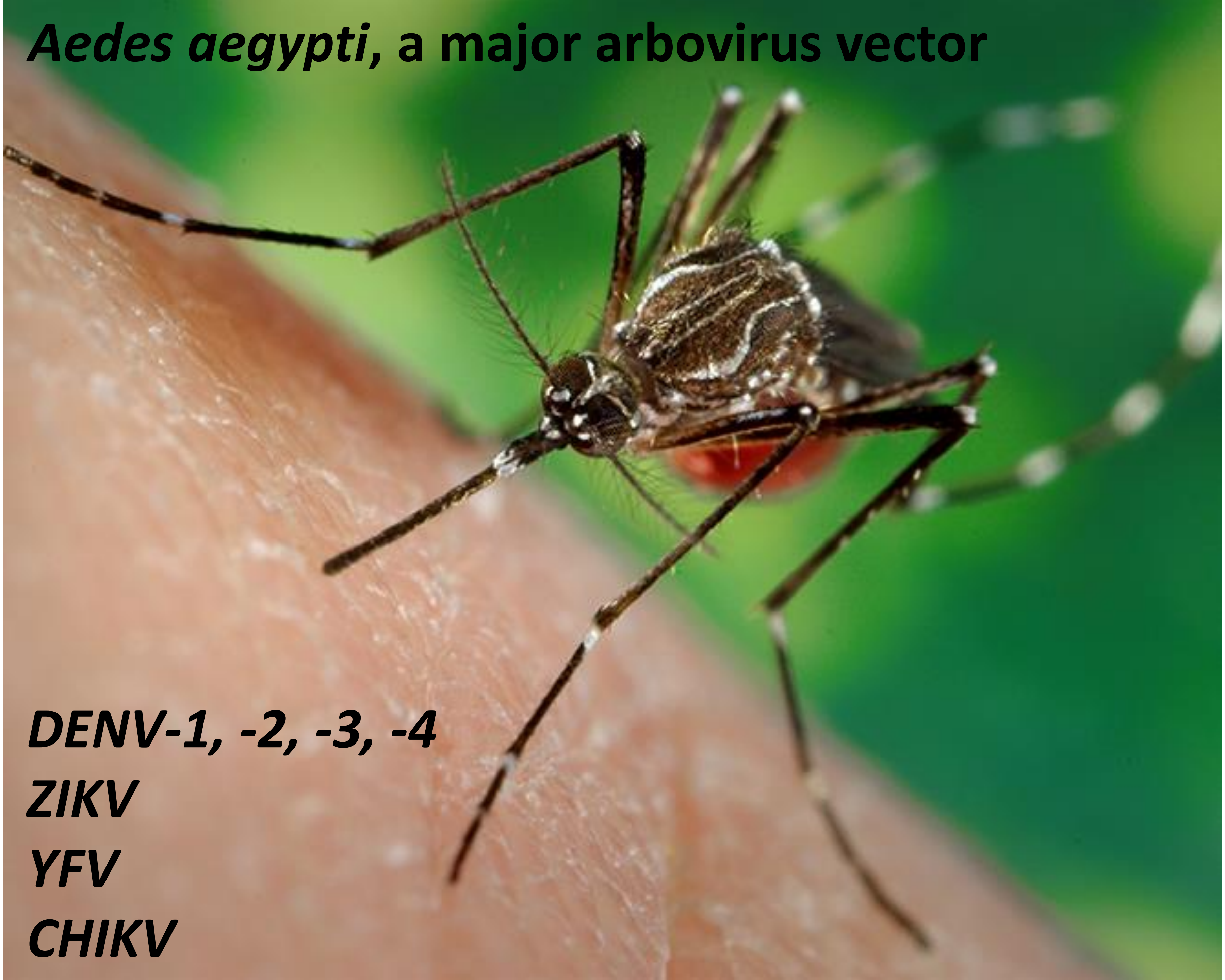
22 June 2018 – *Les Pensières* Center for Global Health

Overview of *Aedes aegypti* biology and interactions with dengue and Zika viruses

Louis Lambrechts

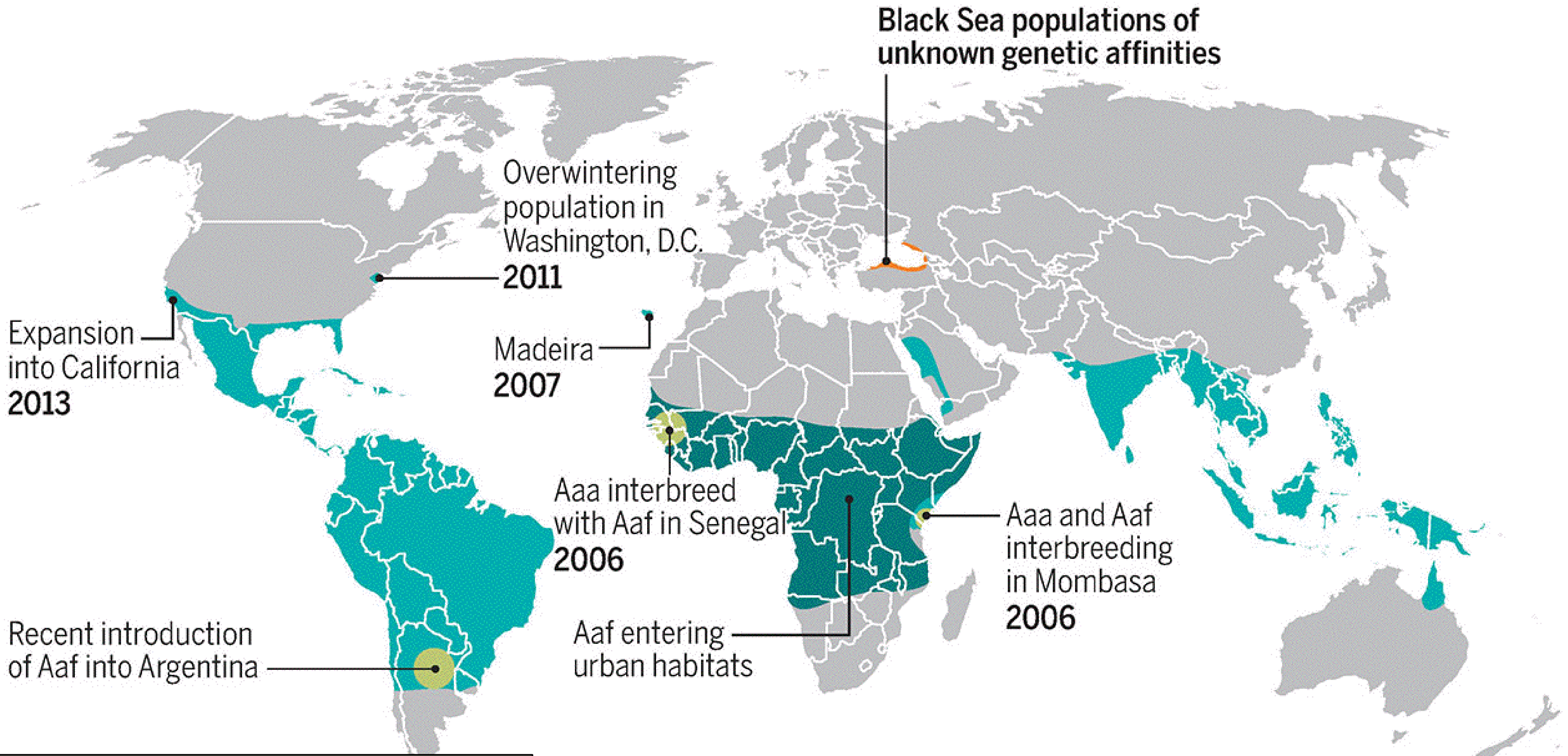
Insect-Virus Interactions, Institut Pasteur-CNRS UMR 2000, Paris, France

Aedes aegypti, a major arbovirus vector

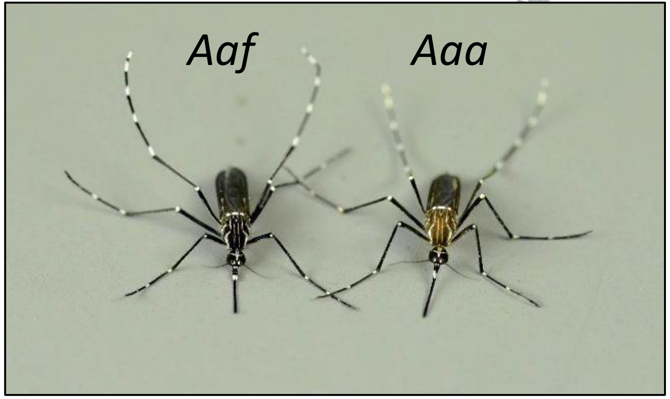


DENV-1, -2, -3, -4
ZIKV
YFV
CHIKV

Worldwide distribution of *Aedes aegypti*



● *Aedes aegypti formosus* (Aaf) ● *Aedes aegypti aegypti* (Aaa)



Powell *Science* 2016; Photo: Lindy McBride

What does make *Aedes aegypti* such a good arbovirus vector?

Vector-borne pathogen transmission

$$R_0 = \frac{ma^2p^nb}{-\ln(p)} \frac{c}{r}$$

R_0 (basic reproduction number) = total number of infectious vector bites that arise from 1 infected person introduced into a susceptible human population

Vector-borne pathogen transmission

$$R_0 = \frac{ma^2p^nb}{-\ln(p)} \underbrace{\frac{c}{r}}_{HUMAN}$$

c = human host competence

r = daily recovery rate
of infected humans

R_0 (basic reproduction number) = total number of infectious vector bites that arise from 1 infected person introduced into a susceptible human population

Vector-borne pathogen transmission

m = vector density per person

a = daily probability of human biting

p = daily probability of vector survival

n = duration in days of extrinsic incubation period

b = vector competence

$$R_0 = \underbrace{\frac{ma^2p^nb}{-\ln(p)}}_{VECTOR}\;\underbrace{\frac{c}{r}}_{HUMAN}$$

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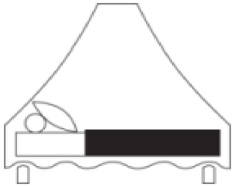

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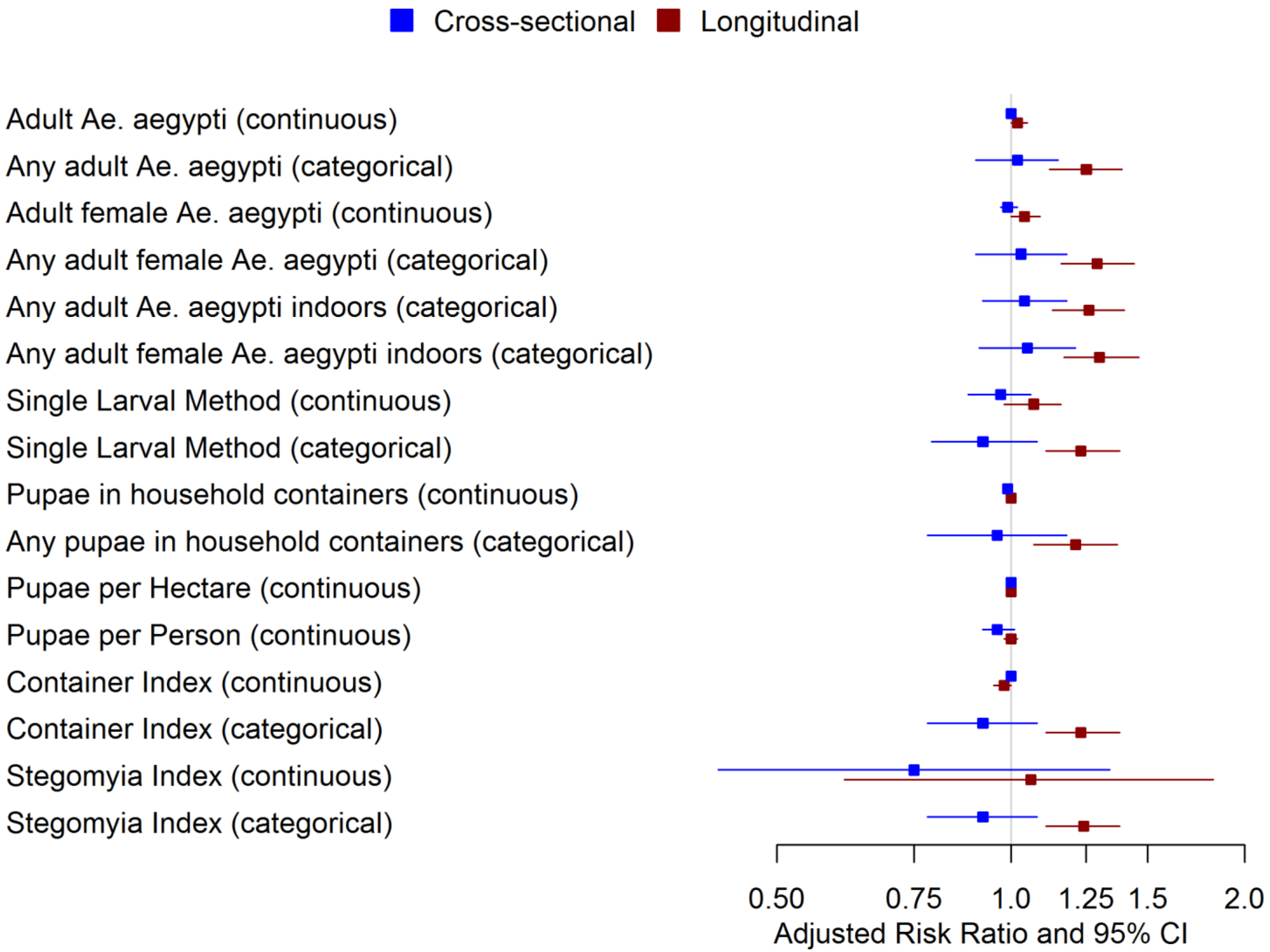
Aedes aegypti abundance and DENV infection risk



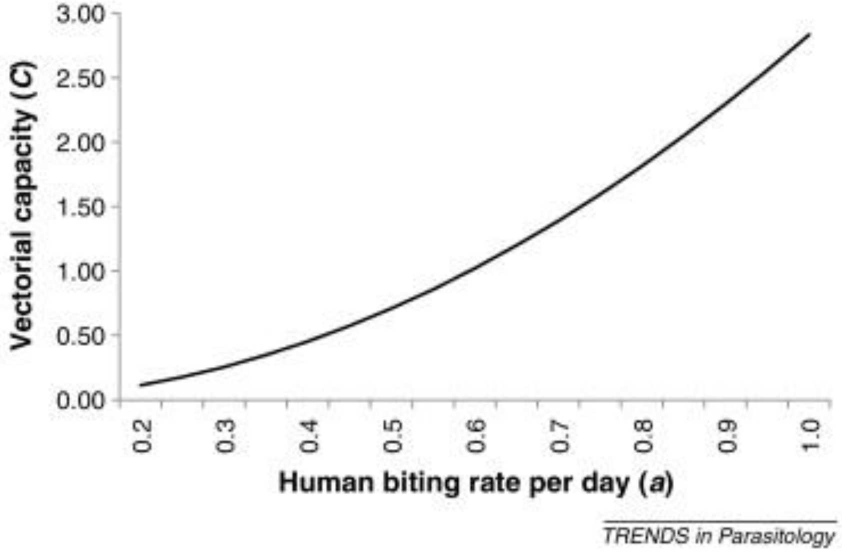
Household-level indicators of *Ae. aegypti* abundance are associated with DENV seroconversion when they are calculated from longitudinal entomological data

Cromwell *et al. PLoS Negl Trop Dis* 2017

Impact of mosquito blood feeding behavior on vector-borne pathogen transmission

Most adult female anautogenous mosquitoes

- One vertebrate blood meal per egg-laying cycle
- Consumption of plant carbohydrates



Aedes aegypti

- >90% blood meals taken on humans
- Multiple blood feeding
- 0.63 to 0.76 blood meals per day
- No sugar feeding when human blood available

Reviewed in Scott & Takken *Trends Parasitol* 2012

Vector-borne pathogen transmission

p = daily probability of vector survival

a = daily probability of human biting

n = duration in days of extrinsic incubation period

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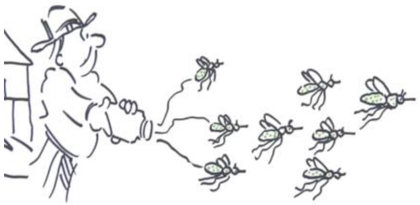

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Genetic determinants of vector-virus interactions

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- *Ae. aegypti* vs. *Ae. albopictus*

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- Larval microbiota
- Vertebrate host factors

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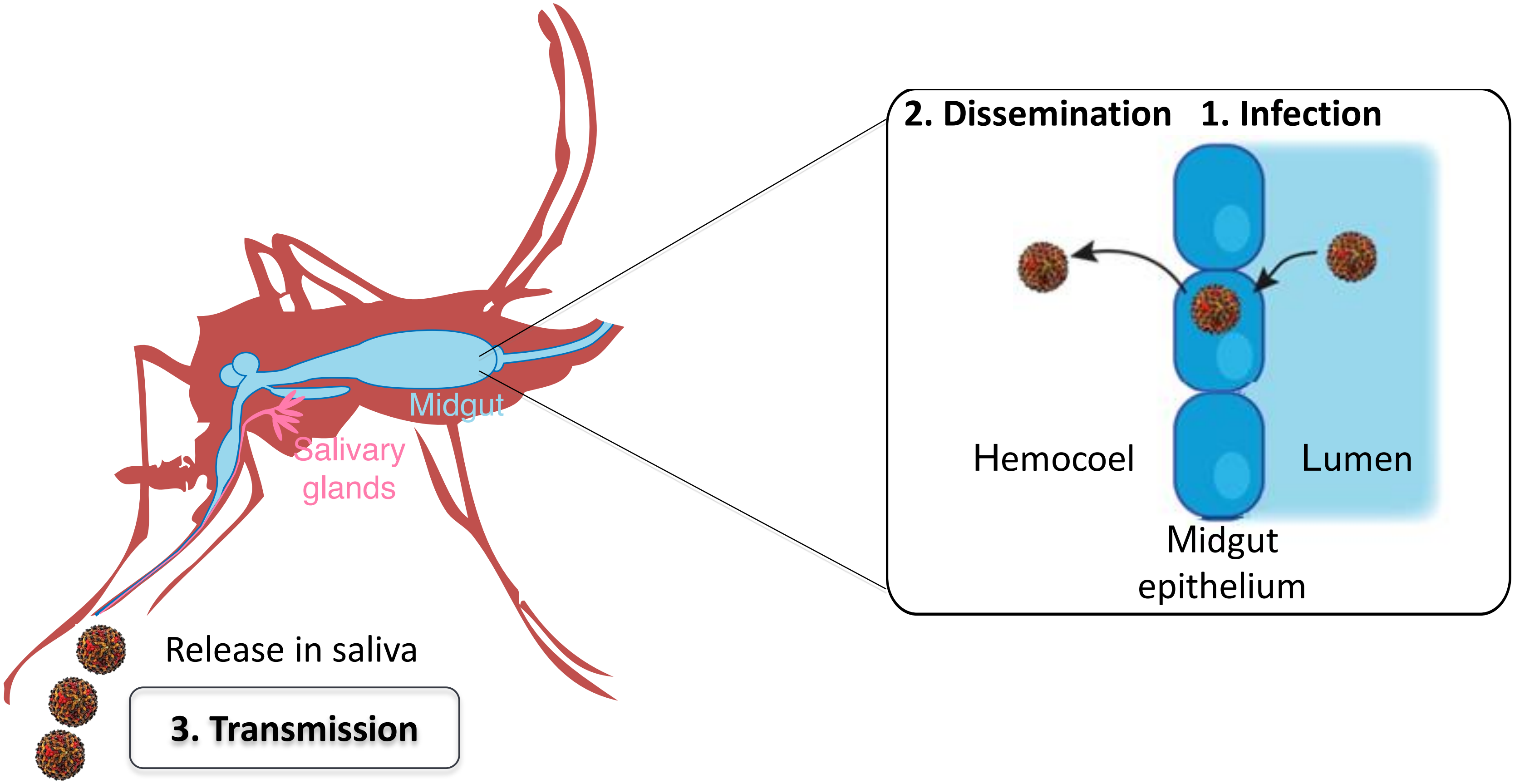
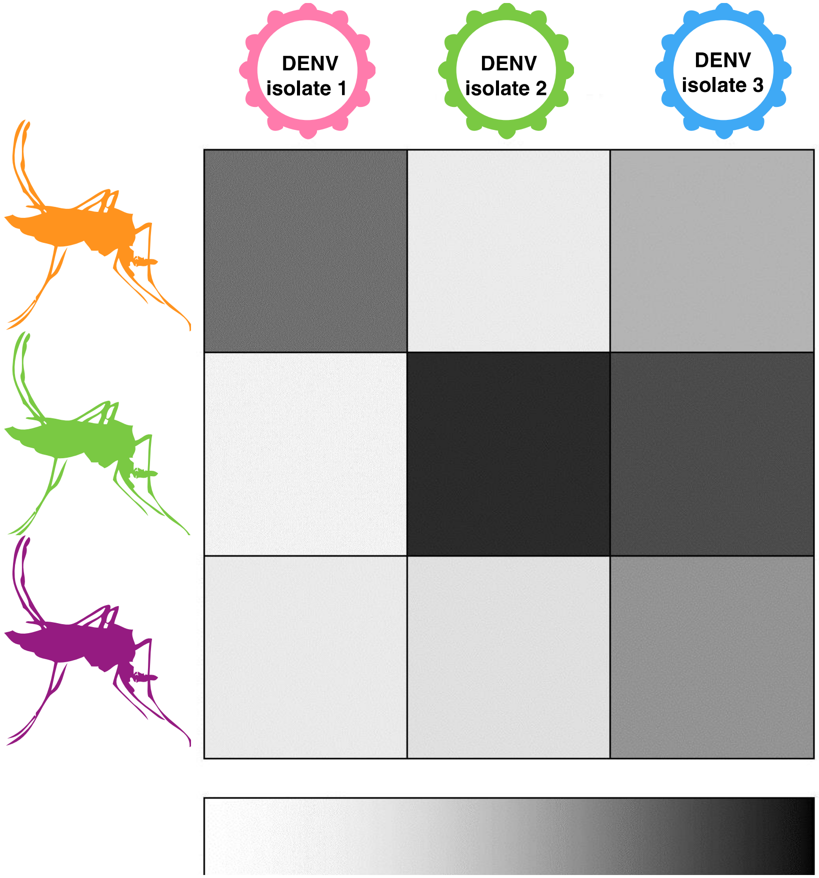
Vector competence

Intrinsic ability to become infected and subsequently transmit a pathogen



Genotype-by-genotype (G x G) interactions

DENV-1 isolates



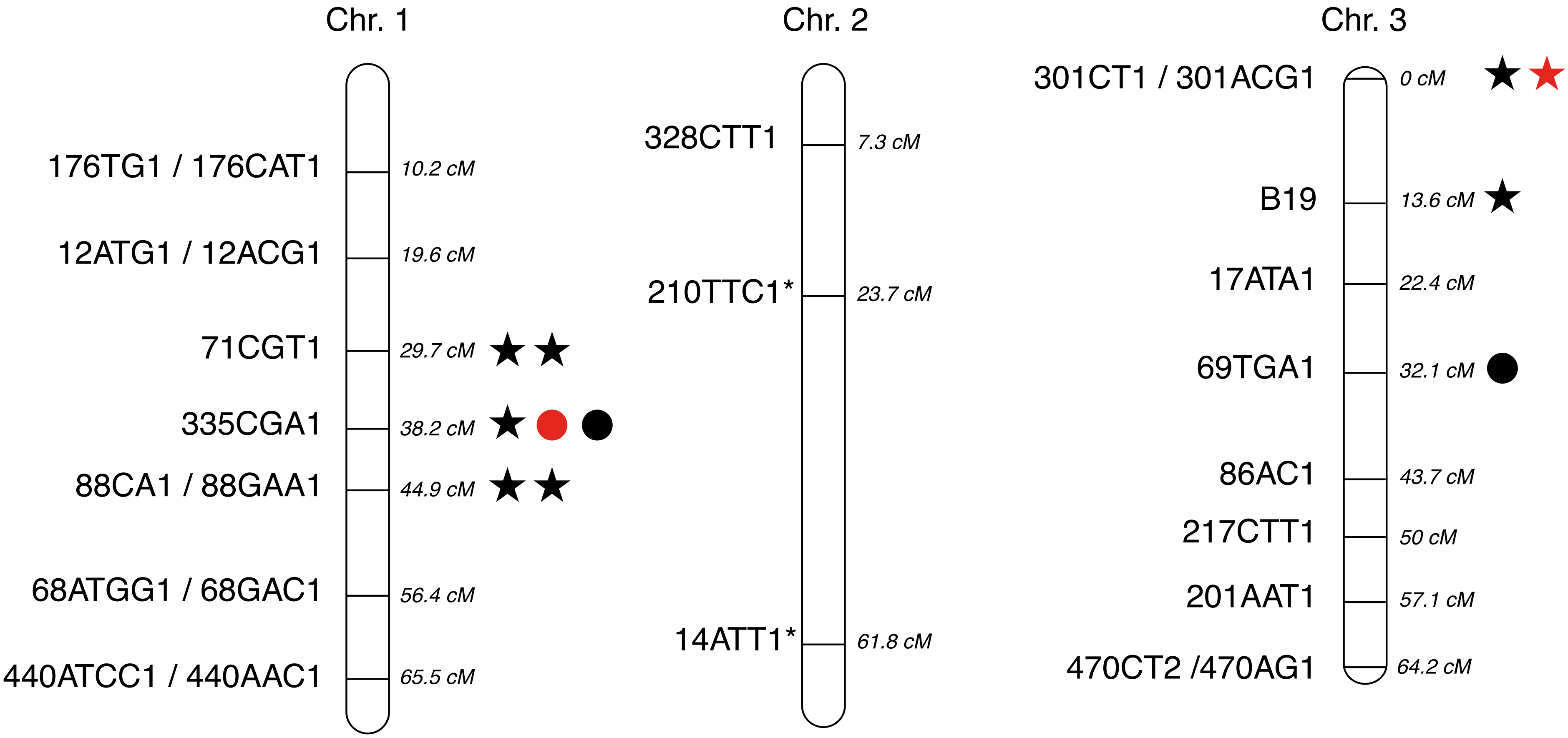
Ae. aegypti genotypes

LOW Vector competence HIGH

Ratchaburi, Thailand

Lambrechts *et al. BMC Evol Biol* 2009; Lambrechts *Trends Parasitol* 2011

Genetic mapping of G x G interactions between *Ae. aegypti* and DENV



Chr. 1

176TG1 / 176CAT1 *10.2 cM*

12ATG1 / 12ACG1 *19.6 cM*

71CGT1 *29.7 cM* ★ ★

335CGA1 *38.2 cM* ★ ● ●

88CA1 / 88GAA1 *44.9 cM* ★ ★

68ATGG1 / 68GAC1 *56.4 cM*

440ATCC1 / 440AAC1 *65.5 cM*

Chr. 2

328CTT1 *7.3 cM*

210TTC1* *23.7 cM*

14ATT1* *61.8 cM*

Chr. 3

301CT1 / 301ACG1 *0 cM* ★ ★

B19 *13.6 cM* ★

17ATA1 *22.4 cM*

69TGA1 *32.1 cM* ●

86AC1 *43.7 cM*

217CTT1 *50 cM*

201AAT1 *57.1 cM*

470CT2 /470AG1 *64.2 cM*

☆ **Infection**

○ **Dissemination**

G x G interaction

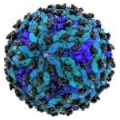
Fansiri *et al. PLoS Genet* 2013

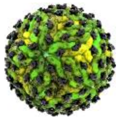
Worldwide survey of *Ae. aegypti* susceptibility to diverse strains of ZIKV

Preparedness
Latin American Network
ZikaPLAN

- **8 field-derived *Ae. aegypti* colonies**

- **6 low-passage ZIKV strains:**

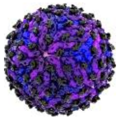

Cambodia
2010


Philippines
2012


F. Polynesia
2013

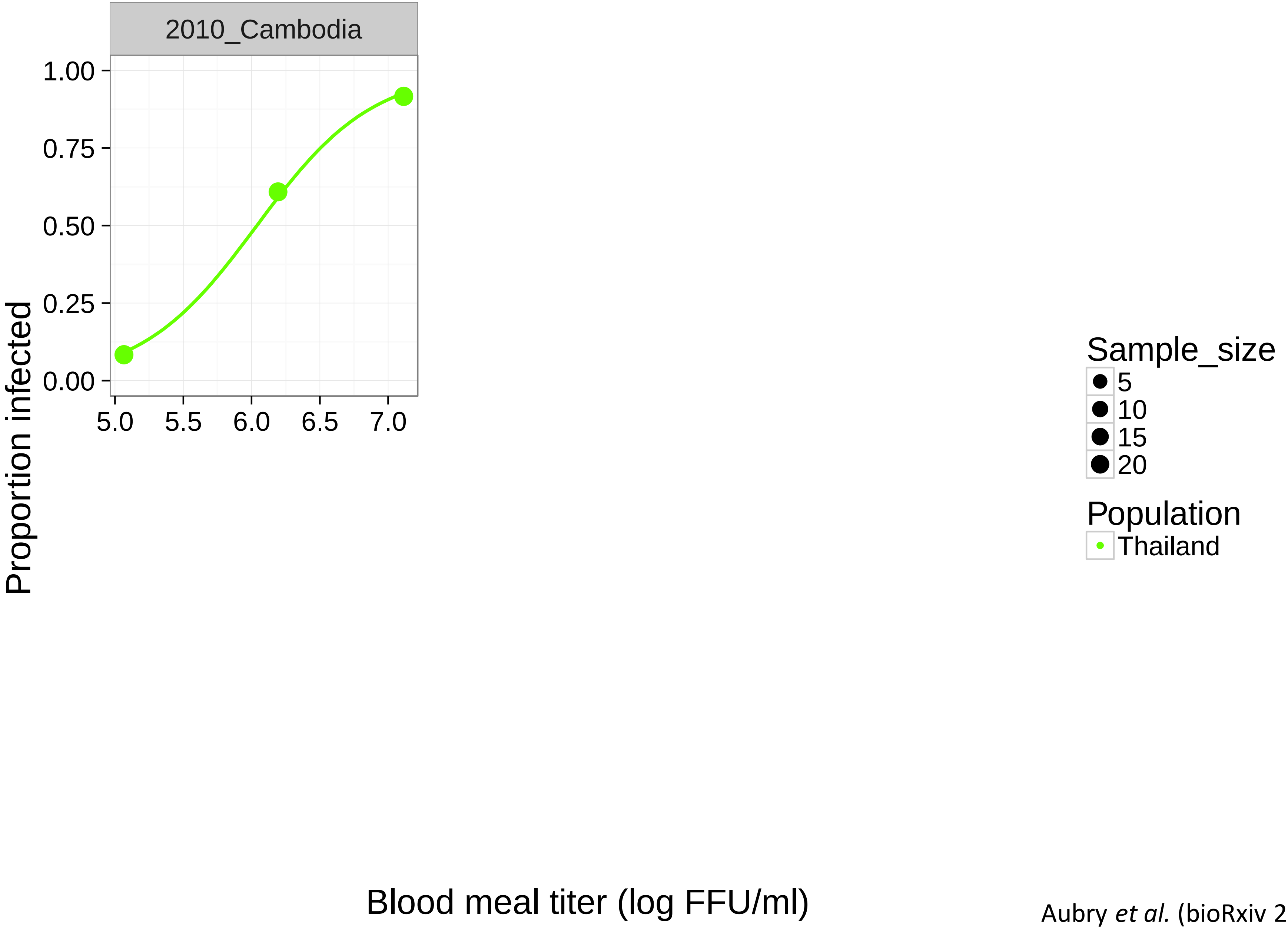

Thailand
2014


Puerto Rico
2015


Senegal
2015

Aubry *et al.* (bioRxiv 2018)

Aedes aegypti susceptibility to ZIKV



Aubry *et al.* (bioRxiv 2018)

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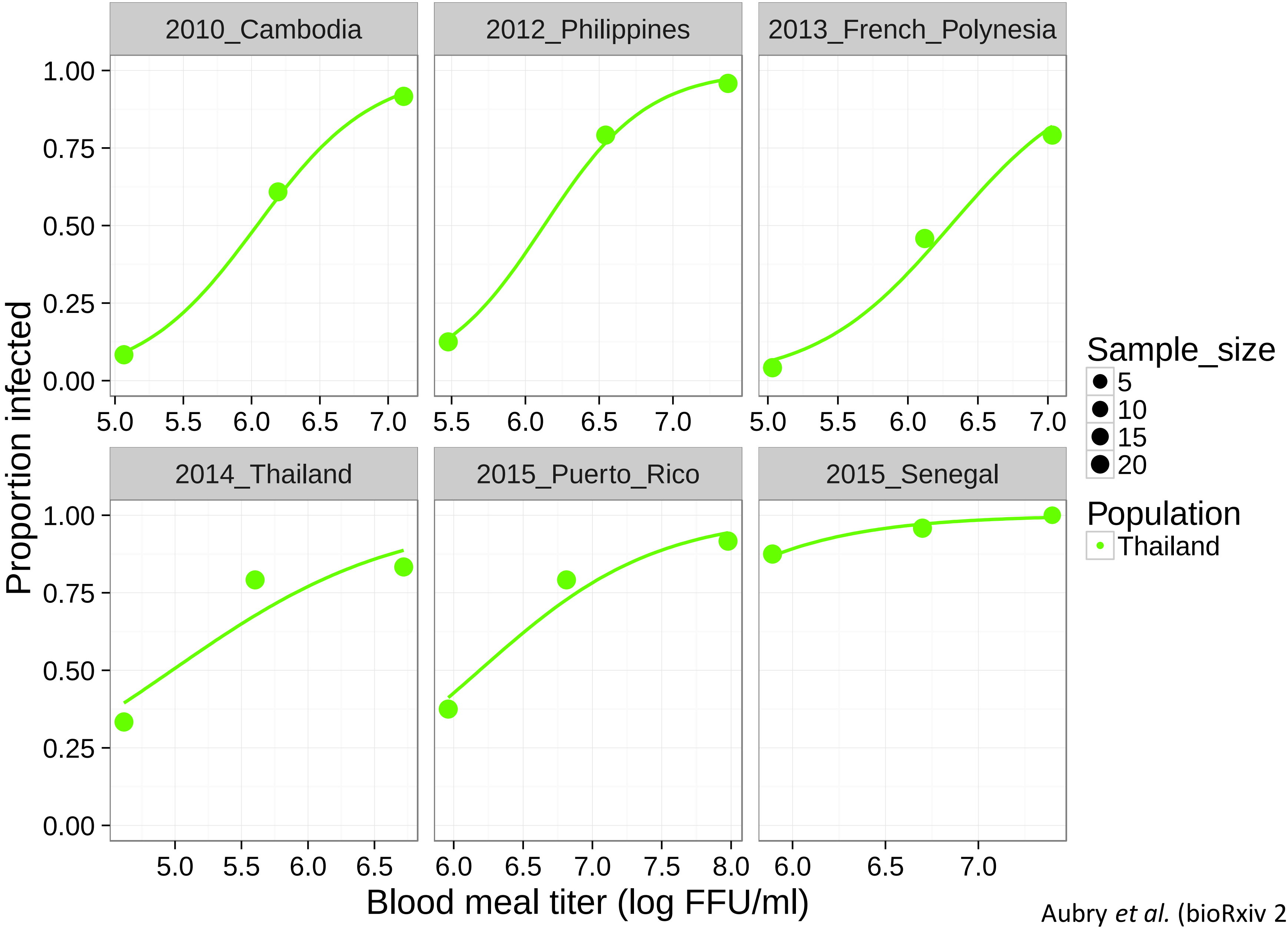
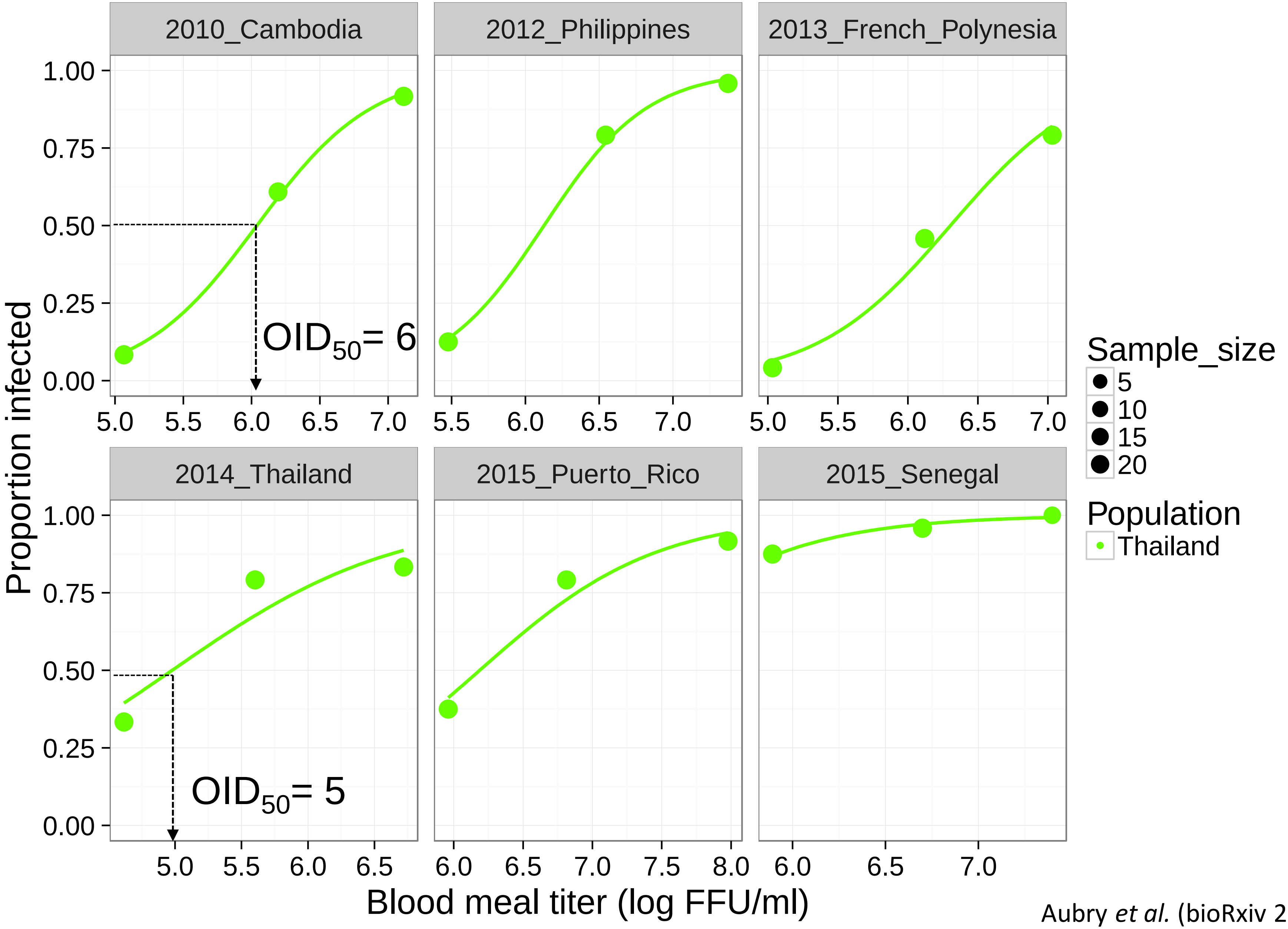


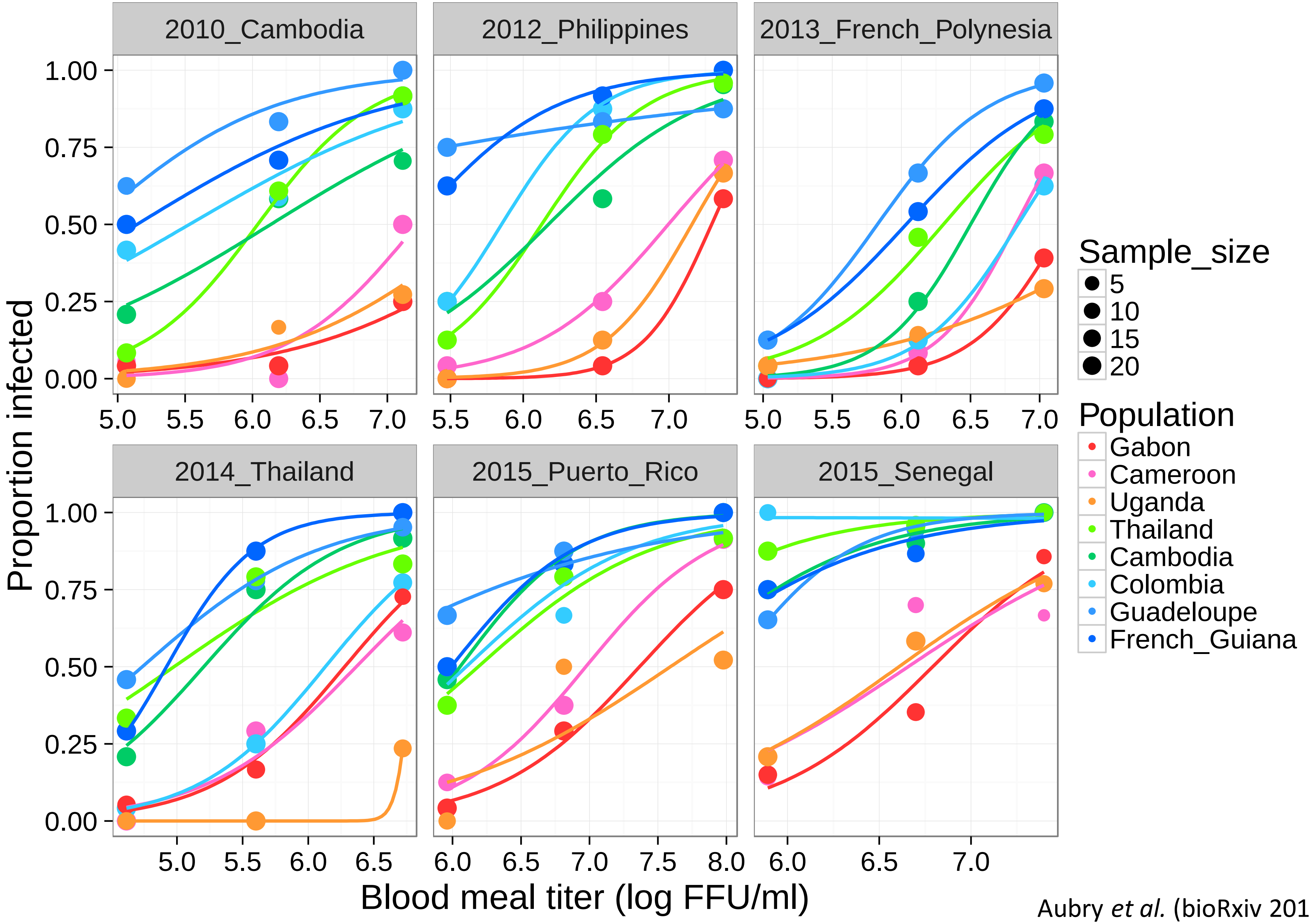
Aubry *et al.* (bioRxiv 2018)

Aedes aegypti susceptibility to ZIKV



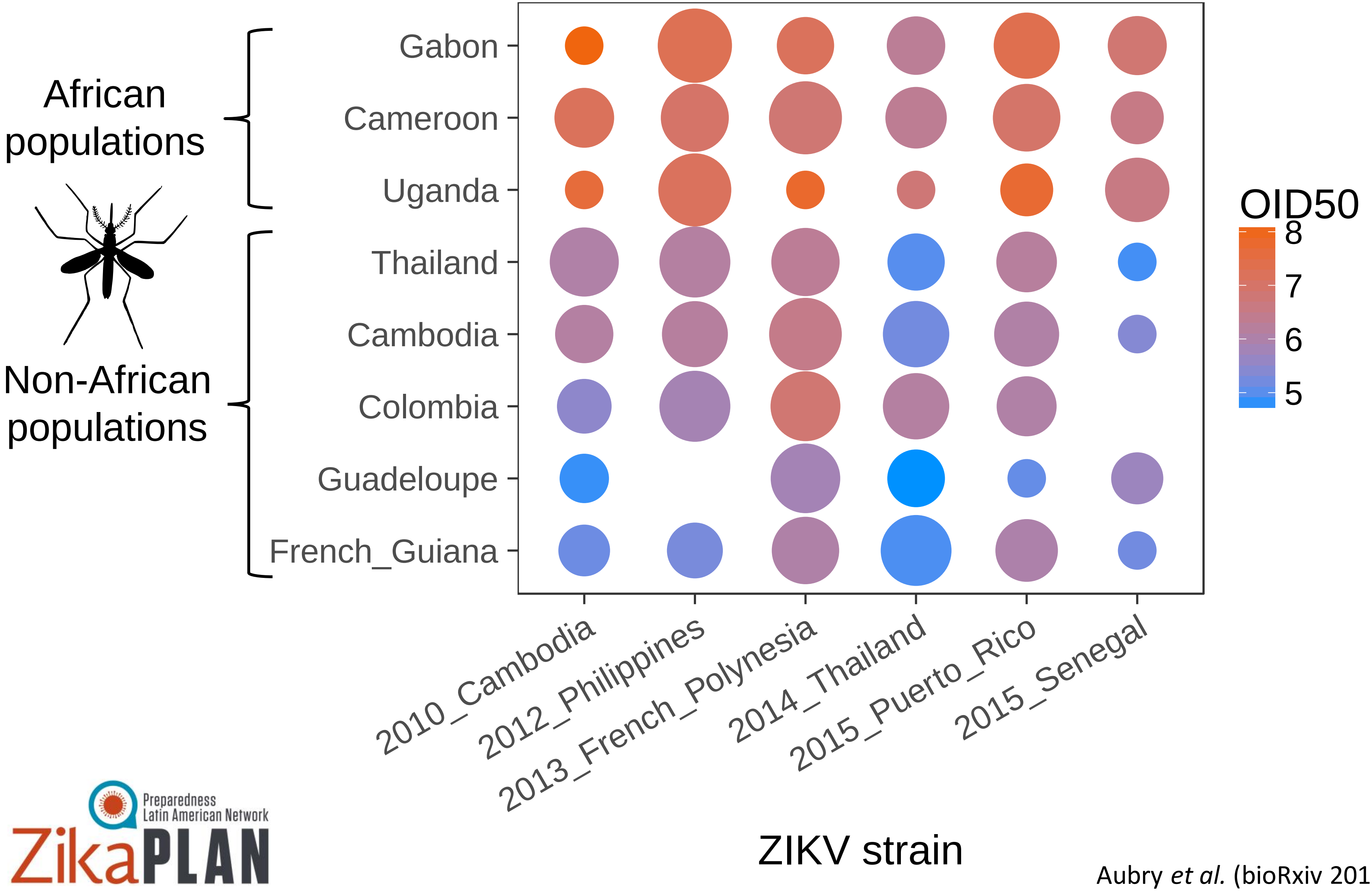
Aubry *et al.* (bioRxiv 2018)

Aedes aegypti susceptibility to ZIKV



Aubry *et al.* (bioRxiv 2018)

African *Ae. aegypti* are less susceptible to ZIKV



Preparedness Latin American Network
ZikaPLAN

Aubry *et al.* (bioRxiv 2018)

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Genetic determinants of vector-virus interactions

- G x G interactions
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Non-genetic determinants of vector-virus interactions

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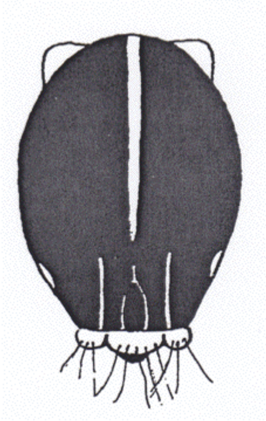
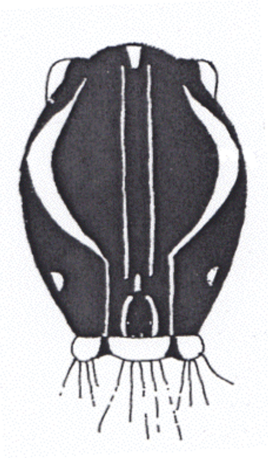
- Vertebrate host factors

Aedes aegypti vs. *Aedes albopictus*

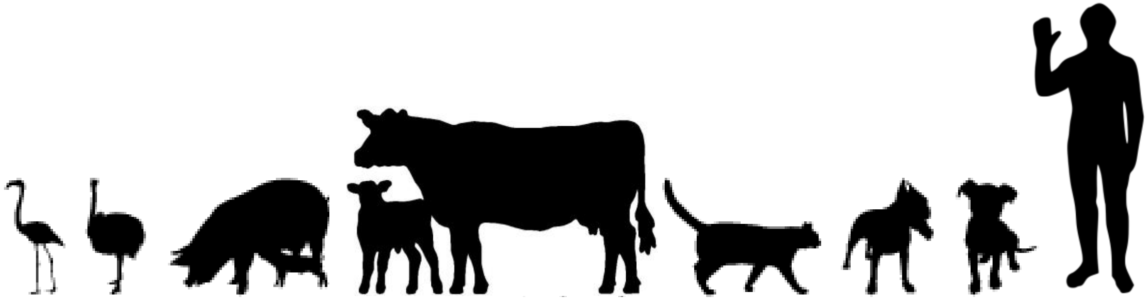
Secondary DENV/ZIKV vector:
Aedes albopictus



Primary DENV/ZIKV vector:
Aedes aegypti



Feeding behavior of *Ae. aegypti* vs. *Ae. albopictus*



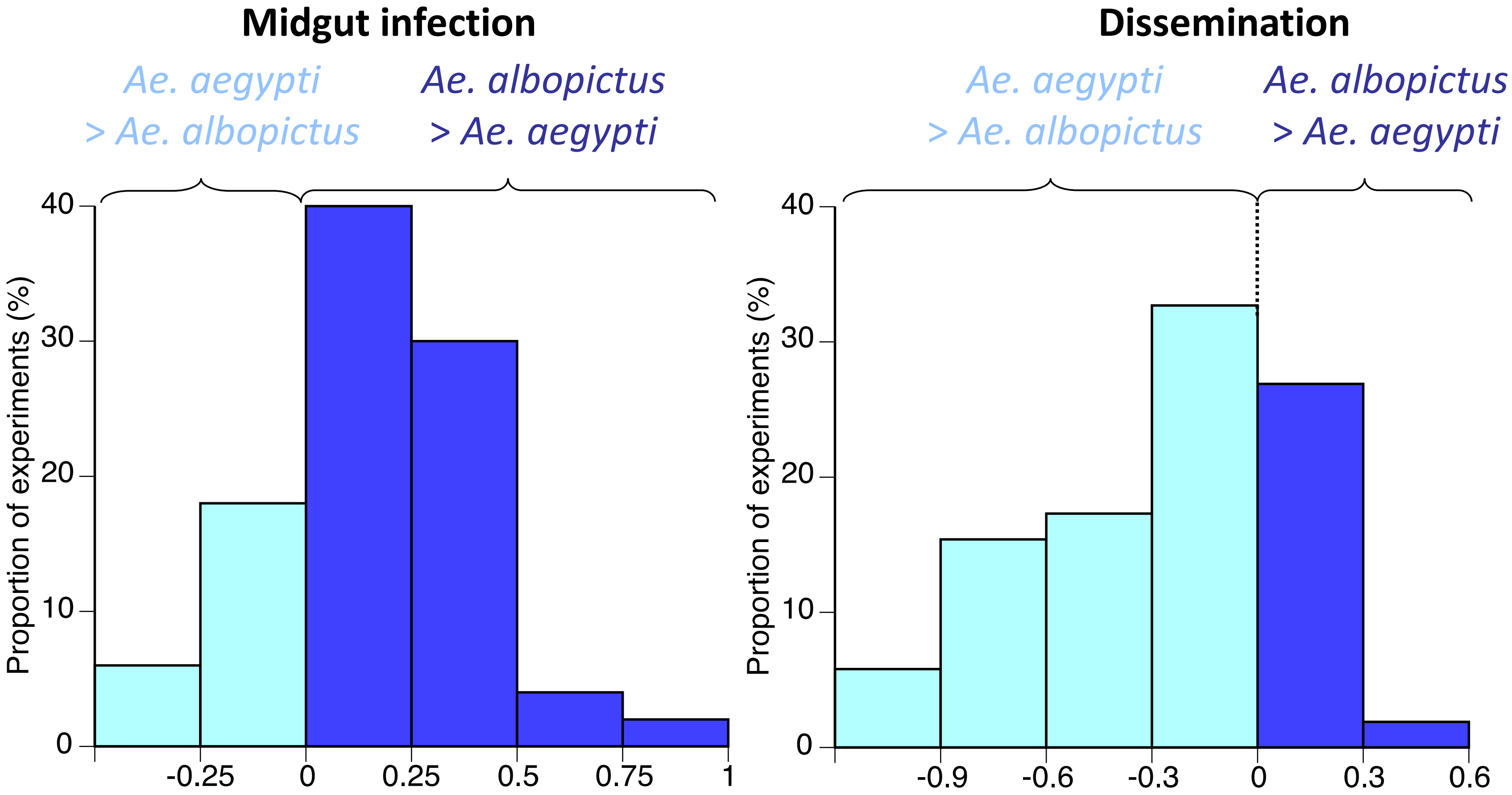
Aedes albopictus
- Day biting
- **Opportunistic**

Aedes aegypti aegypti
- Day biting
- **Anthropophilic**

However, multiple examples of *Ae. albopictus* preference for humans:
- North Carolina (Richards *et al. J Med Entomol* 2006)
- La Réunion Island (Delatte *et al. Vector Borne Zoonotic Dis* 2010)
- Southern Thailand (Ponlawat & Harrington *J Med Entomol* 2005)

DENV competence of *Ae. aegypti* vs. *Ae. albopictus*

Meta-analysis of 91 separate experiments from 14 studies (1971-2009)



Midgut infection

Dissemination

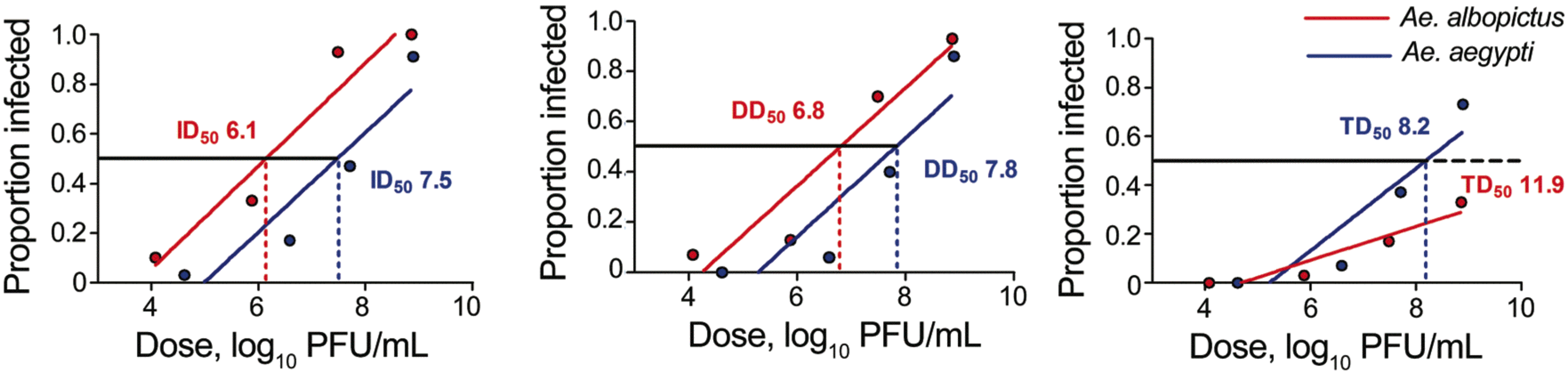
- *Ae. albopictus* 16% more susceptible to midgut infection
- Dissemination 26% less likely than in *Ae. aegypti*

Lambrechts *et al. PLoS Negl Trop Dis* 2010

ZIKV competence of *Ae. aegypti* vs. *Ae. albopictus*

Ae. albopictus is more susceptible but less competent than *Ae. aegypti*

Infection (body) **Dissemination (legs)** **Transmission (saliva)**



- Data shown for 2016 ZIKV strain from Honduras
- Similar results for 2010 ZIKV strain from Cambodia

Ciota *et al. Emerg Infect Dis* 2017

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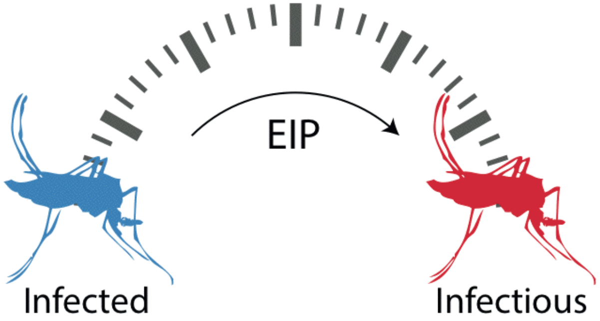
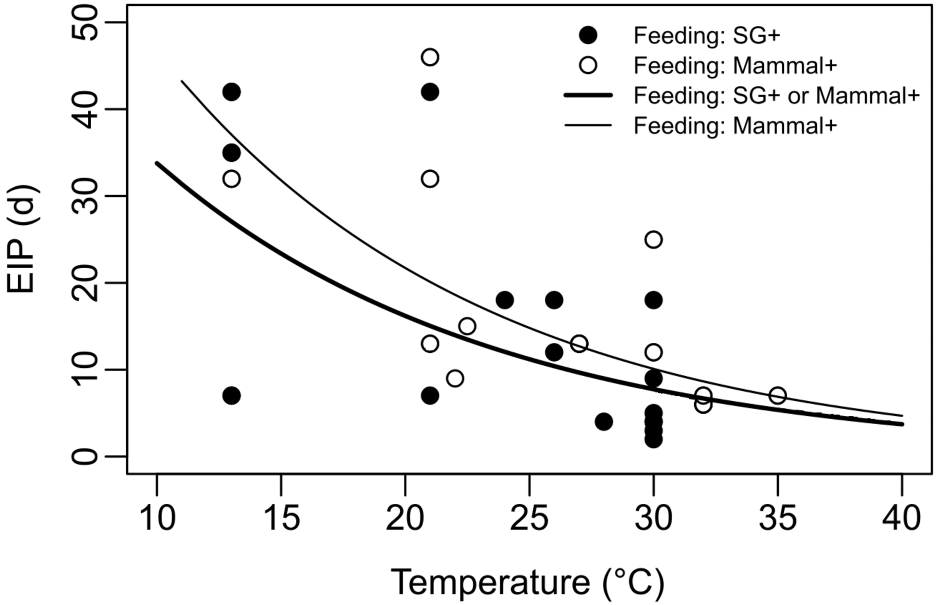
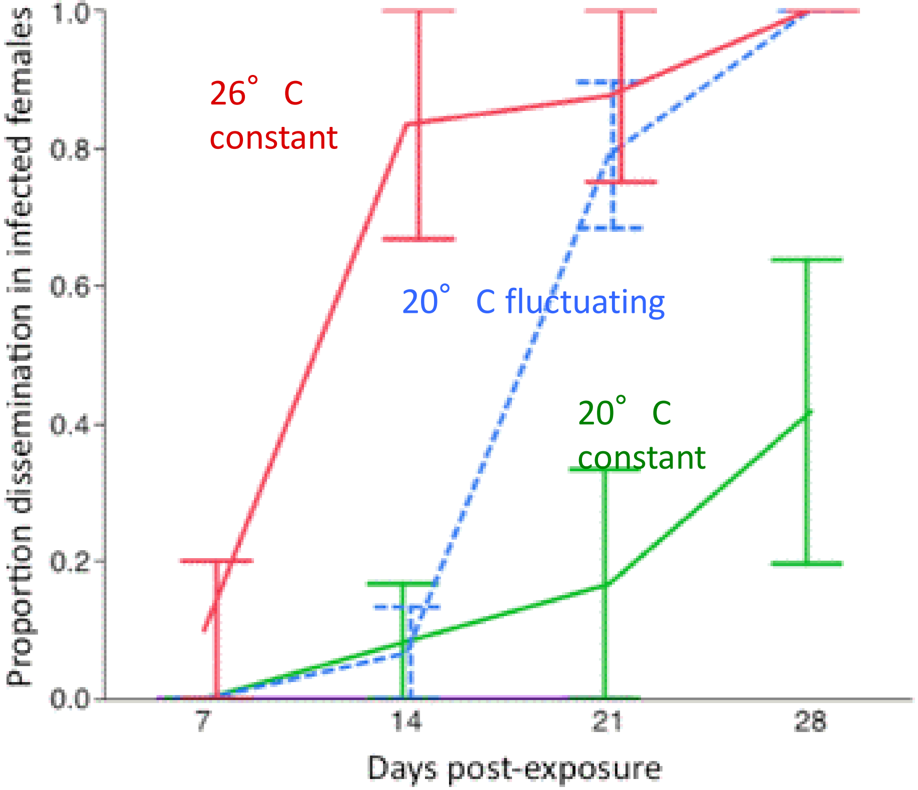
Influence of ambient temperature on DENV extrinsic incubation period in *Ae. aegypti*







Tjaden *et al. PLoS Negl Trop Dis* 2013; Carrington *et al. PLoS Negl Trop Dis* 2013

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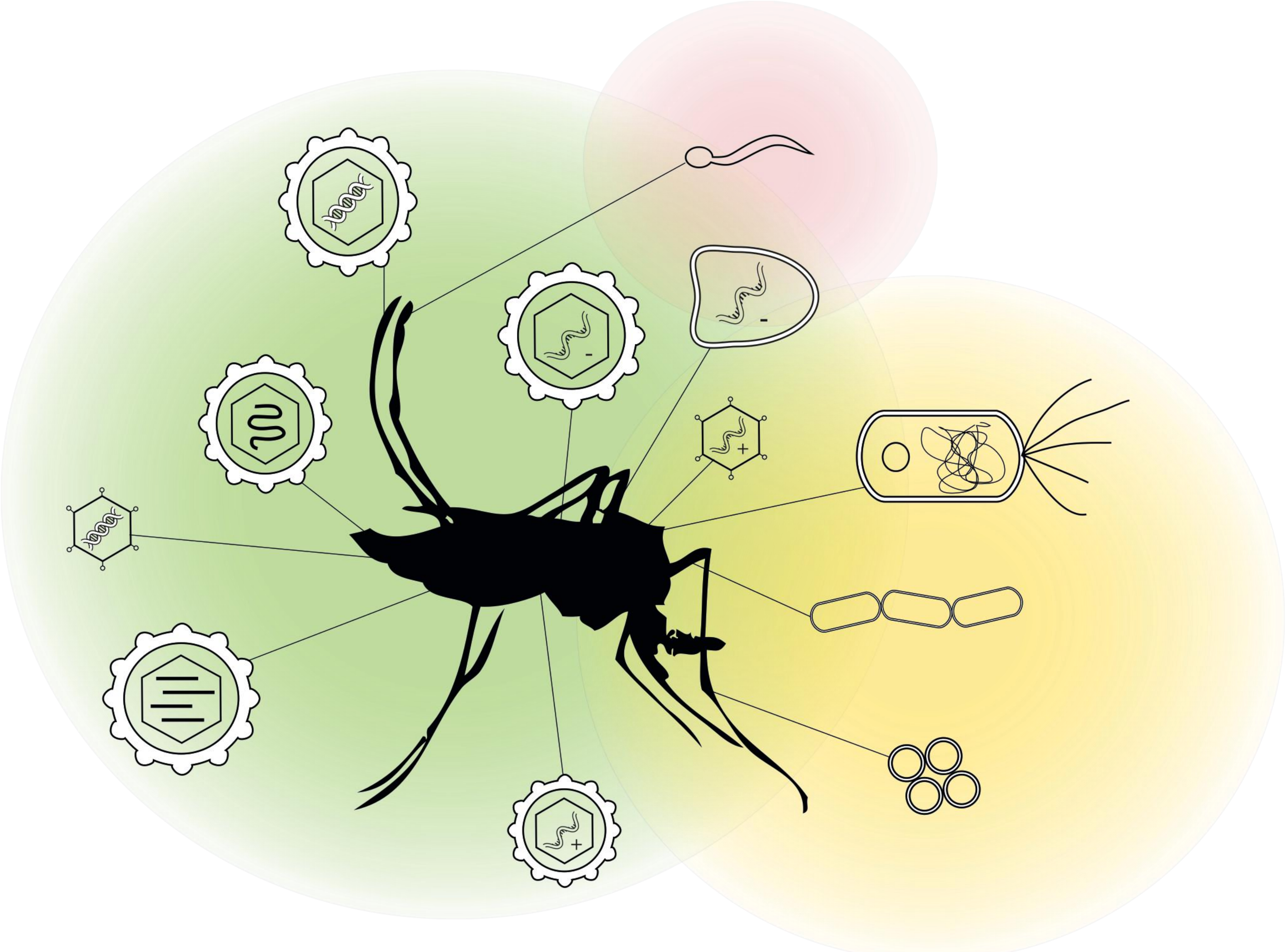
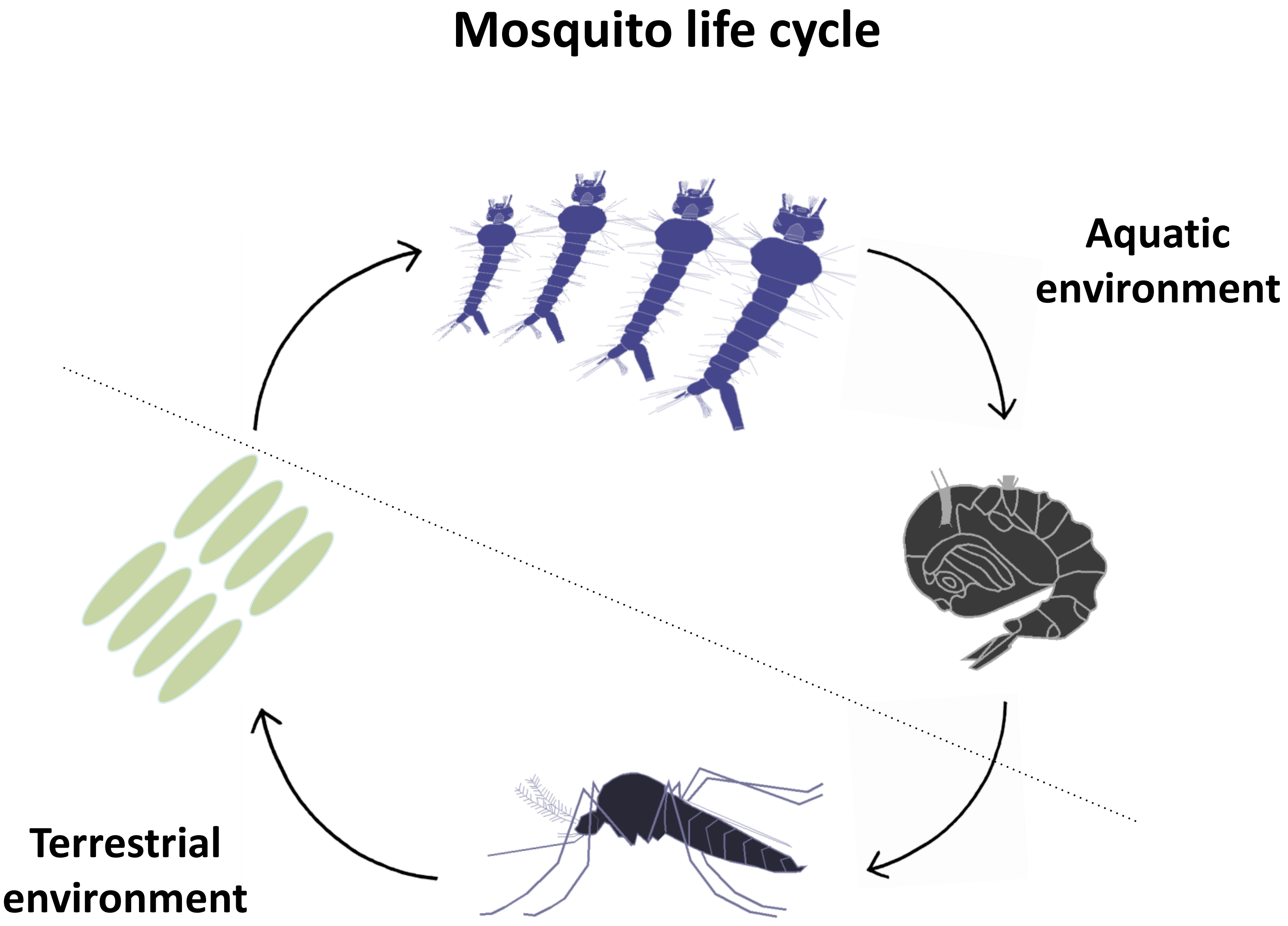
The mosquito 'holobiont'



Carry-over effects of larval microbiota



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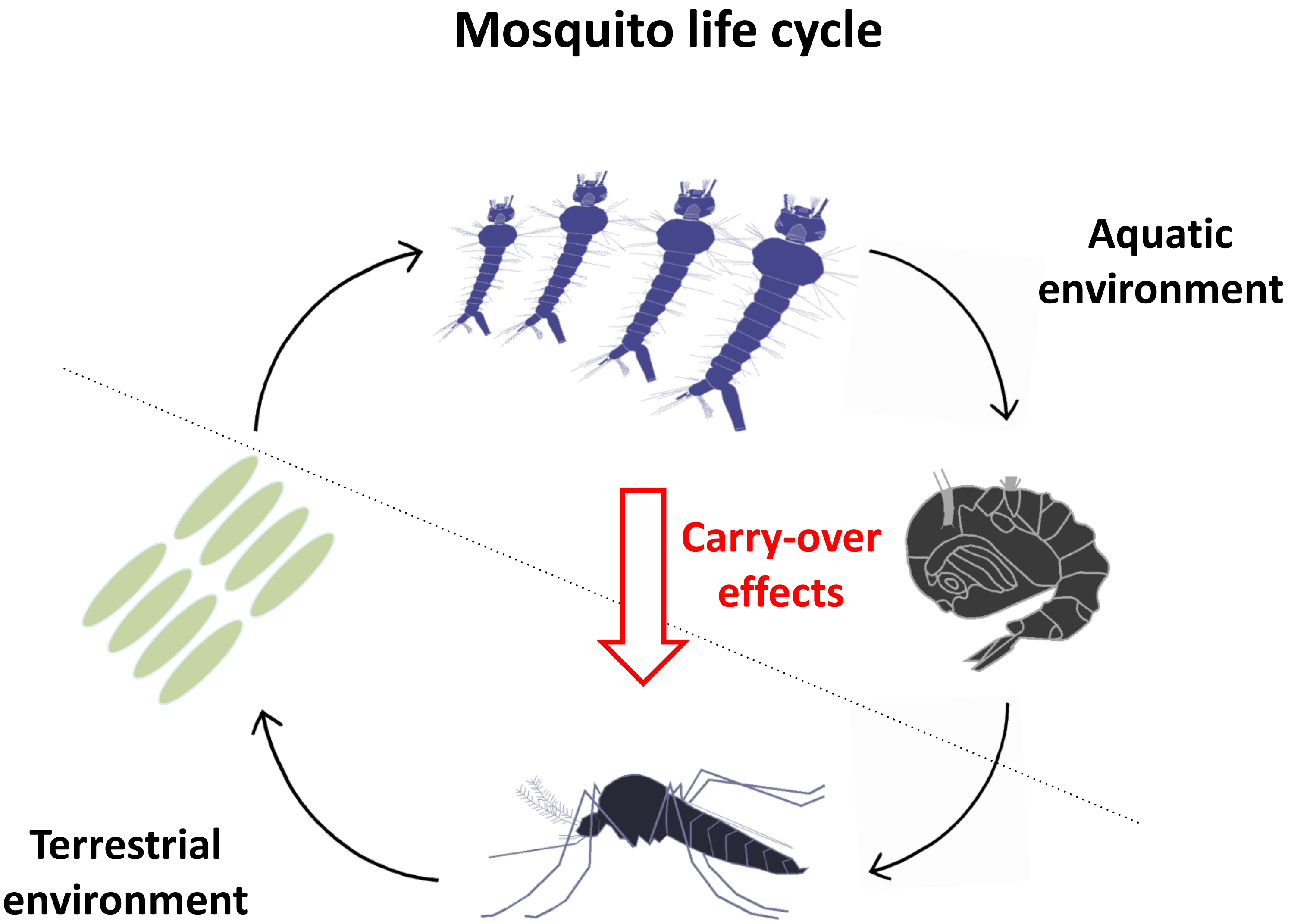
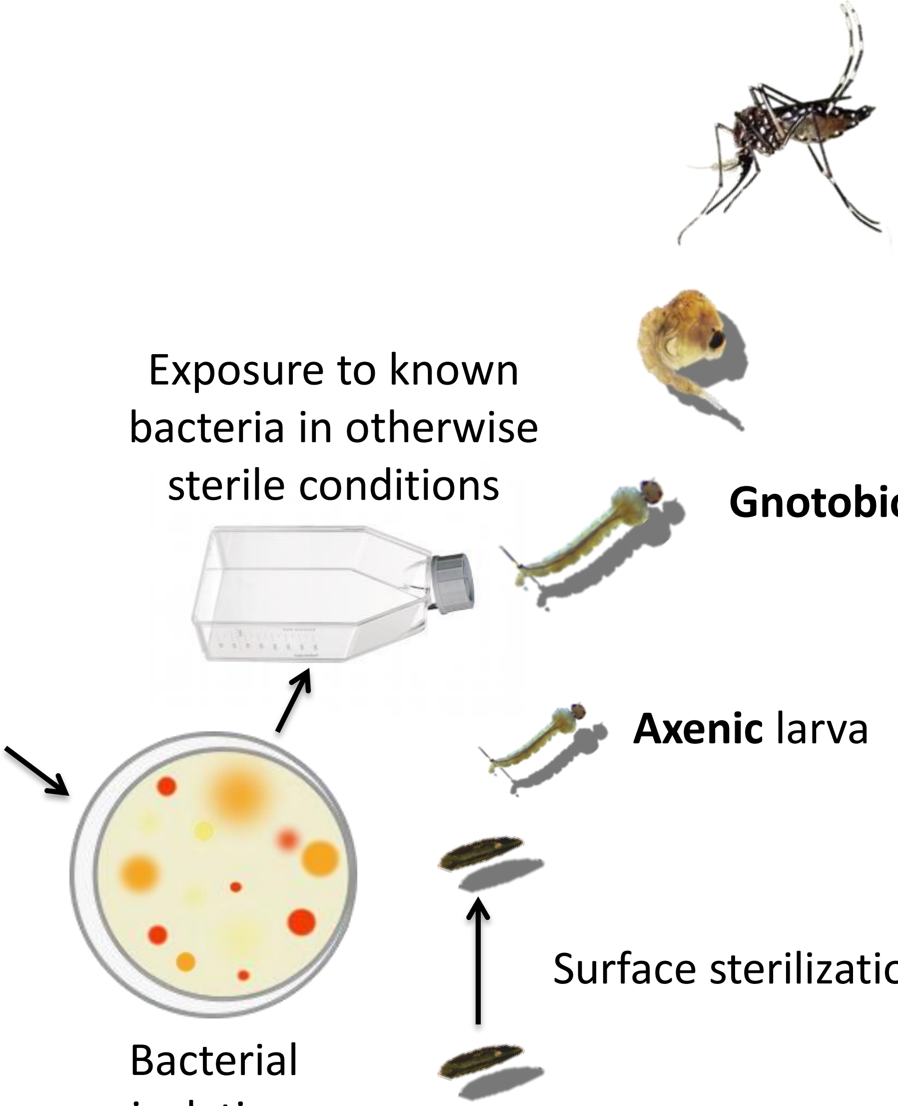


Gnotobiotic mosquitoes

Water sampling from natural breeding sites in Gabon



Bacterial isolation

Exposure to known bacteria in otherwise sterile conditions

Egg

Surface sterilization

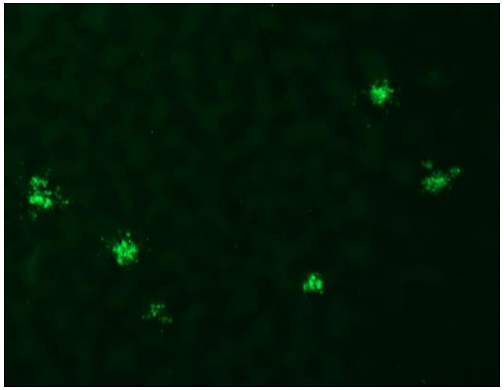
Axenic larva

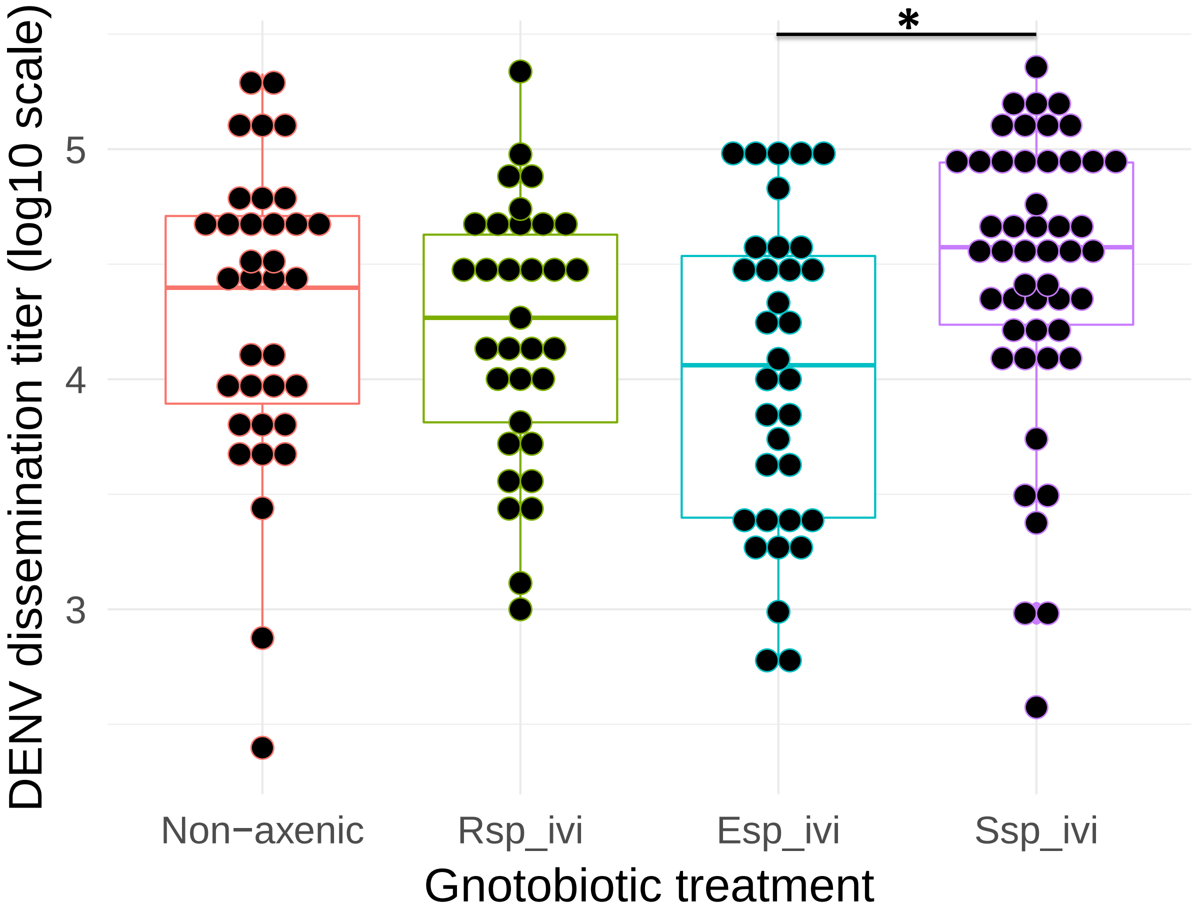
Gnotobiotic larva

Adult vector competence

Dickson *et al. Sci Adv* 2017

Exposure to different bacteria during larval development affects adult DENV vector competence





Non-axenic = control
Rsp_ivi = *Rhizobium* isolate
Esp_ivi = Enterobacteriaceae isolate
Ssp_ivi = *Salmonella* isolate

Dickson *et al. Sci Adv* 2017

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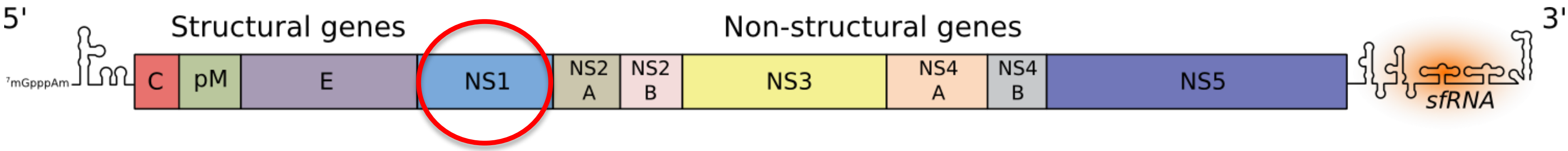
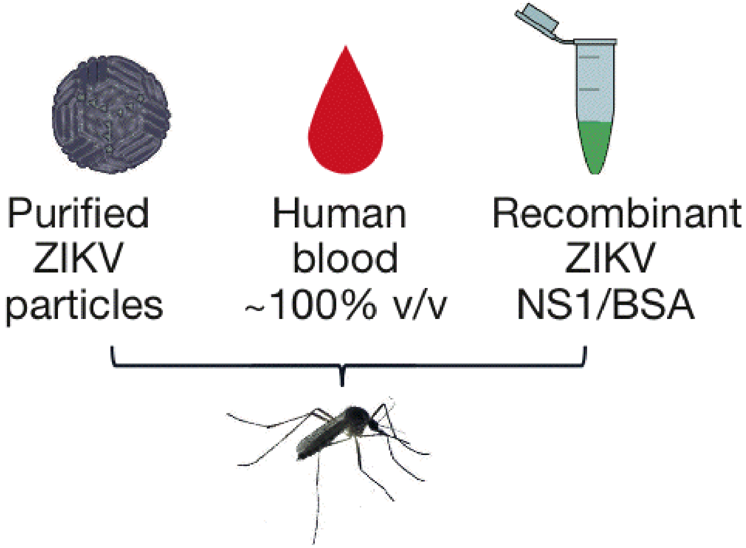
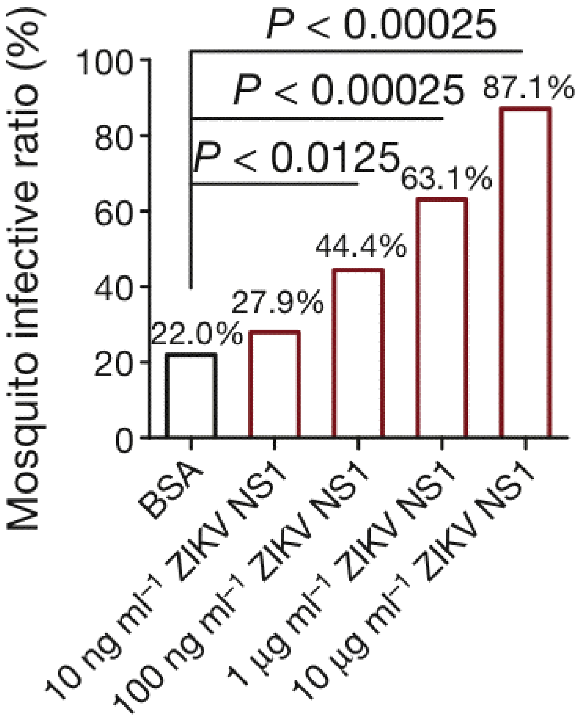
NS1 facilitates ZIKV infection of *Aedes aegypti*

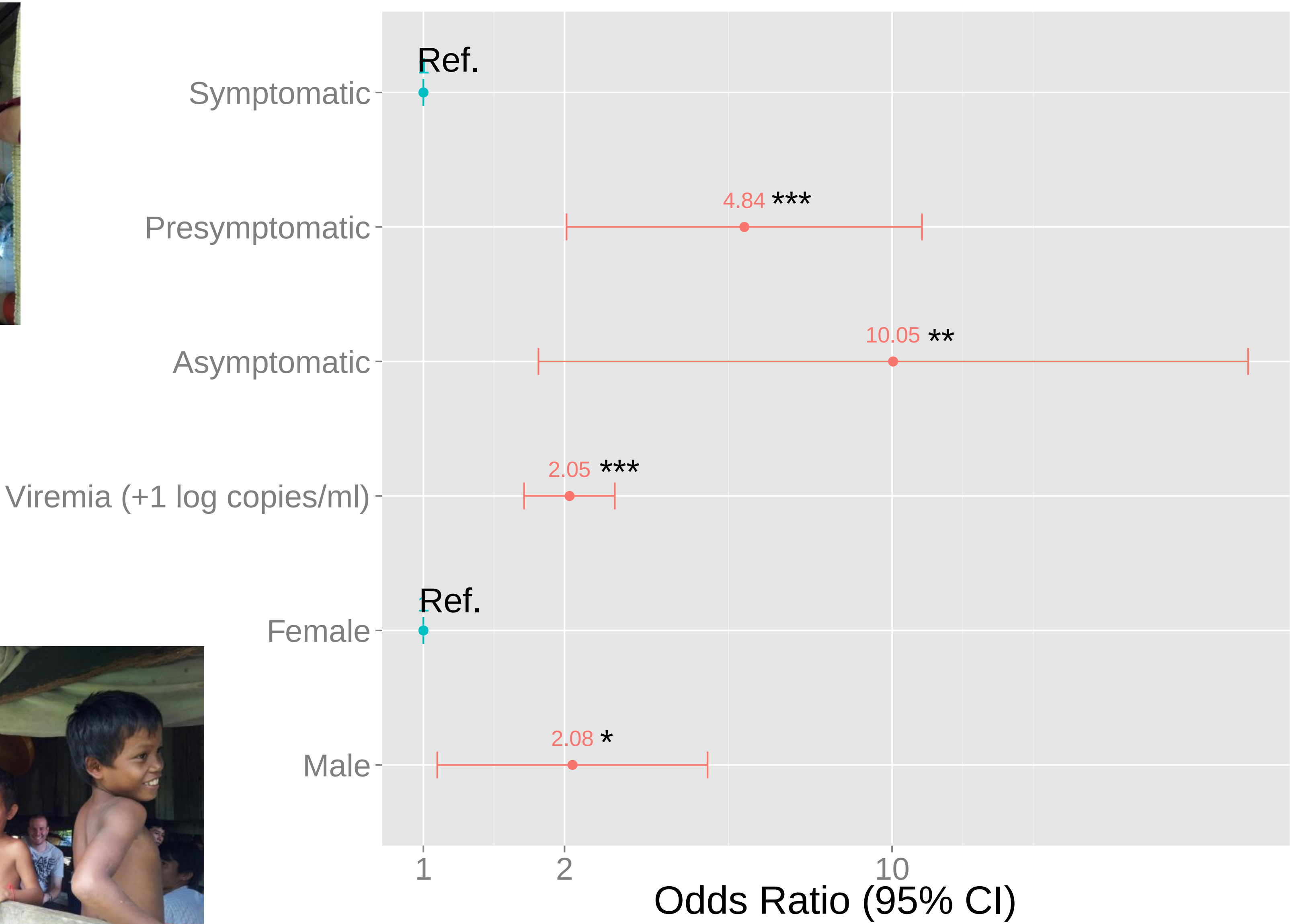






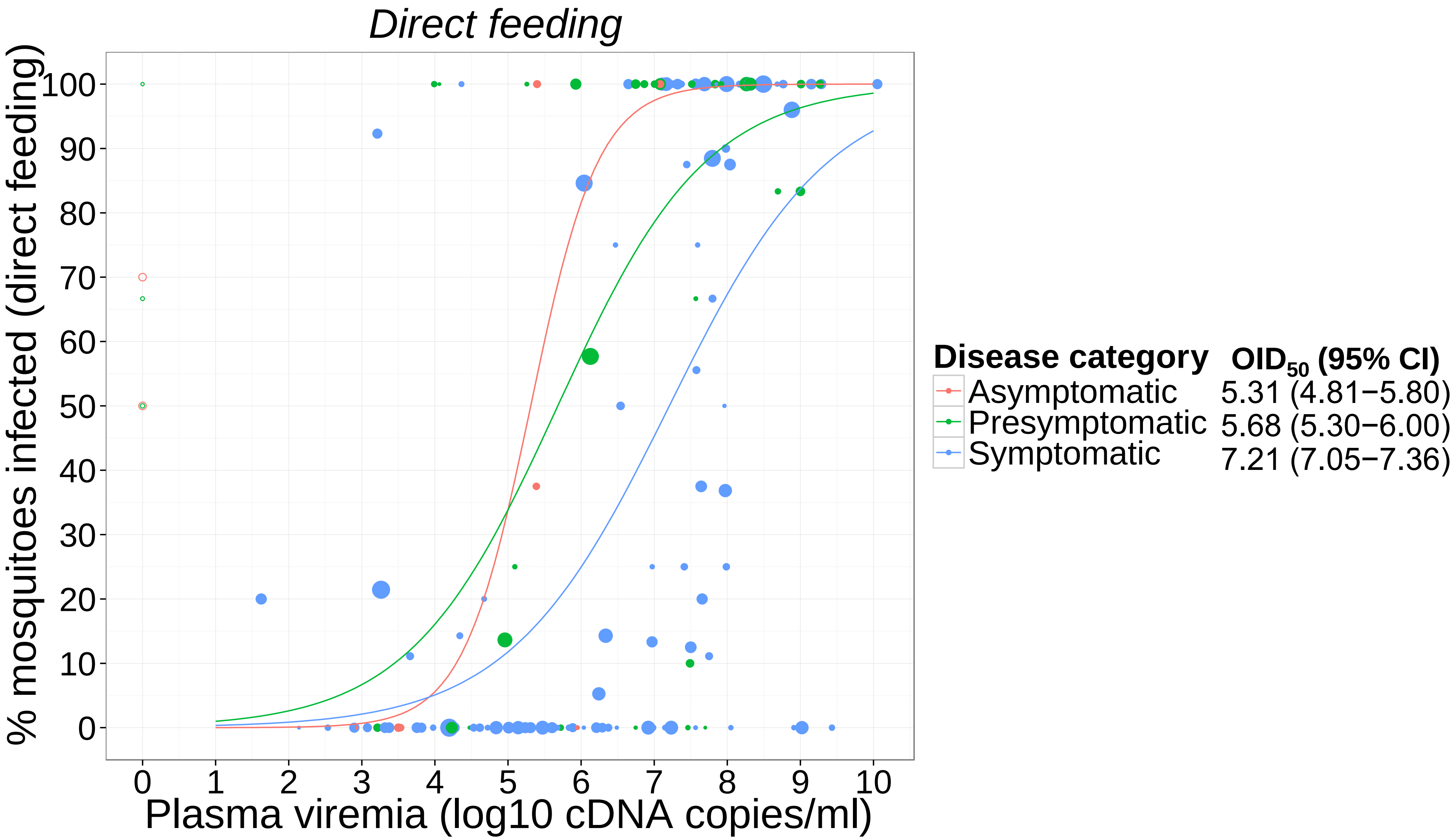
Liu *et al. Nature* 2017

Predictors of successful human-to-mosquito DENV transmission in Cambodia



Duong, Lambrechts *et al. PNAS* 2015

DENV dose response by disease category



Duong, Lambrechts *et al.* *PNAS* 2015

Take home

- *Aedes aegypti* is a **major arbovirus vector** owing to its widespread distribution, human biting behavior and vector competence

- Vector competence is governed by specific **G x G interactions** between mosquito and arbovirus strains

- Arbovirus transmission by mosquitoes is modulated by manifold **biotic and abiotic factors** of the environment

- Understanding variation in vector-virus interactions provides insights into arbovirus epidemiology and supports development of **innovative strategies** to interrupt arbovirus transmission

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Claire Valiente Moro
Guillaume Minard
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AFRIMS Bangkok
Thanyalak Fansiri
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Rick Jarman

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Veasna Duong
IP Dakar
Amadou Sall
Cheikh Diagne
IP Cayenne
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IP Guadeloupe
Anubis Vega-Rua
UniNorte Colombia
Claudia Romero-Vivas
CVR Glasgow
Alain Kohl
UVR Entebbe
Julius Lutwama

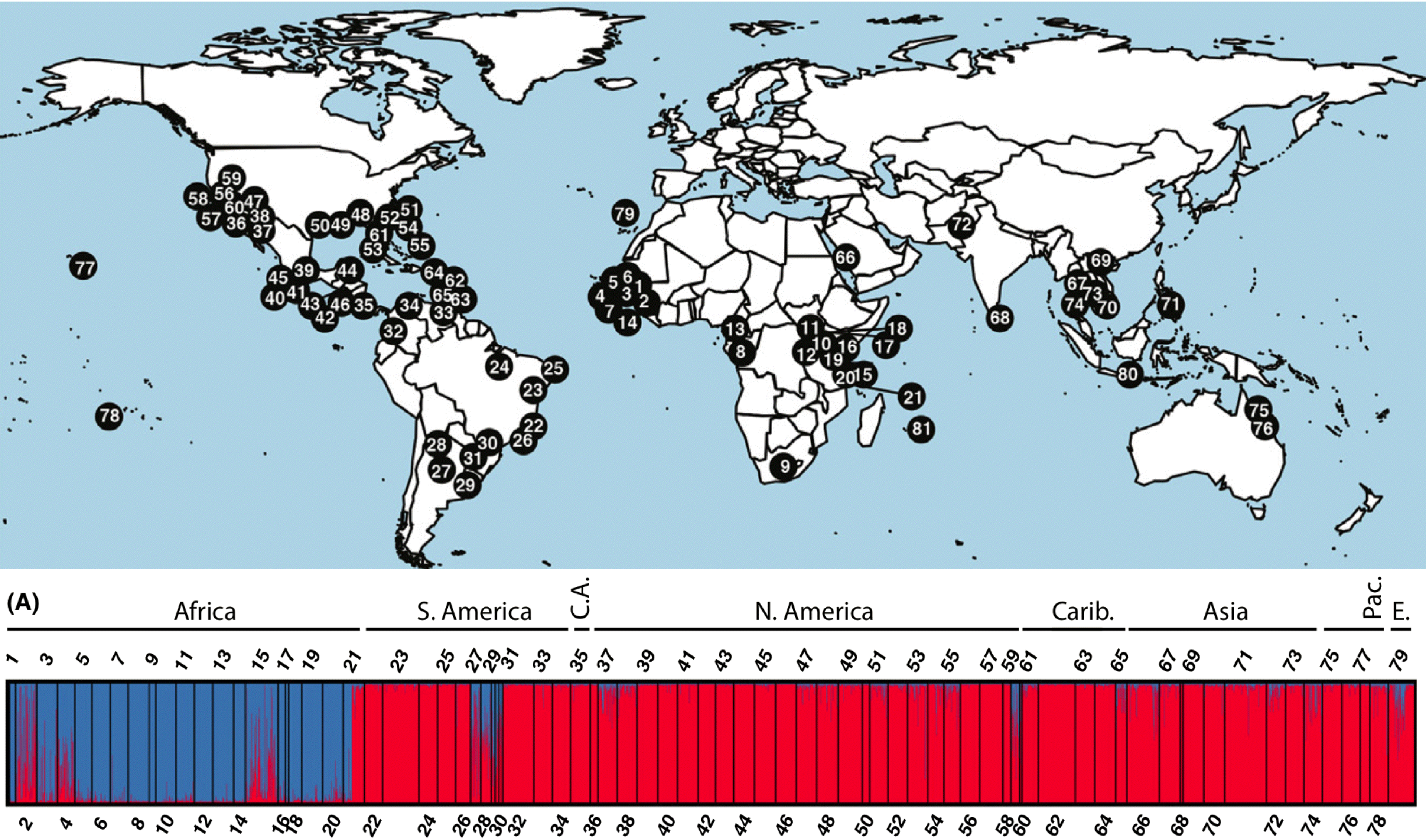
Thank you for your attention

Insect Virus Interactions

http://research.pasteur.fr/en/team/insect-virus-interactions

louis.lambrechts@pasteur.fr

Aedes aegypti subspecies

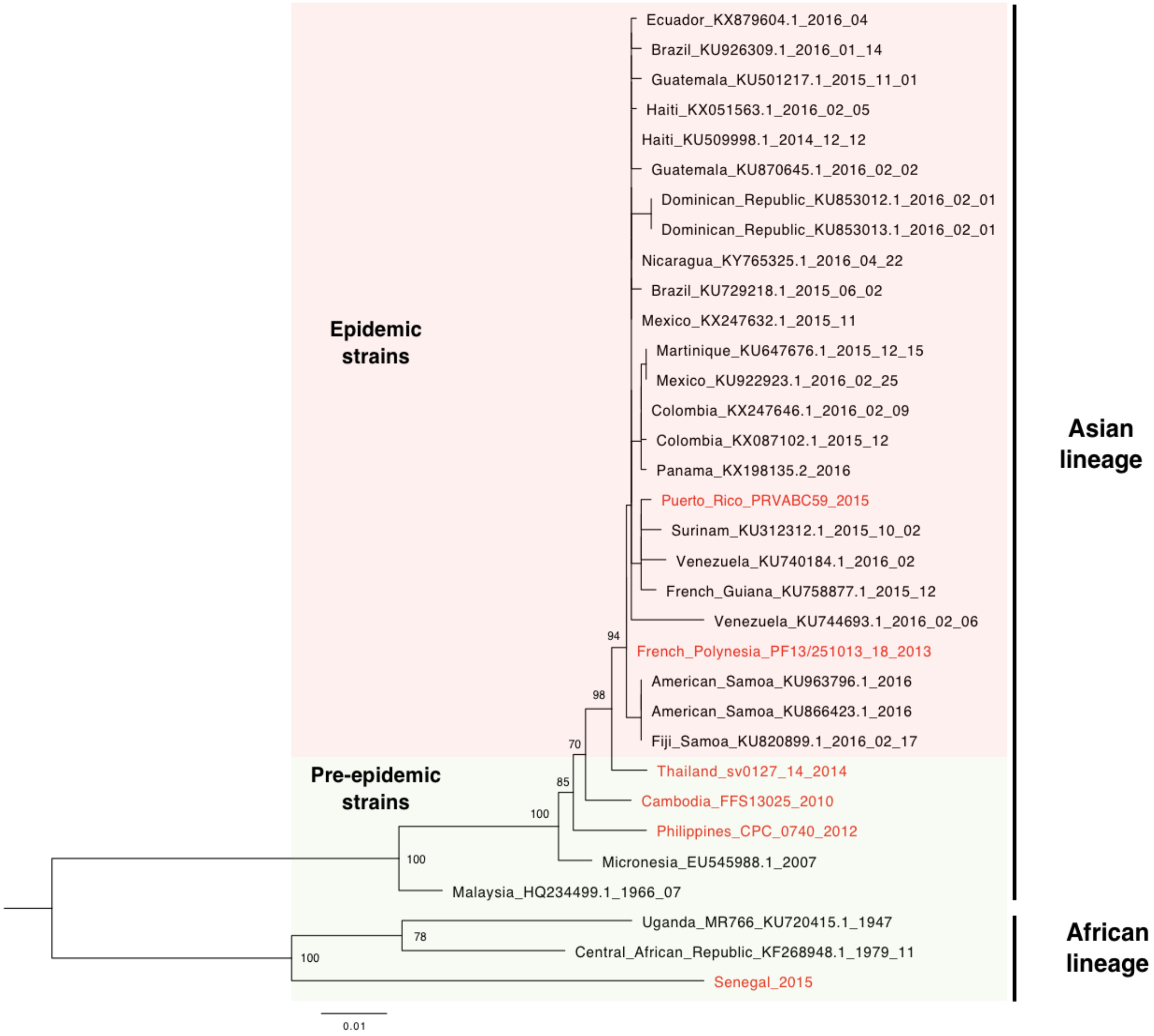


Blue = subspecies *Ae. aegypti formosus*

Red = subspecies *Ae. aegypti aegypti*

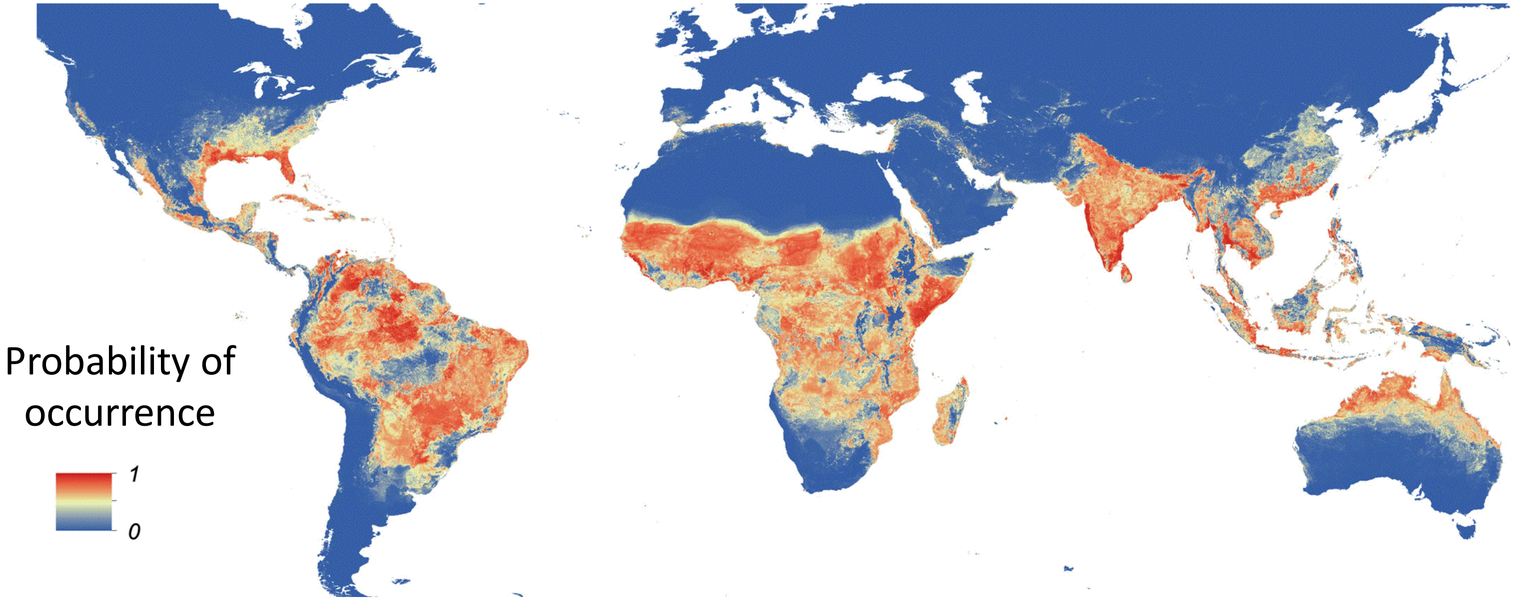
Gloria-Soria *et al. Mol Ecol* 2016

ZIKV strains

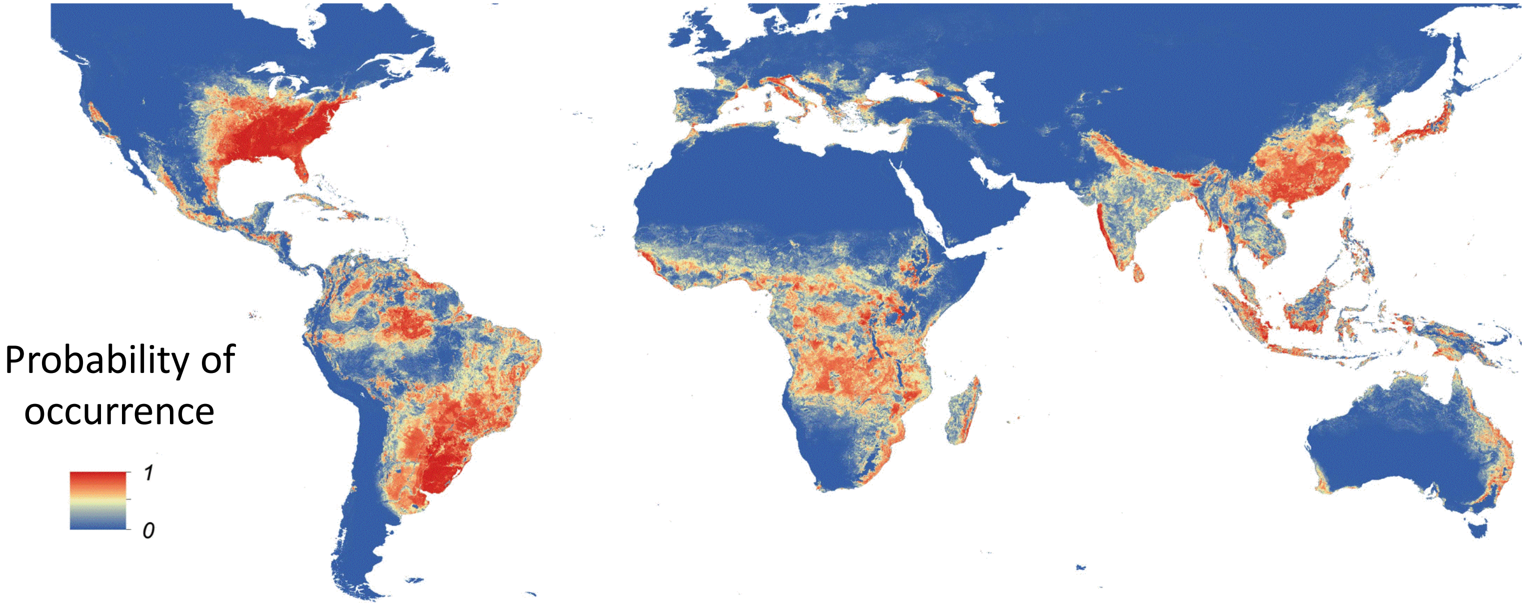


Aubry *et al.* (bioRxiv 2018)

Distribution of *Aedes aegypti* and *Aedes albopictus*



Ae. aegypti



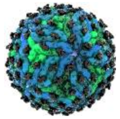
Ae. albopictus

Kraemer *et al. eLife* 2015

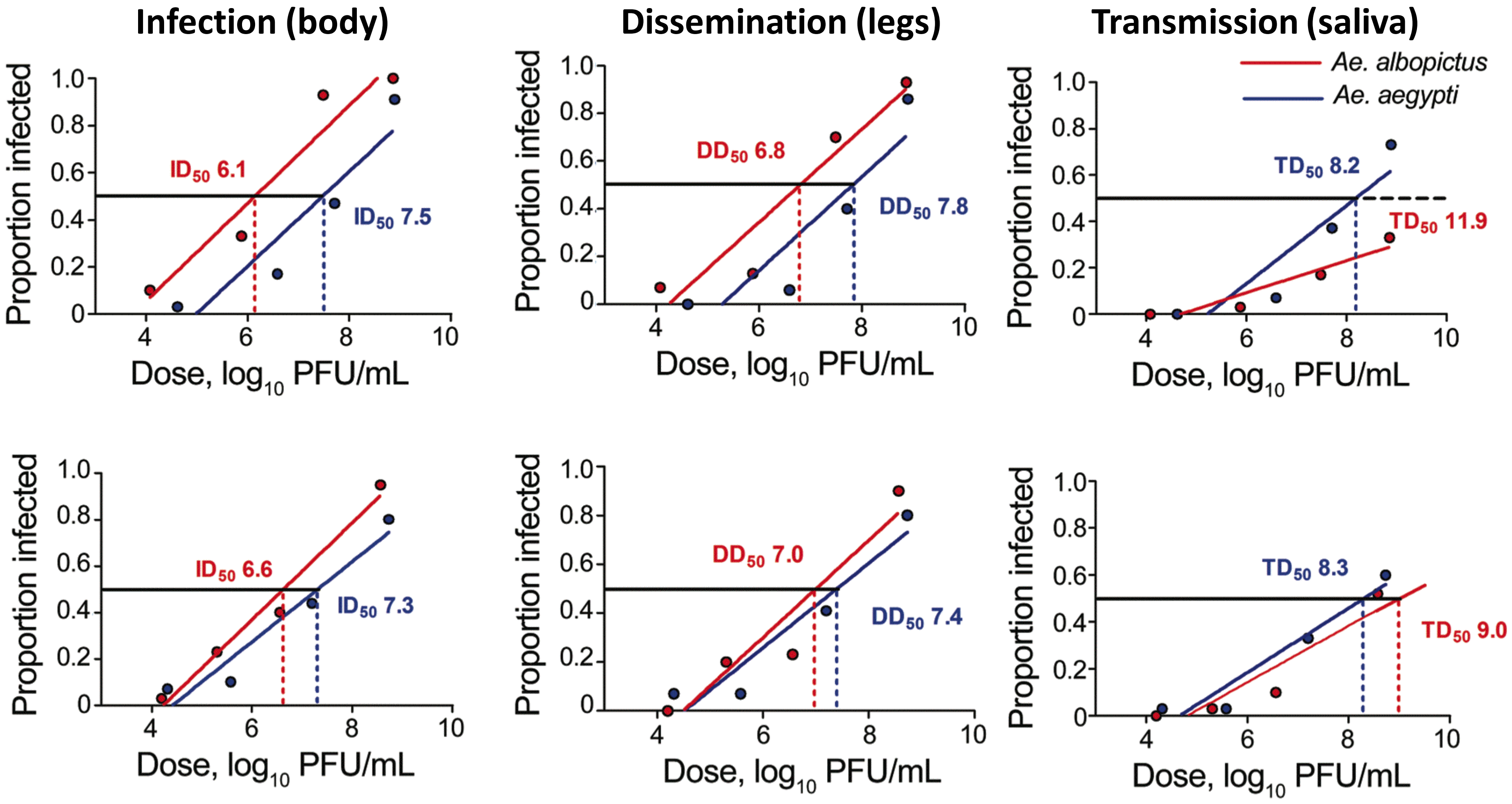
ZIKV competence of *Ae. aegypti* vs. *Ae. albopictus*

Ae. albopictus is more susceptible but less competent than *Ae. aegypti*

Honduras ZIKV strain



Cambodia ZIKV strain



Ciota *et al. Emerg Infect Dis* 2017