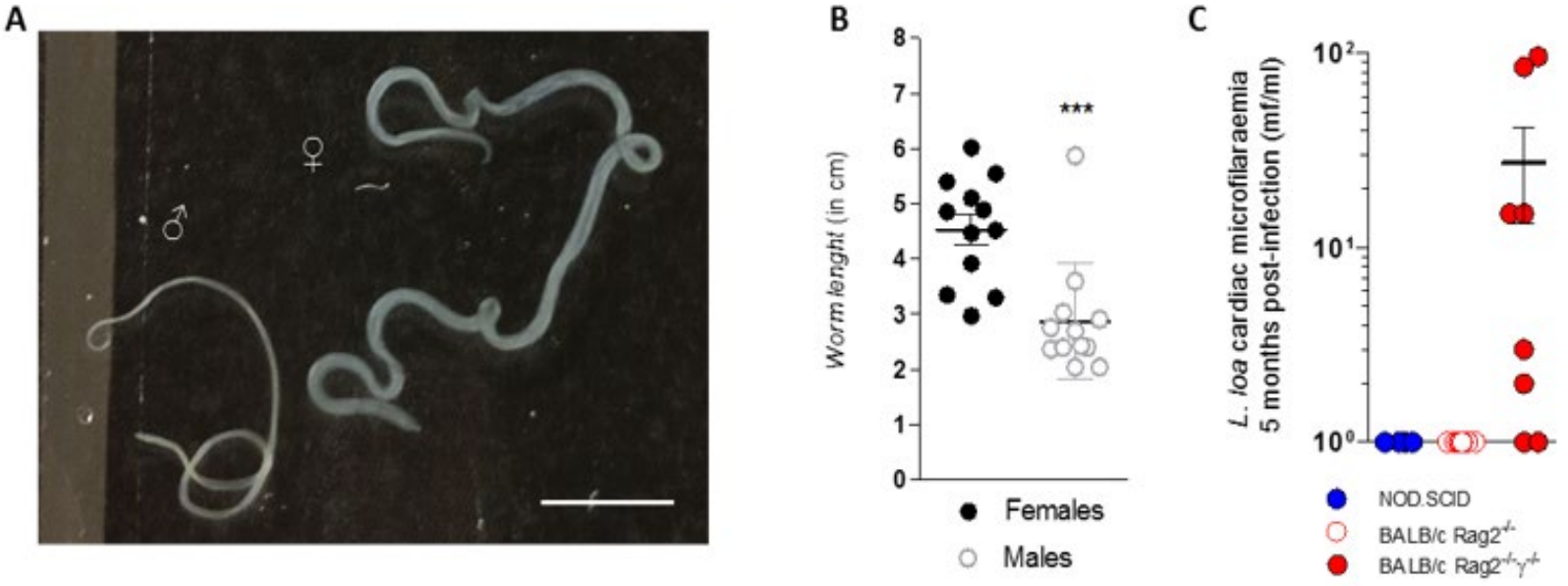
# Mouse models of *Loa loa* for anti-filarial translational research

Nicolas P Pionnier[1, †], Hanna Sjoberg[1, †], Haelly M Metuge[2,3], Valerine C Chunda[2,3], Abdel J Njouendou[2,3], Fanny F Fombad[2,3], Dizzle B Tayong[2,3], Narcisse V Gandjui[2,3], Desmond N Akumtoh[2,3], Patrick W Chounna[2,3], Bertrand L Ndzeshang[2,3], Mark J Taylor[1], Samuel Wanji[2,3] and Joseph D Turner[1, *]

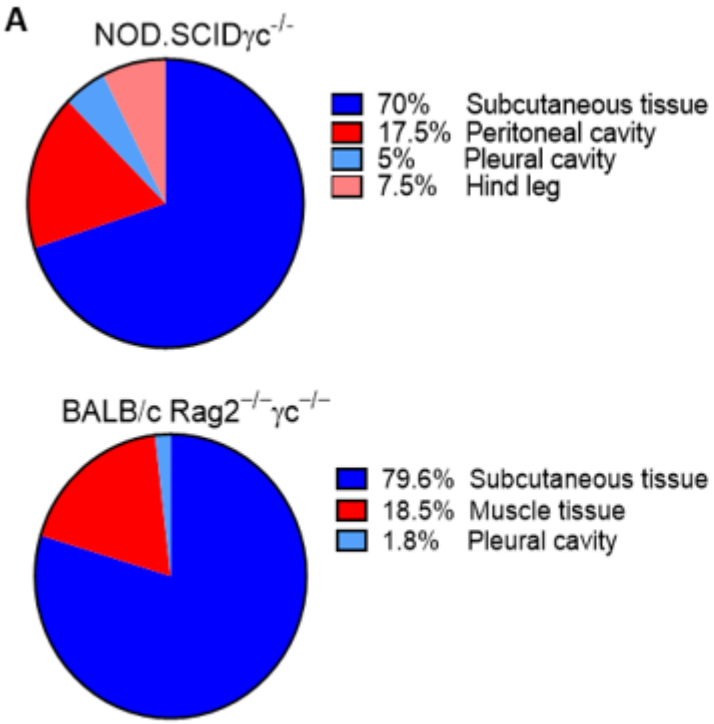
STERILE HOOD + $CO_2$ INCUBATOR

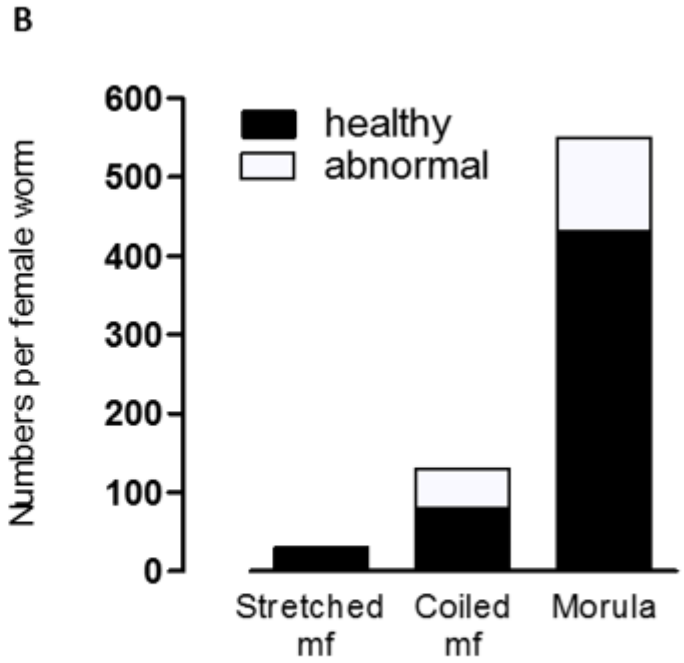
Rearing of sensitive mice within IVCC system

**Recovered *L. loa* adult worms from mice 5 months post-infection were viable and fully mature**

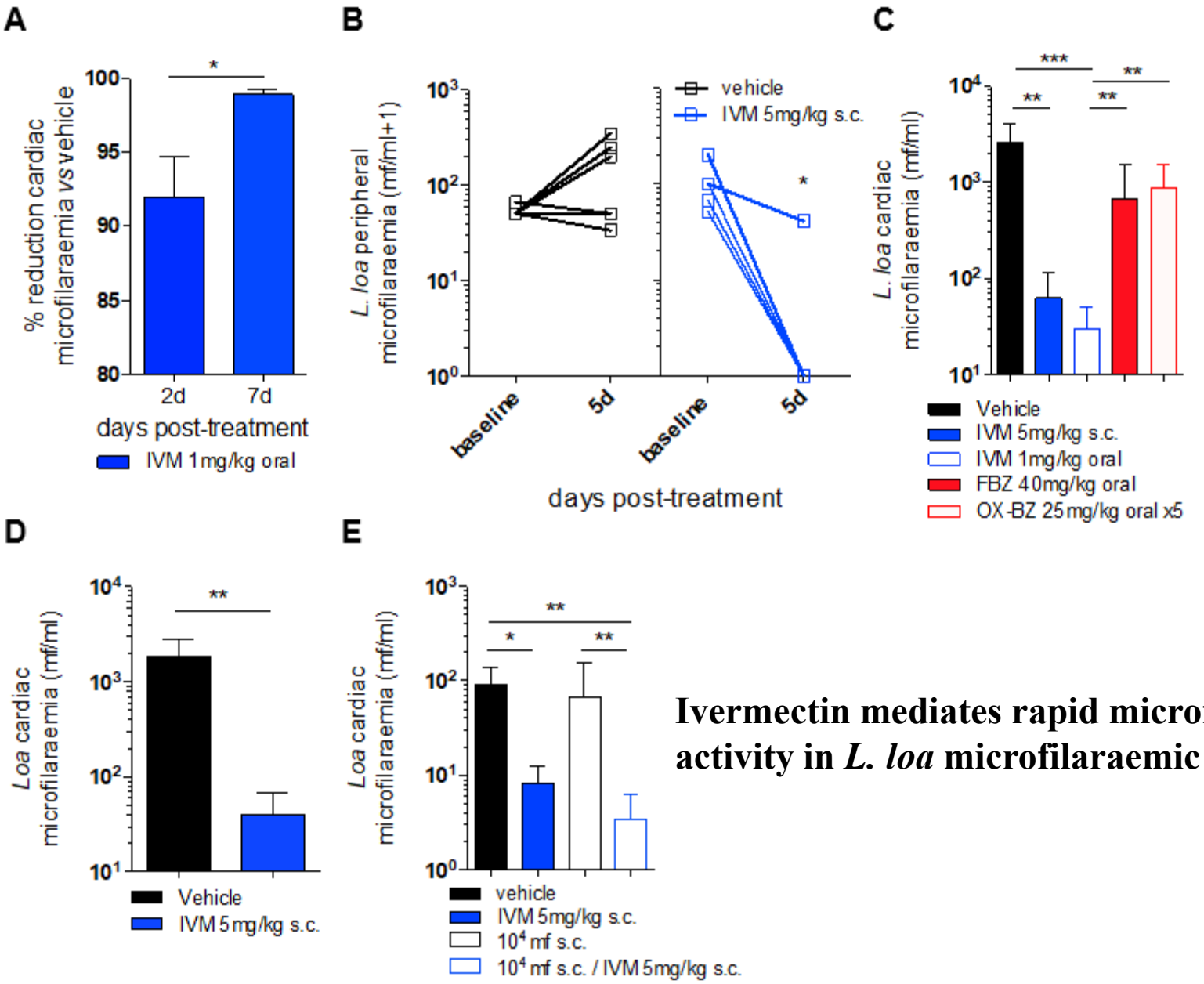


**Tissue distributions of adult *L. loa* in NOD.SCIDγc$^{-/-}$ or BALB/c RAG2$^{-/-}$γc$^{-/-}$ mice 1-month post-infection**




**Embryogram outcome from *L. loa* females recovered from RAG2$^{-/-}$ mice implanted with *L. loa* adults and culled 1 month post-implant**




**Ivermectin mediates rapid microfilaricidal activity in *L. loa* microfilaraemic mice.**

# General platform

Infected Chrysops silacea
(l development)

Production of Infective larvae (L3)

K.O. mice
s.c./i.p. iniection

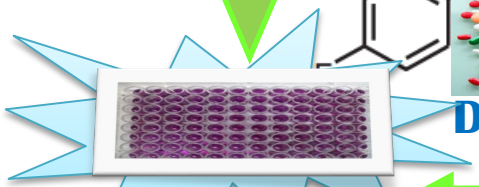
Baboons (animal reservoir of mf)

Production of mf

Cultu re syste m

L4 --> L5
Recovery:
s.c. 20-80%;

Drugs



In vitro drug screening

In vivo drug pre-clinical

Achieveme
developm
ent

Under optimization

K.O. mice
i.v.
injection

In vivo drug model screening

# REFOTDE: VISION FOR THE FUTURE

Hospital and Clinical Research Centre


Laboratory Technology Building
Community and Public Engagement Building
Epidemiology & Global Health Building
Hospital Building

***Thank You For Your Technical and Financial Support***


BILL & MELINDA GATES foundation

universitäts klinikum bonn

MICHIGAN STATE UNIVERSITY

MECTIZAN® DONATION PROGRAM

LSTM LIVERPOOL SCHOOL OF TROPICAL MEDICINE

DFG Deutsche Forschungsgemeinschaft


IRD Institut de Recherche pour le Développement FRANCE

Federal Ministry of Education and Research


MRC Medical Research Council

wellcome

DFID Department for International Development

DNDi Drugs for Neglected Diseases *initiative*

The African Academy of Sciences