MOSQUITO SYMBIONTS AS TOOL FOR CONTRASTING ZIKA INFECTION

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Symbiotic Control: use of symbiotic microbes to interfere with vector competence.

•The expression of effector genes rendering a mosquito vector incapable to transmit pathogens using bacteria as vehicle (Paratransgenesis).

•The interference with microbial symbionts conferring specific adaptations to insect pests (likely related to their capacity to vector diseases).

•Novel biocontrol approaches (*Wolbachia*-like) using maternally inherited symbiont transinfected into mosquitoes in order to interfere with pathogen transmission.

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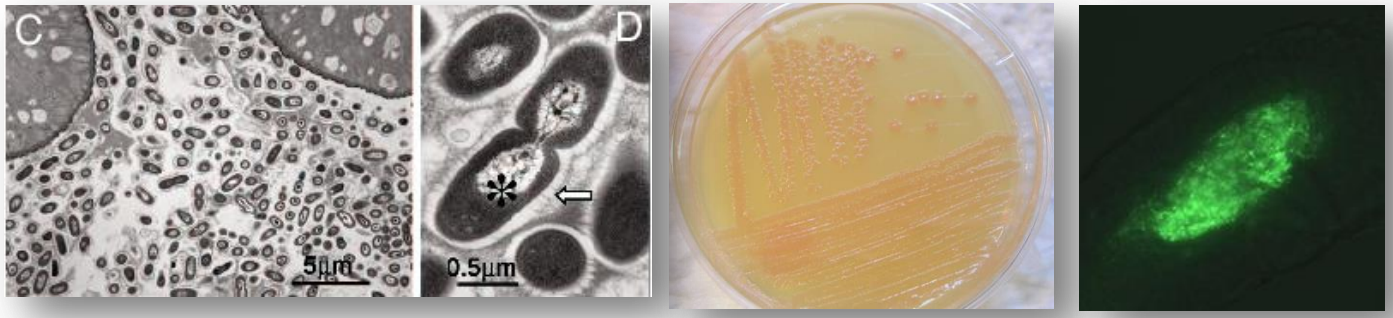
Symbiotic Control:
Asaia as a good candidate.



✓*Proper localization: in the midgut and salivary glands thus overlapping* Plasmodium *localization, and in the gonads.*

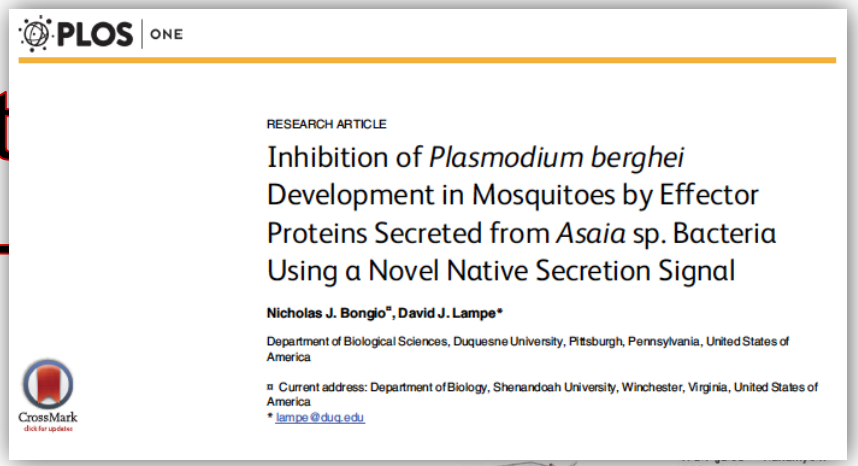
✓*It's cultivable and transformable with exogenous DNA.*

✓*Modified strains of* Asaia *are able to efficiently colonize midgut, salivary glands and gonads*

✓*Transmission occurs through horizontal (co-feeding, mating) and vertical routes (maternal transmission). In particular vertical routes offer the chance to introduce engineered bacteria into mosquito populations in the field!*

Paratransgenesis t
vectors: a semi-

Mancini et al., 2016.
Parasite&Vectors



PLOS | ONE

RESEARCH ARTICLE

Inhibition of *Plasmodium berghei* Development in Mosquitoes by Effector Proteins Secreted from *Asaia* sp. Bacteria Using a Novel Native Secretion Signal

Nicholas J. Bongio¤, David J. Lampe*

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* lampe@duq.edu

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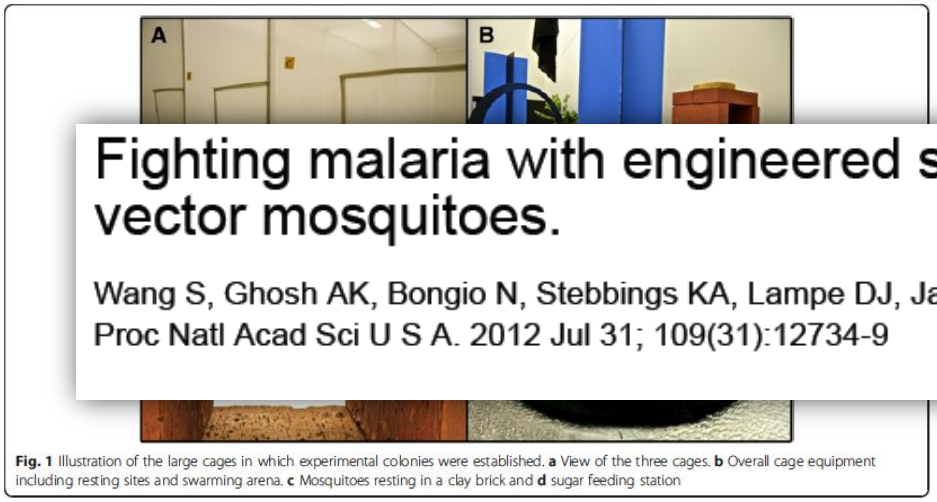
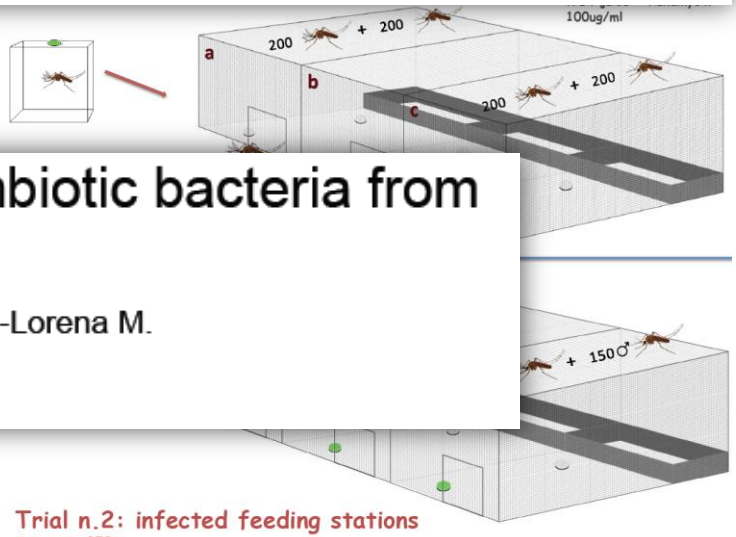


Fig. 1 Illustration of the large cages in which experimental colonies were established. **a** View of the three cages. **b** Overall cage equipment including resting sites and swarming arena. **c** Mosquitoes resting in a clay brick and **d** sugar feeding station

Fighting malaria with engineered symbiotic bacteria from vector mosquitoes.

Wang S, Ghosh AK, Bongio N, Stebbings KA, Lampe DJ, Jacobs-Lorena M.
Proc Natl Acad Sci U S A. 2012 Jul 31; 109(31):12734-9



Trial n.2: infected feeding stations (Asaia^{GFP})

Conclusions: Our results demonstrate the considerable ability of modified *Asaia* to colonise different populations of malaria vectors, including pecies where its association is not primary, in large environments. The data support the potential to employ transgenic *Asaia* as a tool for malaria control, disclosing promising perspective for its field application with suitable effector molecules.

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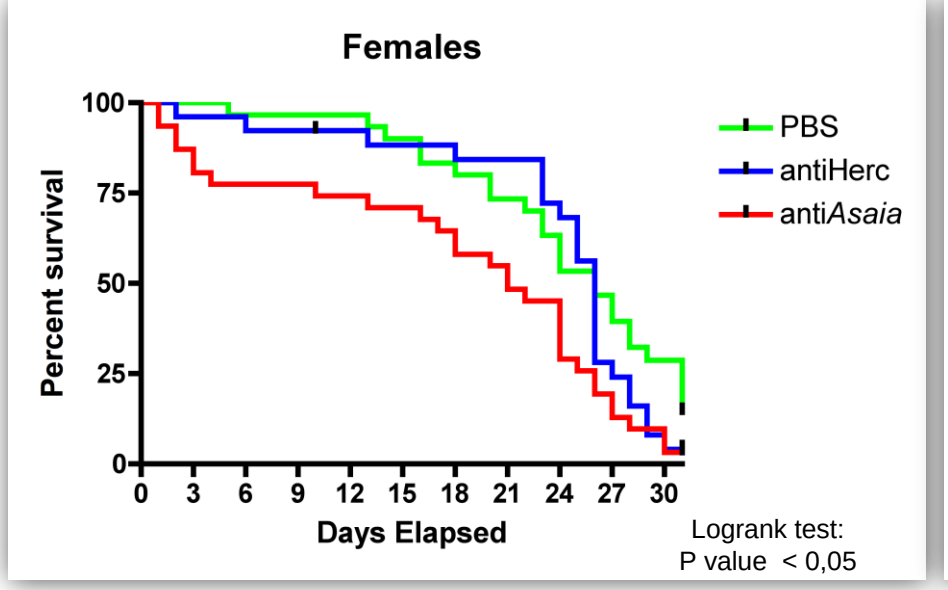
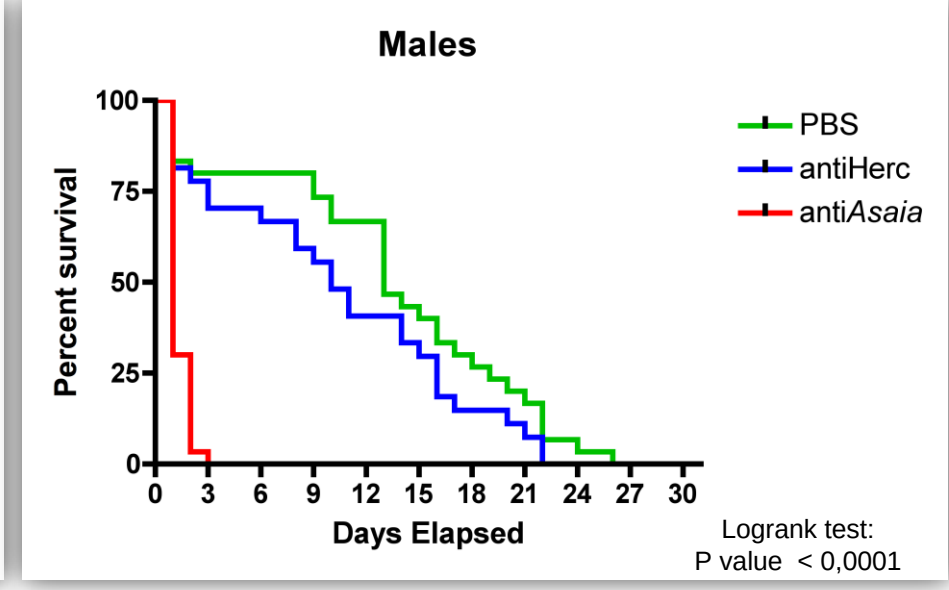
May *Asaia* provide useful adaptations to its host?

- ✓ Delayed larval development in *Anopheles* mosquitoes deprived of *Asaia* bacterial symbionts (Chouaia et al, 2012).
- ✓ *Asaia* accelerates larval development of *Anopheles gambiae* (Mitraka et al, 2013).

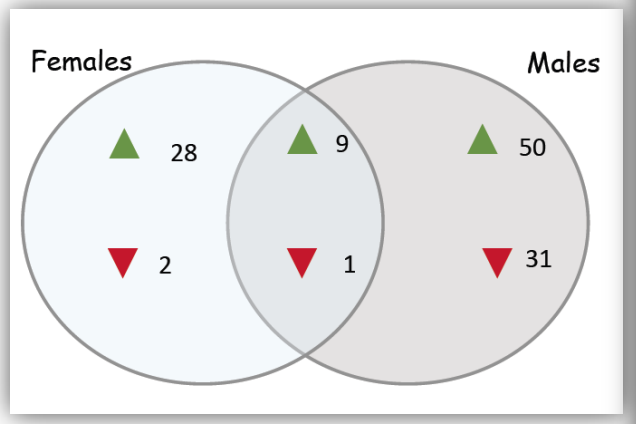
May *Asaia* provide useful adaptations to its adult host?

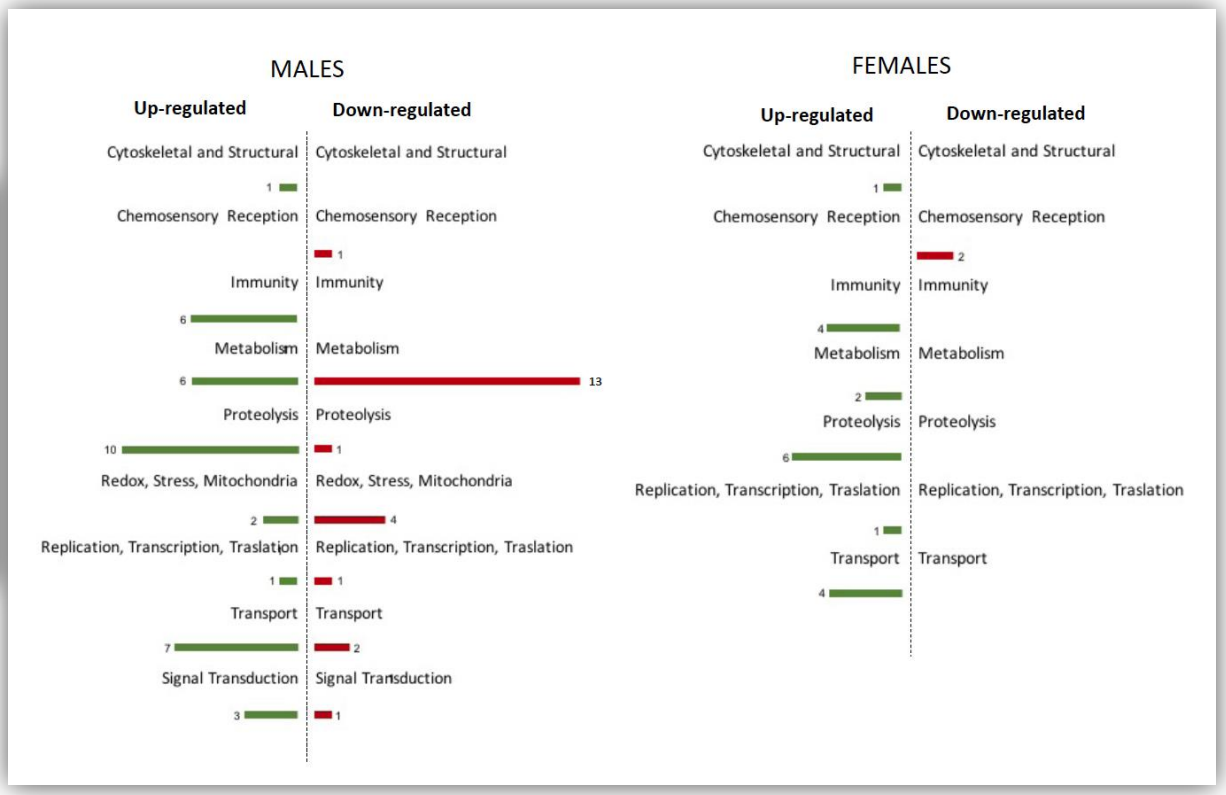




An. stephensi were thoracically injected with an anti-*Asaia* mAbs.

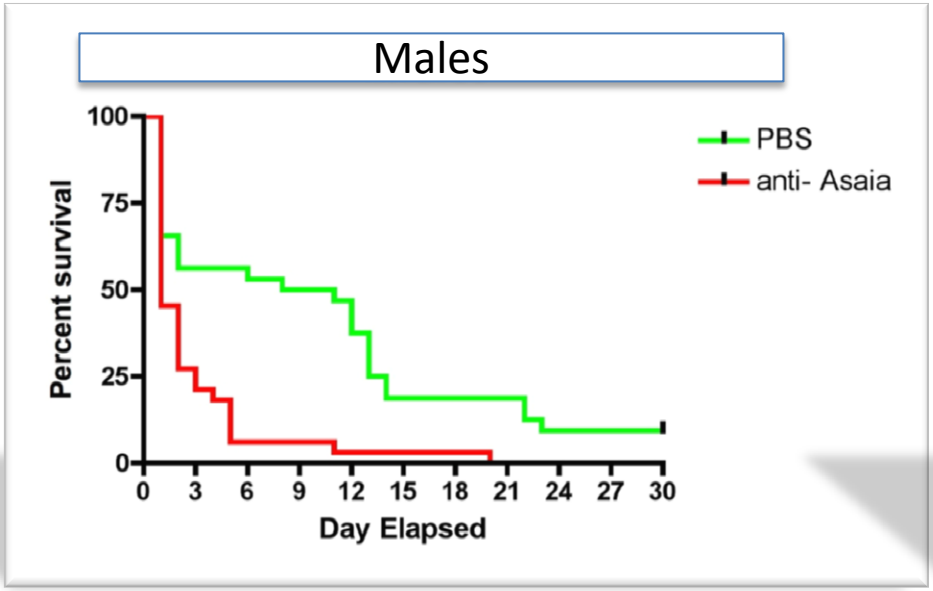
May *Asaia* provide useful adaptations to its adult host?

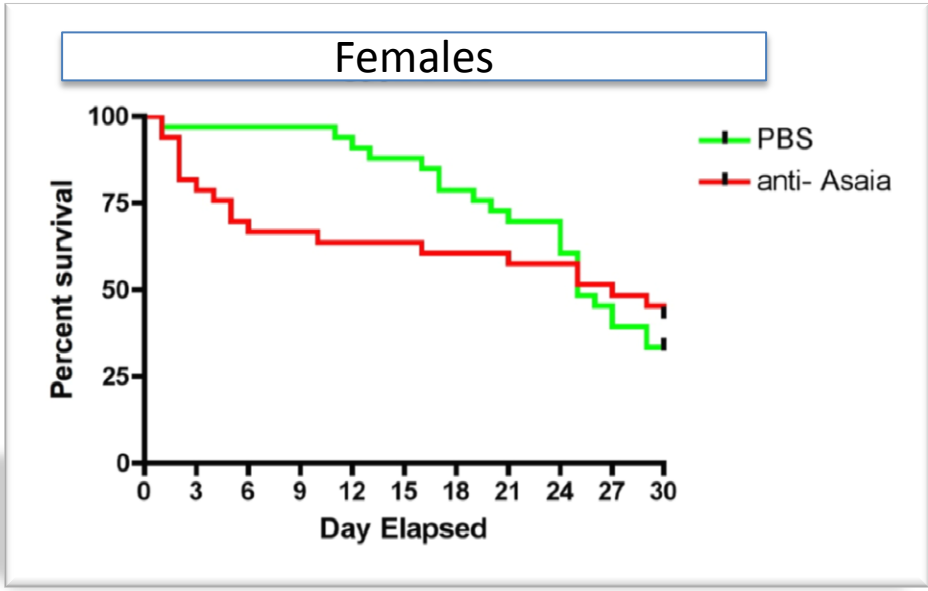




- ✓ mAb Anti-*Asaia* treatment followed by microarray analysis, reveals a sex biased gene modulation.

What in *Ae. aegypti?* (preliminary results)





Logrank test:

P value Males < 0,0001

Logrank test:

P value Females (0,9049)

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Does *Asaia* directly interfere with *Zika* development?

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RESEARCH ARTICLE

Chromobacterium Csp_P Reduces Malaria and Dengue Infection in Vector Mosquitoes and Has Entomopathogenic and *In Vitro* Anti-pathogen Activities

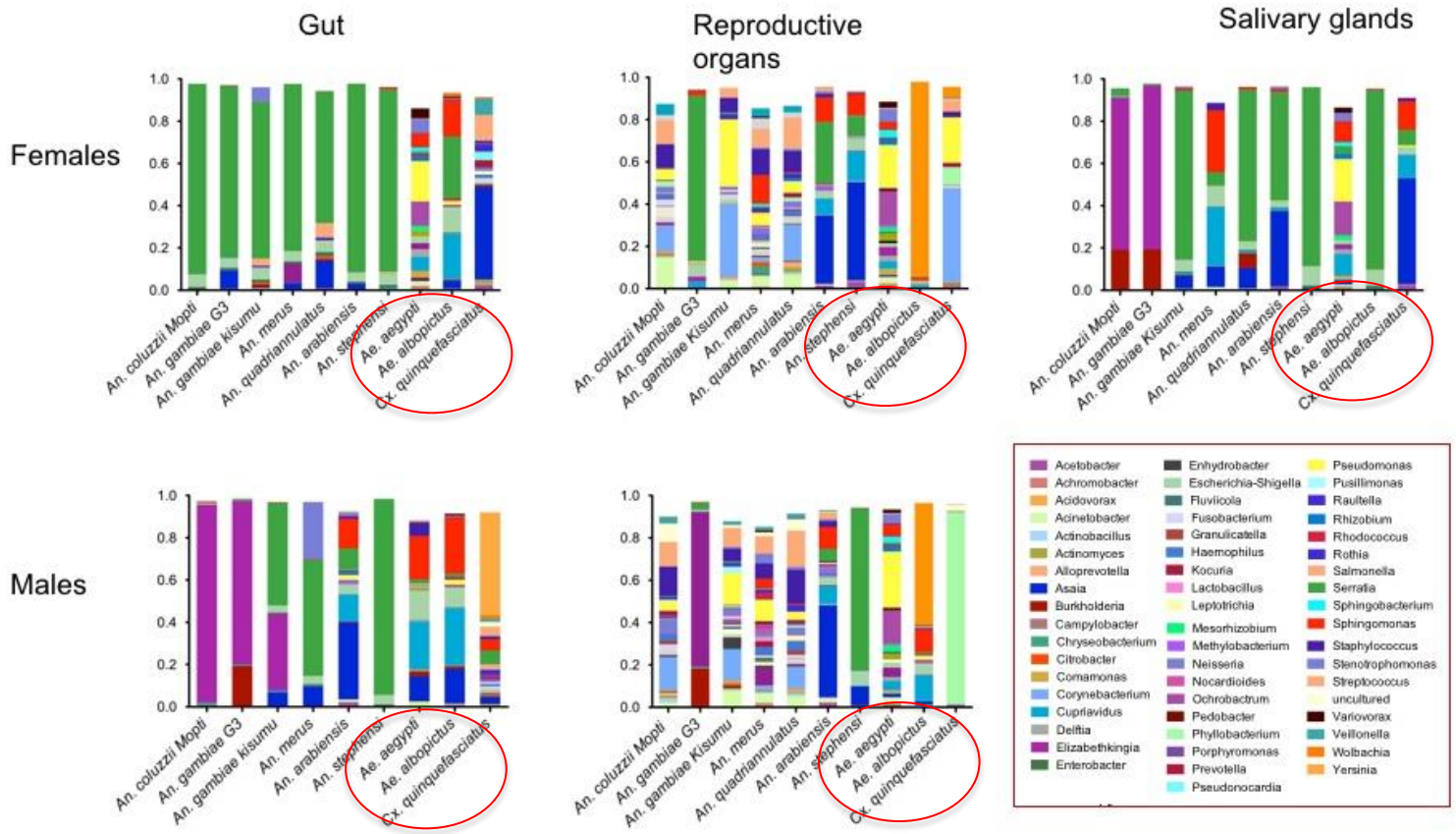
Jose Luis Ramirez, Sarah M. Short, Ana C. Bahia, Raul G. Saraiva, Yuemei Dong, Seokyoung Kang, Abhai Tripathi, Godfree Mlambo, George Dimopoulos

Published: October 23, 2014 • http://dx.doi.org/10.1371/journal.ppat.1004398

- Shacking conditions

- HPLC
- LC-MS and NMR analyses

Metagenomic analaysis in three different organs of several mosquito species/strains



Asaia distribution among different mosquito species/strains is not homogeneous.

Many more symbionts maybe employed to develop innovative MBD control approaches

Take home message

✓*Asaia* provides good evidences for its employment in paratransgenic applications that are on the road from lab to field.

✓Its involvement in other types of symbiotic control applications are still questionable and further experiments are ongoing. Those against Zika virus may open some new avenue in the contrast of this viral infection.

✓The high complexity of the microbiota in different organs of several lab strains of different mosquito species, suggests that a relevant number of bacterial symbionts maybe employed to develop innovative MBD control approaches, Zika infection included.

Credits

Collaborations:

Roberta Spaccapelo & Anastasia Accoti (University of Perugia)

George Dimopoulos & Sarah Short
(Johns Hopkins, Baltimore)

Antonino Di Caro
(Spallanzani Hospital, Rome)

SEVENTH FRAMEWORK PROGRAMME

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