



**QIMR Berghofer**  
Medical Research Institute



## Sornchai Looareesuwan Medal Lecture

“New Tools in the Neglected Tropical Diseases Armoury”



Prof. Donald Peter McManus



International Tropical Medicine Meeting  
14<sup>th</sup> December 2018

**Parasites have killed more humans  
than all the wars in history!**



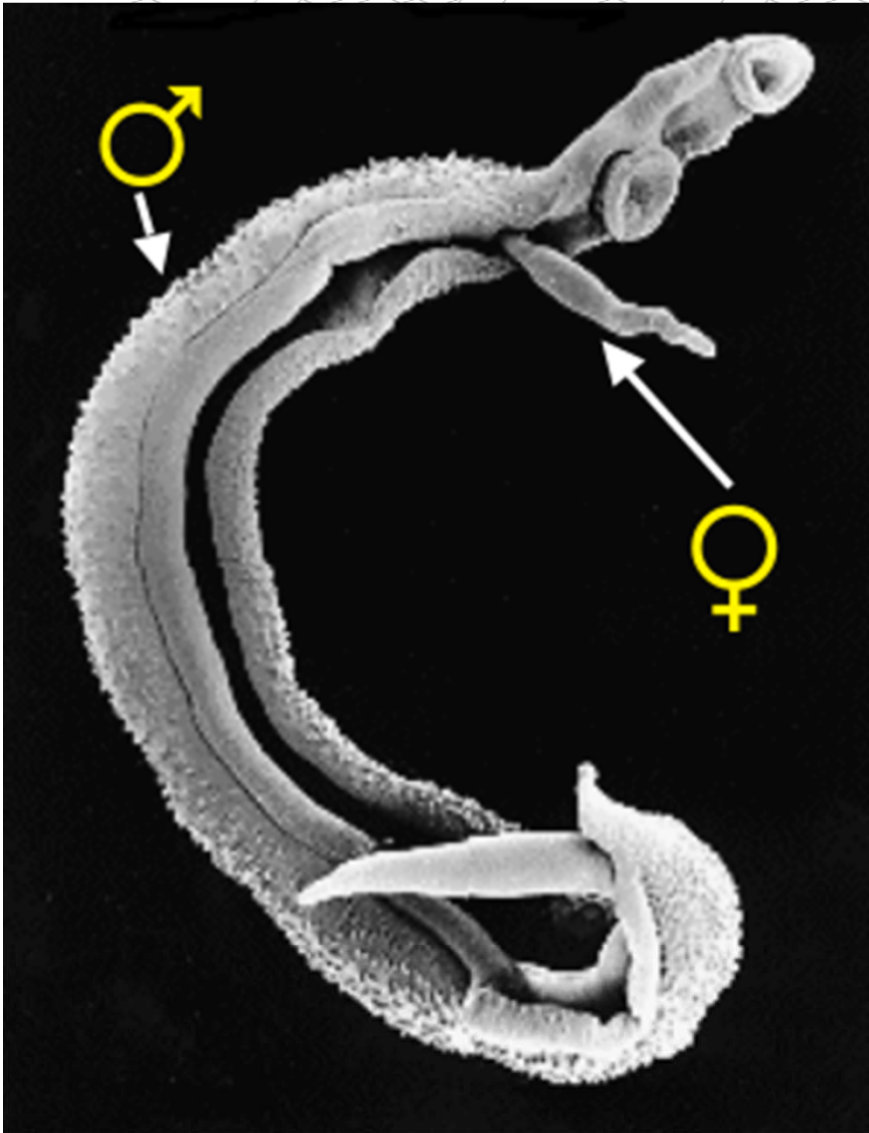


Image 1a

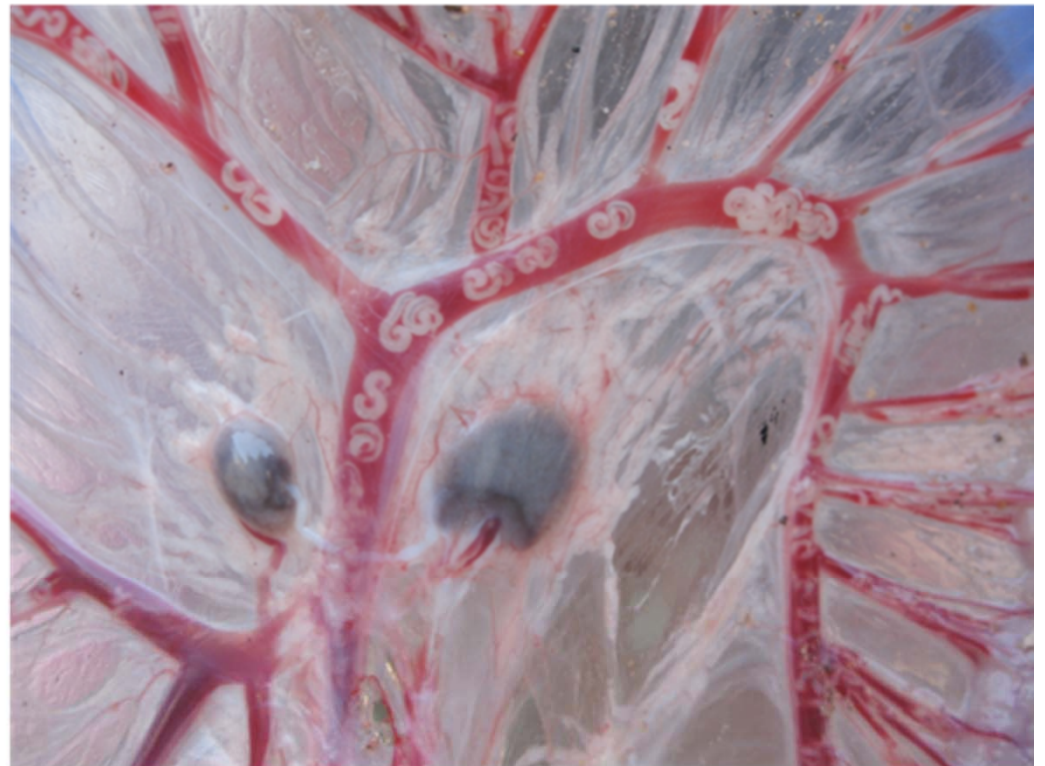


Image 1b





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## Concept: Innovation, Translation, and Impact - Lecture Overview

1. *New Diagnostics for Schistosomiasis*
2. *High Quality Reference Genomes of Neglected Pathogens: a Platform for Development of Targeted Interventions*
3. *The Magic Glasses Asia Research Program for the Prevention of Intestinal Worms*
4. *Outcomes of a Multicomponent Schistosomiasis Control Trial in China*
5. *Polyparasitism and the gut microbiome in humans from the Philippines*





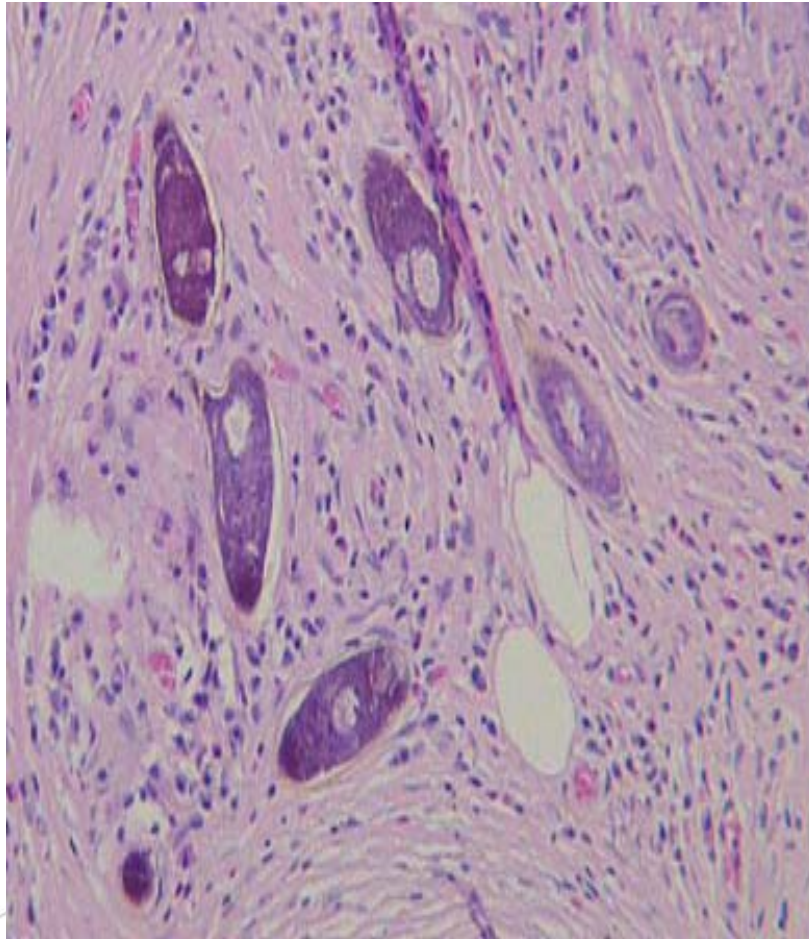


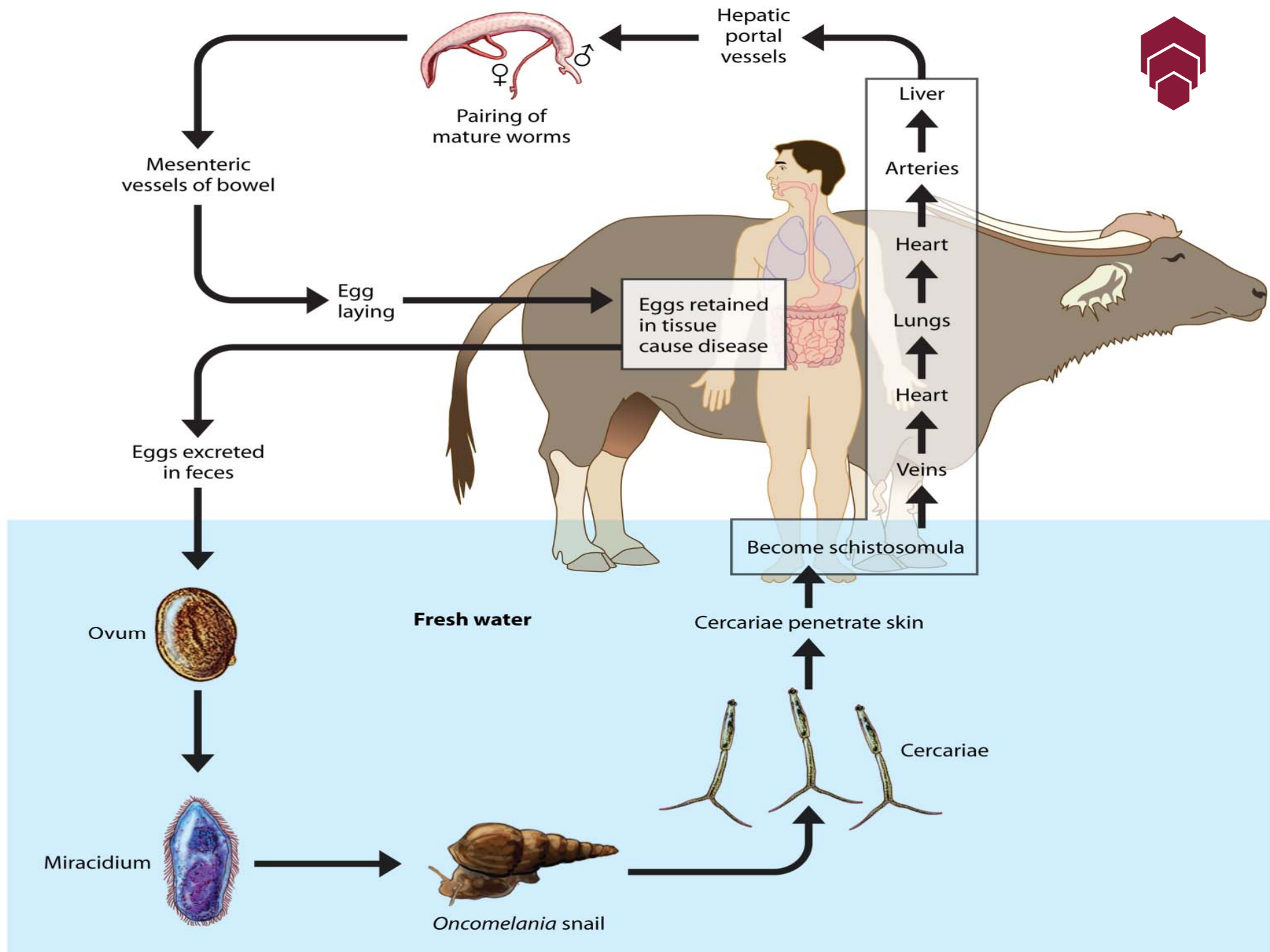
# **1. *New Diagnostics for Asian Schistosomiasis***

## **Schistosomiasis in China and the Philippines**


- In China, very successful control efforts – reduced infection prevalence from 11.6 million Chinese in 1950s to 290,000 in 2015.
- Schistosomiasis control has been/is of high priority for the Chinese Government along with HIV/AIDS and TB.
- Elimination now on the horizon.
- In contrast, in the Philippines control has been sporadic and complicated due to inadequate funding and the zoonotic nature of schistosomiasis. There are approximately 865,000 people infected and another seven million at risk of infection.

# ***Schistosoma* eggs cause pathology and disease**







- 
- **Elimination through integrated intervention approaches is the focus of current schistosomiasis control efforts.**
  - **Precise diagnosis of schistosome infections will be critical in achieving these goals, particularly in areas such as China where extensive control has reduced schistosomiasis to very low levels to the point where elimination is now on the horizon.**

# Three new diagnostic tools for *Schistosoma japonicum* we developed and tested:

1. A real-time polymerase chain reaction (qPCR)-based (for humans and animals) assay for humans and animals.
2. A droplet digital PCR assay detecting *S. japonicum* cell free DNA (cfDNA) in serum, urine, salivary glands, and feces.
3. An IgG-based serum antibody ELISA incorporating a combination of two recombinant *S. japonicum* antigens.



# 1. Real-time PCR diagnosis of *Schistosoma japonicum* in low transmission areas of China – pilot study

- Mass drug treatment and reservoir host removal in endemic areas has decreased *S. japonicum* prevalence to <5%
- Kato-Katz and MHT have low sensitivity at low intensity infections
  - How then to determine true prevalence and assess elimination interventions?
  - MHT and qPCR (*nad1* gene) on human and animal stools from four provinces in



He et al. *Infectious Diseases of Poverty* (2018) 7:8  
DOI 10.1186/s40249-018-0390-y

Infectious Diseases of Poverty

RESEARCH ARTICLE

Open Access

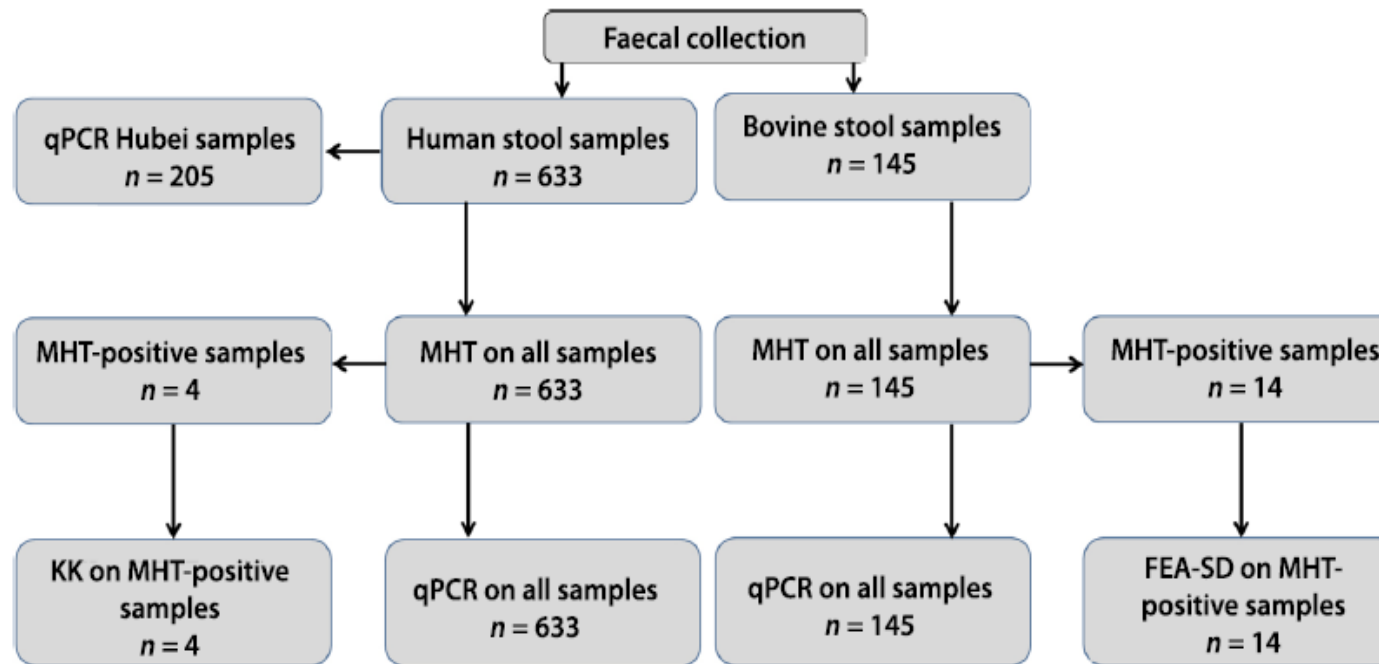
## Real-time PCR diagnosis of *Schistosoma japonicum* in low transmission areas of China



Pei He<sup>1†</sup>, Catherine A. Gordon<sup>2†</sup>, Gail M. Williams<sup>3</sup>, Yuesheng Li<sup>1,2</sup>, Yuanyuan Wang<sup>1</sup>, Junjian Hu<sup>1</sup>, Darren J. Gray<sup>2,3,4</sup>, Allen G. Ross<sup>5</sup>, Donald Harn<sup>6</sup> and Donald P. McManus<sup>2\*</sup>



# Real-time PCR diagnosis of *Schistosoma japonicum* in low transmission areas of China



**Fig. 2** Flow diagram showing breakdown of the diagnostic techniques and numbers of human and bovine stool samples subjected to analysis

# Procedure for analysis of human/bovine faeces for the presence of *S. japonicum* DNA

Stool  
Collection



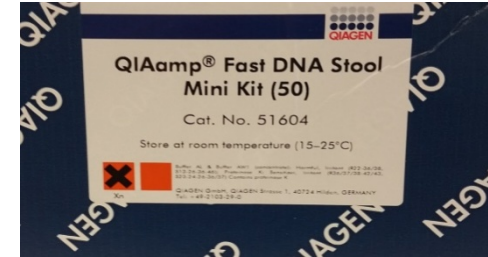
Fix (80% ethanol)



Weigh (200mg)  
& wash (H<sub>2</sub>O)



Extract using  
Qiagen Stool kit  
as per protocol



Add Inhibitex buffer  
and vortex



Heat (95°C),  
centrifuge



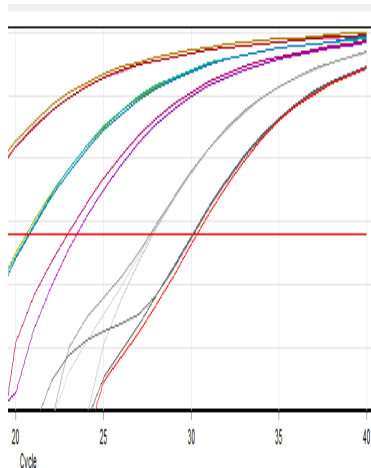
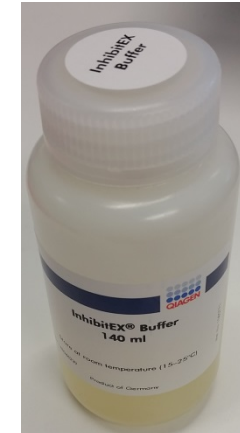
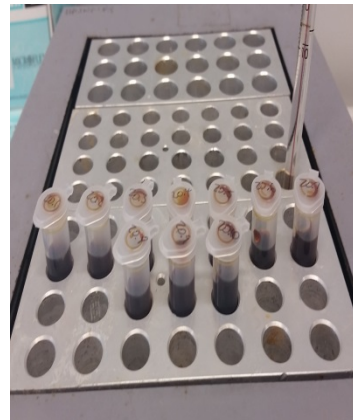
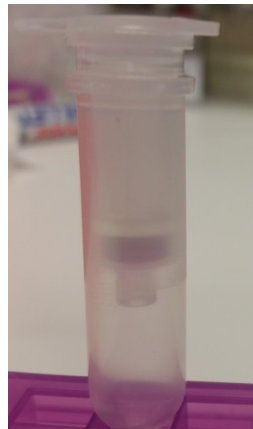
Proteinase K  
to  
supernatant,  
heat 70°C



Apply to  
spin  
column



qPCR from DNA



# Real-time PCR diagnosis of *Schistosoma japonicum* in low transmission areas of China

**Table 2** Prevalence of *S. japonicum* in humans by the MHT and qPCR assay

Province	Village	N	MHT			qPCR			P-value (McNemar)
			No. Positive	Prevalence (%)	95% CI	No. Positive	Prevalence (%)	95% CI	
Anhui	Zhongxing	89	0	0.00	.	9	10.11	3.73, 16.50	0.003
	Muxiahe	69	0	0.00	.	4	5.80	1.42, 11.45	0.046
Jiangxi	Xiguang	107	1	0.93	-0.92, 2.79	11	10.28	4.43, 16.13	0.002
	Biaoen	100	0	0.00	.	13	13.00	6.29, 19.71	< 0.001
Hunan	Yuewu	63	3	4.76	-0.64, 10.17	17	26.98	15.72, 38.25	< 0.001
Hubei	Xiti	123	.	.	.	8	6.50	2.08, 10.92	0.0043
	Yanchuan	82	.	.	.	8	9.76	3.20, 16.32	0.004
<b>Total</b>		<b>633</b>	<b>4</b>	<b>0.93</b>	<b>0.02, 1.85</b>	<b>70</b>	<b>11.06</b>	<b>9.46, 15.78</b>	<b>&lt; 0.0001</b>



The final row of each table is in bold to denote that these are total numbers

**Table 3** Prevalence of *S. japonicum* in bovines by the MHT and qPCR assay

Village	N	MHT			qPCR			P-value (McNemar)
		No. positive	Prevalence (%)	95% CI	No. positive	Prevalence (%)	95% CI	
Xiguang	63	5	7.90	1.07, 14.80	14	22.22	11.67, 32.78	0.007
Biaoen	51	1	1.96	-2.00, 5.90	9	17.65	6.82, 28.48	0.005
Wuyi	38	1	2.63	-2.70, 7.96	5	13.16	1.90, 24.42	0.046
Yuewu	30	7	2.33	7.27, 39.40	17	56.67	37.85, 75.49	0.002
Animal type								
Cattle	70	9	12.90	4.82, 20.90	23	32.86	21.58, 44.14	0.0005
Buffalo	112	5	4.46	0.58, 8.34	22	19.64	12.17, 27.12	< 0.0001
<b>Total</b>	<b>182</b>	<b>14</b>	<b>7.69</b>	<b>3.78, 11.60</b>	<b>45</b>	<b>24.73</b>	<b>18.40, 31.05</b>	<b>&lt; 0.0001</b>



The final row of each table is in bold to denote that these are total numbers



# Is elimination of schistosomiasis in China by 2025 feasible?

## In a 5 year (2016-2020) ongoing NHMRC project we are:

- Monitoring the impact of the National Schistosomiasis Control Programme in 16 sentinel villages in the Dongting and Poyang Lakes areas of the P.R. China.
- We are using a field-verified loop-mediated isothermal amplification (LAMP)-based assay (snails) and our real-time PCR diagnostic (bovines, humans) alongside the currently implemented methods (Miracidial Hatching Test and Kato Katz).
- The true endemic picture and impact of schistosomiasis control in the P.R. China can only be measured accurately by implementing more sensitive diagnostic techniques than are used currently.

*2. High Quality Reference Genomes  
of Neglected Pathogens: a Platform  
for Development of Targeted  
Interventions*

# From *Schistosoma japonicum* (397 Mb) to *Echinococcus granulosus* (152 Mb)

Vol 460 | 16 July 2009 | doi:10.1038/nature08140

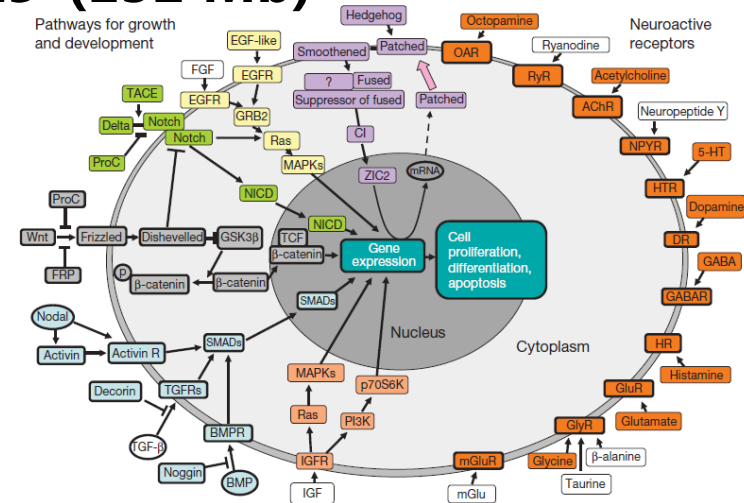
nature

ARTICLES

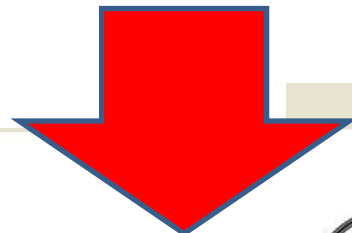
## The *Schistosoma japonicum* genome reveals features of host-parasite interplay

The *Schistosoma japonicum* Genome Sequencing and Functional Analysis Consortium\*

*Schistosoma japonicum* is a parasitic flatworm that causes human schistosomiasis, which is a significant cause of morbidity in China and the Philippines. Here we present a draft genomic sequence for the worm. The genome provides a global insight into the molecular architecture and host interaction of this complex metazoan pathogen, revealing that it can exploit host nutrients, neuroendocrine hormones and signalling pathways for growth, development and maturation. Having a complex



151.6 Mb

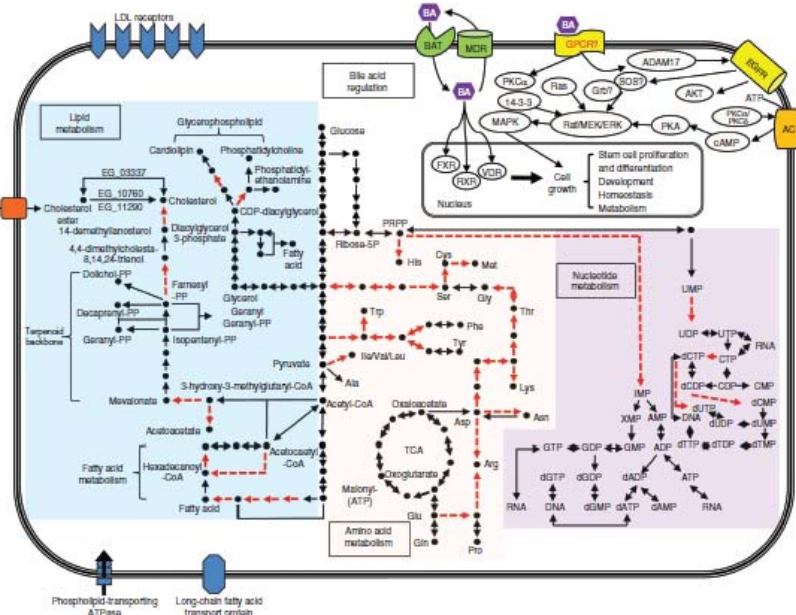


nature genetics

OPEN

## The genome of the hydatid tapeworm *Echinococcus granulosus*

Huajun Zheng<sup>1,12</sup>, Wenbao Zhang<sup>2,12</sup>, Liang Zhang<sup>1,3,12</sup>, Zhuangzhi Zhang<sup>4</sup>, Jun Li<sup>5</sup>, Gang Lu<sup>1</sup>, Yongqiang Zhu<sup>1</sup>, Yuezhu Wang<sup>1</sup>, Yin Huang<sup>1</sup>, Jing Liu<sup>3</sup>, Hui Kang<sup>1</sup>, Jie Chen<sup>1</sup>, Lijun Wang<sup>1</sup>, Aojun Chen<sup>1</sup>, Shuting Yu<sup>1</sup>, Zhengchao Gao<sup>1</sup>, Lei Jin<sup>1</sup>, Wenyi Gu<sup>1</sup>, Zhiqin Wang<sup>1</sup>, Li Zhao<sup>4</sup>, Baoxin Shi<sup>4</sup>, Hao Wen<sup>2</sup>, Renyong Lin<sup>2</sup>, Malcolm K Jones<sup>5,11</sup>, Brona Brejova<sup>6</sup>, Tomas Vinar<sup>6</sup>, Guoping Zhao<sup>1,3</sup>, Donald P McManus<sup>5</sup>, Zhu Chen<sup>1,7-9</sup>, Yan Zhou<sup>3</sup> & Shengyue Wang<sup>1,3,10</sup>



ARTICLES







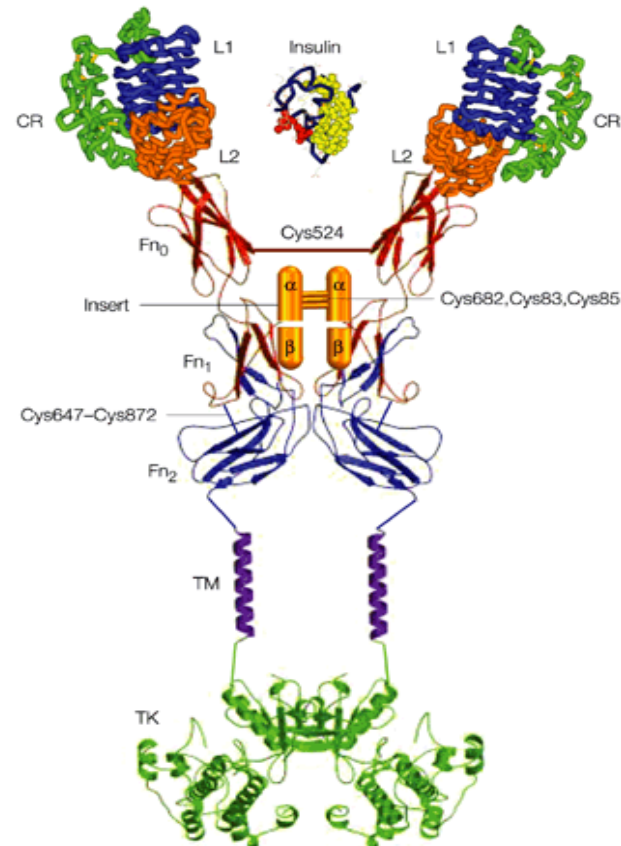
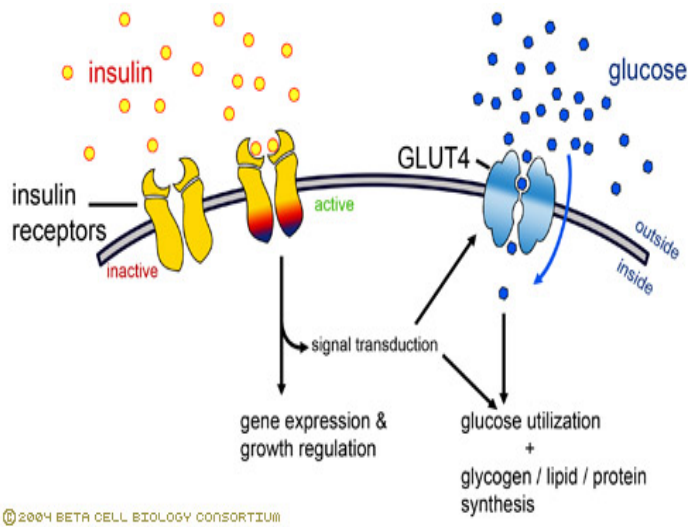




**McManus – Kenya, 1981 Collecting hydatid cysts for biochemical analysis** © Queensland Institute of Medical Research | 19



# A new vaccine candidate: insulin receptor



**$\alpha$  Subunit**  
LD domain  
of S<sub>J</sub>IR-1 (1181aa)  
and S<sub>J</sub>IR-2 (1089aa)

**$\beta$  Subunit**  
TK domain  
of S<sub>J</sub>IR-1 (352aa)  
and S<sub>J</sub>IR-2 (609aa)

Nature Reviews | Drug Discovery

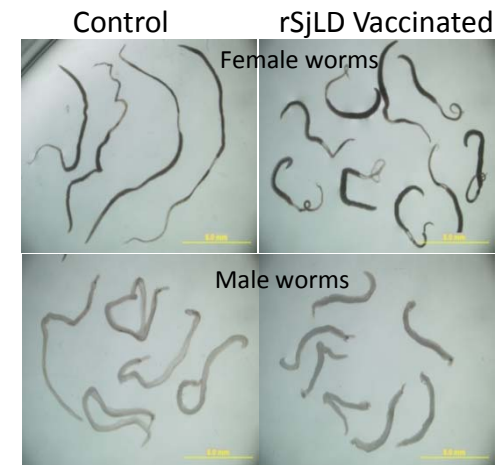
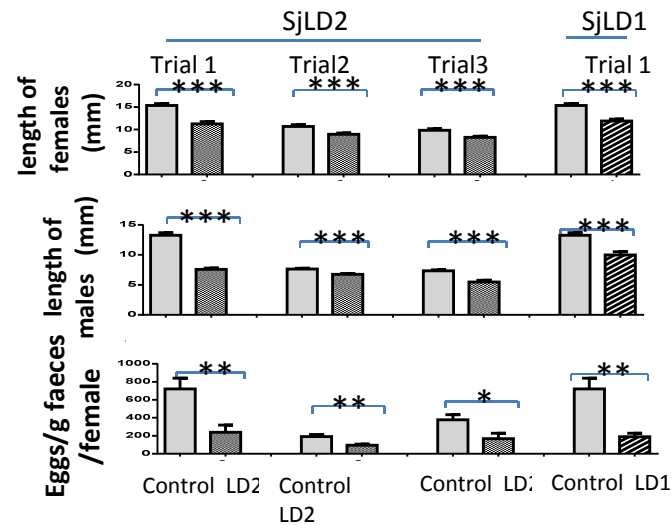


# Transmission blocking vaccine candidates

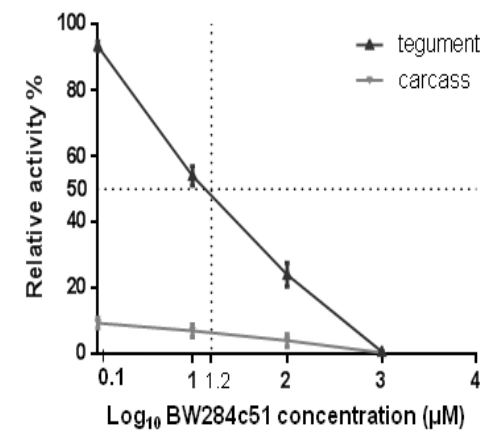
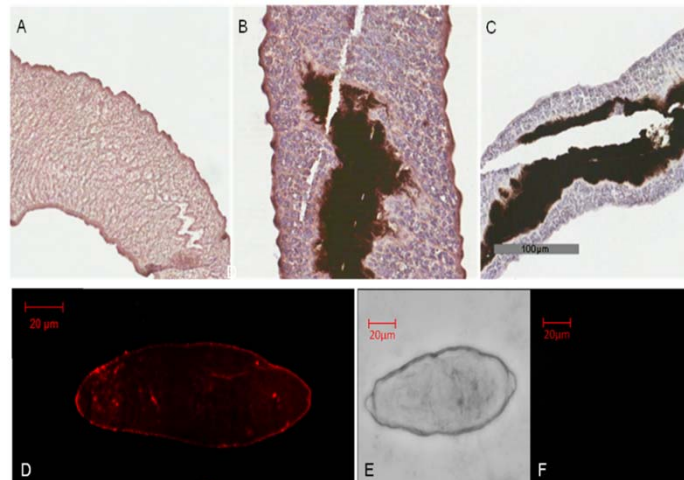
## Hong You, Marina Harvie, Biniam Tebeje, Xiaofeng Du



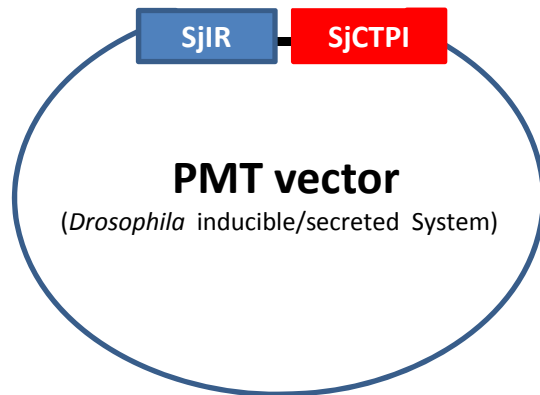
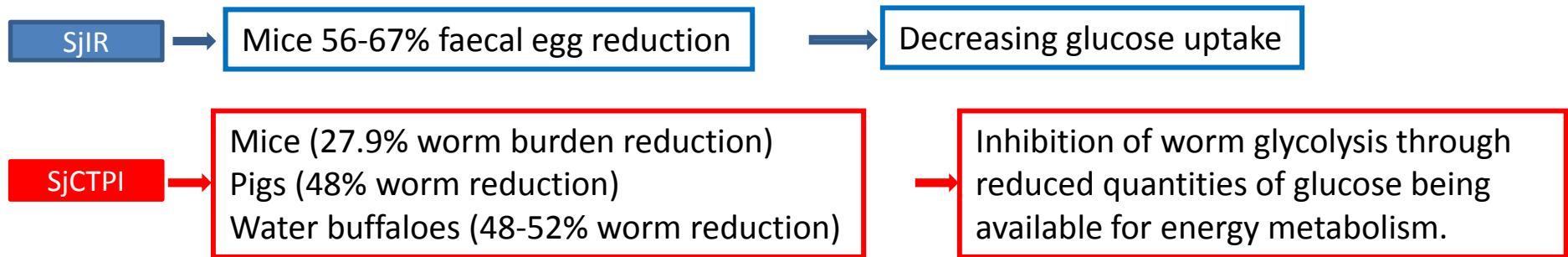
1. Ligand domain of the *S. japonicum* insulin receptor (SjIR) fusion proteins induced a significant retardation in worm growth (12-42% reduction in worm lengths) and depressed fecundity (56-67% faecal egg reduction) against cercarial challenge in the murine model.



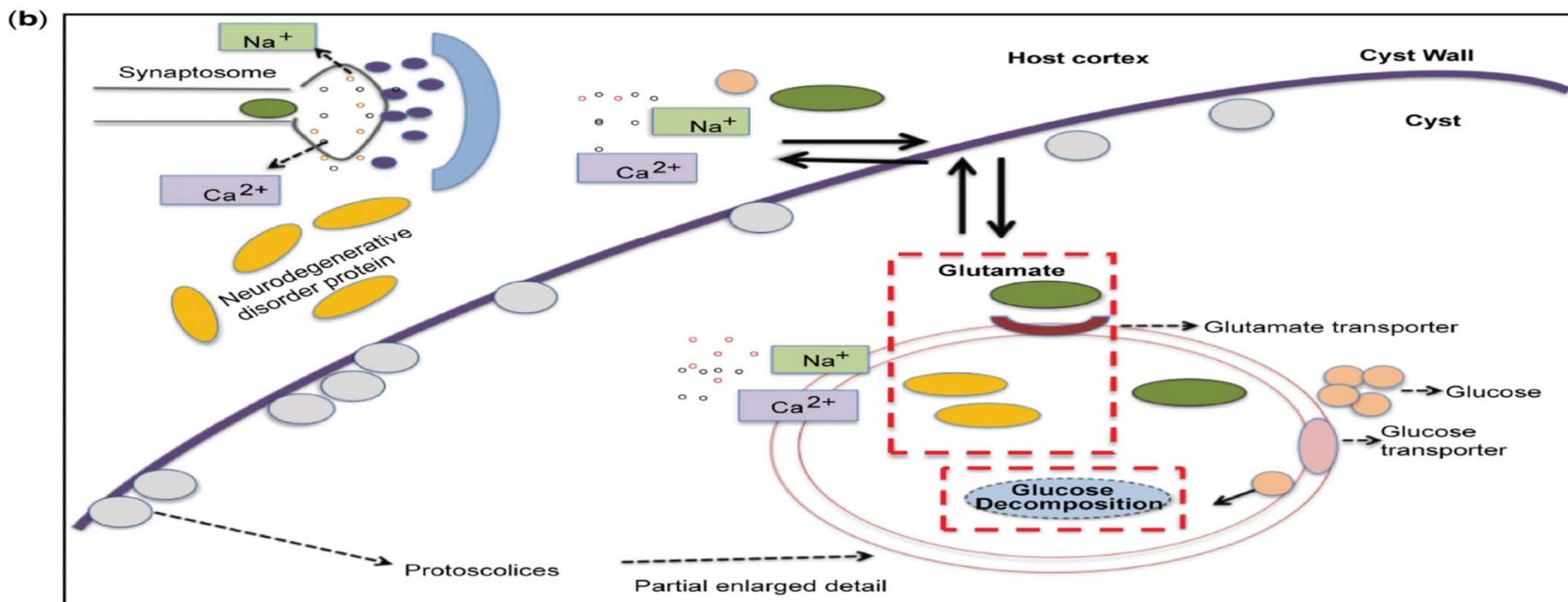
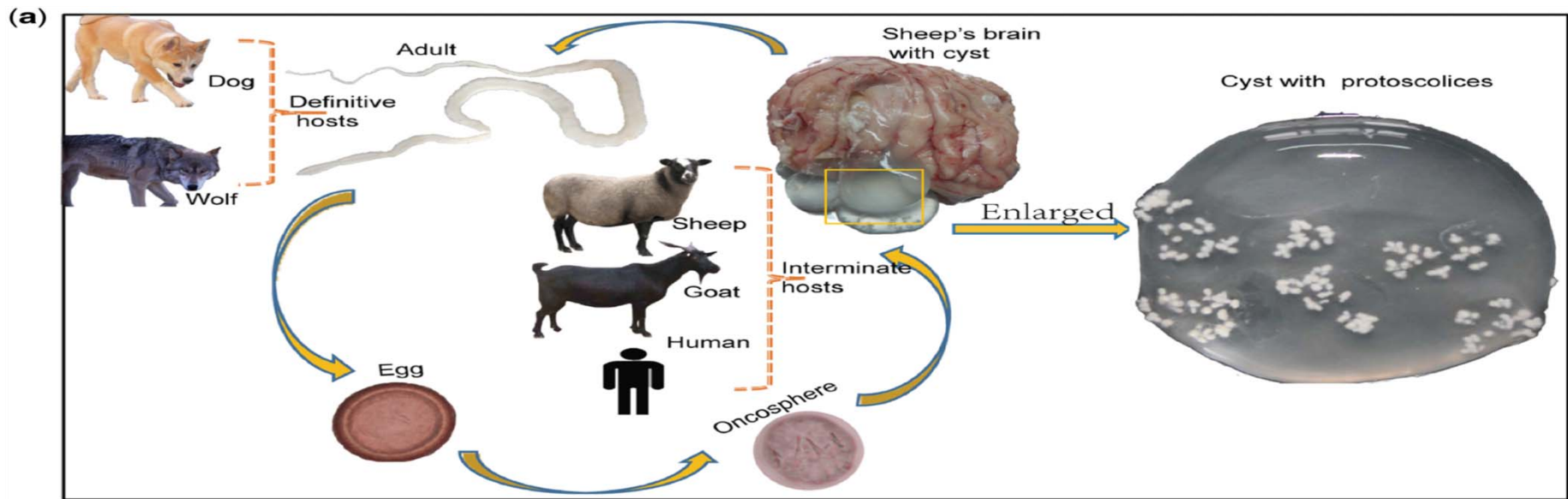
2. *S. japonicum* acetylcholinesterase (SjAChE) is located on the surface of adult worms and schistosomula. The relatively high abundance of AChE activity (90%) present on the surface of adult *S. japonicum*, suggests SjAChE is a good drug or vaccine target.



# Current work: Novel multivalent vaccine



To generate highly efficacious veterinary-based multivalent transmission blocking vaccines in bovines against schistosome infection in endemic areas in China/Philippines in the future.



Genome of the tapeworm *Taenia multiceps* (240 Mb) sheds light on understanding parasite biology and the control of devastating coenurosis disease. *DNA Research* 2018.

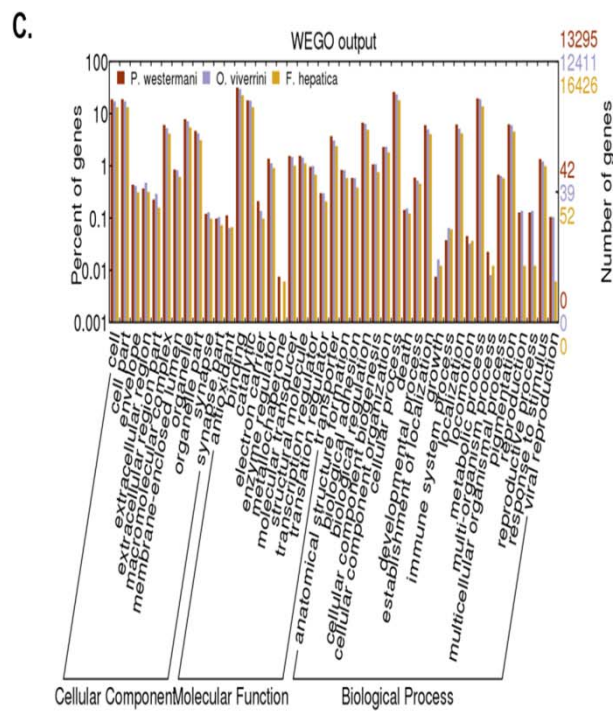
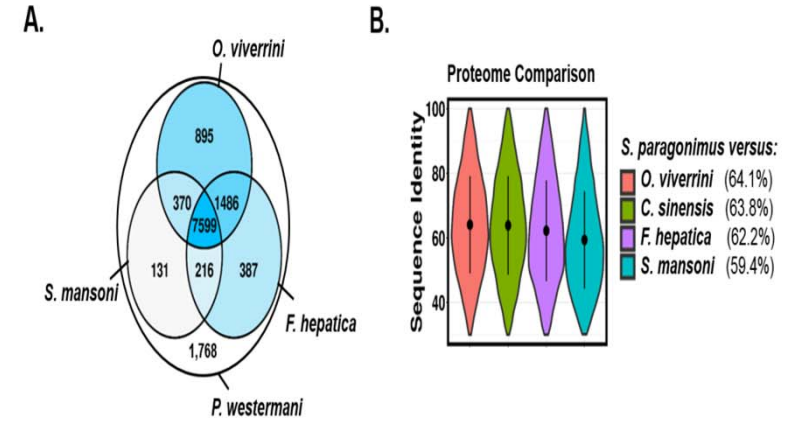
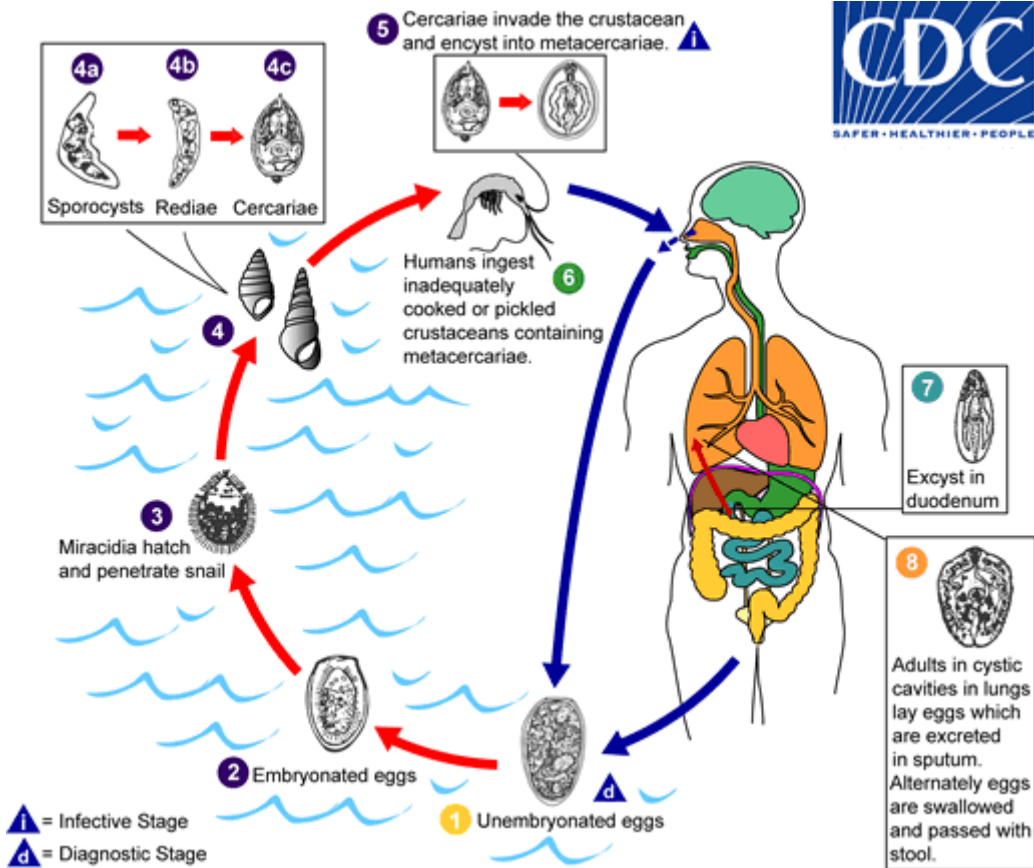




***PLOS PATHOGENS* (in press) - Whole-genome sequence (374 Mb) of the bovine blood fluke *Schistosoma bovis* reveals further evidence for interspecies hybridization with *S. haematobium***

- ***S. bovis* primarily infects bovines, with important economic consequences in affected countries.**
- **However, it is also a close relative of the human, carcinogenic parasite *Schistosoma haematobium*, which is a serious health issue in many countries in Sub-Saharan Africa.**
- **The close relationship and overlapping geographical distribution of *S. bovis* and *S. haematobium* allows these to hybridise in the wild increasing their genetic diversity and presenting the risk of zoonotic transmission, i.e. the transmission from animals to humans.**
- **By whole-genome sequencing and assembly of an *S. bovis* worm pair we present evidence that fertile hybrids are indeed present in the wild, presenting the risk of transmission from animal reservoirs to humans.**
- ***S. bovis* has recently come into the spotlight as a possible emerging health threat following the molecular identification of *S. haematobium-bovis* hybrids from children in Senegal and during recent schistosomiasis outbreaks in Corsica.**
- **A tropical parasitic disease has invaded Europe, thanks to a hybrid of two infectious worms.**

# Whole-genome sequence (1.1 Gb) of the oriental lung fluke *Paragonimus westermani* (*GigaScience* in press)



# *Biomphalaria glabrata* genome - 916 Mb



ARTICLE

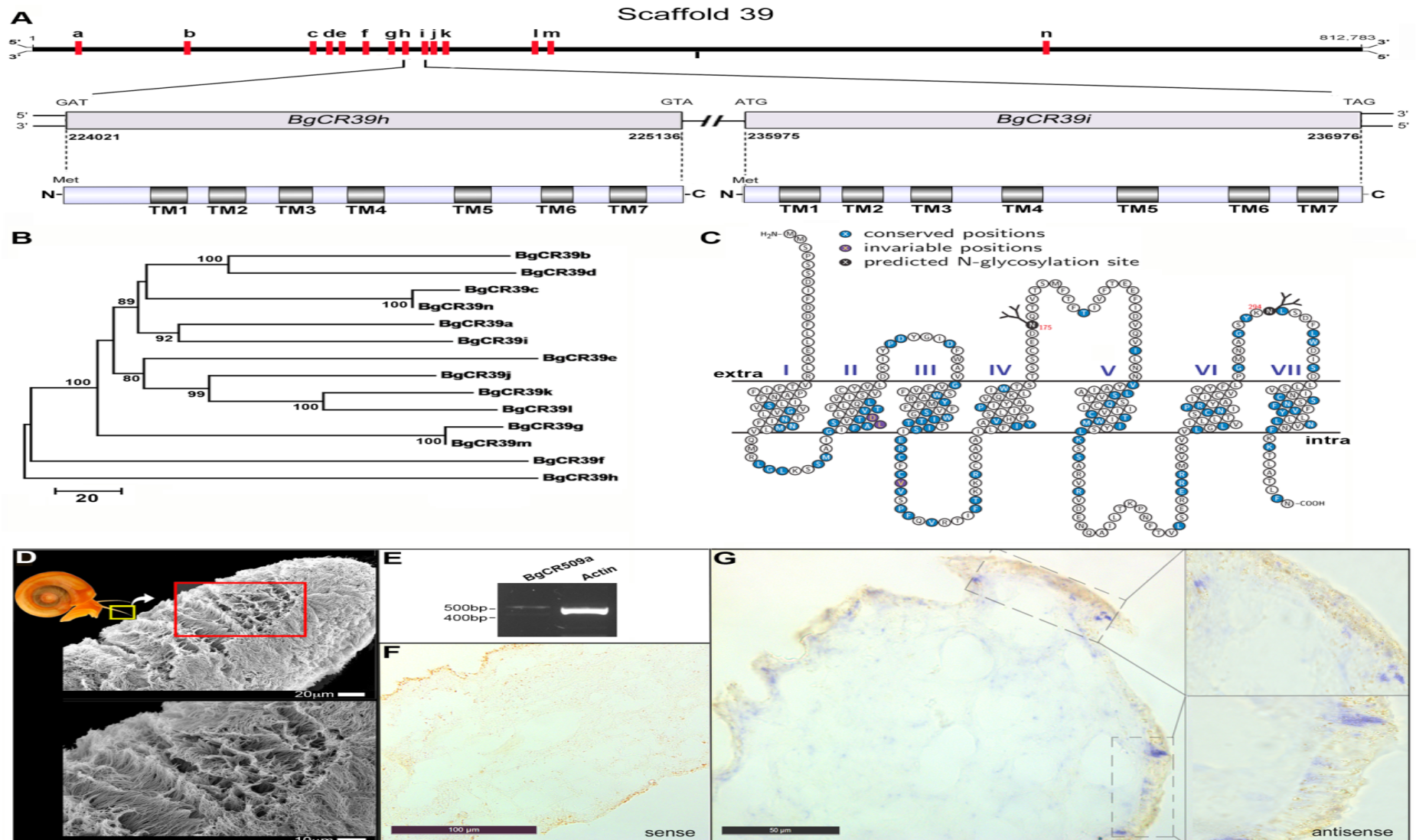
Received 25 Feb 2016 | Accepted 30 Mar 2017 | Published 16 May 2017

DOI: [10.1038/ncomms15451](https://doi.org/10.1038/ncomms15451)

OPEN

Whole genome analysis of a schistosomiasis-transmitting freshwater snail

# Candidate chemosensory receptors of *B. glabrata*.





# Research offers sniff of success over 'snail fever' (Scott Cummings, USC)

- “The work in Australia involved a long standing collaboration with **Professor Don McManus at the QIMR Berghofer Medical Research Institute in Brisbane**, which can house the snails for research.”
- “We discovered that pheromones released by the snail may be used by the parasite to locate the host snail.”
- “We also identified the olfactory receptors used by the snail to smell, and the neurohormones used by the snail to reproduce and grow.”
- “There is potential to change these pheromones, receptors or neurohormones to prevent the parasite from entering the host snail.”

### 3. *The Magic Glasses Asia Research Program for the Prevention of Intestinal Worms*





Roundworm *Ascaris lumbricoides*



Whipworm *Trichuris trichiura*

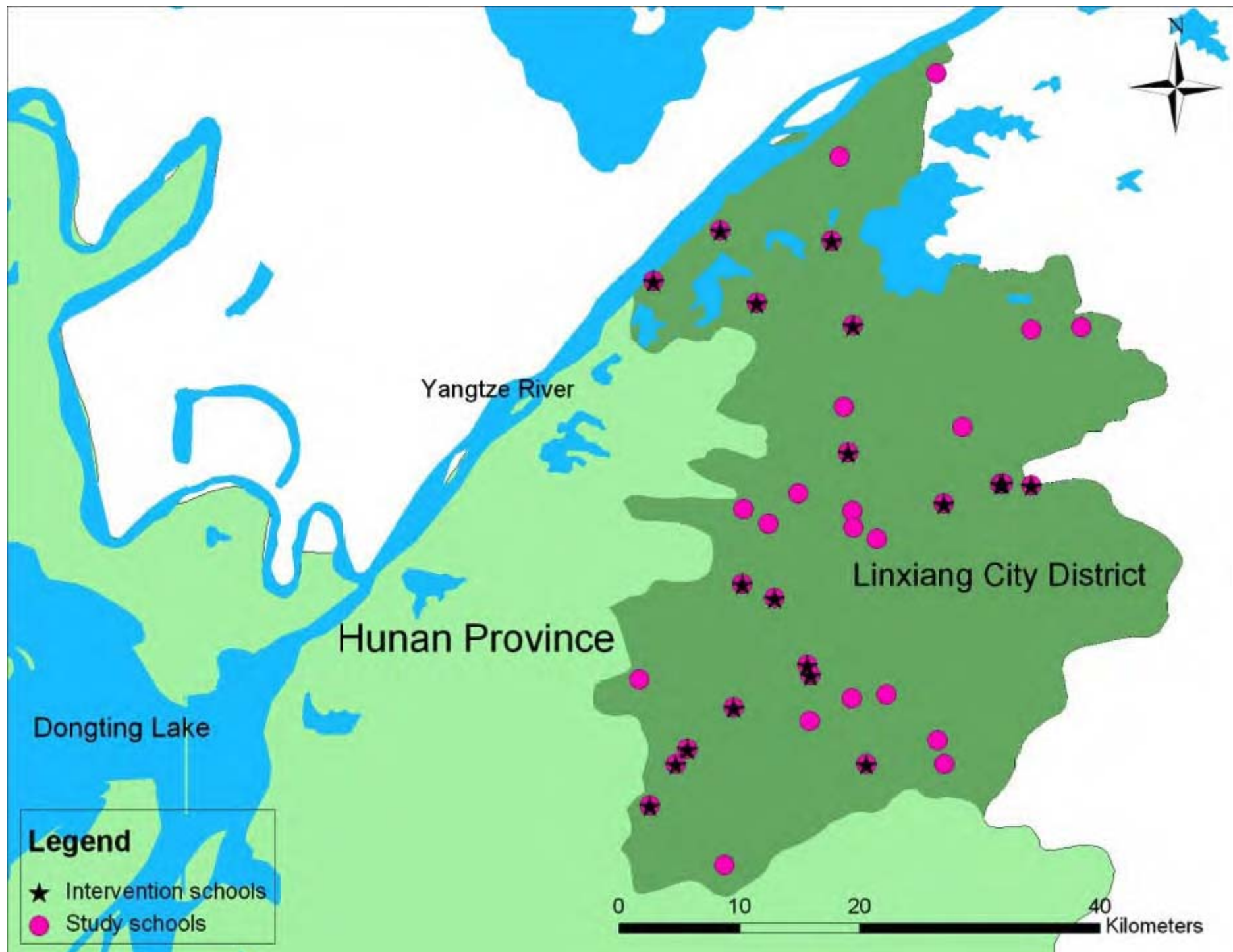


Hookworm  
*Necator americanus*,  
*Ancylostoma duodenale*

# HUNAN TRIAL: STUDY AREA







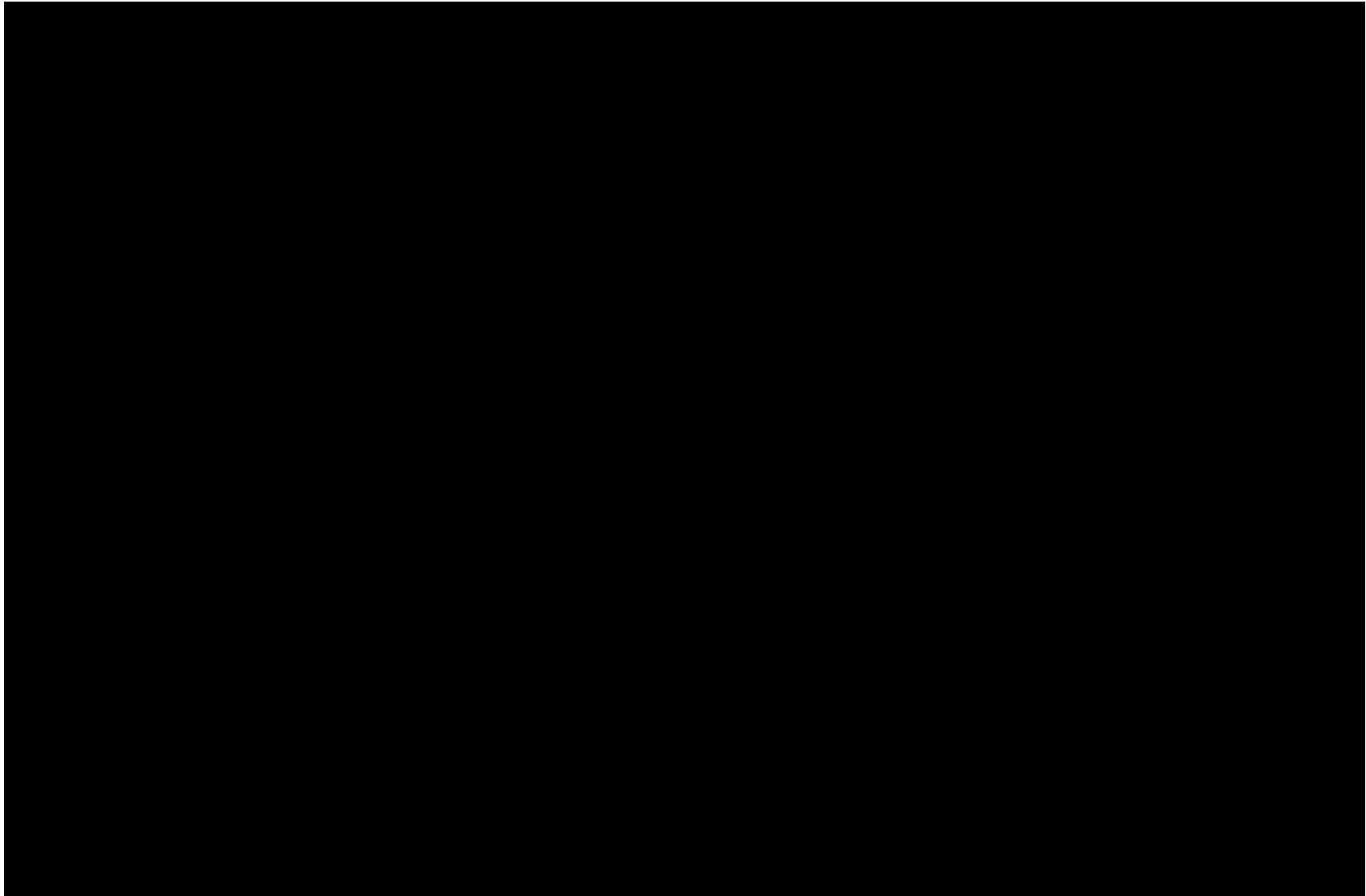
## Research question

Does an education package including an educational video increase the students' knowledge and change their behaviour, resulting in fewer STH infections?

- **3 end-points:**
- Infection incidence
- Knowledge
- Behaviour

- Cluster-randomized intervention trial
- 38 schools: 19 intervention, 19 control
- N = 1718 children, age 9-10 years

## **STUDY DESIGN**





# Health education works!



**PROOF OF PRINCIPLE ESTABLISHED THAT OUR VIDEO-BASED HEALTH EDUCATIONAL PACKAGE WIDENS STUDENT KNOWLEDGE AND CHANGES BEHAVIOUR, RESULTING IN FEWER STH INFECTIONS.**

*The NEW ENGLAND JOURNAL of MEDICINE*

ORIGINAL ARTICLE

## Health-Education Package to Prevent Worm Infections in Chinese Schoolchildren

Franziska A. Bieri, M.Sc., Darren J. Gray, Ph.D., Gail M. Williams, Ph.D.,  
Giovanna Raso, Ph.D., Yue-Sheng Li, Ph.D., Liping Yuan, Ph.D.,  
Yongkang He, M.P.H., Robert S. Li, B.Inf.Tech., Feng-Ying Guo, B.A.,  
Sheng-Ming Li, B.A., and Donald P. McManus, D.Sc.



# 学校健康教育视频控制土源性线虫病项目启动及培训会

云南景洪 2013年10月9日

整治火灾隐患 确保消防安全



# Magic Glasses II

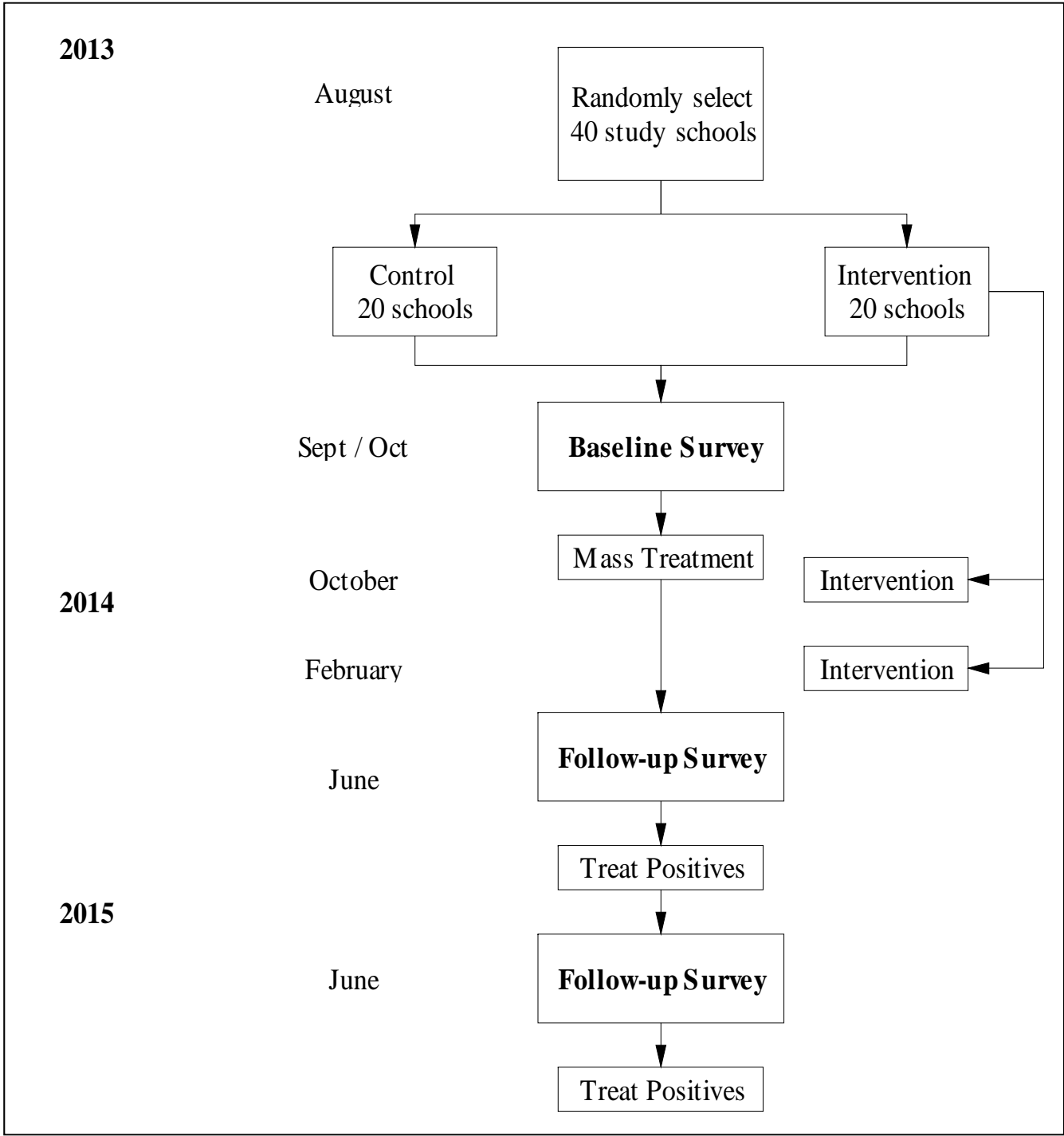
- Partner: Yunnan Institute of Parasitic Diseases
- Study location:
  - Yunnan Province, China
  - Xishuangbanna Prefecture (Jinghong and Menghai Counties)
  - South Yunnan, borders with Myanmar
  - Approx 30% Han, 30% Dai, remainder ~25 ethnic minorities
- Cluster RCT





Study Area  
Prevalence up to 80%









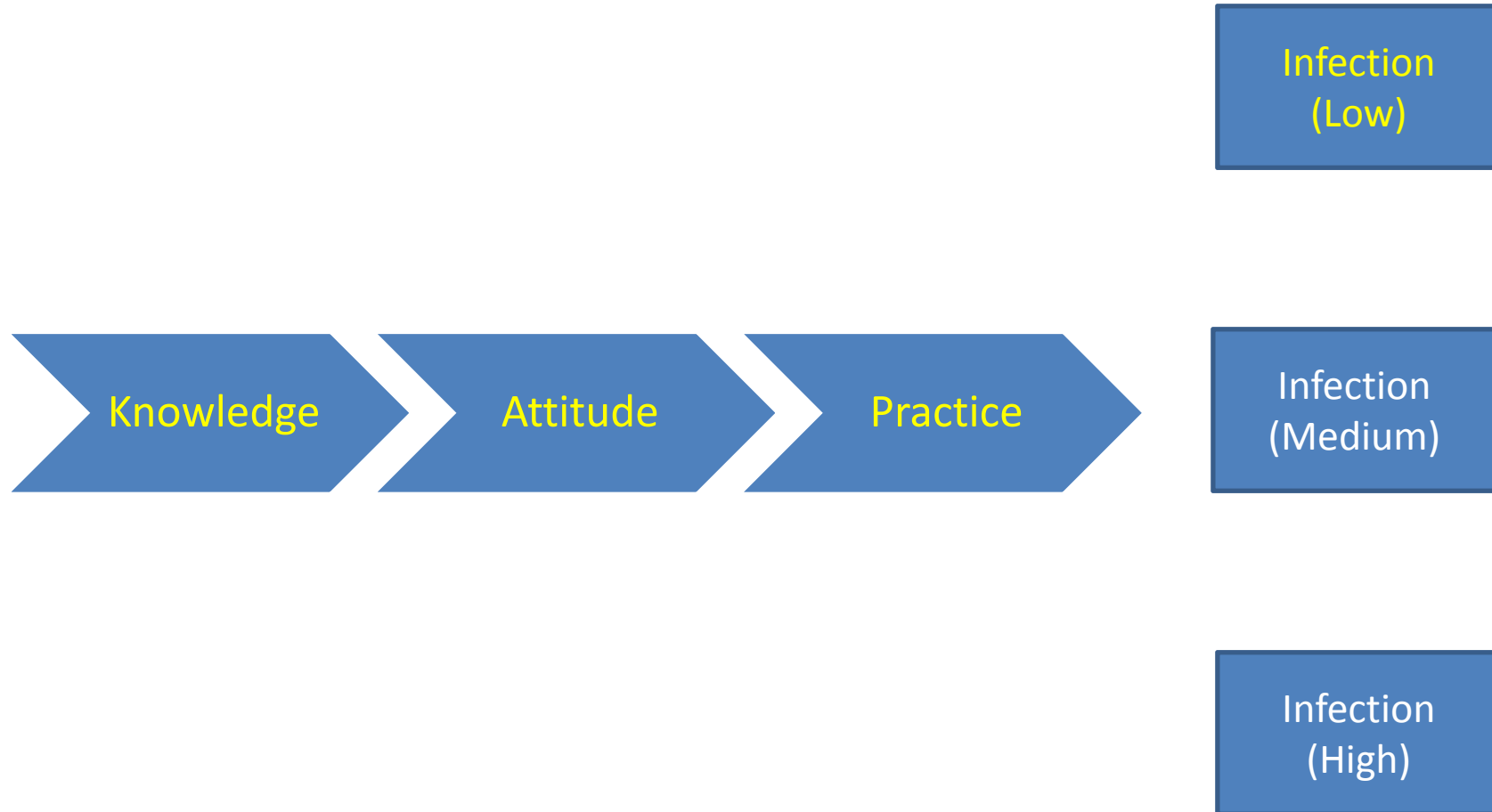


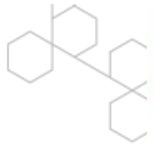


# Baseline Infection

Parasite	Control				Intervention			
	N	Prevalence (%)	N	GMEPG	N	Prevalence (%)	N	GMPEG
<b><i>A. lumbricoides</i></b>	988	7.0 (5.4 – 8.6)	69	1649 (1047 – 2559)	989	10.0 (8.1 – 11.9)	99	3180 (2211 – 4574)
<b>Hookworm</b>	988	21.0 (18.4 – 23.5)	207	214 (176 – 260)	989	21.6 (19.1 – 24.2)	214	167 (137 – 204)
<b><i>T. trichiura</i></b>	988	10.5 (8.6 – 12.4)	104	88.1 (67.6 – 115)	989	18.1 (15.7 – 20.5)	179	145 (113 – 187)
<b>Any STH</b>	988	30.5 (27.6 – 33.3)	-	-	989	34.7 (31.7 – 37.7)	-	-

# Impact of Magic Glasses





**Magic Glasses works!!! But high STH (especially *Trichuris*) prevalence and multiple ethnicities affected the infection incidence endpoint.**

# What's Next?



- **Up-scaling**
- **Incorporation into National STH control program for China?**
- **Laguna Province, the Philippines (trial completed; analysis underway);**
- **Phu Tho Province, Vietnam (trial underway).**



# Magic Glasses Philippines (MGP)

- To evaluate the impact of the video-based educational package (for use in schools), culturally adapted for the Philippines, on STH infections in schoolchildren in Laguna Province

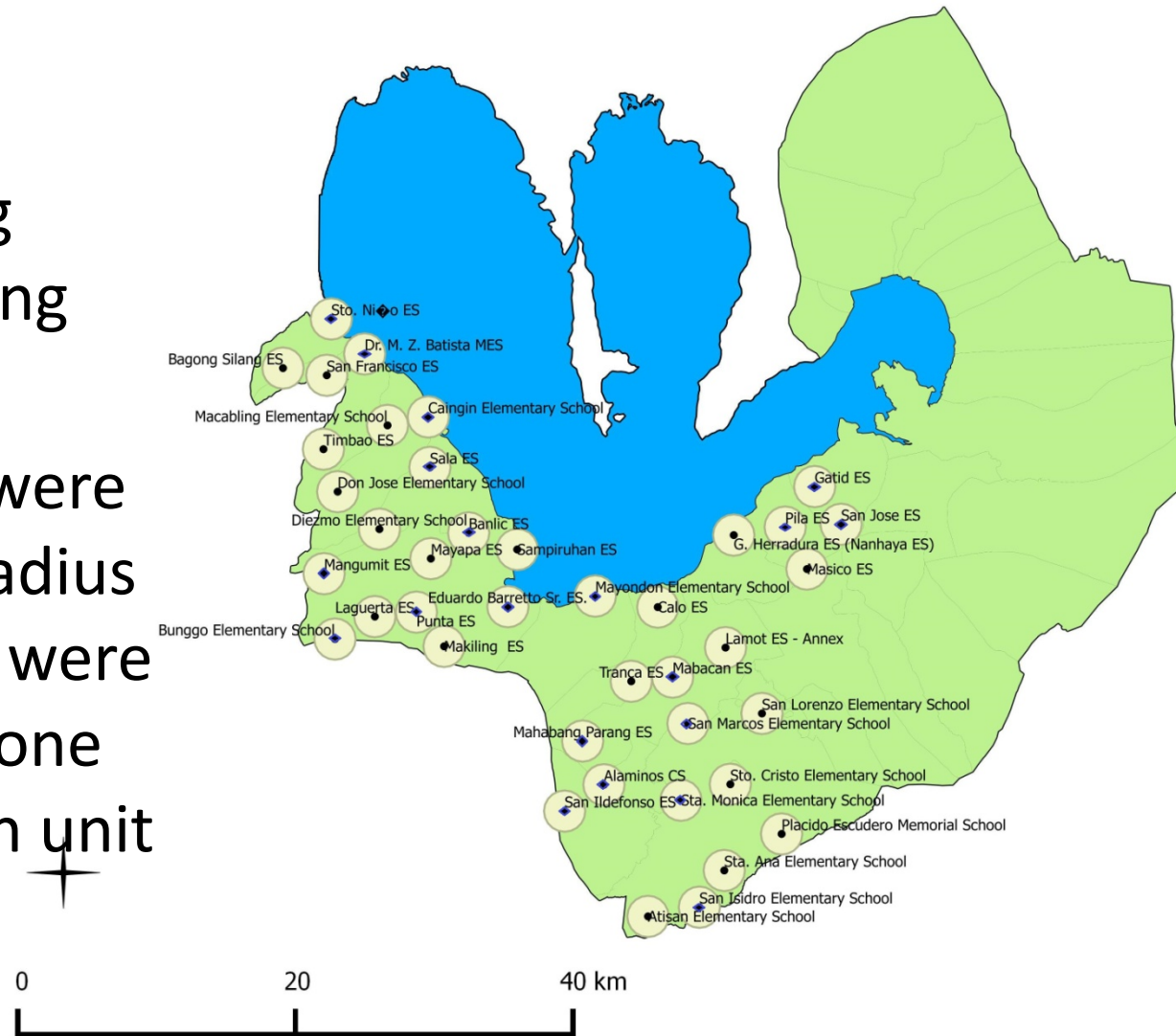


# Study Area (close to Manila)



# Selection of schools

- Schools were selected using spatial sampling frame
- Schools who were within 3 km radius of each other were grouped into one randomisation unit





# Study Governance

Magic Glasses Philippines Steering Committee Meeting, November 2017

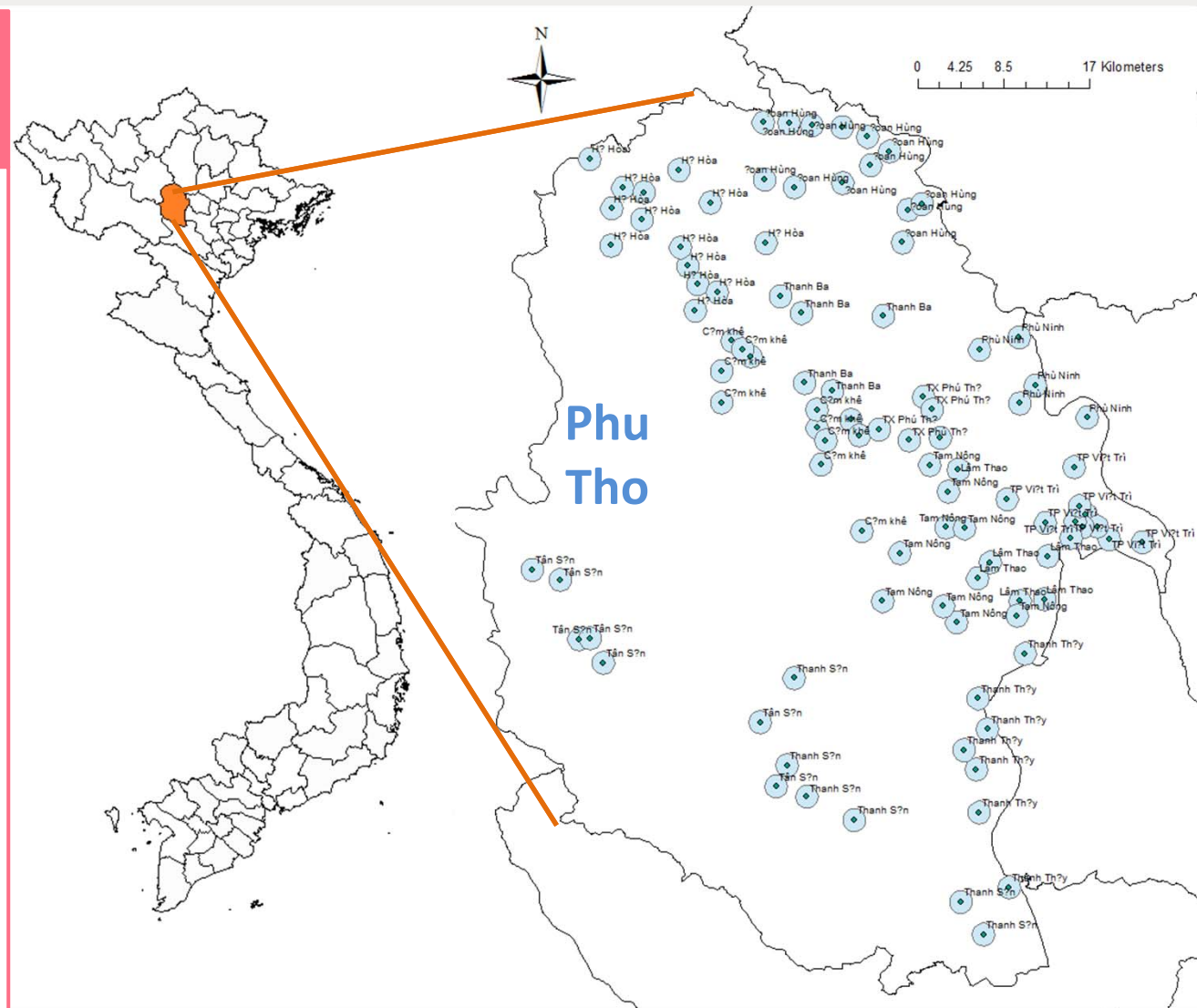




# Magic Glasses RCT in Vietnam

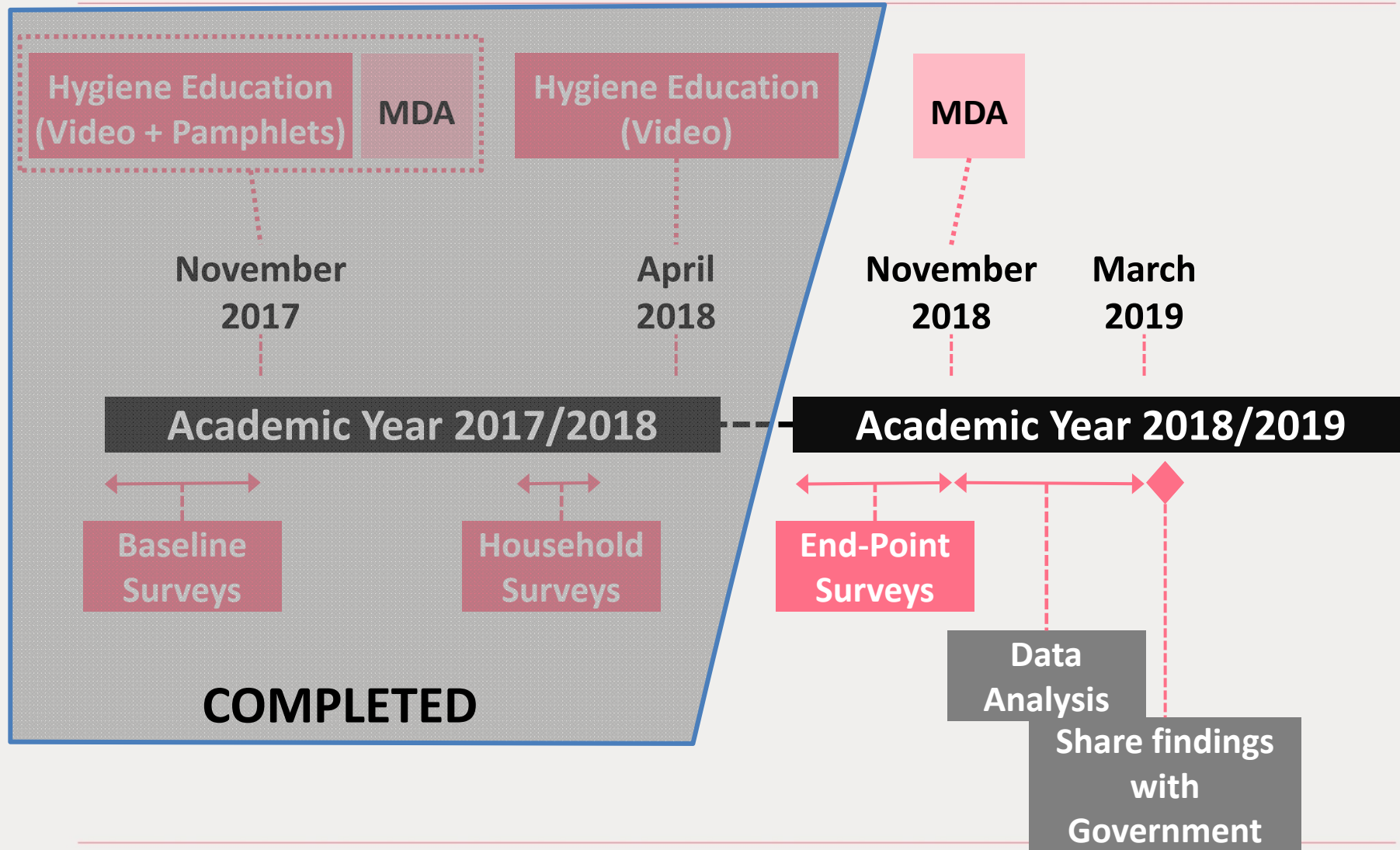
## Study Site: Phu Tho province

- Cluster RCT
- **100** primary schools randomly-selected (out of a total of ~300 schools in Phu Tho)
  - **48** schools randomly assigned to intervention cohort
  - **52** schools randomly assigned to control cohort
- **6,000** grade 3 & 4 children (8-10 years of age)



# Magic Glasses RCT in Vietnam

## -Timeline for study



# Evidence-Based Scale-Up

-Using results from RCT to inform deworming policy in Vietnam

This study aims to provide evidence to the Government of Vietnam to help with developing a nationwide strategy to combat STH

Evidence-based decision on scale-up of integrated deworming & hygiene education intervention

RCT shows reduction in STH reinfection

- Advocate for integrated program (deworming + hygiene education) to be implemented in ALL at-risk provinces
- Advocate for Magic Glasses intervention to be included in national curriculum

RCT shows no reduction in STH reinfection

- Advise Gov of Vietnam to continue with deworming alone

- Current control strategy: mass drug administration -  
> reinfection, resistance
- Health education and behaviour change needed to prevent infection sustainably

## **PUBLIC HEALTH SIGNIFICANCE**



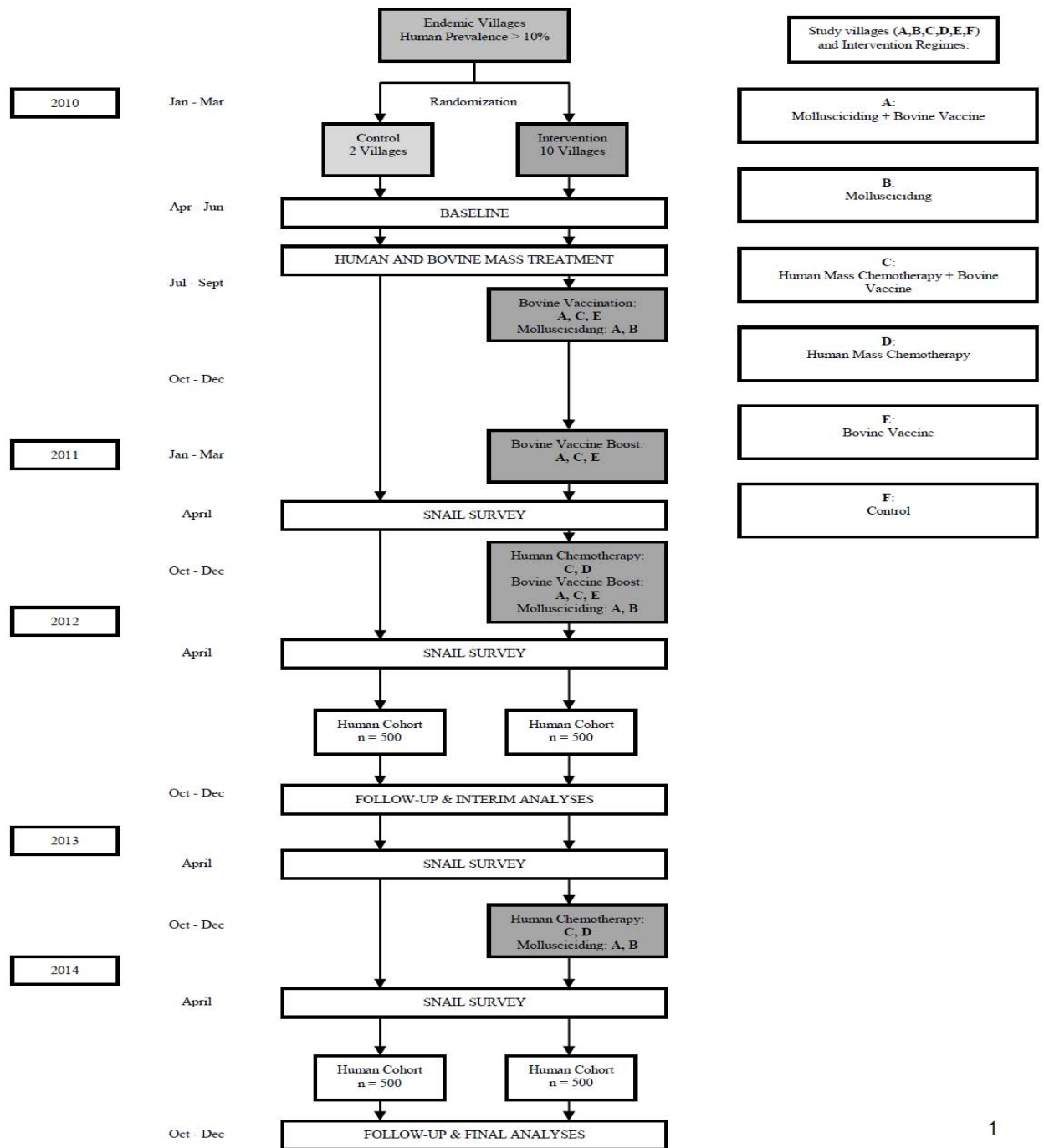
#### 4. A 4-year cluster-randomised intervention trial in Hunan Province (2010-2014)



## Intervention matrix which conceptually highlights the factorial study design used in village groups A–F

Intervention	Bovines: <b>SjTPI</b> vaccine	Bovines: placebo vaccine
Mollusciciding	2 villages (A)	2 villages (B)
Human Mass Chemotherapy	2 villages (C)	2 villages (D)
Neither	2 villages (E)	2 villages (F) Control

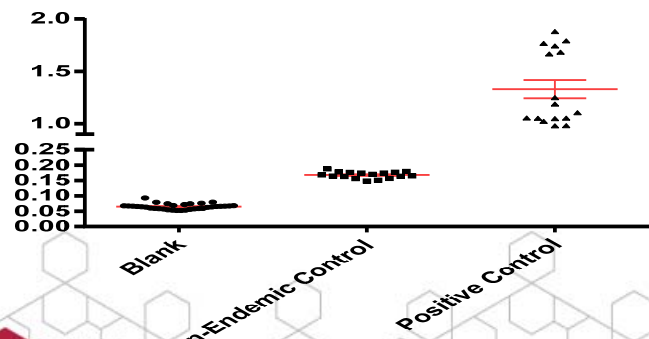
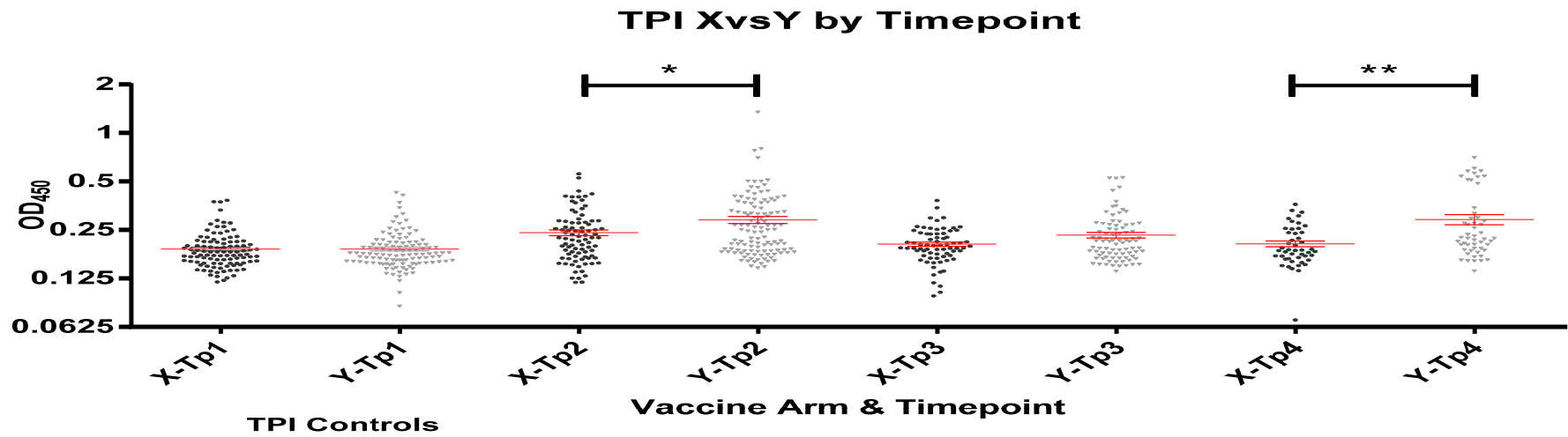
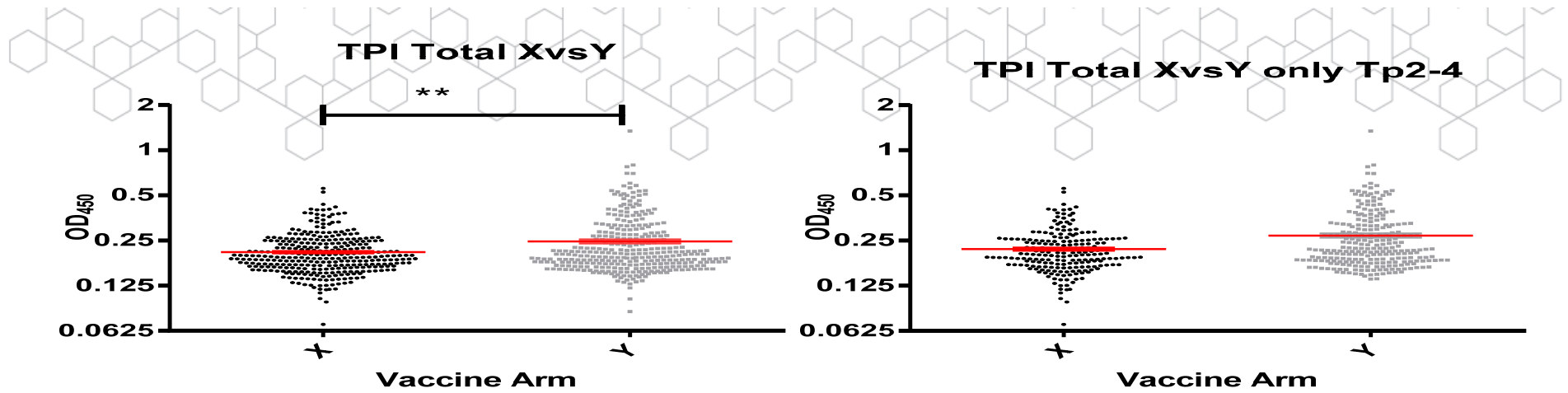
“A” villages received mollusciciding + bovine *Schistosoma japonicum* **triose-phosphate isomerase (SjTPI)** vaccine. “B” villages received mollusciciding + bovine placebo vaccine. “C” villages received human mass chemotherapy (praziquantel, PZQ) + bovine SjTPI vaccine. “D” villages received human mass chemotherapy (PZQ) + bovine placebo vaccine. “E” villages received bovine SjTPI vaccine. “F” villages were controls and received bovine placebo vaccine.



# OUTCOMES

- This study is the first to report on the outcomes of a trial to test a schistosomiasis vaccine in the field.
- This type of factorial design has not been applied hitherto in field/clinical trials of populations before.
- Over the post-baseline period, human treatment and mollusciciding separately showed a halving of infection rates
- The active vaccine group had significantly higher anti-TPI antibody levels compared to the placebo vaccine after the primary prime boost vaccination. The TPI response was maintained after the first boost and increased after the second boost.





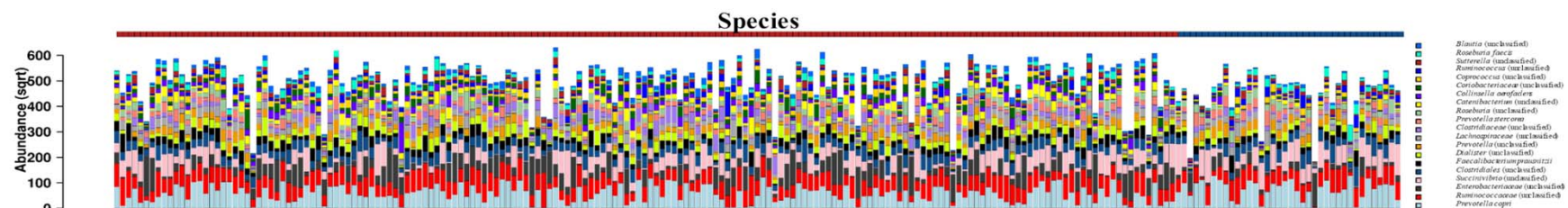
# OUTCOMES

- There was a reduction in schistosome egg output in vaccinated bovines.
- This did not translate into a reduction in human infection rates over the course of the trial.
- Results of the TPI vaccine component of the trial are inconclusive.
- Due in part to activities undertaken by the China National Schistosomiasis Control Program and the Hunan Veterinary Authorities, over which we had no jurisdiction. Removal of buffaloes in one village; treatment of buffaloes and people in other villages; killing of buffaloes due to an outbreak of brucellosis. The trial design was compromised as a result and this reduced power and contaminated outcome measures in relation to comparing the active vaccine to the placebo.
- Very low local schistosome prevalence may have impacted on natural boosting of the vaccine.
- Modify the TPI vaccine formulation and/or combine with another antigen (insulin receptor) to produce a more effective multivalent vaccine. Almost identical trial completed in the Philippines. Natural boosting of the TPI vaccine will be higher. Data being analysed.

## 5. Polyparasitism and the gut microbiome in humans from the Philippines

- We examined the gut microbiome in individuals with polyparasitism from two cohorts in the Philippines (Palapag) utilising DNA sequencing based profiling (amplicon sequencing of the gene encoding microbial 16S rRNA (*rrs*)).
  - Polyparasitism was high with 70.32% (n=219) of study participants harbouring at least two helminth parasite species, and 16% harbouring at least five species.
  - Increasing numbers of helminth co-infections, in particular with the gut-resident intestinal worms, were significantly associated with increasing bacterial diversity.
  - We clearly demonstrate that human infection with helminth parasites led to an increase in bacterial diversity, a feature which is often associated with a healthy gut.
  - The increased numbers of so called ‘beneficial’ bacteria, such as *Faecalibacterium*, we report in the helminth-infected individuals points to a positive association leading to the concept that helminth parasites can in certain circumstances be beneficial commensal organisms.
- Take home message: More worms = better gut health? Due to helminth-mediated immune modulation, or due to changes to the gut environment caused by the presence of these worms.**

### Abundance profile:





# Major collaborators and support

Hong You, Feng Zheng, Guo Jiagang, Li Yuesheng, Honggen Chen, Shengyue Wang, Hu Wei, Zeguang Han, Zhu Chen, Allen Ross, Gail Williams, Catherine Gordon, Kosala Weerakoon, Marina Harvie, Biniam Tebeje, Alex Loukas, Don Harn, Jurg Utzinger, Robert Bergquist, Darren Gray, Geoff Gobert, Mal Jones, Rachel White, Shiwanthi Ranasinghe, Patrick Driguez, Pengfai Cai, Francois Villinger, **Mary Duke**, Istvan Toth, Denise Doolan, Phil Felgner, Els Meeusen, Hamish McWilliam, Remi Olveda, Veronica Tallo

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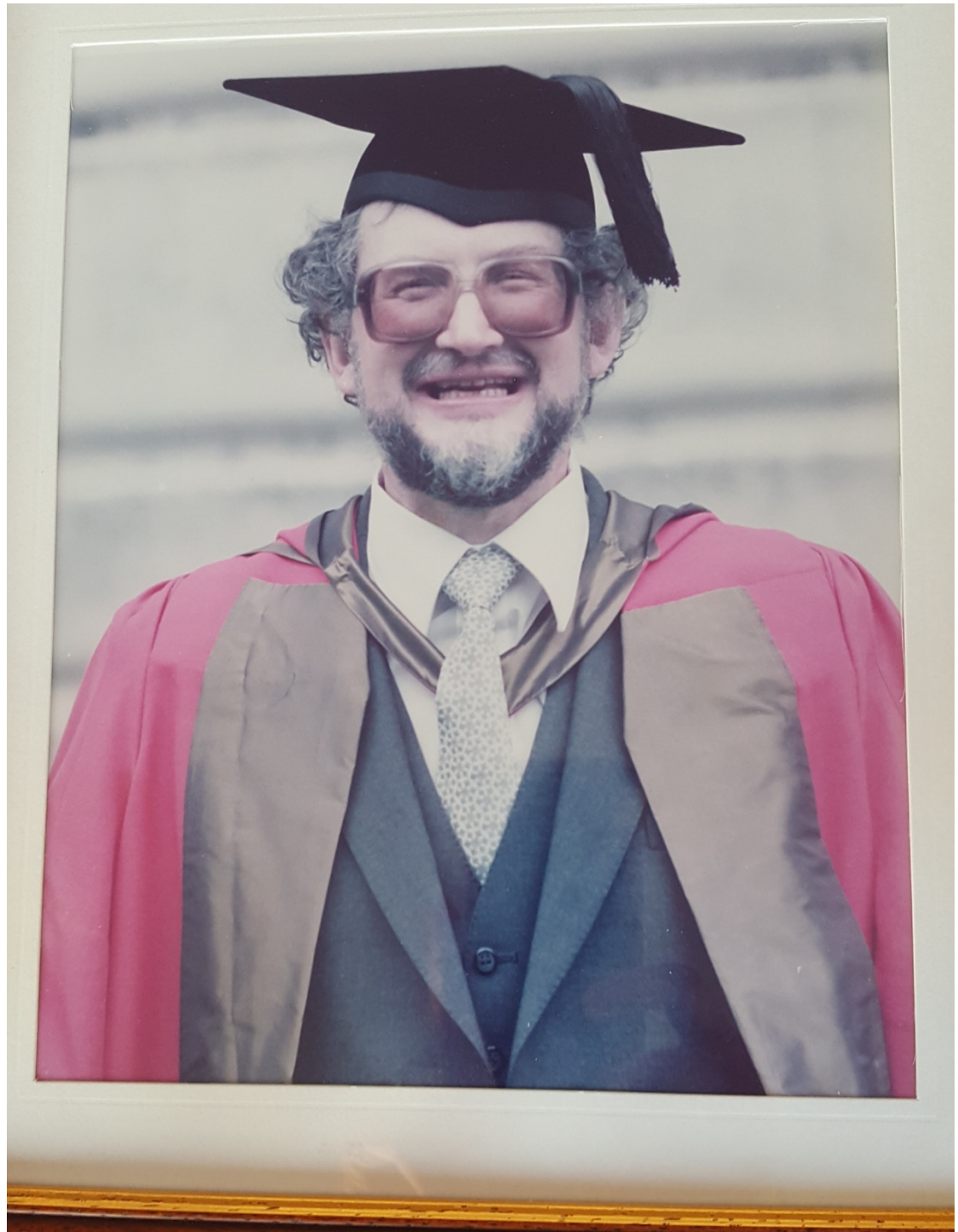
Queensland Institute of Medical Research

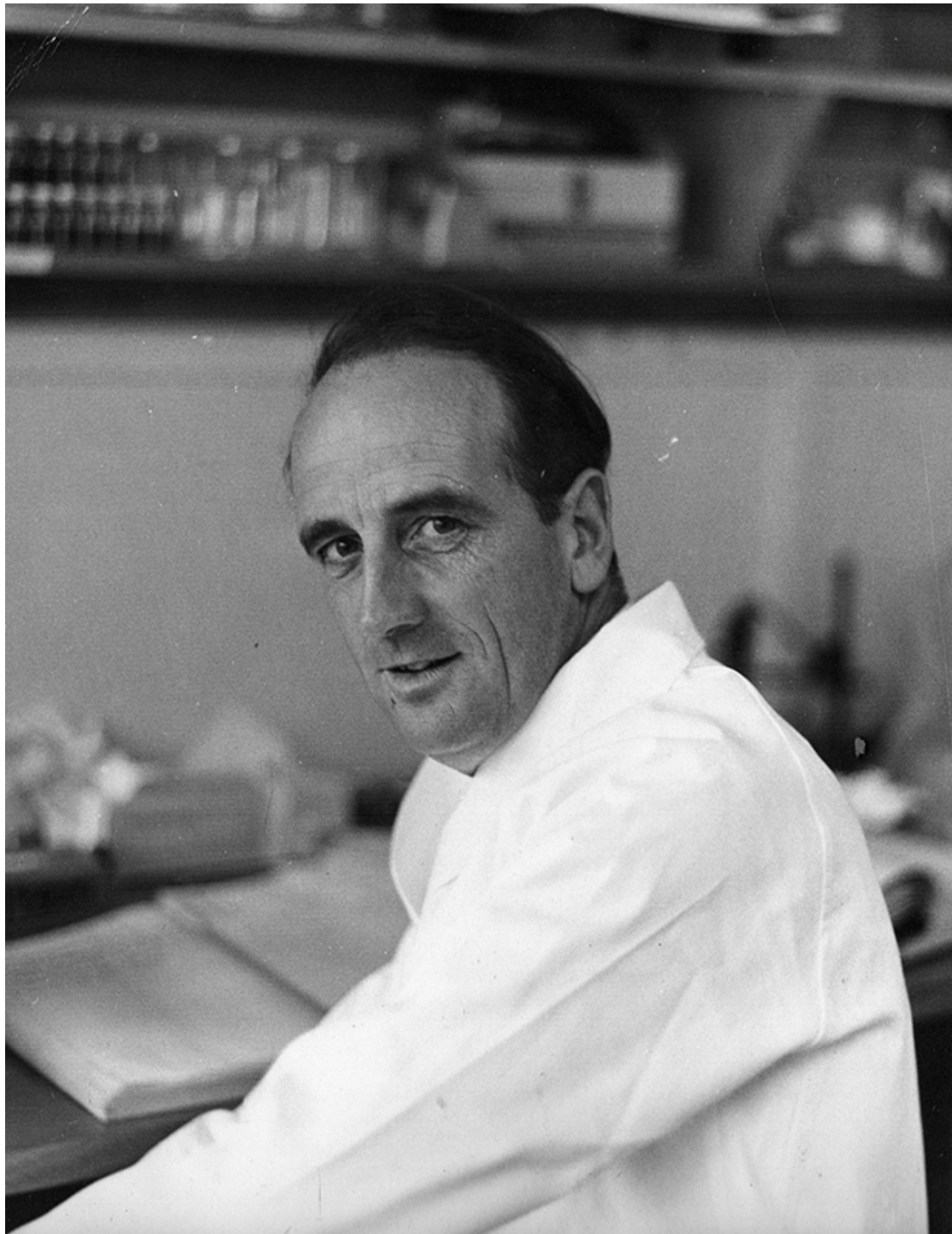
wellcome trust



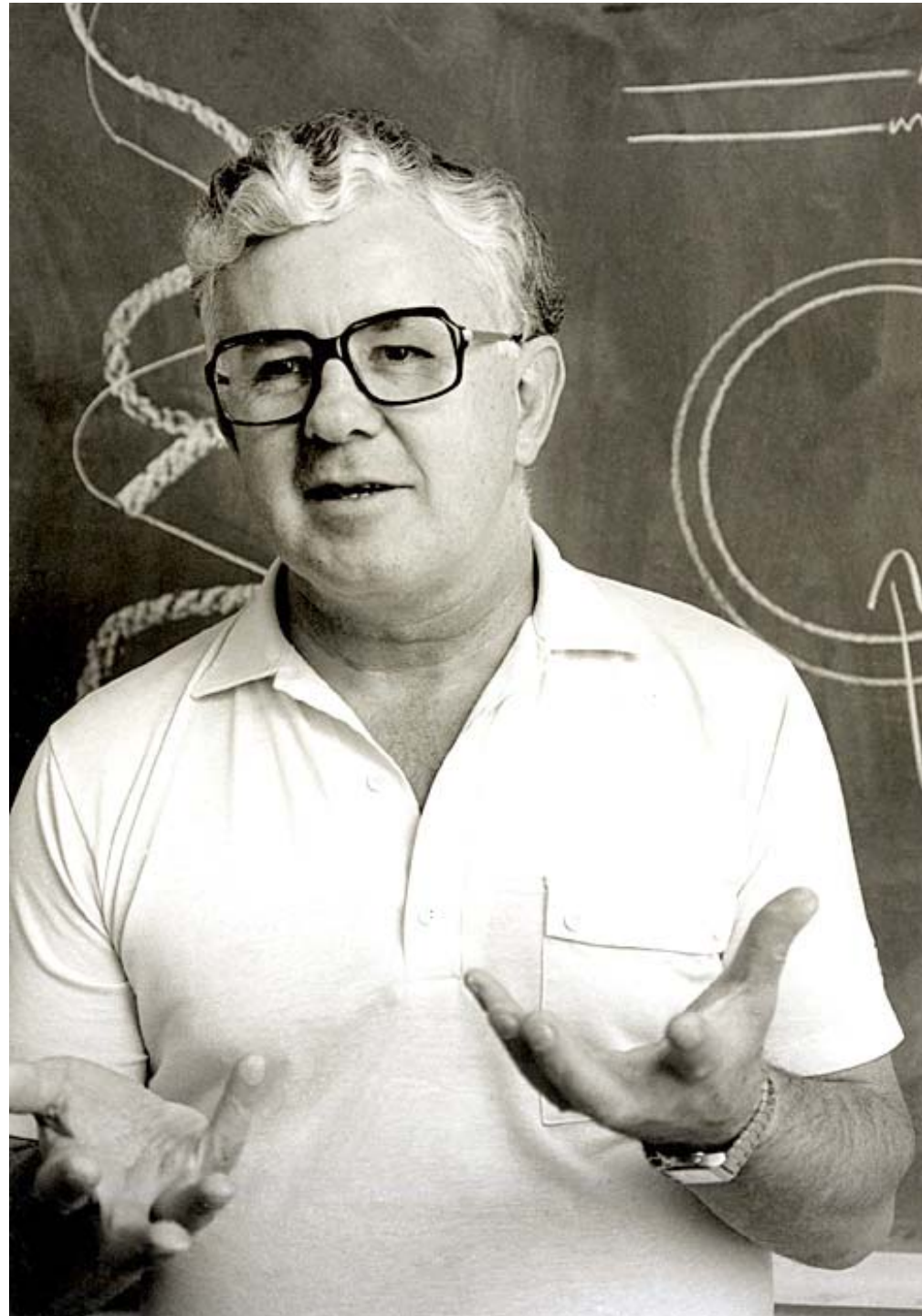
**Dana Foundation**  
**Sandler Foundation**  
**UBS Optimus Foundation**  
**Chenhall Estate**

Receiving this prestigious award, time to reflect and show my appreciation for three mentors who guided my research career.









For the Primer, visit doi:10.1038/s41572-018-0013-8

**→** Schistosomiasis is a neglected tropical disease caused by infection with parasitic flatworms of the genus *Schistosoma*. The clinical manifestations (intestinal, hepato-splenic and urogenital schistosomiasis) are caused by inflammatory responses to worm eggs trapped in the tissues.

**EPIDEMIOLOGY**

The *Schistosoma* spp. that can infect humans have different geographical distributions: *Schistosoma mansoni* is prevalent in Africa, South America and the Caribbean islands; *Schistosoma japonicum* in China and the Philippines; and *Schistosoma haematobium* in Africa and the Middle East.

**PATHOPHYSIOLOGY**

After contact with contaminated water, the resulting miracidia infect an intermediate snail host where they develop into cercariae, which produce cercariae (the human-infecting stage) that are released into the water.

**!** The progression of infection can be divided into three overlapping stages

**Rx MANAGEMENT**

Oral praziquantel is safe and efficacious against all species of adult worms and is also used in chemopreventive programmes based on mass drug administration (MDA) to populations living in schistosomiasis-endemic areas. However, praziquantel does not prevent reinfection, and the development of drug resistance is a concern. The antimalarial drugs artesunate and artemether are effective against immature worms and could be used for the chemoprophylaxis of high-risk groups; however, their use is not recommended in malaria-endemic areas to avoid the selection of resistant *Plasmodium* spp. parasites (the aetiological agents of malaria).

**OUTLOOK**

A multifaceted approach will be required to achieve the WHO target of global elimination of schistosomiasis. Interventions should include precision diagnosis and surveillance (particularly in settings where the disease burden is decreasing thanks to successful control programmes), the development of a vaccine and new anti-schistosomal drugs, and interruption of transmission with combined MDA and snail control programmes.

**Don McManus**  
**Molecular Parasitology**  
**Laboratory, QIMR Berghofer**

**THANK YOU**

Symptoms vary based on the *Schistosoma* species and the stage of infection. Intestinal schistosomiasis may present with intermittent abdominal pain and bloody diarrhoea. Hepato-splenic disease is characterized by periportal fibrosis and portal hypertension, which can result in the development of oesophageal varices that, if they rupture, can lead to fatal haemorrhage. Typical signs of urogenital schistosomiasis are haematuria and pelvic

discomfort. In endemic areas, diagnosis relies on detection of parasite eggs under a microscope; more-sensitive, point-of-care assays based on the detection of worm antigens in the serum are urgently needed.

**QUALITY OF LIFE**

Schistosomiasis is a debilitating disease with non-specific morbidity (such as anaemia) that, in children, can lead to malnutrition and impaired growth and cognitive development, and in adults can result in reduced work efficiency and economic productivity.

**DIAGNOSIS**

**ESTABLISHED ACUTE INFECTION**  
In individuals continuously exposed to infection, the worm burdens gradually decline as partial immunity develops

**ACUTE INFECTION**  
Cercariae penetrate skin and cause a localized pruritic (itching) reaction, called cercarial dermatitis

**ACUTE INFECTION**  
schistosomiasis occurs as schistosomula (the larval stage after cercariae) migrate to the lungs and liver and mature into adult worms

**ESTABLISHED ACUTE INFECTION**  
In individuals continuously exposed to infection, the worm burdens gradually decline as partial immunity develops

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