Wolbachia as a Novel Approach to Control Arboviruses Transmitted by *Aedes aegypti*

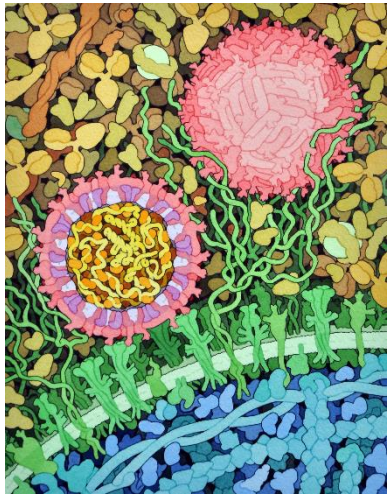

Photo credit: PDB-101

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University of Wisconsin-Madison
24 February 2017

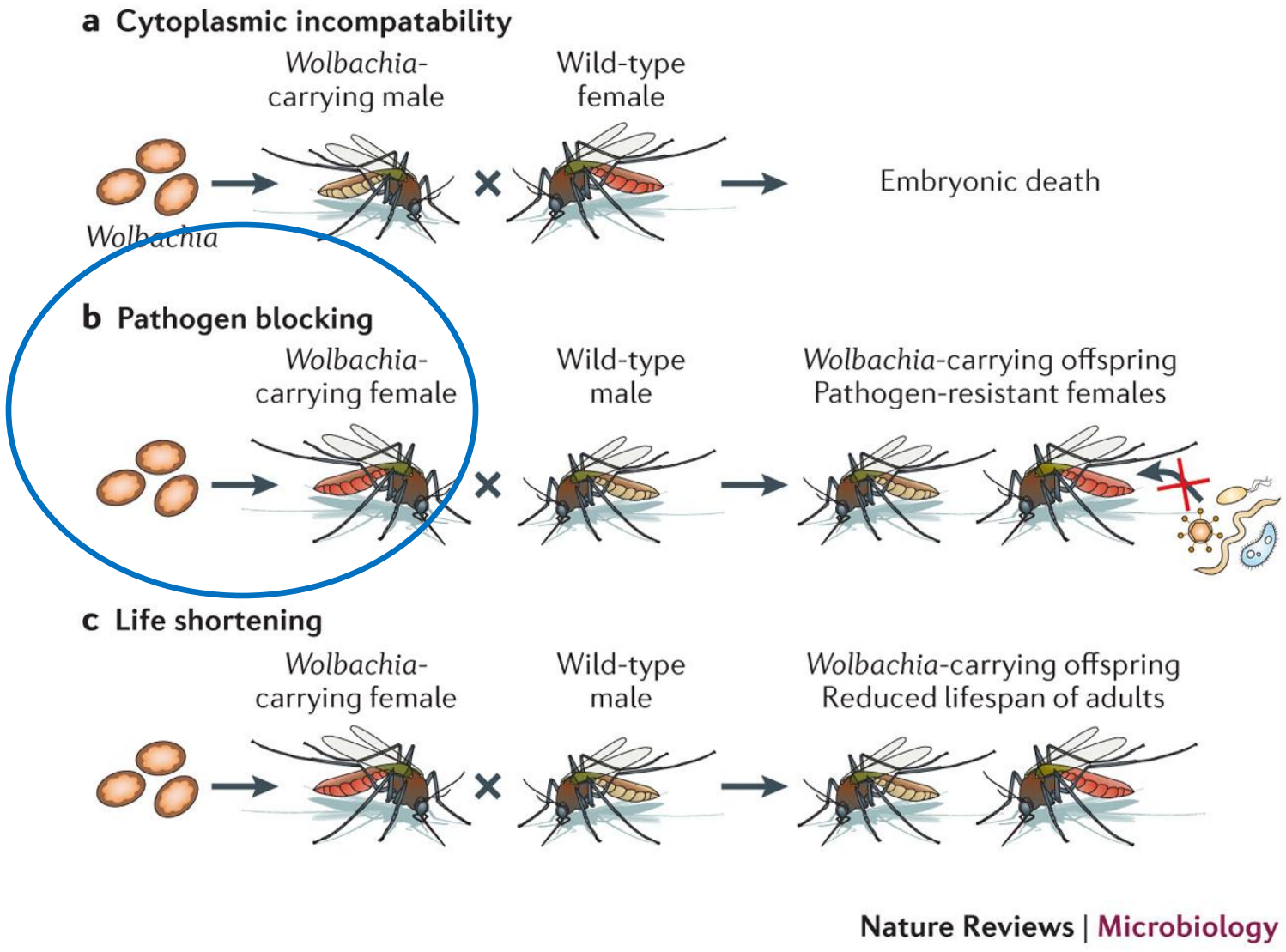
Facilitating *Ae. aegypti* transmitted arboviruses . . .

- Lack of effective mosquito control
- Collapsed public health infrastructure
- Unplanned Urbanization
  - Habitat for mosquitoes
- Pesticide resistant vectors
- Economics, politics, etc.
- **No vaccines or effective treatment**

What is *Wolbachia*?

- Naturally occurring bacteria
- Lives inside insect cells
- Transmitted from parent to offspring through the insect's eggs
- Cannot be transmitted to warm-blooded animals
- Safe for humans, animals and the environment

The Eliminate Dengue Program (EDP)



The *w*Mel strain of *Wolbachia* reduces transmission of DENV

PLoS Negl Trop Dis. 2015 Jun 26;9(6):e0003894. doi: 10.1371/journal.pntd.0003894. eCollection 2015.

Wolbachia Reduces the Transmission Potential of Dengue-Infected Aedes aegypti.

Ye YH[1], Carrasco AM[1], Frentiu FD[2], Chenoweth SF[3], Beebe NW[4], van den Hurk AF[5], Simmons CP[6], O'Neill SL[1], McGraw EA[1].

PLoS Negl Trop Dis. 2014 Feb 20;8(2):e2688. doi: 10.1371/journal.pntd.0002688. eCollection 2014.

Limited dengue virus replication in field-collected Aedes aegypti mosquitoes infected with Wolbachia.

Frentiu FD[1], Zakir T[1], Walker T[1], Popovici J[1], Pyke AT[2], van den Hurk A[2], McGraw EA[1], O'Neill SL[3].

Nature. 2011 Aug 24;476(7361):454-7. doi: 10.1038/nature10356.

Successful establishment of Wolbachia in Aedes populations to suppress dengue transmission.

Hoffmann AA[1], Montgomery BL, Popovici J, Iturbe-Ormaetxe I, Johnson PH, Muzzi F, Greenfield M, Durkan M, Leong YS, Dong Y, Cook H, Axford J, Callahan AG, Kenny N, Omodei C, McGraw EA, Ryan PA, Ritchie SA, Turelli M, O'Neill SL.

Nature. 2011 Aug 24;476(7361):450-3. doi: 10.1038/nature10355.

The wMel Wolbachia strain blocks dengue and invades caged Aedes aegypti populations.

Walker T[1], Johnson PH, Moreira LA, Iturbe-Ormaetxe I, Frentiu FD, McMeniman CJ, Leong YS, Dong Y, Axford J, Kriesner P, Lloyd AL, Ritchie SA, O'Neill SL, Hoffmann AA.

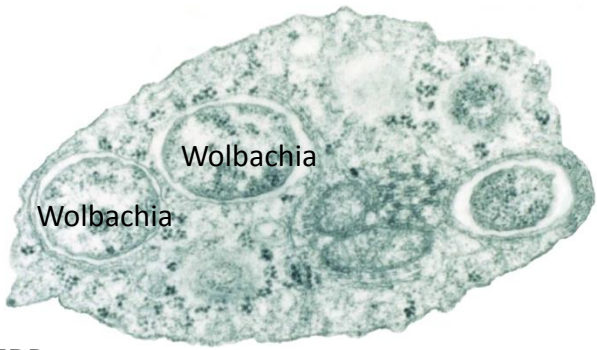


Photo credit: EDP

EDP Sites around the World

ELIMINATE DENGUE
OUR CHALLENGE

Can the *w*Mel strain of *Wolbachia* reduce transmission of viruses related to DENV in *Aedes aegypti*?

Vector-Virus Interactions in the Laboratory

Wolbachia-infected *Ae. aegypti*
From Colombia (wMELCOL)

Wild-type *Ae. aegypti* from Colombia (WT)

Bloodmeal titer 6.02 $\log_{10}$ PFU/ml
ZIKV strain PRVABC59 (Puerto Rico)

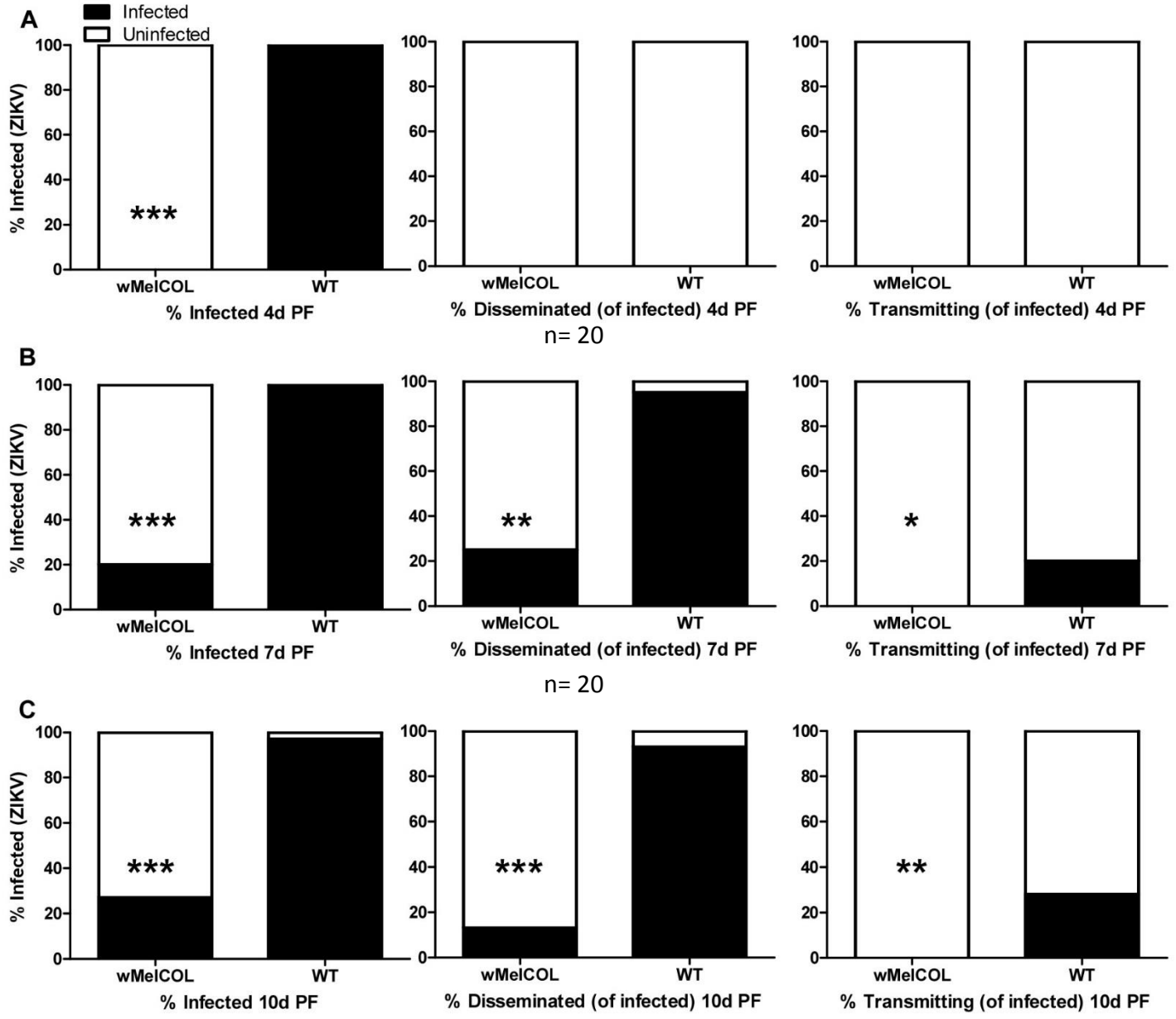
wMELCOL + ZIKV

Harvest:
Bodies
Legs
Salivary Secretions
4, 7, 10 d PF

Screen for infectious virus via Plaque Assay

WT + ZIKV

The *w*Mel strain of *Wolbachia* blocks transmission of ZIKV



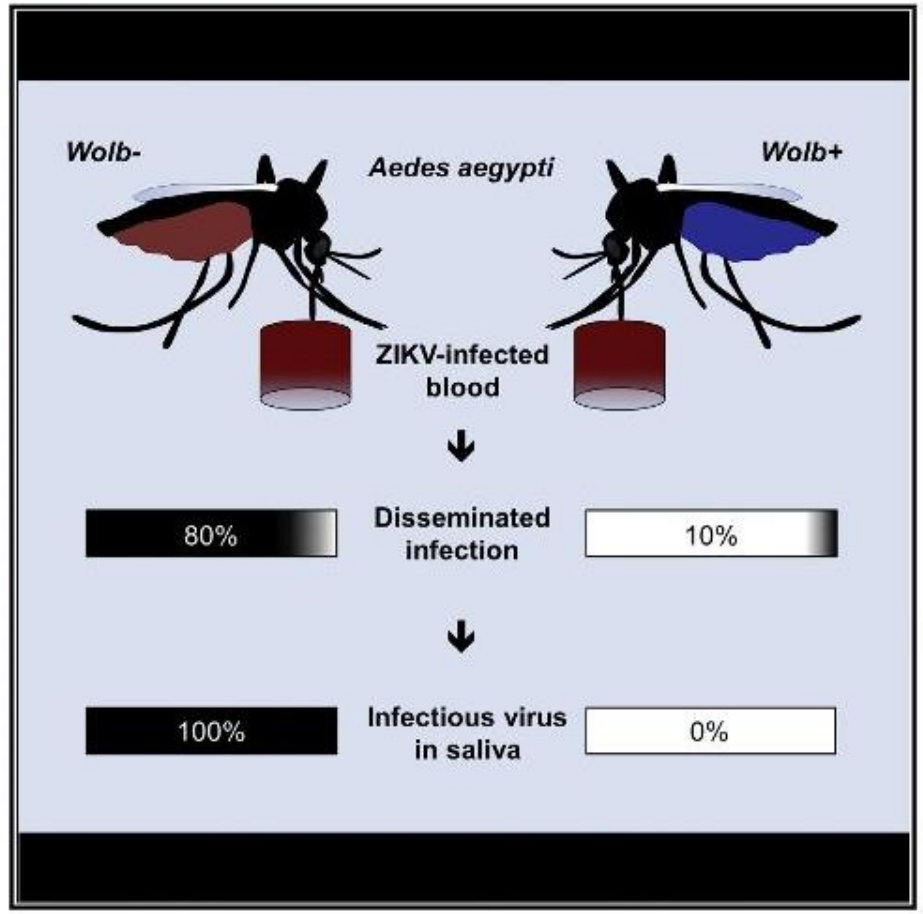
*, p<0.05
**, p<.01
***, p<0.001
Exact unconditional test

Aliota et al. (2016) Sci Reports

Cell Host & Microbe

Wolbachia Blocks Currently Circulating Zika Virus Isolates in Brazilian *Aedes aegypti* Mosquitoes

Graphical Abstract



Highlights

- Mosquitoes harboring *Wolbachia* were resistant to current circulating Zika virus isolates

Authors

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In Brief

Strategies to combat Zika virus (ZIKV) and its mosquito vector are urgently needed. Dutra et al. report that *Wolbachia*-carrying mosquitoes are highly resistant to ZIKV and display reduced virus prevalence and intensity. Saliva from *Wolbachia*-carrying mosquitoes did not contain infectious virus, suggesting the possibility to block ZIKV transmission.

Vector-Virus Interactions in the Laboratory

Wolbachia-infected *Ae. aegypti*
From Colombia (wMELCOL)

Wild-type *Ae. aegypti* from Colombia (WT)

Bloodmeal titer 9.44 $\log_{10}$ PFU/ml
CHIKV strain 99659 (British Virgin Islands)

wMELCOL + CHIKV

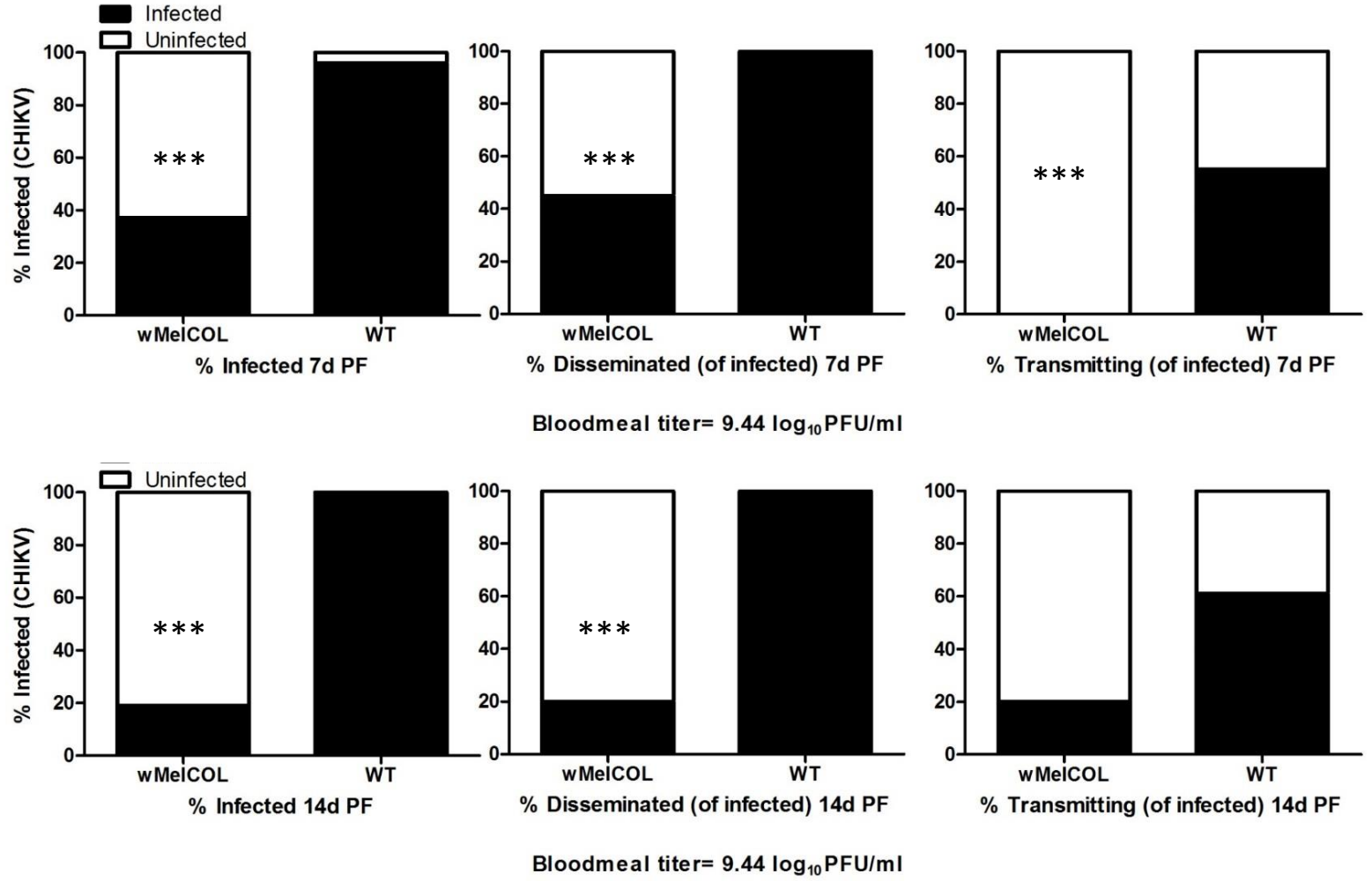
Harvest:
Bodies
Legs
Salivary Secretions
7 & 14 d PF

Screen for infectious virus via Plaque Assay

WT + CHIKV

Aliota et al. (2016) PLoS NTD

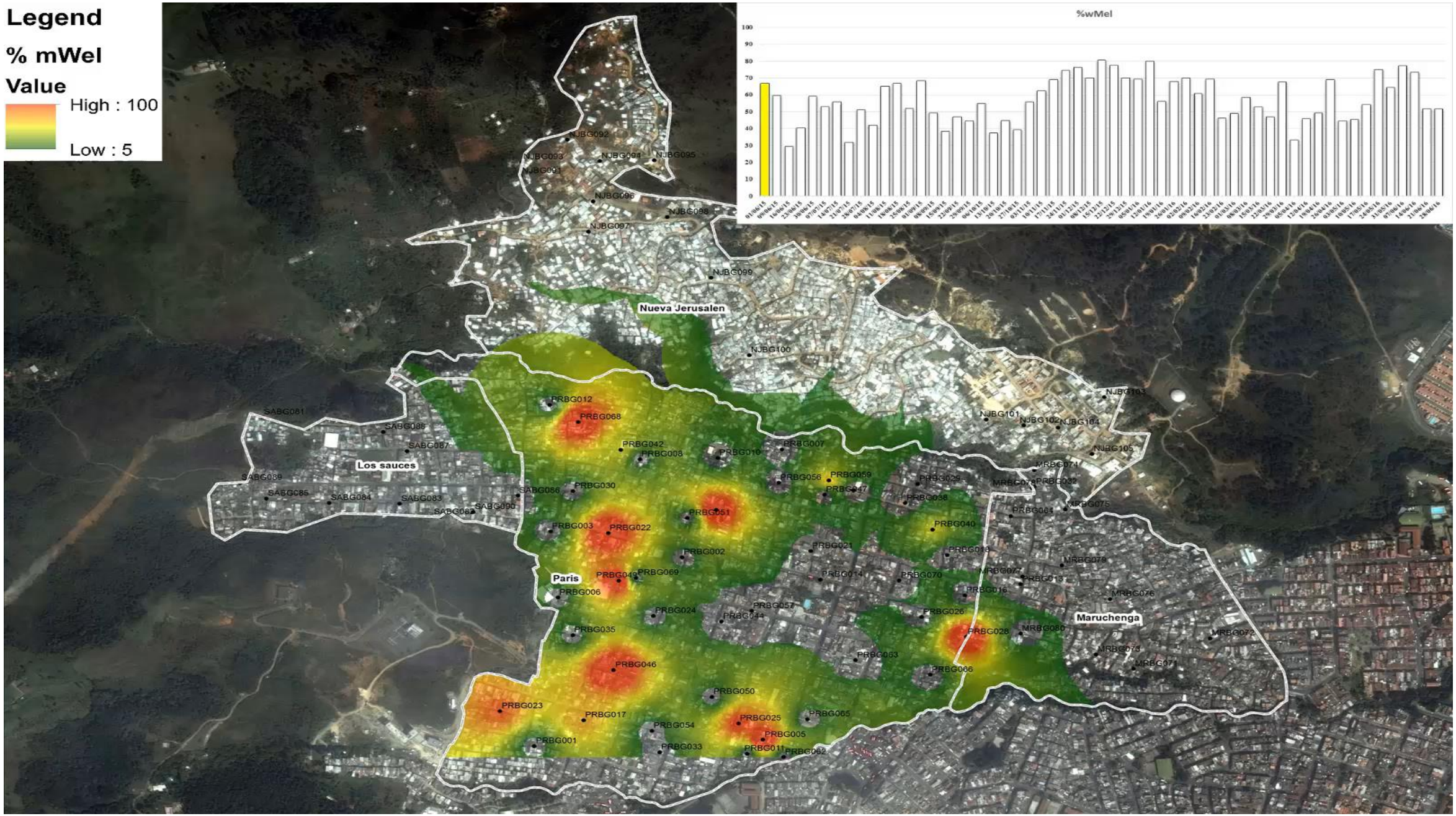
The *w*Mel strain of *Wolbachia* reduces transmission of CHIKV



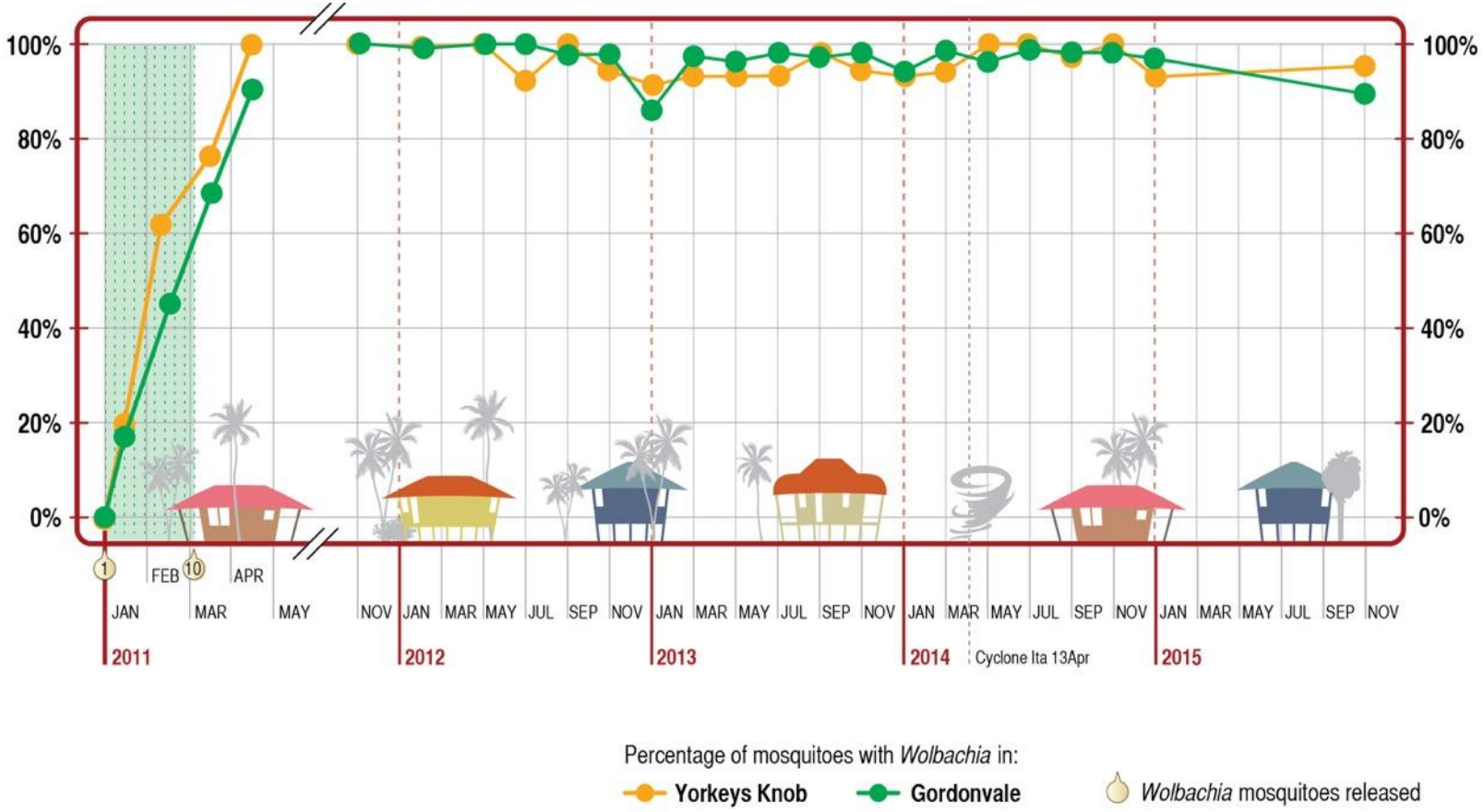
*, p<0.05
**, p<.01
***, p<0.001
Exact unconditional test

Aliota et al. (2016) PLoS NTD

Mosquitoes with *Wolbachia* released starting in May 2015 in Bello, Colombia


Legend
% mWel
Value
High : 100
Low : 5
%wMel
Nueva Jerusalen
Los sauces
Paris
Maruchenga

Wolbachia is self-sustaining after deployment



- *Wolbachia* still at high levels in mosquito populations
- No locally acquired dengue cases

Next: Large Scale *Wolbachia* Release in Medellin (~2.5 million)

Wolbachia biocontrol – effective and safe

- Implemented in over 50 communities (over 192,768 total population)
- Large scale implementations > 5 million people over next 2 years

Australia

- Cairns (2011-15): 17 field sites & 41,899 population
- Townsville (2014-16): 29 field sites & 90,000 population

Vietnam

- Central Vietnam (2013-15): 1 field site & 3,250 population
- Serological surveys (145 volunteers) pre & post release – test for antibodies to *Wolbachia*

Indonesia

- Yogyakarta (2014-15): 4 field sites & 9,233 population
- Serological surveys (100 volunteers) pre & post release – test for antibodies to *Wolbachia* (results pending)

Brazil

- Rio de Janeiro (2015): 2 field sites & 3,621 population

Colombia

- Bello (2015): 1 field site & 44,765 population

In Summary……

- The *w*Mel strain of *Wolbachia* blocks transmission of Zika virus in *Aedes aegypti* .
- Also have reduced vector competence for dengue virus (Ye et al. (2015) PLoS NTD; Frentiu et al. (2014) PLoS NTD; etc. etc.) and chikungunya virus (Aliota et al. (2016) PLos NTD; van den Hurk et al. (2012) PLoS NTD).
- Successful pilots undertaken now in 5 countries.
- Large scale releases commencing in Colombia and Brazil and randomized trials commencing at two sites in SE Asia.
- Community led, sustainable, cost effective intervention.

Acknowledgements

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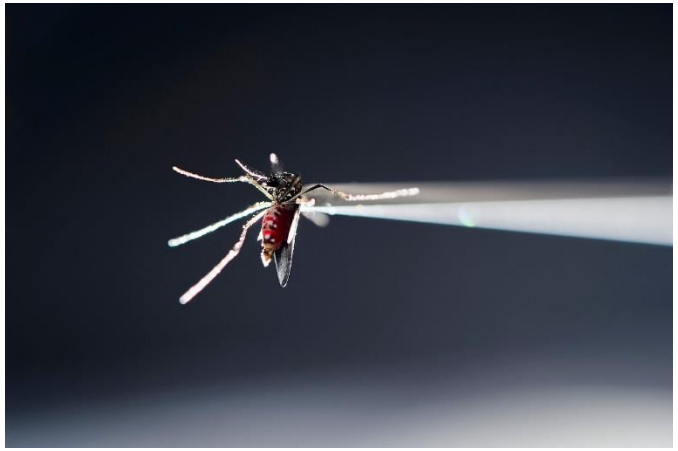

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