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Investigating neglected infectious diseases at the interface between ecology and anthropology



Strategic Funds for the Promotion of Science and Technology

Helminths in pigs: the impact of *Taenia solium* and *Taenia asiatica* in Asia

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MEXT Special Fund (2003-2005, 2010-2012)

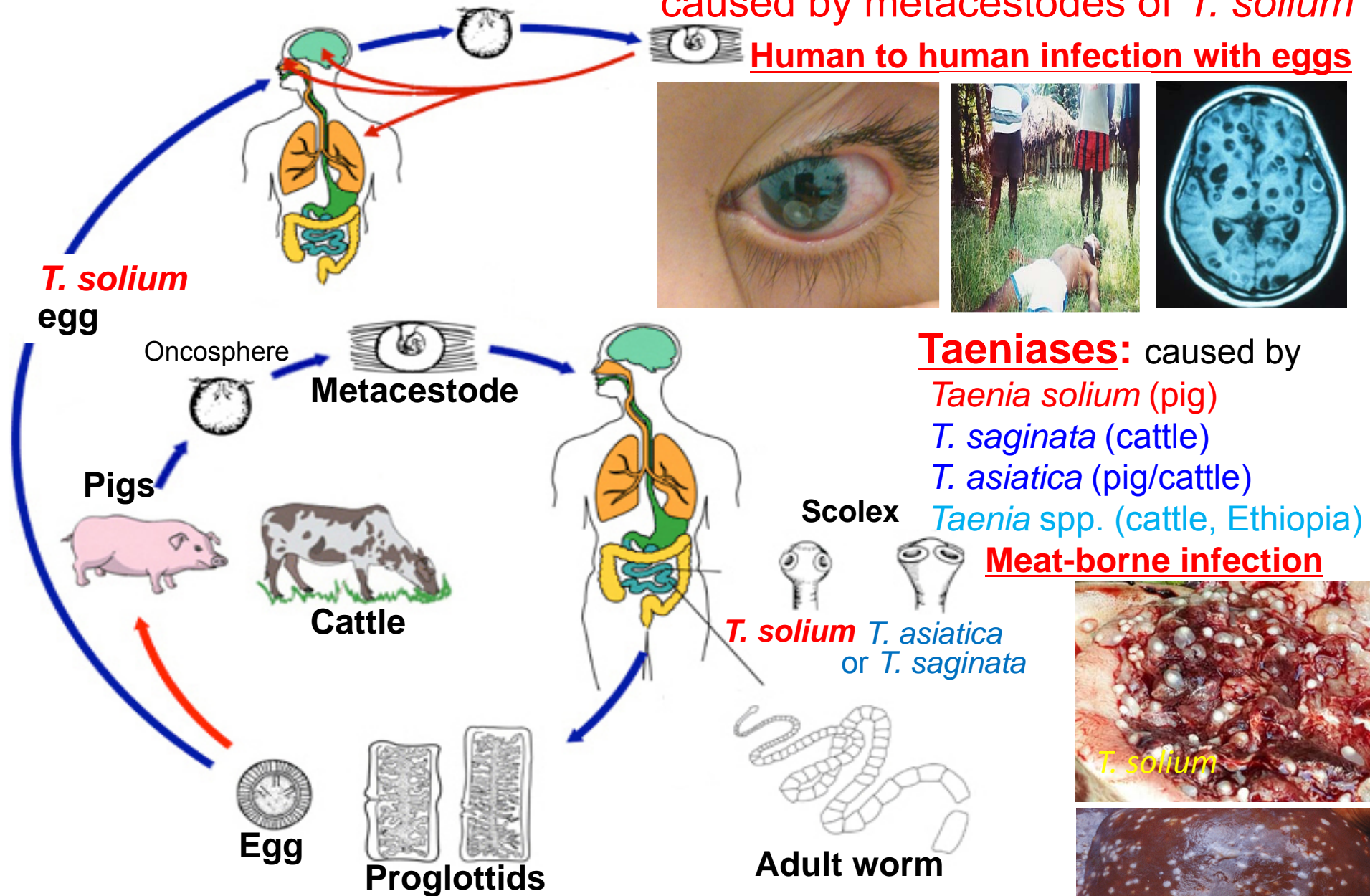
MEXT Hokkaido Translational Research Fund (2007-2011)

Assoc Editor: PLoS Negl Trop Dis

Editorial Board: Acta Tropica, Parasitology, etc.

from Flisser

Cysticercosis (CC), Neurocysticercosis (NCC): most neglected NTD caused by metacestodes of *T. solium*
Human to human infection with eggs

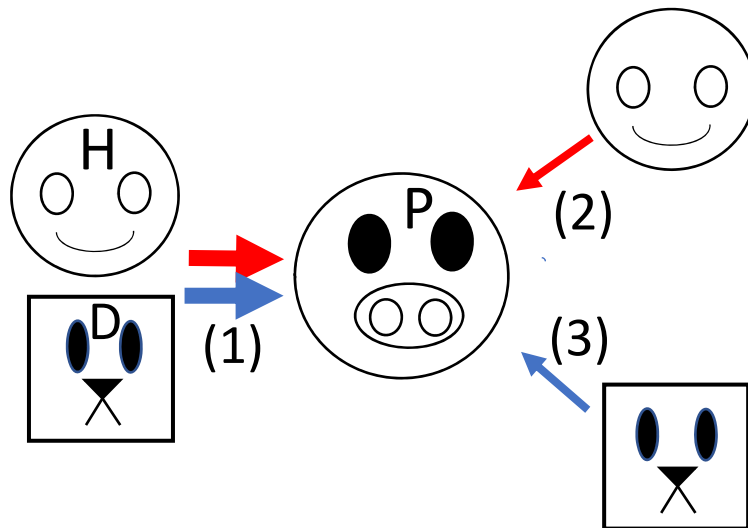


Taeniases: caused by
Taenia solium (pig)
T. saginata (cattle)
T. asiatica (pig/cattle)
Taenia spp. (cattle, Ethiopia)
Meat-borne infection



(modified from Ito & Budke. Travel Med Infect Dis 2014; 12: 582-591)

Eggs of
T. solium and/or *T. asiatica*
from human feces



Eggs of
T. hydatigena etc.
from dog feces

Pigs contaminated with cysticerci of *T. solium* and/or *T. asiatica* from humans and/or *T. hydatigena* etc. from dogs in remote or rural areas of developing countries.

- (1) Humans (H) and dogs (D) have free access to pigs (P) or vice versa:
Pigs are contaminated with *T. solium* and/or *T. asiatica* and *T. hydatigena*.
- (2) Humans have free access to pigs and vice versa:
Pigs contaminated with *T. solium* and/or *T. asiatica*.
- (3) Dogs have free access to pigs and vice versa:
Pigs contaminated with *T. hydatigena*.
- (4) Humans have no access to pigs and vice versa:
Pigs are free of *T. solium* and/or *T. asiatica* cysticercosis.

Fully developed Metacestodes
in NOD/Shi-*scid* female mice 5 months
after injection of *in vitro* hatched
oncospheres

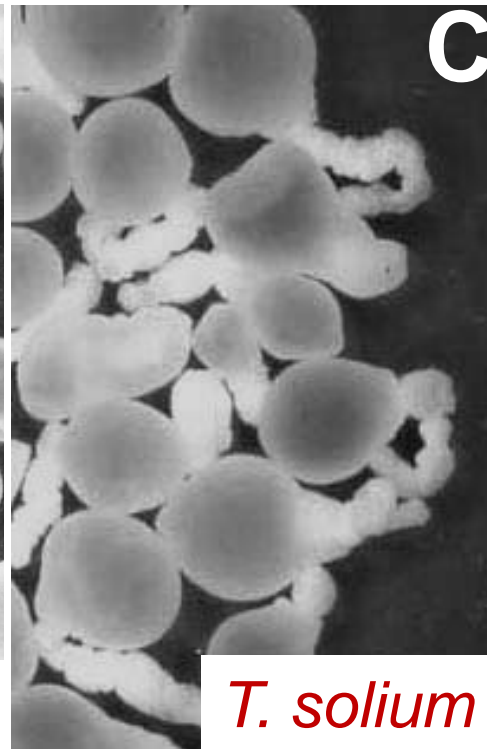
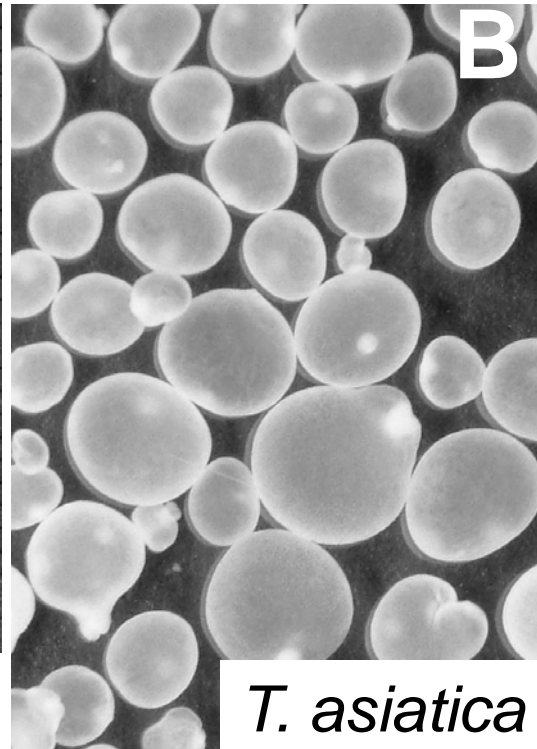
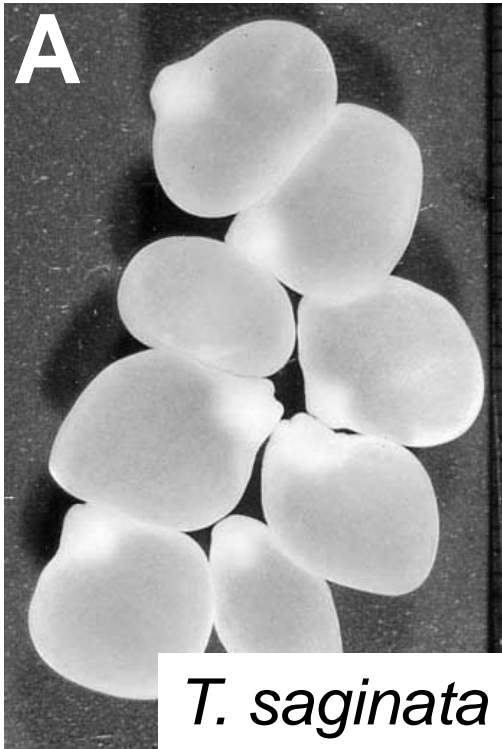


T. saginata **A**



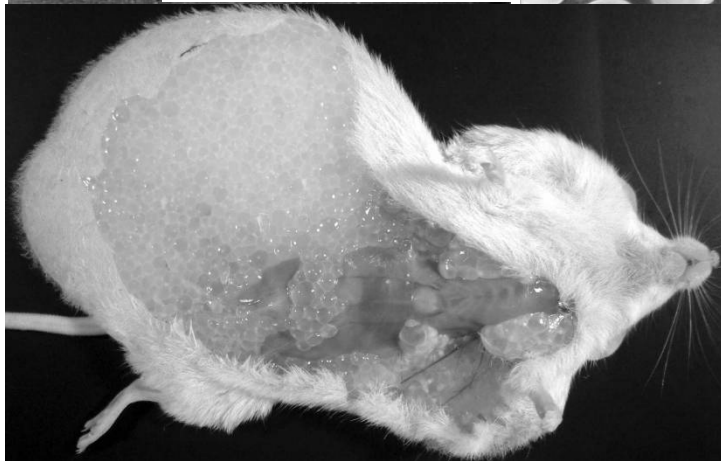
T. asiatica **B**

Cysticerci of *Taenia saginata* (A), *T. asiatica* (B) and *T. solium* (C) fully developed in NOD/Shi-*scid* ♀ mouse



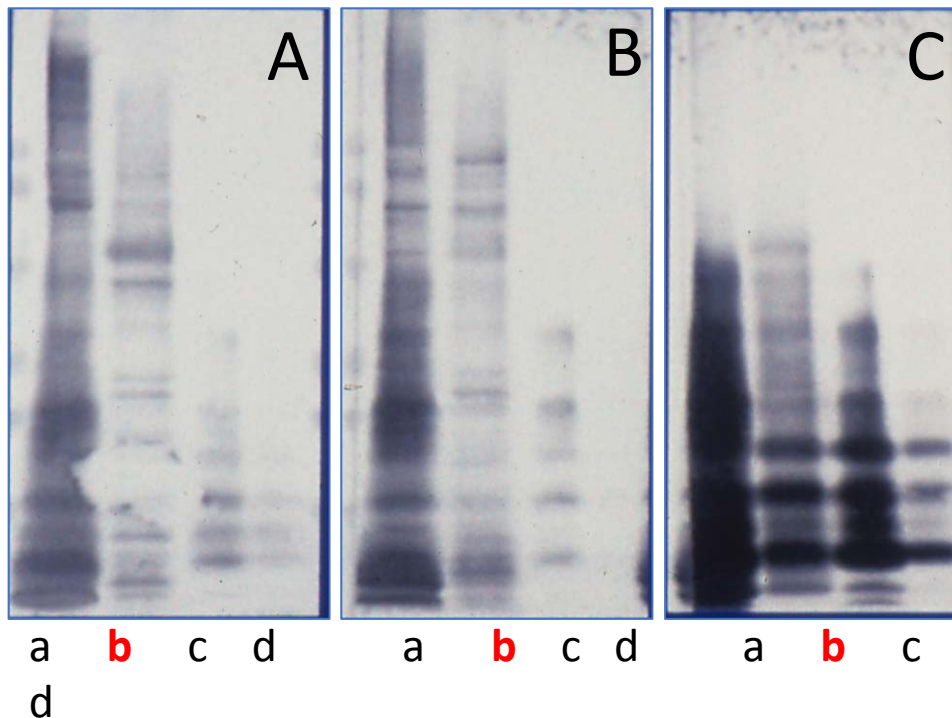
C Fan's group did experimental infection using C3H/HeN, BALB/cAnN, C57BL/6N ♀ mice injected s.c. with in vitro hatched oncospheres. I hesitated to do oral infection using *scid* mice! Oral inoculation should be done using C3H/HeN ♀ mice.

I expect that some mammals other than pigs are suitable host!



1st Topic: serology for cysticercosis in humans and pigs

Is there 100% specific serology for human CC?



EITB (WB) vs ELISA:

No species specific diagnostic antigens but CC in humans are exclusively (>99.999..) caused by *T. solium*!

Any antigens from other *Taenia* species can serve for detection of human CC!

Figure. Comparative evaluation of diagnostic native antigens of *T. solium* cysticerci

a: cyst fluid of *Taenia solium*,

b: lentil lectin affinity purified glycoproteins (Tsang et al. 1989), Gold standard?

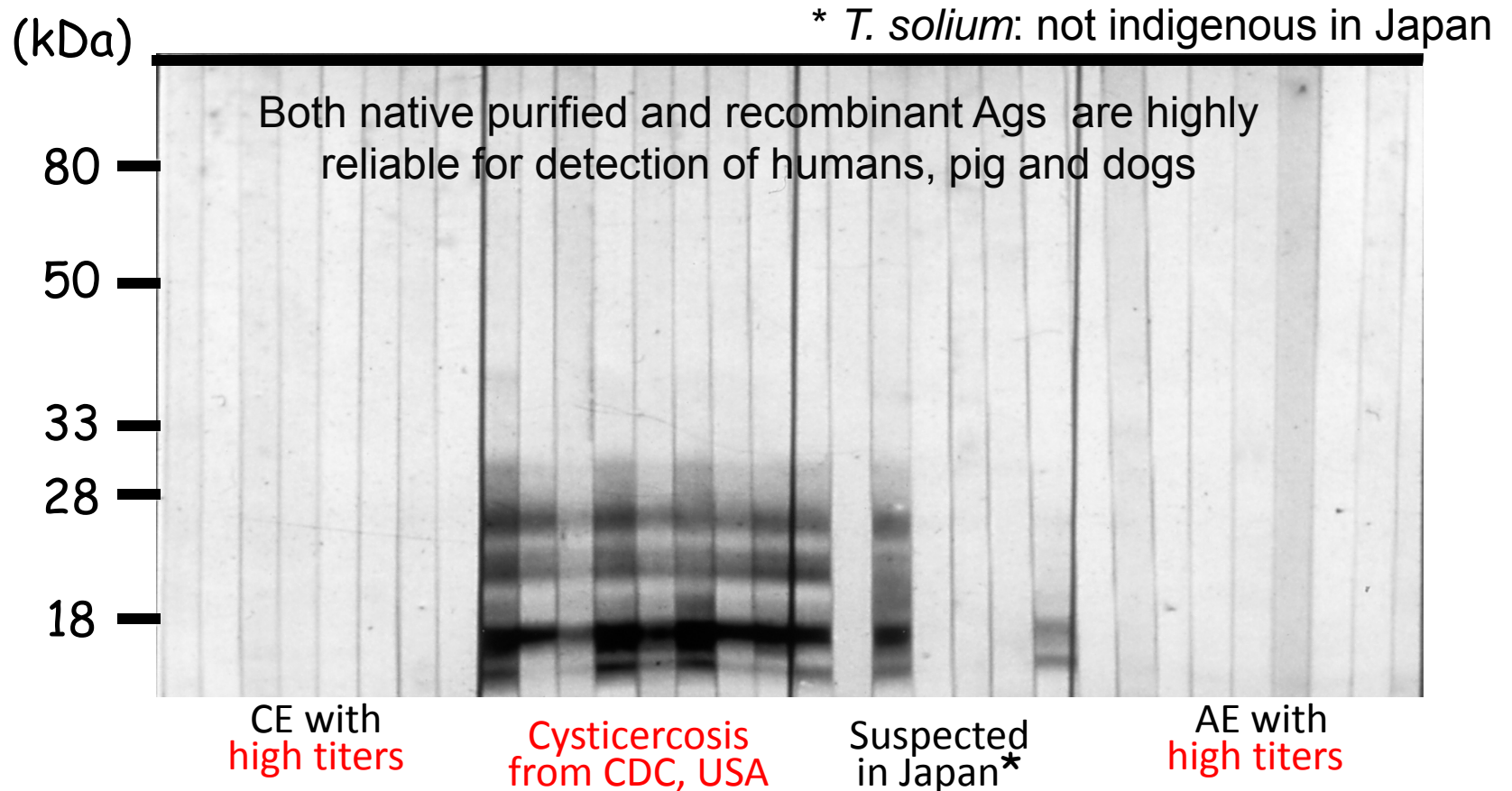
c, d: two fractions purified by preparative isoelectric focusing (PIF)(Ito et al. 1998).

Panel A: incubated with pooled sera from pigs confirmed infected with *T. solium*.

Panel B: incubated with pooled sera from NCC patients.

Panel C: incubated with rabbit anti fraction c of PIF.

Antigens purified by preparative isoelectric focusing were applicable for both ELISA and EITB (WB) with similar results (First report)



Differential Serodiagnosis of Cysticercosis by Immunoblot
(modified from Ito A et al. 1998. Am J Trop Med Hyg 59: 291)
ELISA using recombinant Ag1V1/Ag2 chimeric protein
(Sako Y et al. 2000. J Clin Microbiol 38, 4439)

Antibody responses to GPs of *T. solium* from Asia vs Africa/America

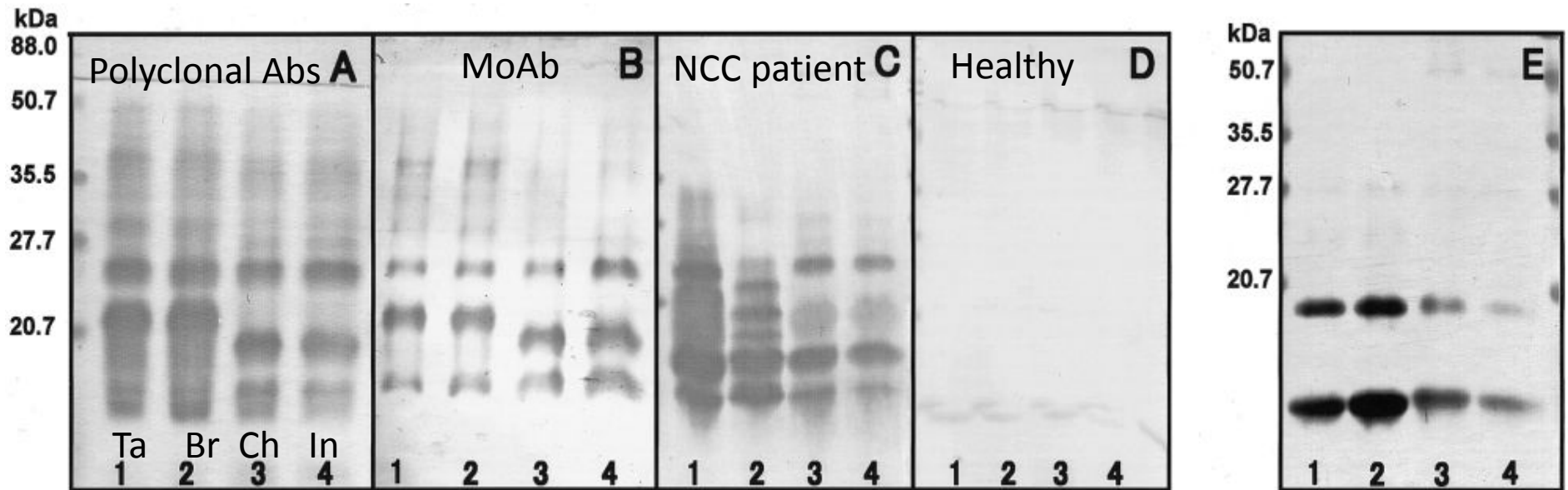


Figure. Immunoblots of *T. solium* glycoproteins (GPs) purified by affinity chromatography using monoclonal antibody (4F10).

Panel A: Native GPs against polyclonal rabbit serum

Panel B: Native GPs against moAb (4F10)

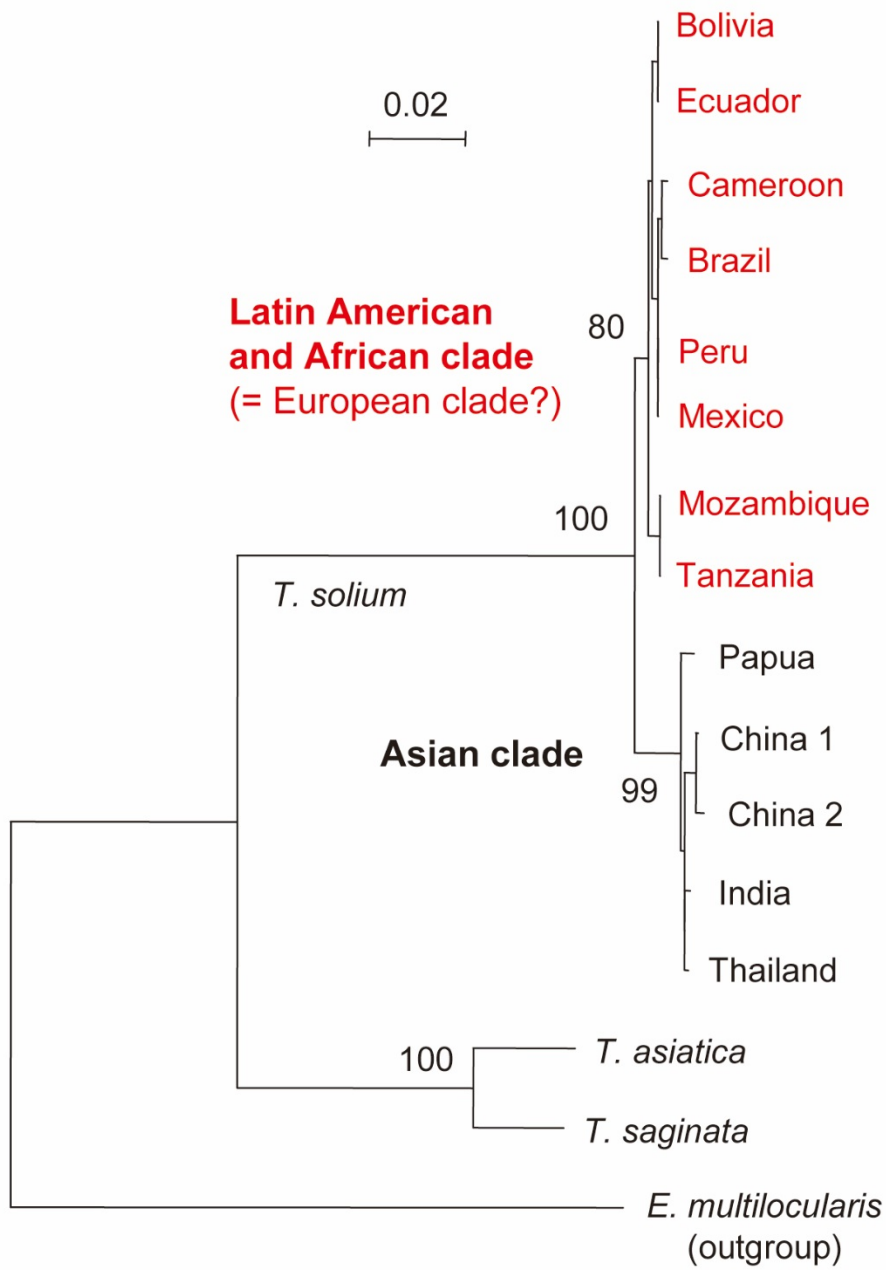
Panel C: Native GPs against serum from a neurocysticercosis patient

Panel D: Native GPs against a healthy person

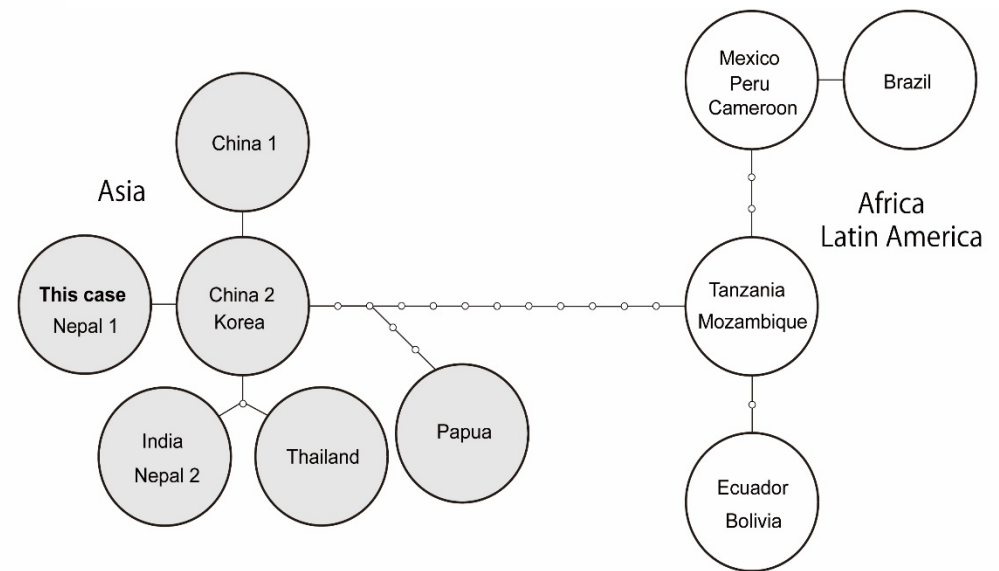
Panel E: Native GPs after treatment with N-glycosidase against moAb (4F10)

Lane 1: Tanzania, Lane 2: Brazil, Lane 3: China, Lane 4: Indonesia

(from Sato MO et al. 2006. J Infect Dis 194, 1783-1790)



- Taeniasis and (neuro)cysticercosis
- Pigs as intermediate hosts, Humans as definitive/intermediate* hosts
- Worldwide distribution, in developing countries (Asia, Africa and Latin America)
- **Two distinct genetic populations (Asian and Afro-American)**



Where was the infection acquired from?

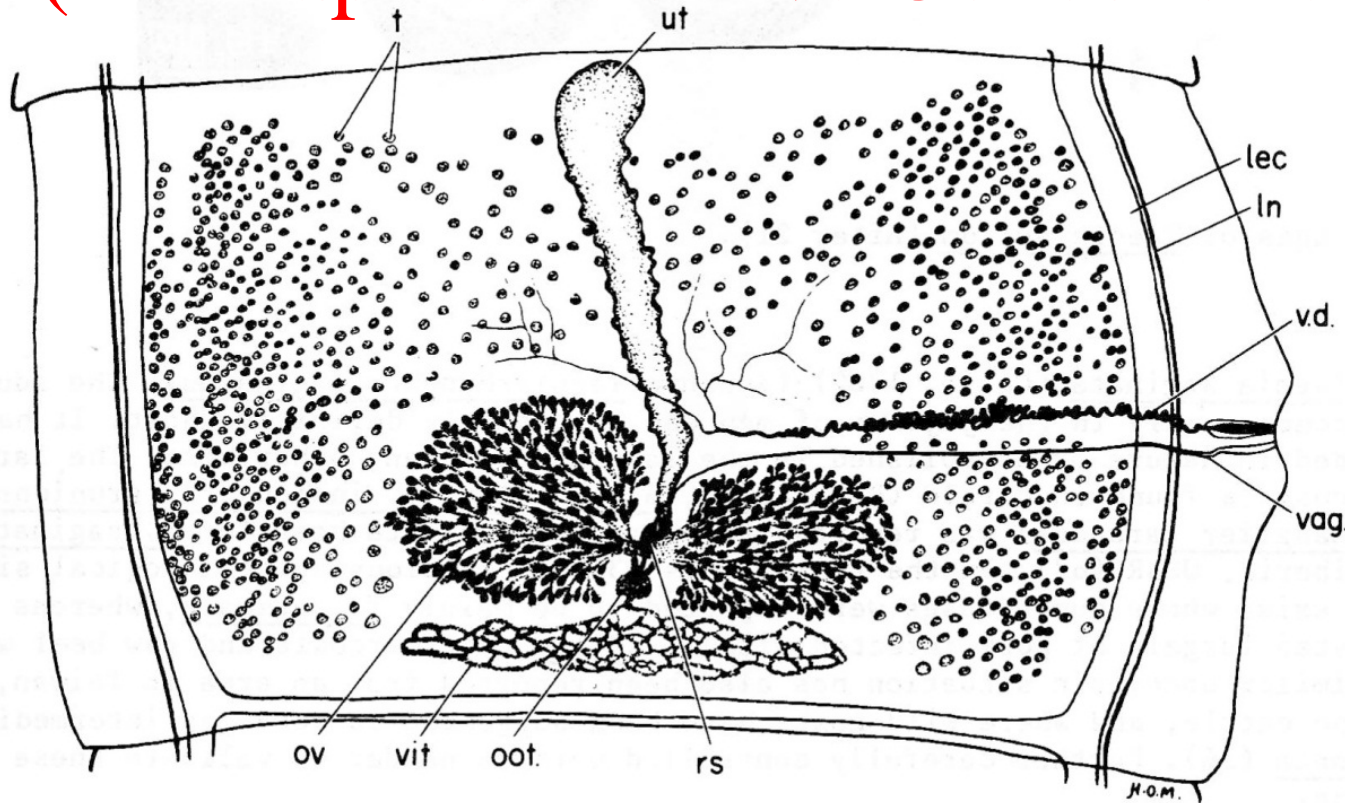
Yanagida *et al.* 2010 J Trav Med 17, 206-8
 Jongwietiwes *et al.* 2011. J Trav Med 18, 284-7

***: *T. solium* is originally a human parasite!**

Strategy of Reproduction in cestodes:

*The majority of platyhelminthes:
Hermaphroditism.*

Self-fertilization vs Cross-fertilization
(Hermaphroditism vs Gonochorism)



from Soulsby E.J.L. 1982. Veterinary Clinical Parasitology

Hypothesis of *Taenia solium* distribution

European *T. solium* ?

Asian *T. solium*

Out of Africa

South American *T. solium*

African *T. solium*

World Miller Projection

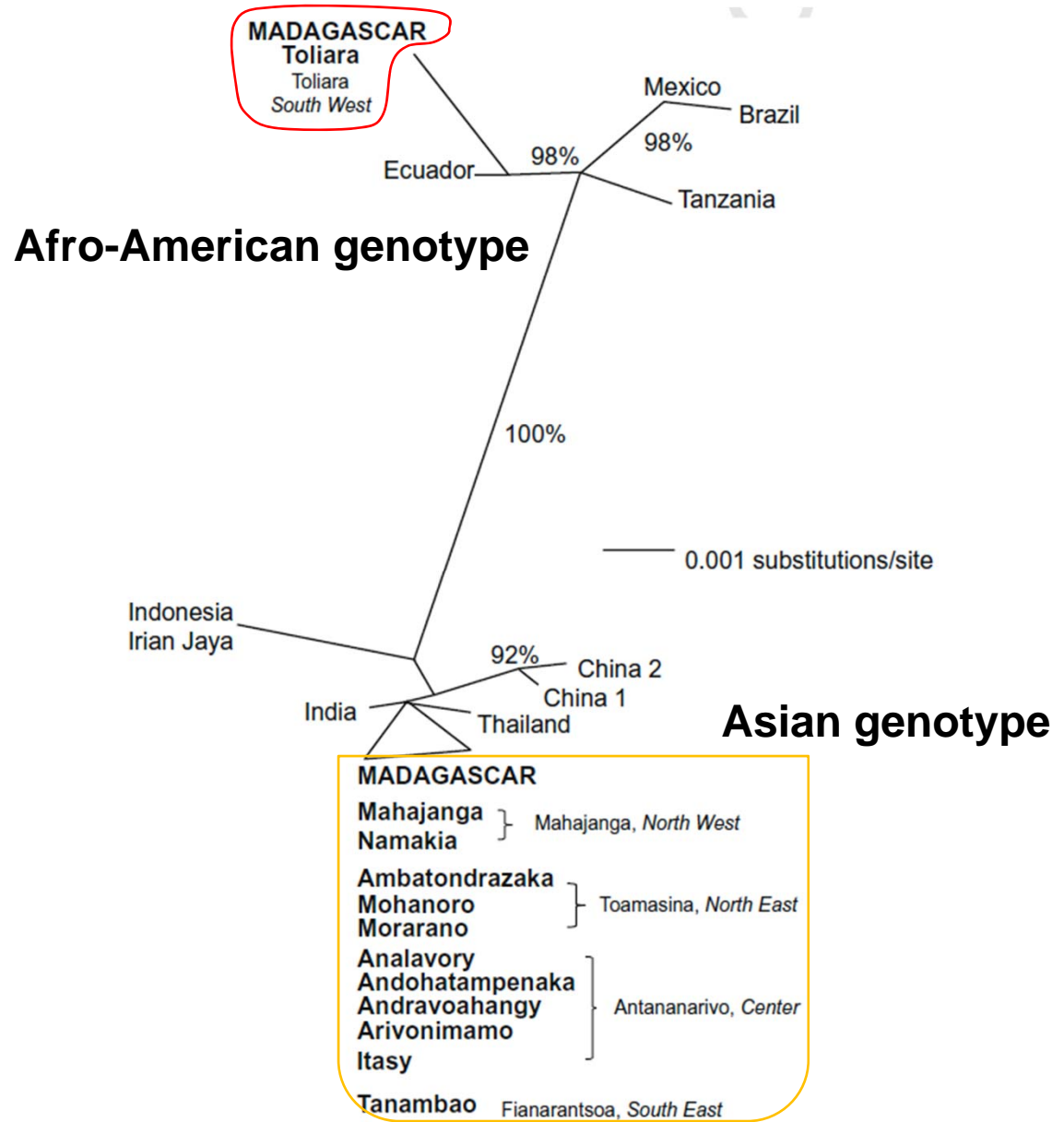
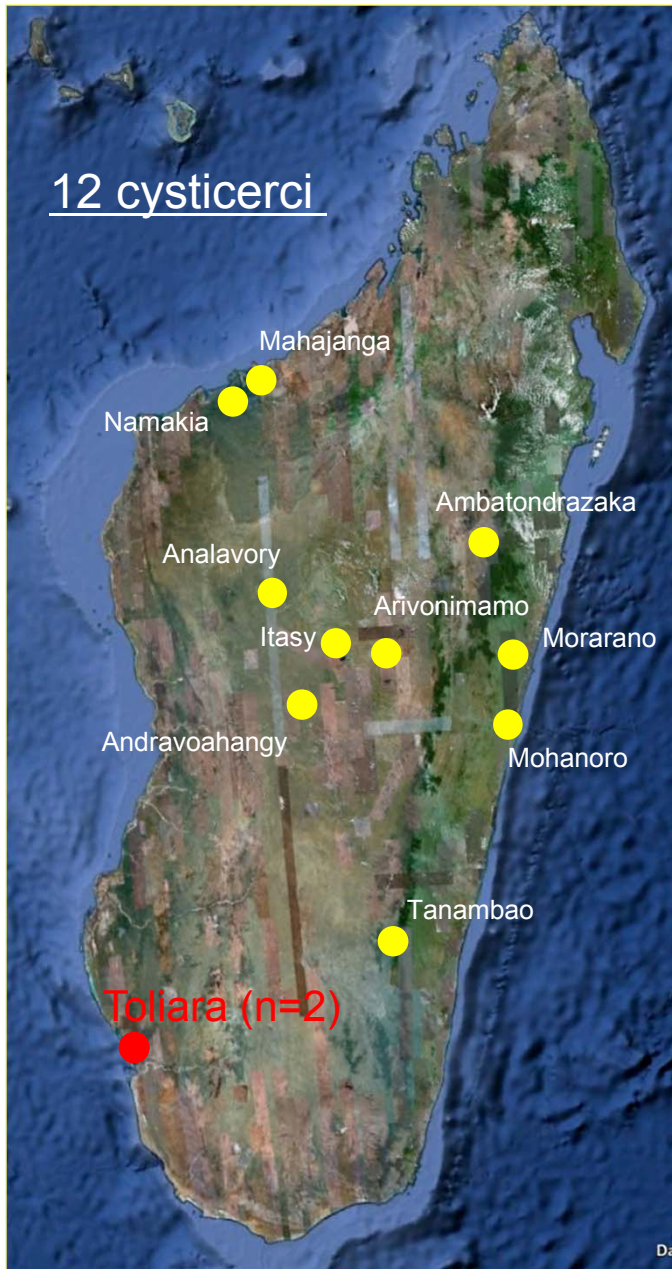
1:100,000,000 Scale at Equator



Nakao M et al. 2002. Parasitology 124, 657-662

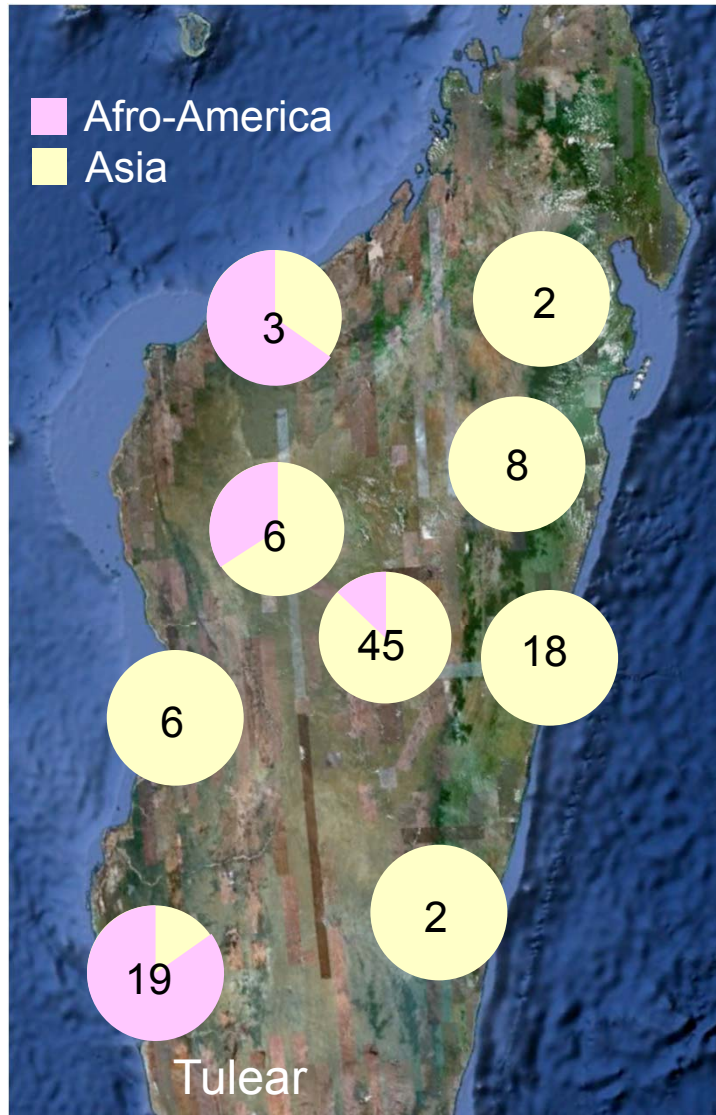
ANTARCTICA

Two genotypes of *T. solium* in Madagascar

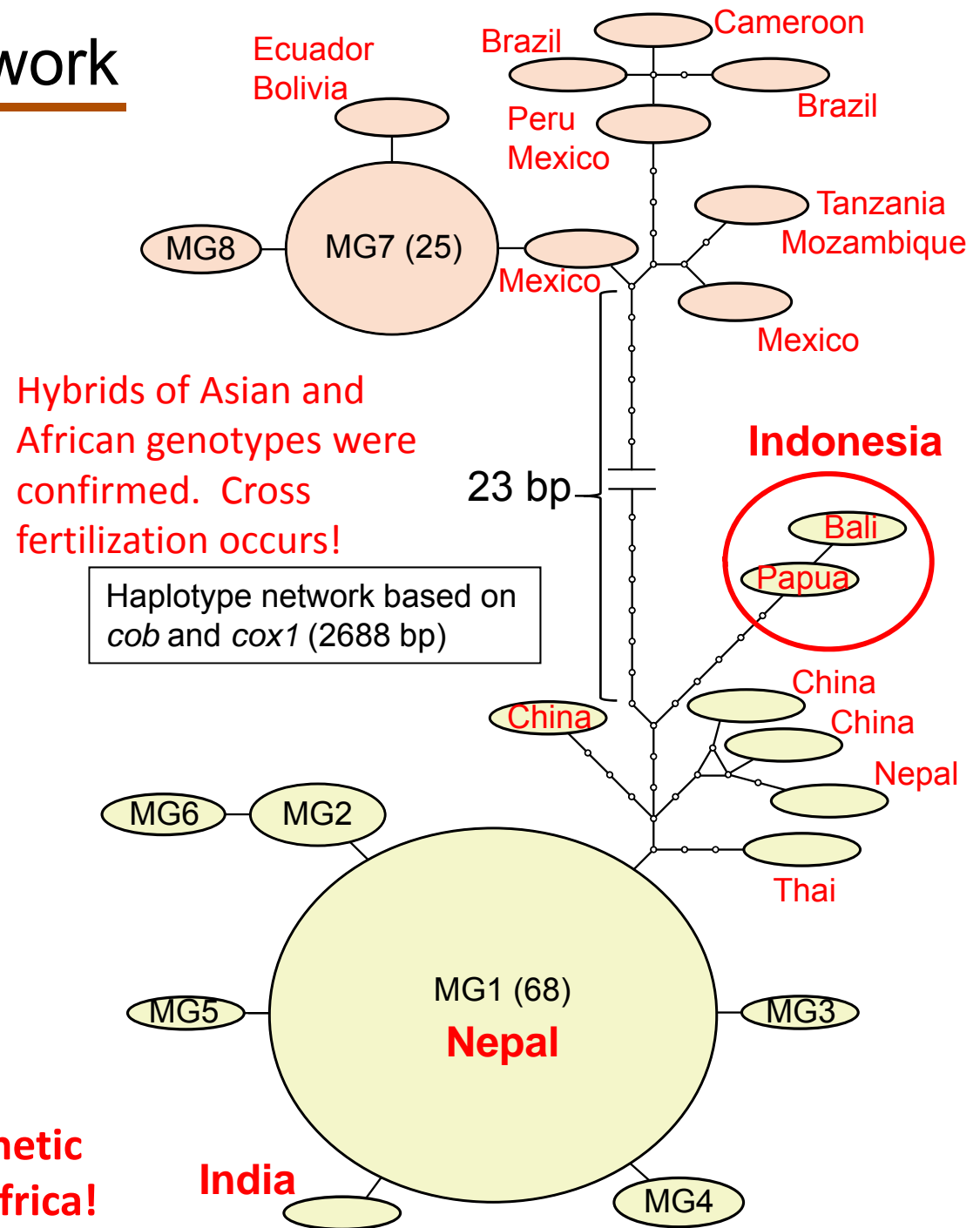


(Michelet et al. 2010 *Molecular Phylogenetics and Evolution*)

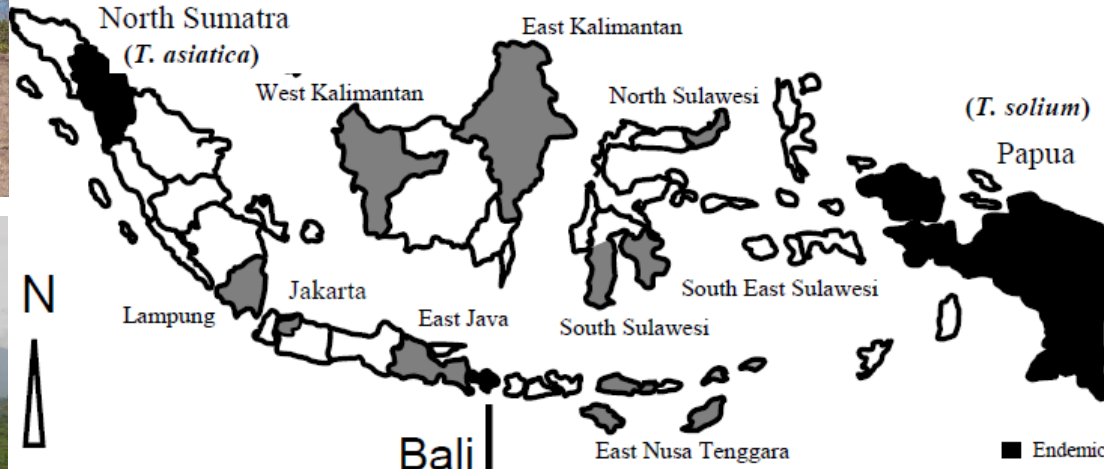
mtDNA haplotype network



We are interested in analyzing genetic diversity in pigs and *T. solium* in Africa!



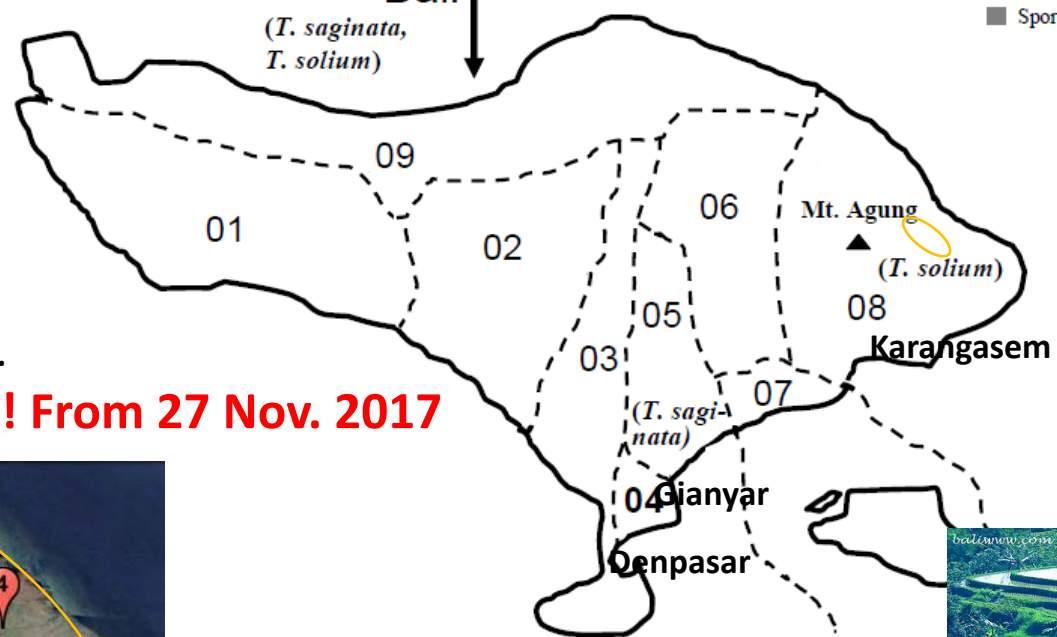
Taeniasis/Cysticercosis in Bali, Indonesia



Endemic areas suspected to be focal in villages on the eastern slope of Mt. Agung, Karangasem

Natural disasters may cause outbreaks beyond our expectation.

Mt. Agung's eruption! From 27 Nov. 2017



Pork Lawar (uncooked or cooked minced pork with blood) VS Beef Lawar (uncooked beef without blood)



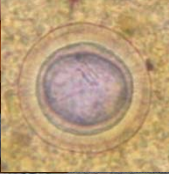
Spicy minced raw pork salad (Larb Moo Dib) in Thailand





Thai-Myanmar Border Refugees villages in Tak Prov

Feb 2012, April 2012, Dec 2012



Taeniasis carriers easily escape from the villages to Bangkok!

Three *Taenia* species are sympatrically distributed in Kanchanaburi Province, Thailand

Nov 2006



Myanmar

Border

Thailand

Feb 2011

Tibetan villages in Sichuan, China

International research projects from 2006 JSPS

The importance of real-time identifications

Oct 2010

GPS on foot

Cooked pork was delicious!?

Molecular identification of the *Taenia* parasite

Oct 2011



Hieroglyph of the House in Chinese



Old Chinese

Wild boar (or adult pig 猪) opening its mouth under roof: error
Pig opening its mouth under floor: **correct**

Pig toilet (pig sty latrine) (猪厠)

China Han dynasty (206BC~AD220)

Still common in remote areas

Jejudo, Korea : common until 1960s

Okinawa, Japan: until the World War II

All other parts, Japan: Human feces were used as fertilizer

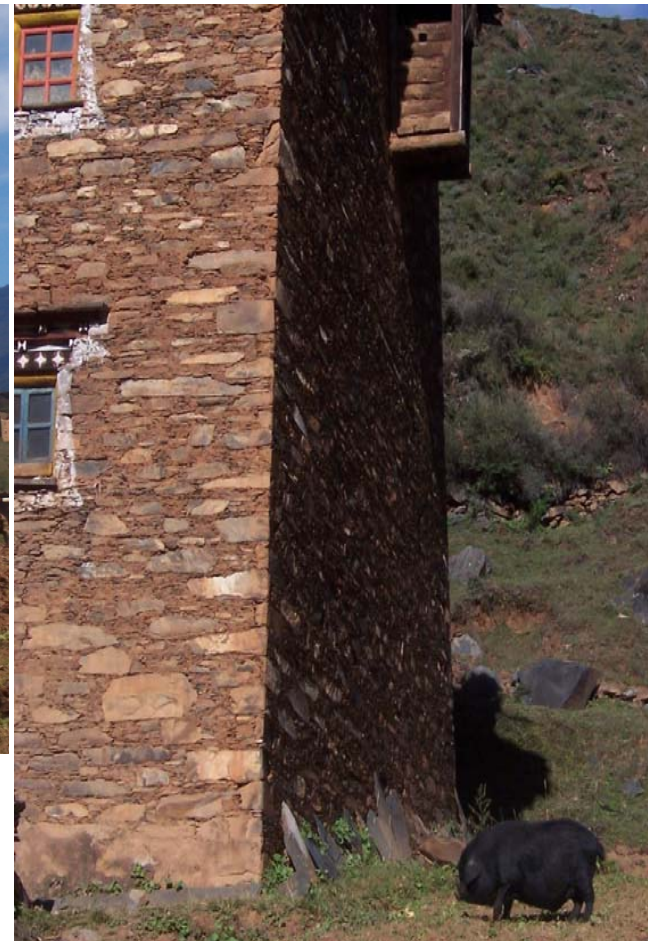


from Wikipedia



2005/10/15

Winter season: indoor latrine.
Under the latrine, pigs are waiting for
the special foods



2011/10/27

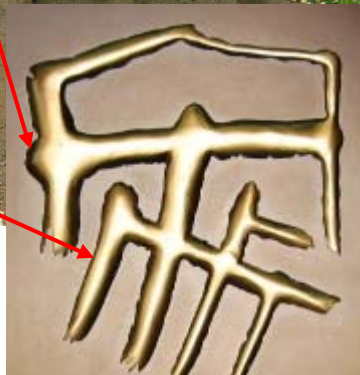


What is meant by the “house” in Chinese?



pigs
豚

mammal



T. solium and *T. asiatica*
and pigs

House/Home

家



Bride or
Daughter-in-law

嫁

↑
female

Taenia solium Cysticercosis:
Community based NTD

If pathogen free, green ecology!



The origin of 家

Approximately 2500 years ago!?

Southern part of China, Vietnam, Lao PDR

from Wikipedia