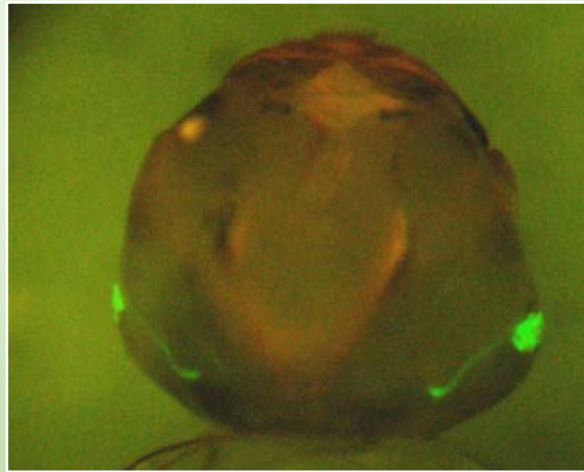
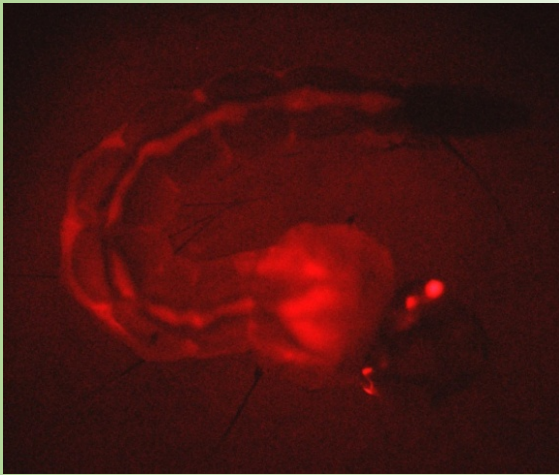




Aedes aegypti control programmes in Brazil

Margareth L. Capurro
mcapurro@icb.usp.br



Dengue Prevention and 35 Years of Vector Control in Singapore

Eng-Eong Ooi,* Kee-Tai Goh,† and Duane J. Gubler‡

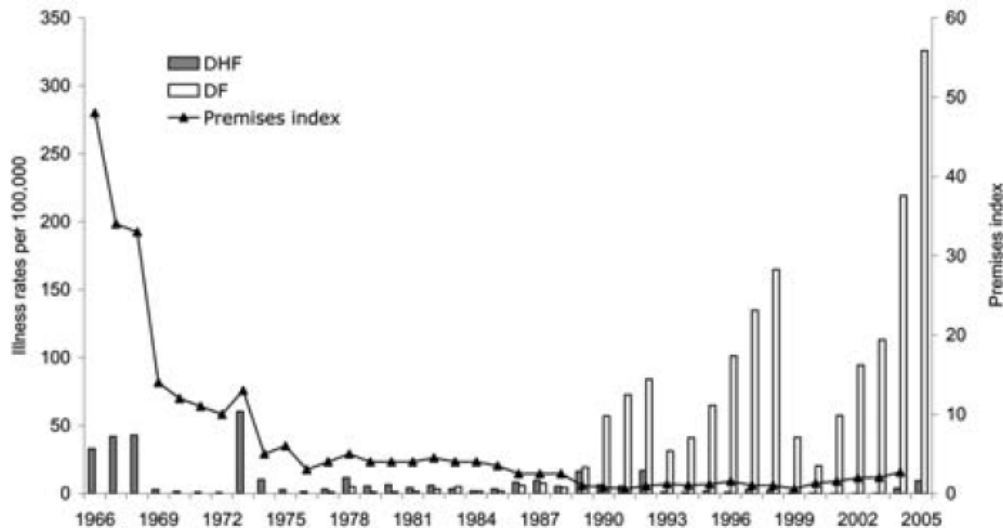
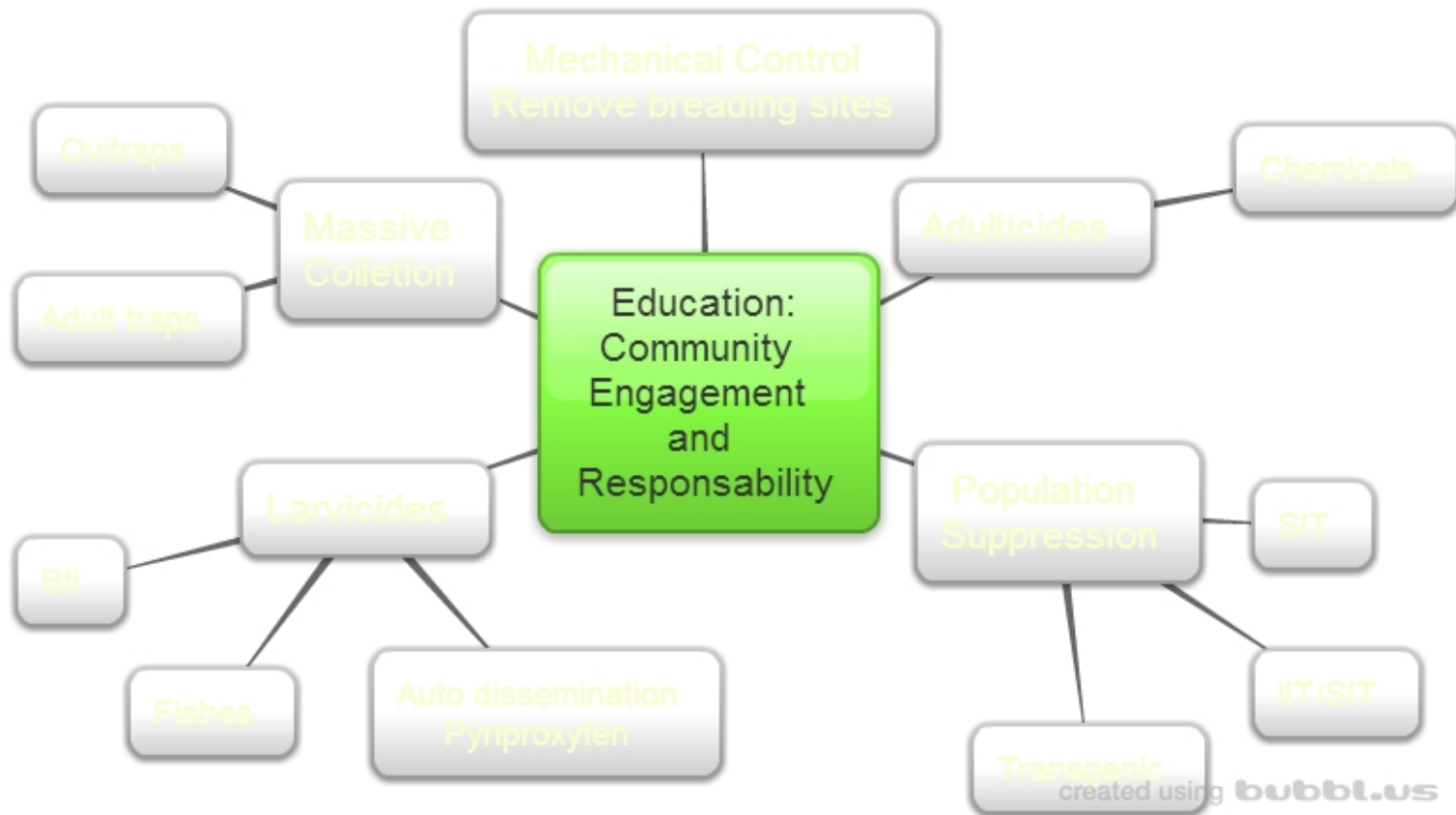


Figure 1. Annual incidence dengue fever (DF) and dengue hemorrhagic fever (DHF) and the premises index, Singapore, 1966–2005. DHF was made a notifiable disease in 1966, while DF became a notifiable disease in 1977. The annual incidences of DF and DHF reported in this figure were calculated from the number of reported cases each year from 1966 to 2004. The annual premises index is expressed as a percentage of the premises in which *Aedes aegypti* or *A. albopictus* larvae were found divided by the number of premises visited by environmental health officers.

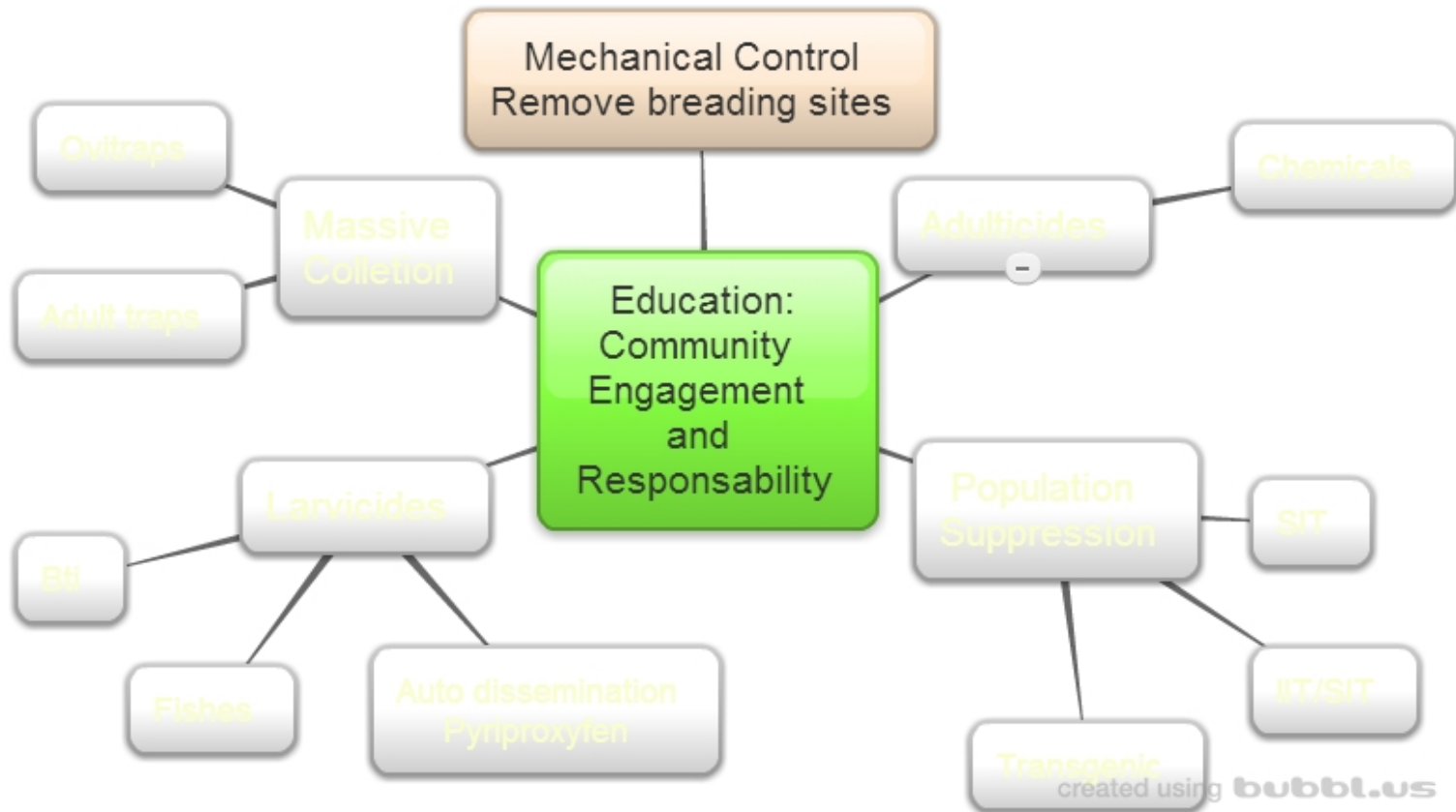
Emerging Infectious Diseases •
www.cdc.gov/eid • Vol. 12, No. 6,
June 2006

After a 15-year period of low incidence, dengue has reemerged in Singapore in the past decade. We identify potential causes of this resurgence. A combination of lowered herd immunity, virus transmission outside the home, an increase in the age of infection, and the adoption of a case-reactive approach to vector control contribute to the increased dengue incidence. Singapore's experience with dengue indicates that prevention efforts may not be sustainable. For renewed success, Singapore needs to return to a vector control program that is based on carefully collected entomologic and epidemiologic data. Singapore's taking on a leadership role in strengthening disease surveillance and control in Southeast Asia may also be useful in reducing virus importation.

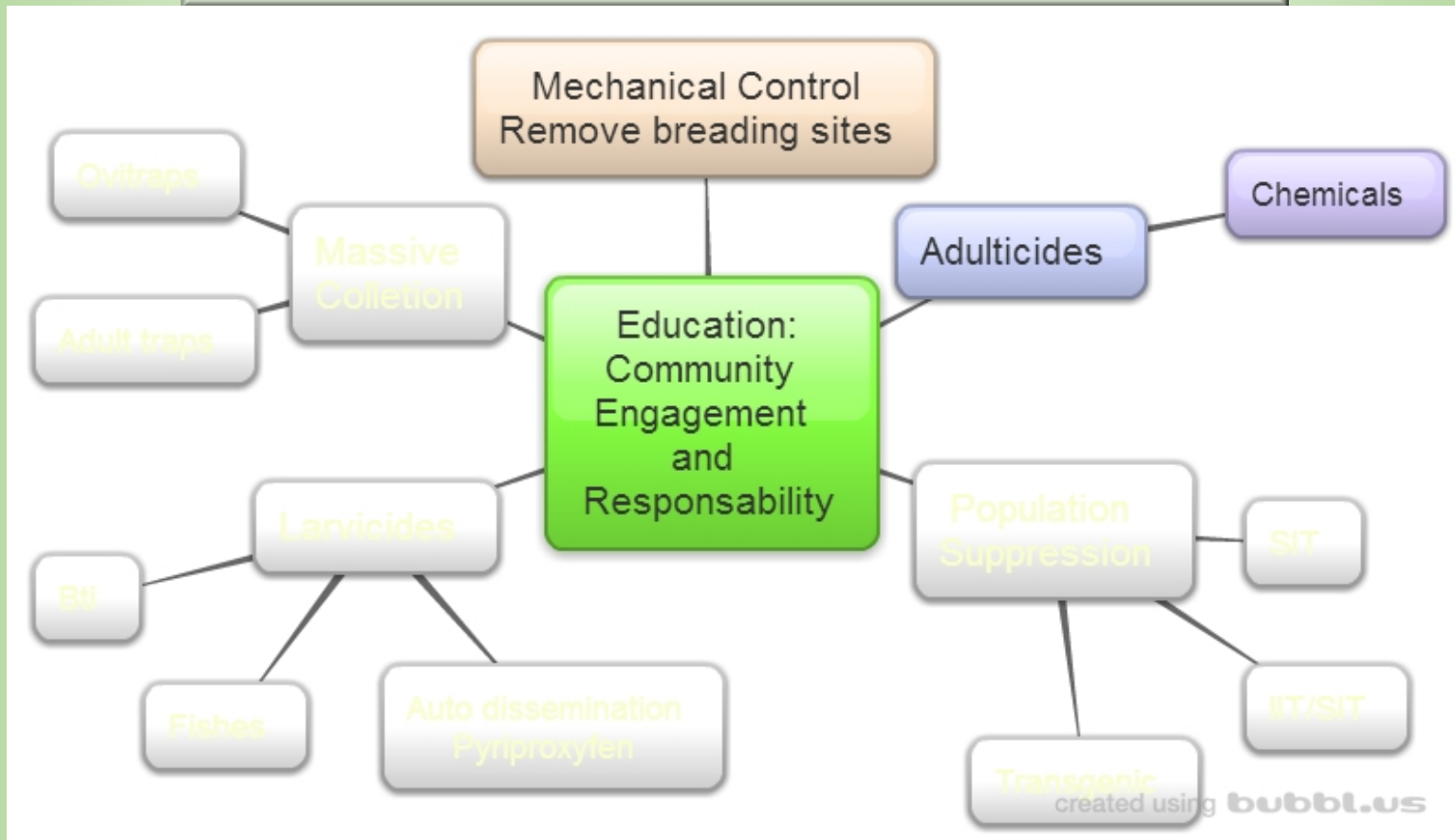
Integrate Control for *Aedes aegypti* Population Suppression



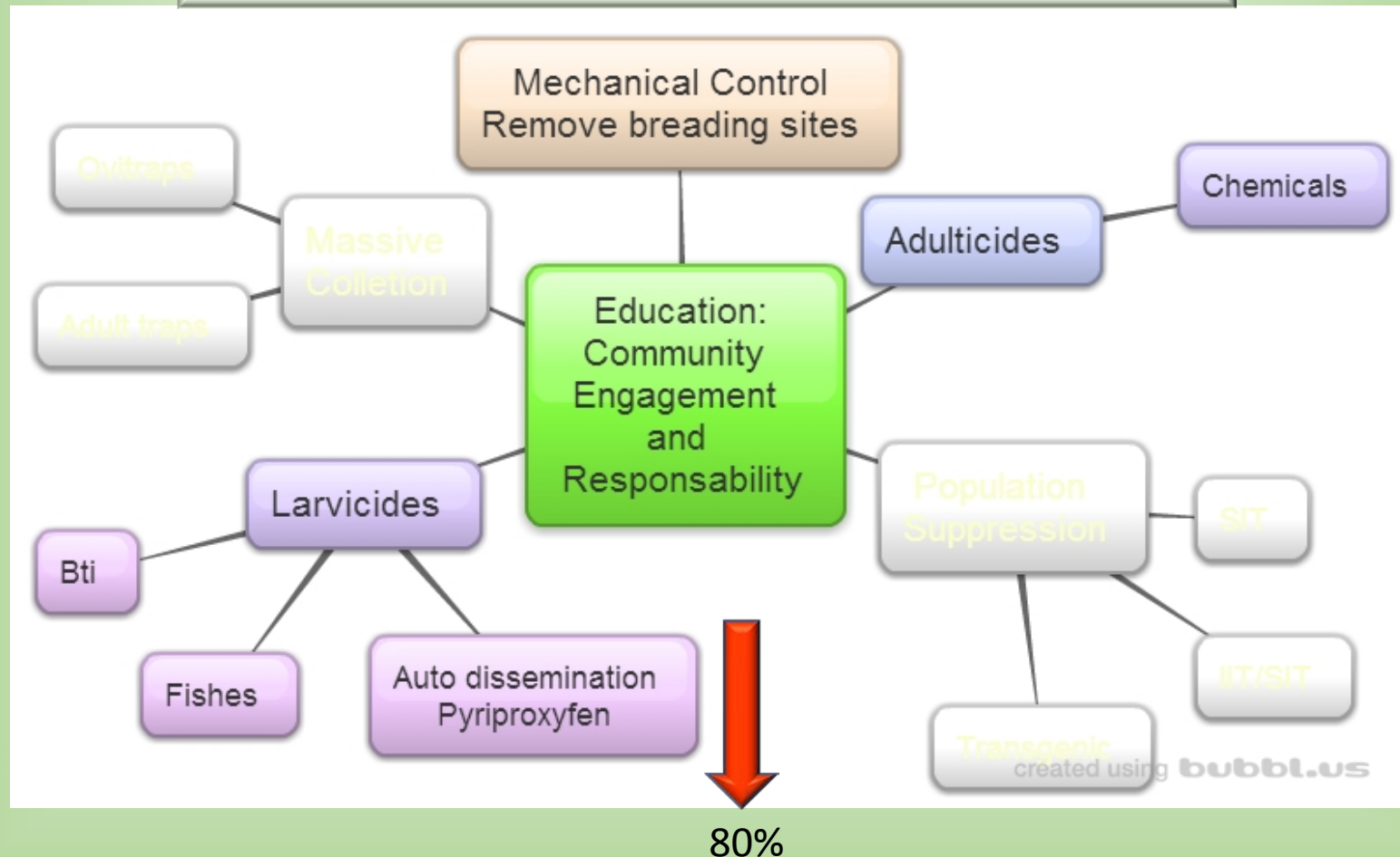
Integrate Control for *Aedes aegypti* Population Suppression



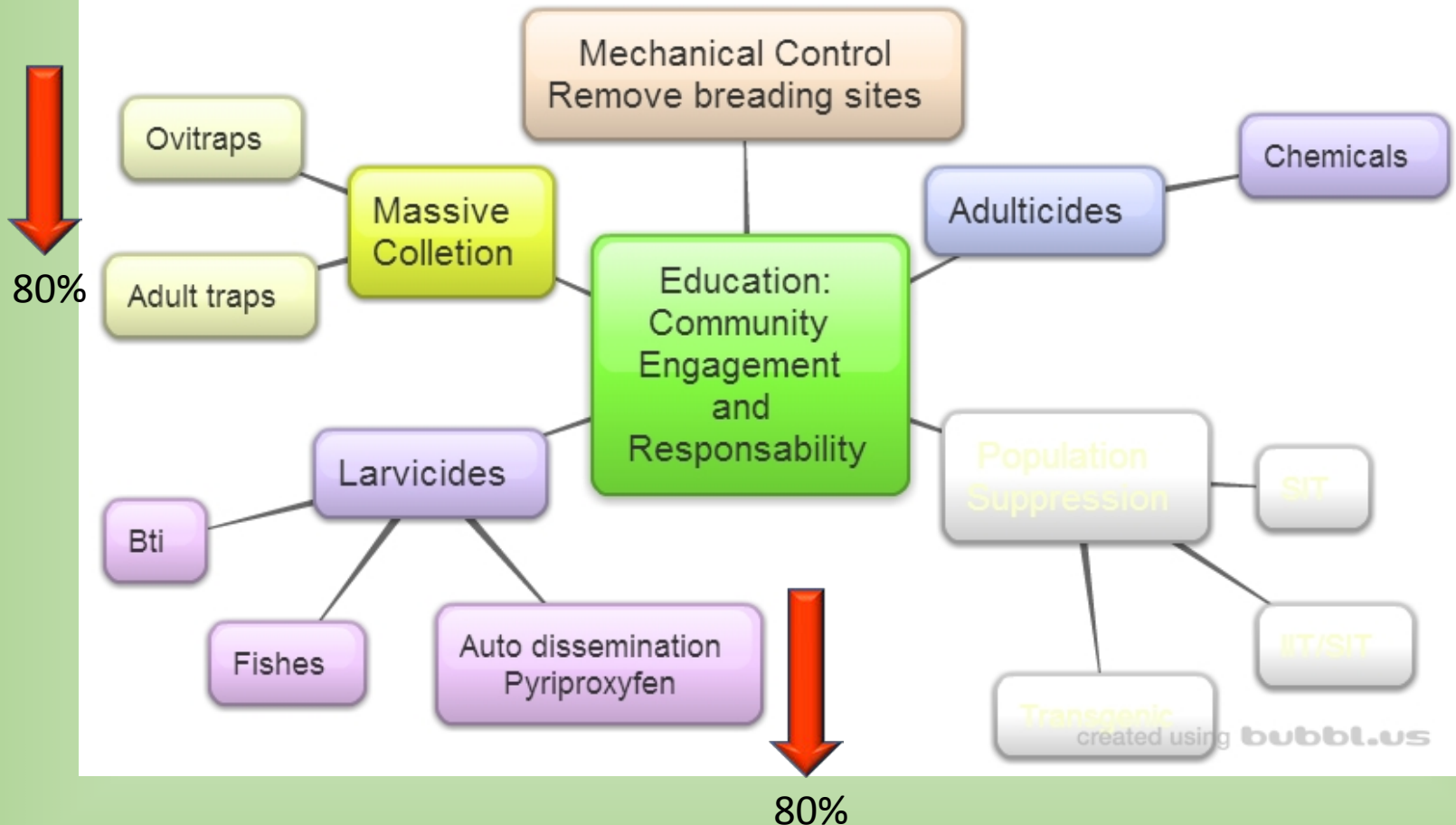
Integrate Control for *Aedes aegypti* Population Suppression



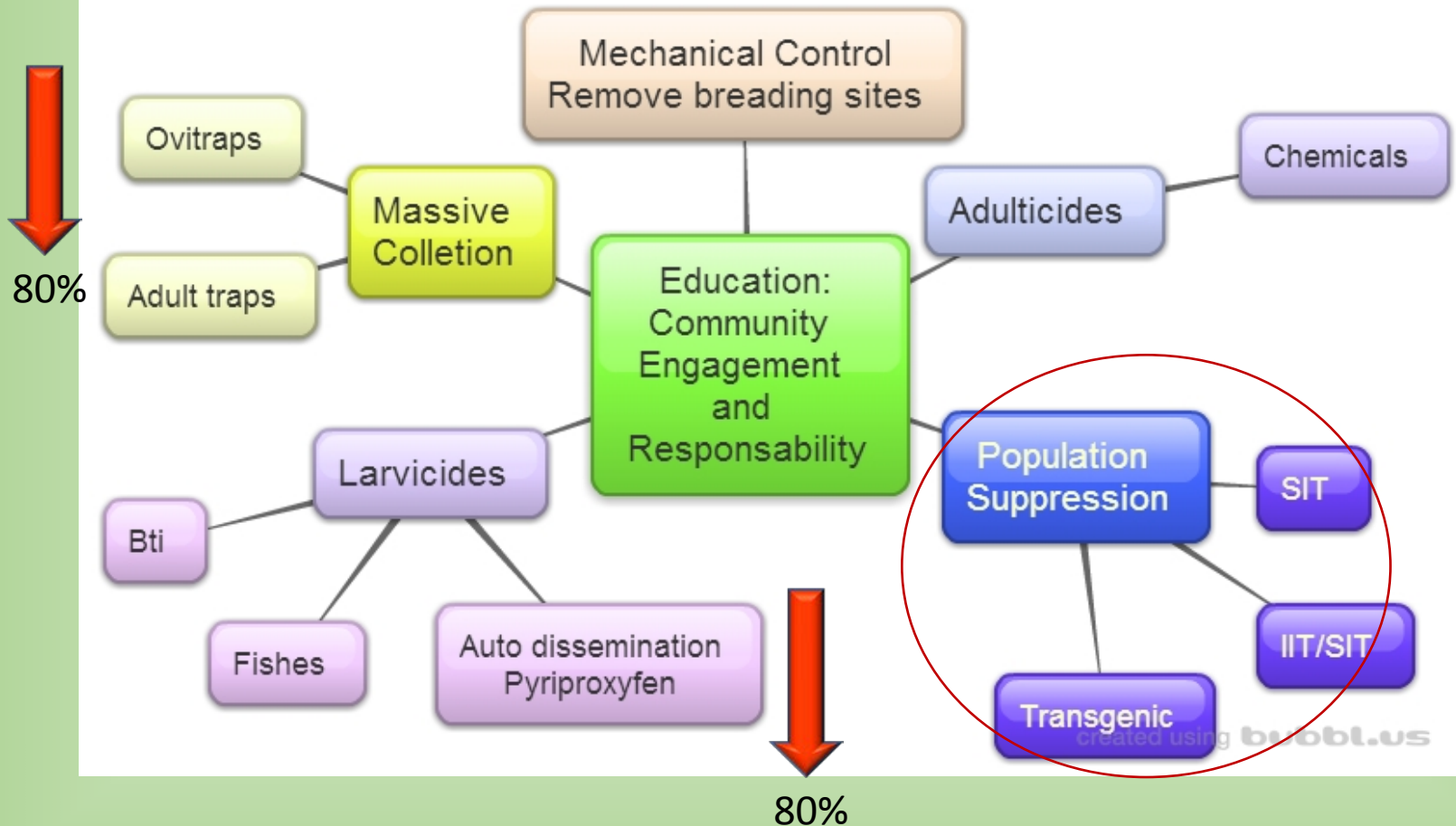
Integrate Control for *Aedes aegypti* Population Suppression

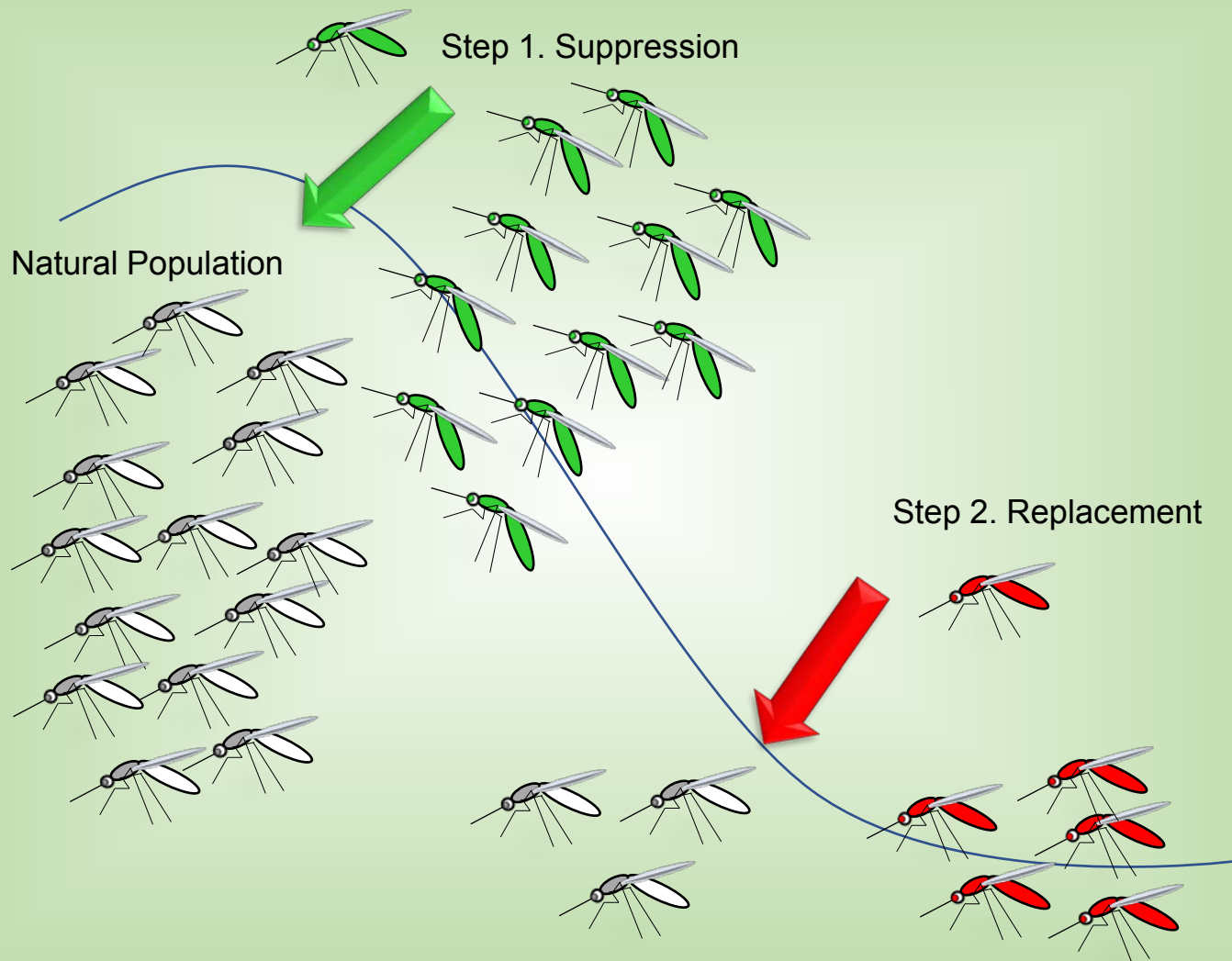


Integrate Control for *Aedes aegypti* Population Suppression



Integrate Control for *Aedes aegypti* Population Suppression





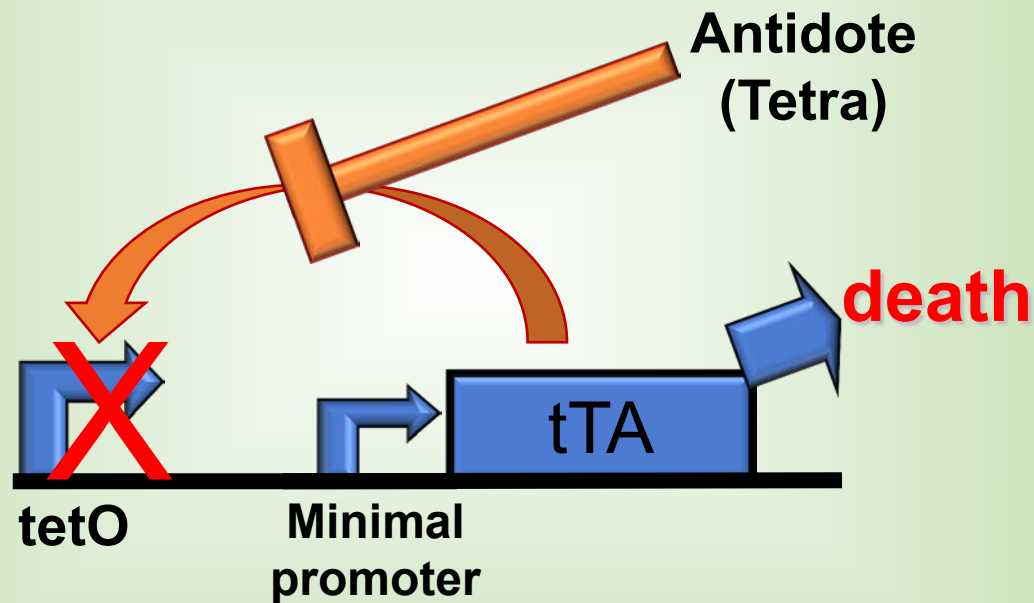
Open Field Release of **OX513A** *Aedes aegypti* Transgenic line evaluation



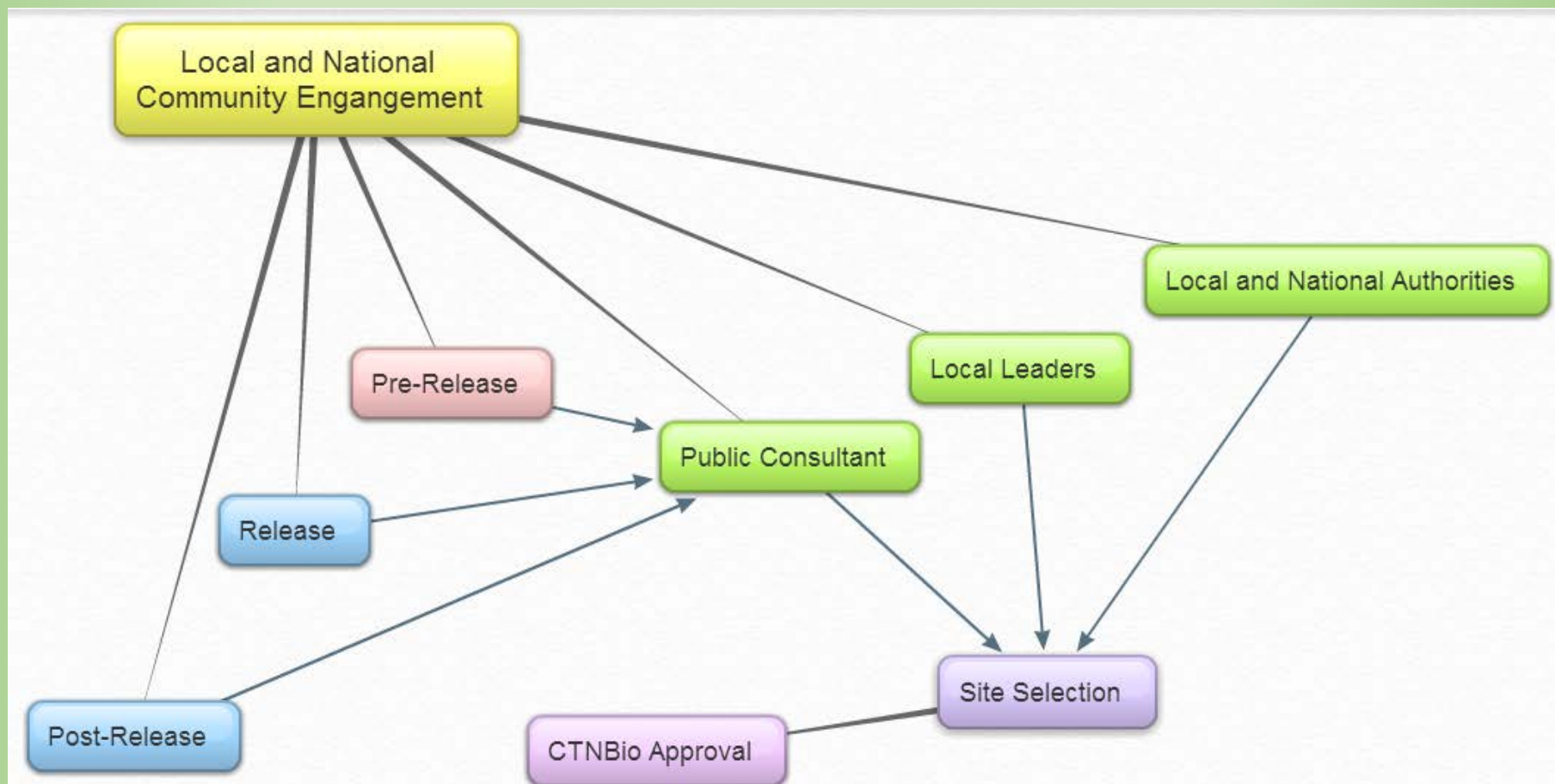
Projeto Aedes Transgênico



Repressive of Insects carrying a Dominant Lethal gene (RIDL)



Thomas *et al.* 2000 Science 287: 2474-6



Video Article

Mass Production of Genetically Modified *Aedes aegypti* for Field Releases in Brazil

Danilo O. Carvalho^{1,2}, Derric Nimmo¹, Neil Naish¹, Andrew R. McKemey¹, Pam Gray¹, André B. B. Wilke³, Mauro T. Marrelli³, Jair F. Virginio⁴, Luke Alphey^{1,5}, Margareth L. Capurro^{2,6}



COLONY
4 to 6 million eggs/week

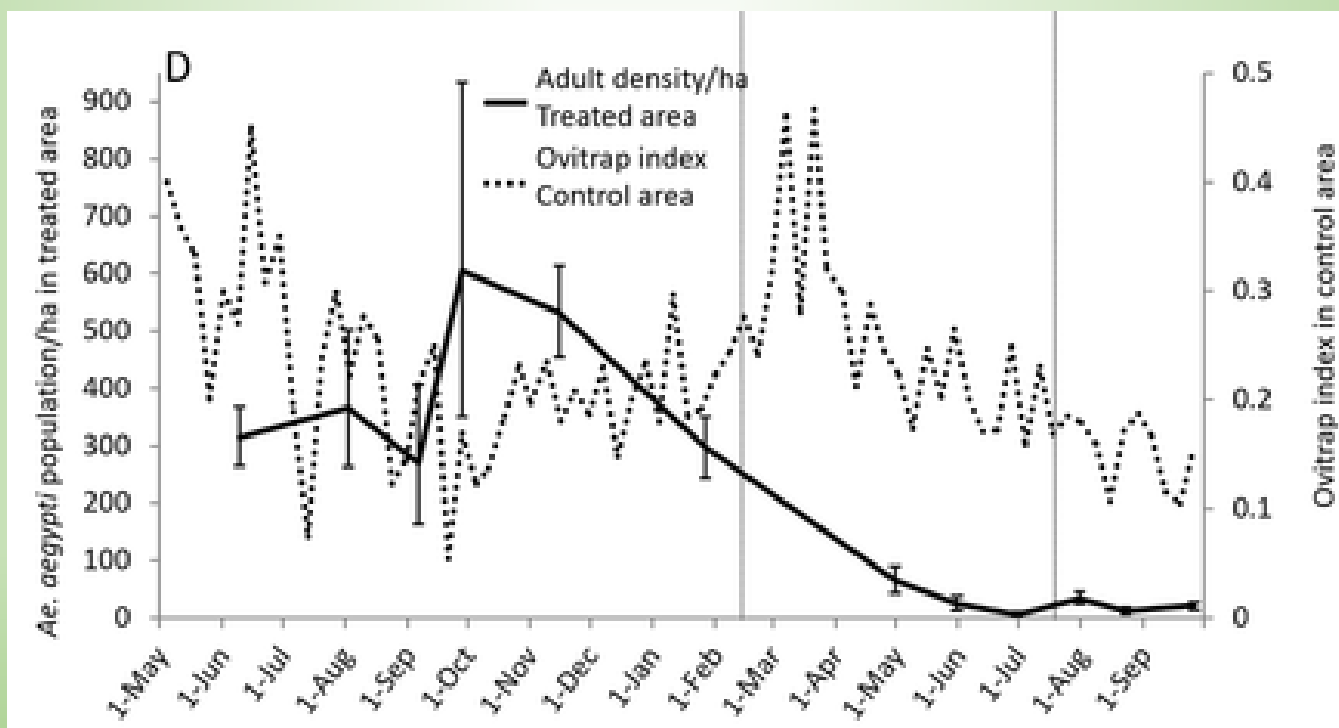


Males for releases
1,5 million/week

RESEARCH ARTICLE

Suppression of a Field Population of *Aedes aegypti* in Brazil by Sustained Release of Transgenic Male Mosquitoes

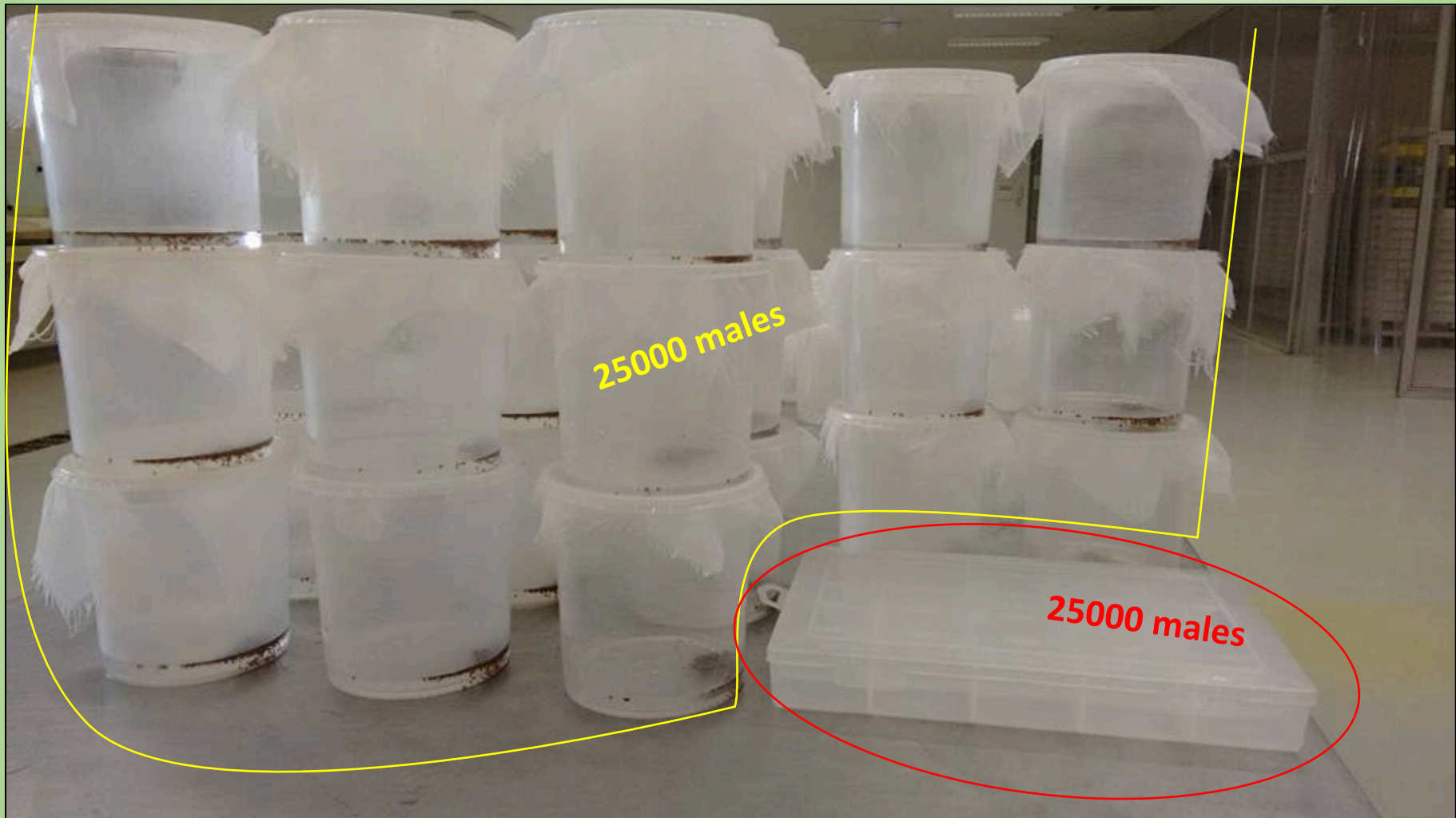
Danilo O. Carvalho^{1,2}*, Andrew R. McKemey¹*, Luiza Garziera³, Renaud Lacroix¹, Christl A. Donnelly⁴, Luke Alphey^{1,5,6}, Aldo Malavasi³, Margareth L. Capurro^{2,7}



Project Phase 2 – Jacobina - Bahia



Pupa Transportation



Pupa transportation (LEMI)



C25



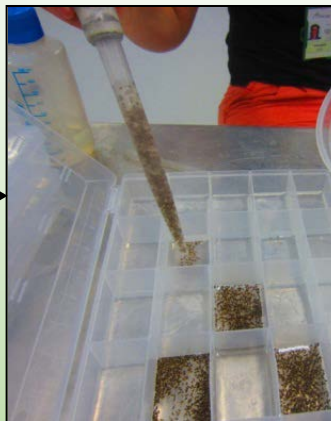
BOD 16°C ON



180,000 per container

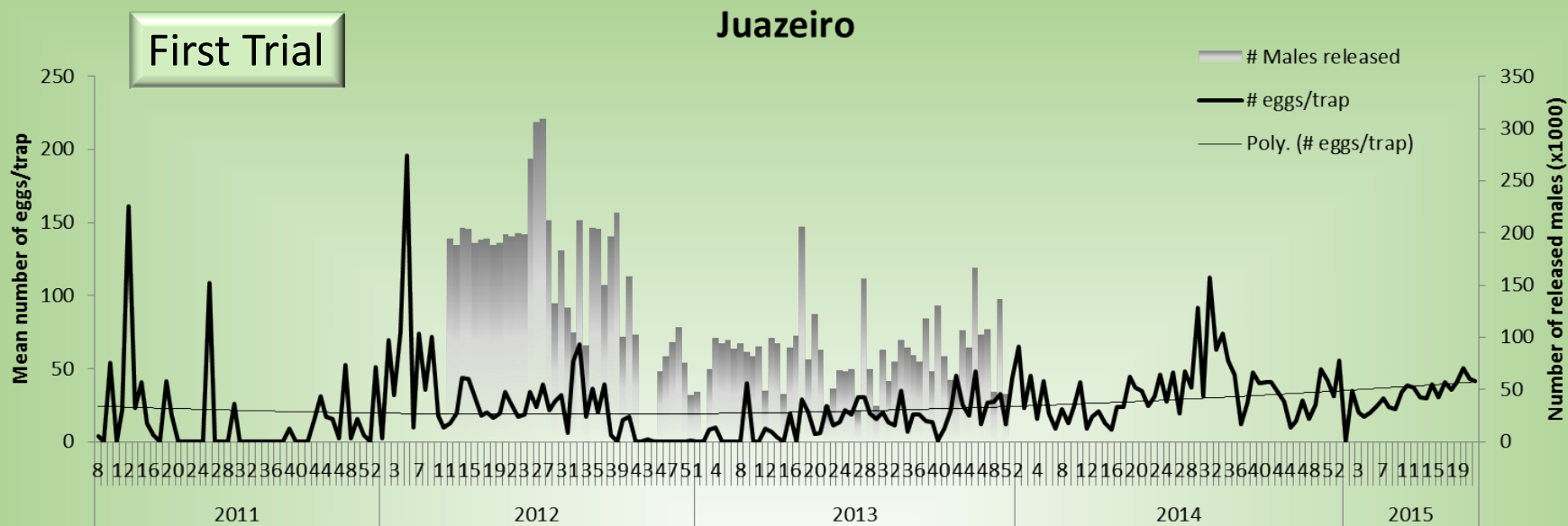


Arriving at LEMI
Emergency , Monitoring and Information Lab

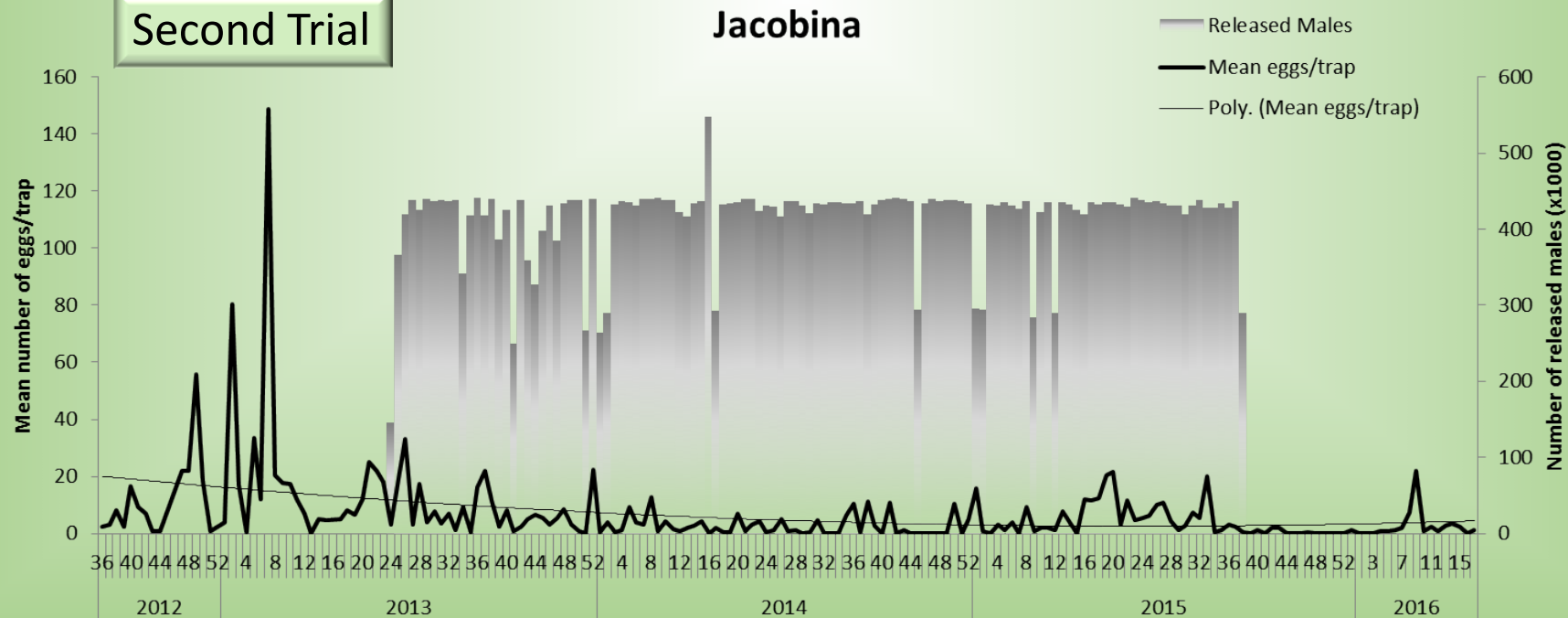


Preparation for release

First Trial



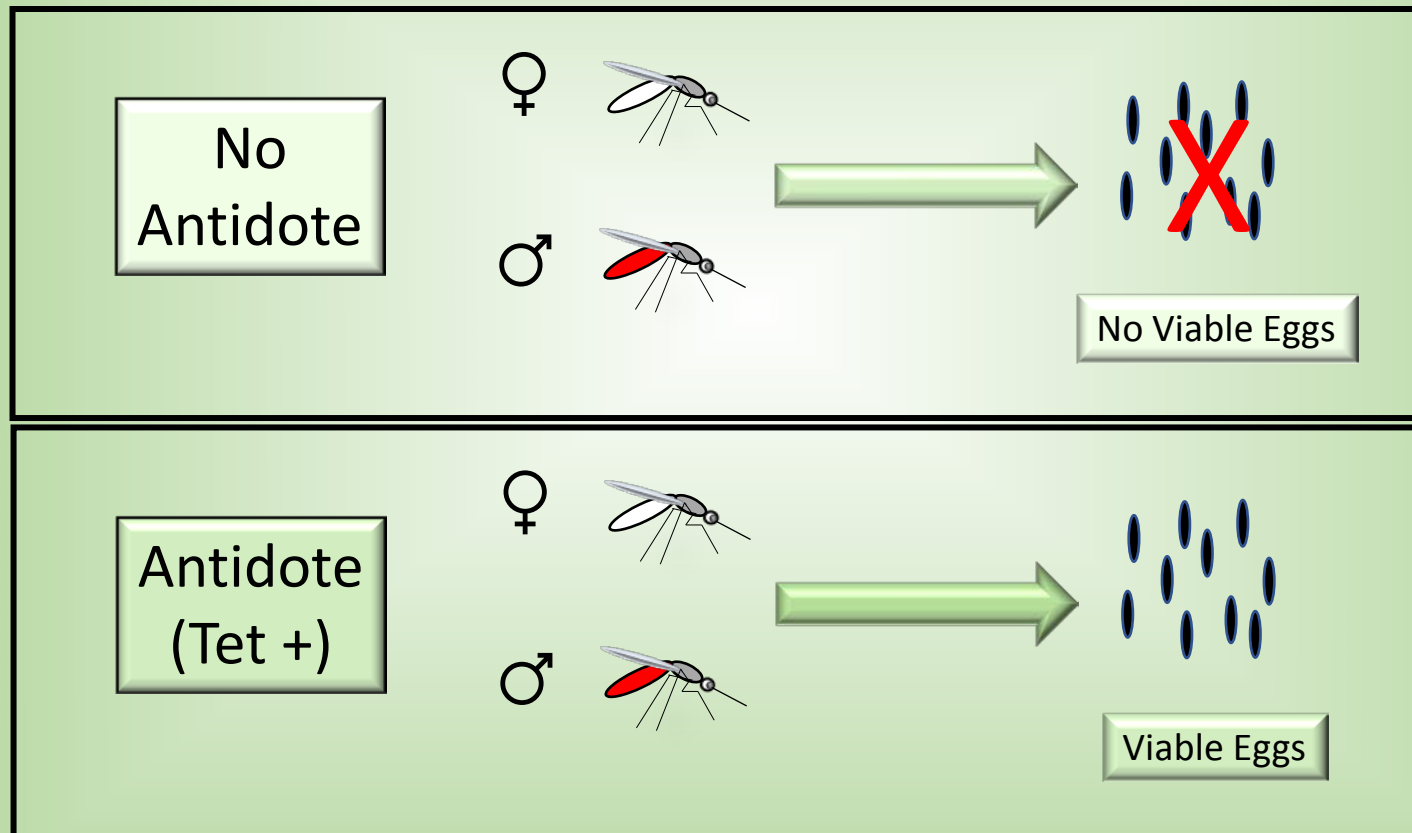
Second Trial



What do we learn?

- We need Genetic Sexing Strain (GSS)
- Producing Sterile male strain (no Larvae)
- Use of tetracycline only in colonies

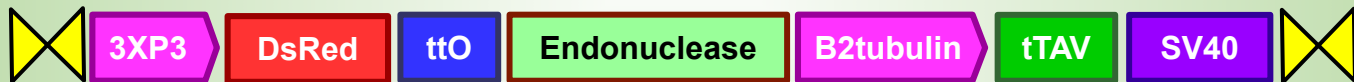
Sterility Conditional Construct - SCC



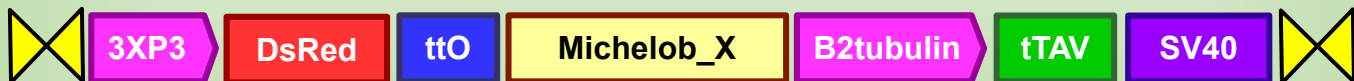
SCC Transgenes

- Two Effector molecules:

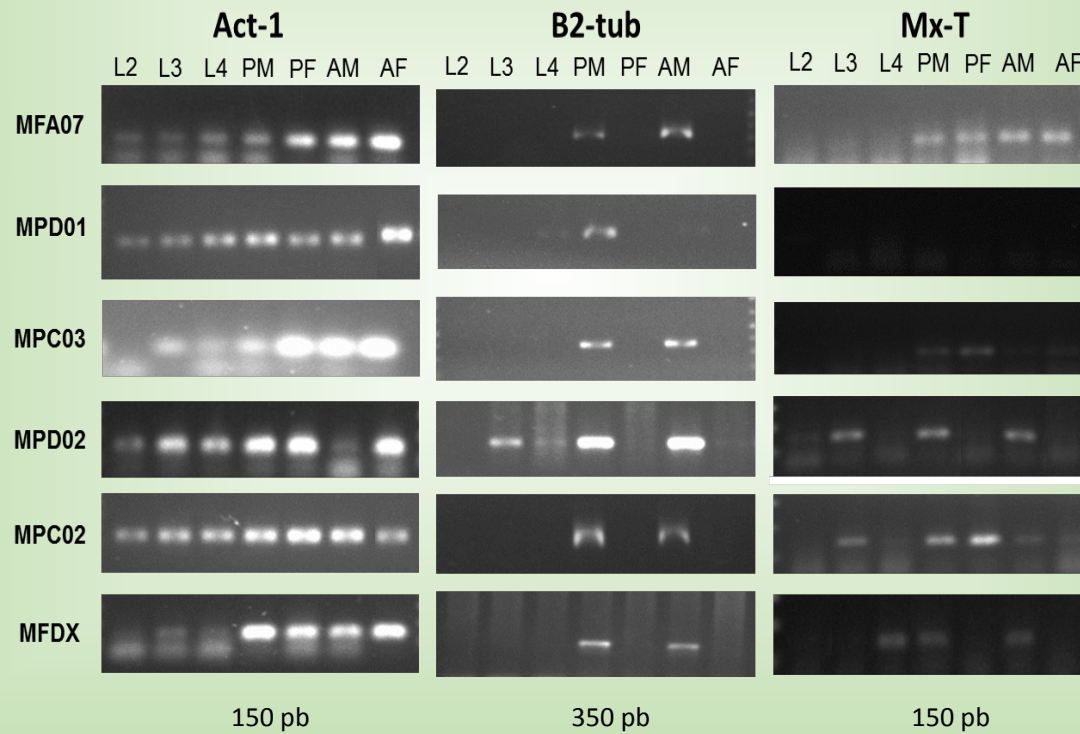
Endonuclease



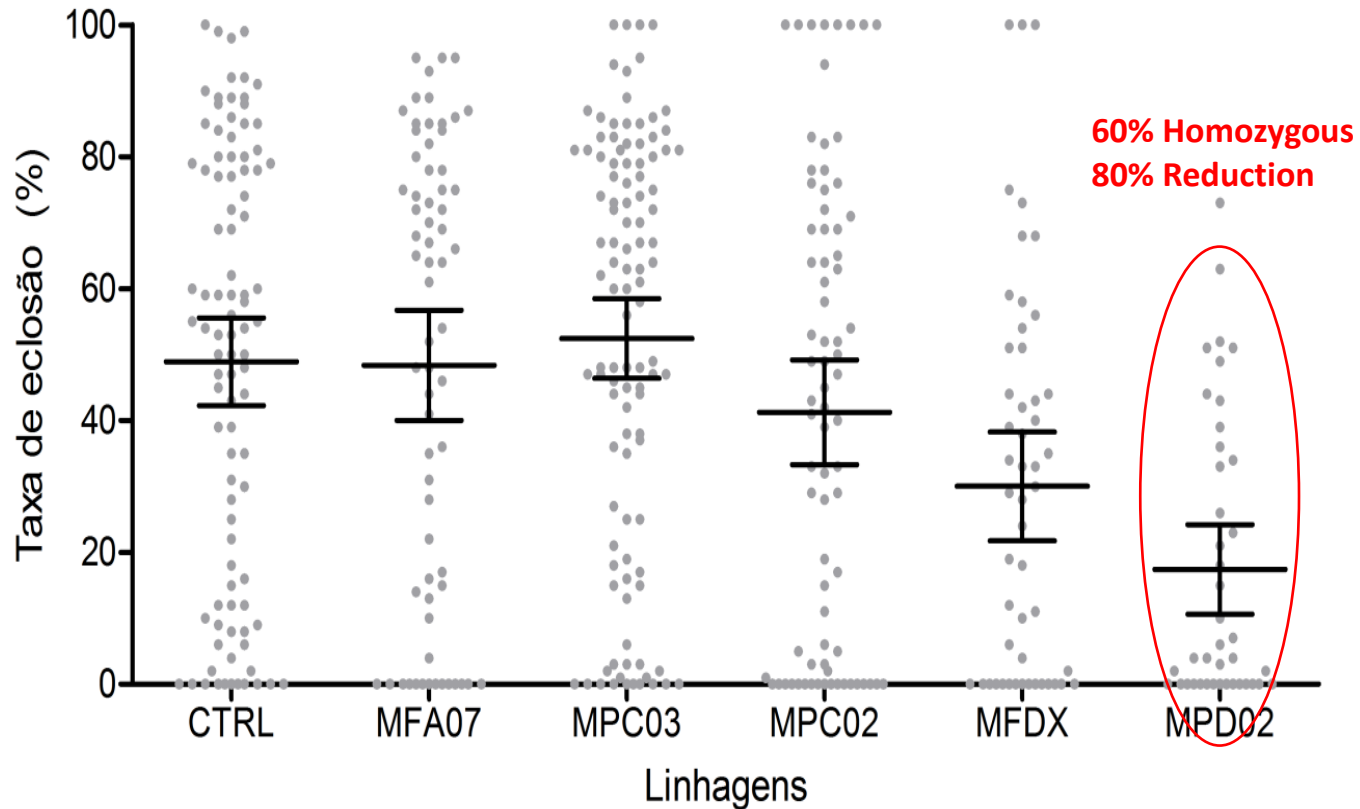
IAP Antagonist



Transgenic Lines



Sterile Conditional Construct (SCC)



Improving transgenic lines
Aedes aegypti and *Aedes albopictus*

- Producing Sterile male strain (no Larvae) ✓
- Producing GSS (Genetic Sexing Strain)

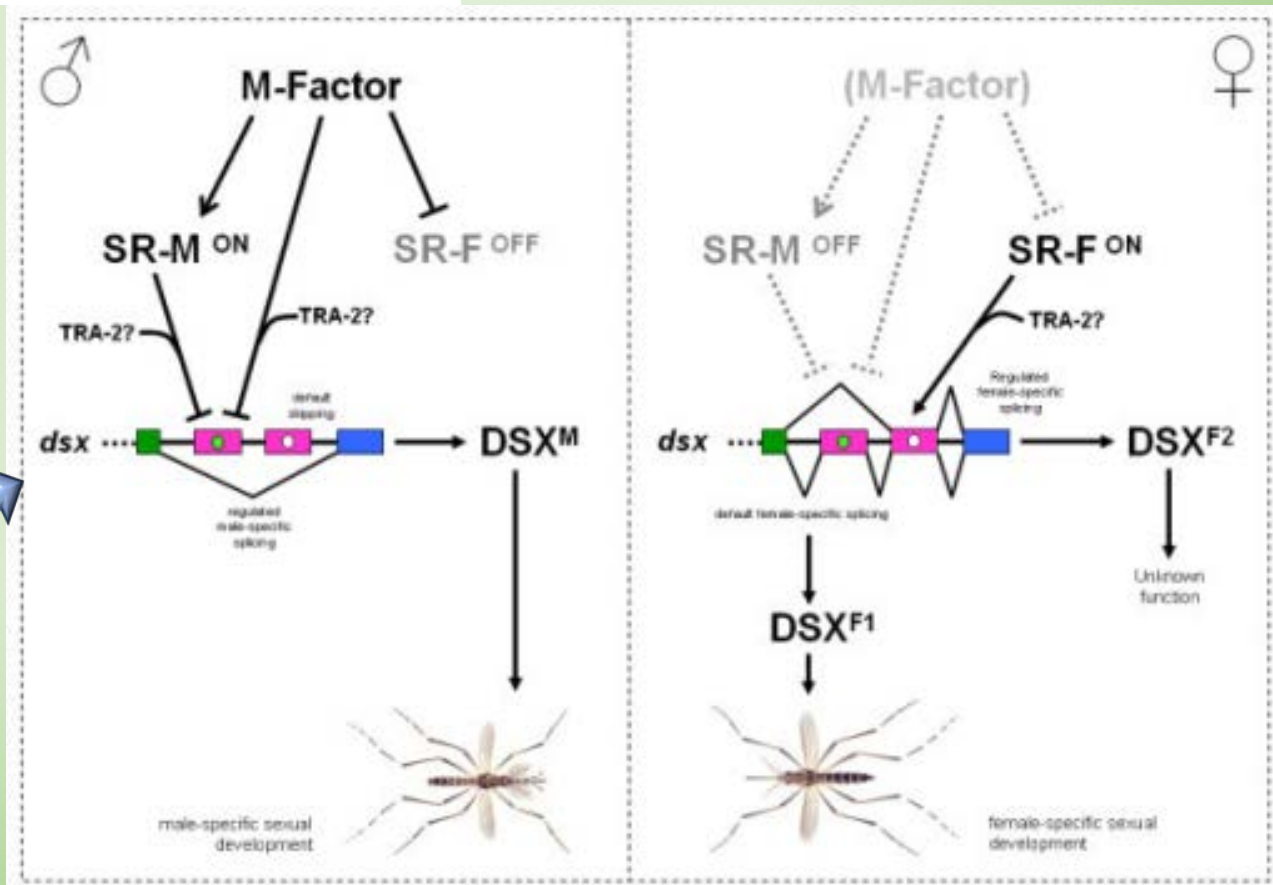


RESEARCH ARTICLE

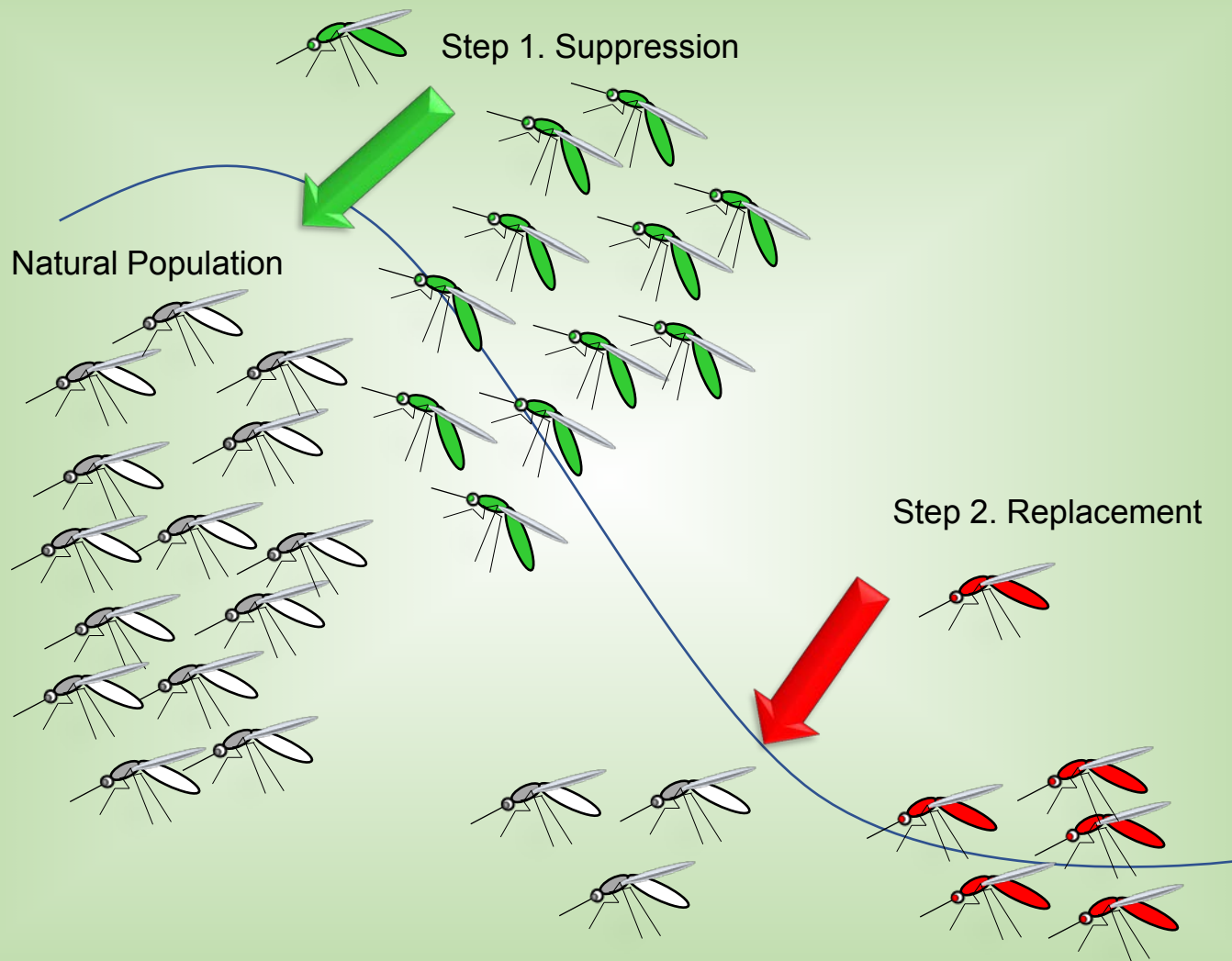
Open Access

Genomic organization and splicing evolution of the *doublesex* gene, a *Drosophila* regulator of sexual differentiation, in the dengue and yellow fever mosquito *Aedes aegypti*

Marco Salvemini^{1†}, Umberto Mauro^{1,2†}, Fabrizio Lombardo³, Andreina Milano¹, Vincenzo Zazzaro¹, Bruno Arcà^{3,4}, Lino C. Polito^{1,5}, Giuseppe Saccone^{1*}



Dsx knockout

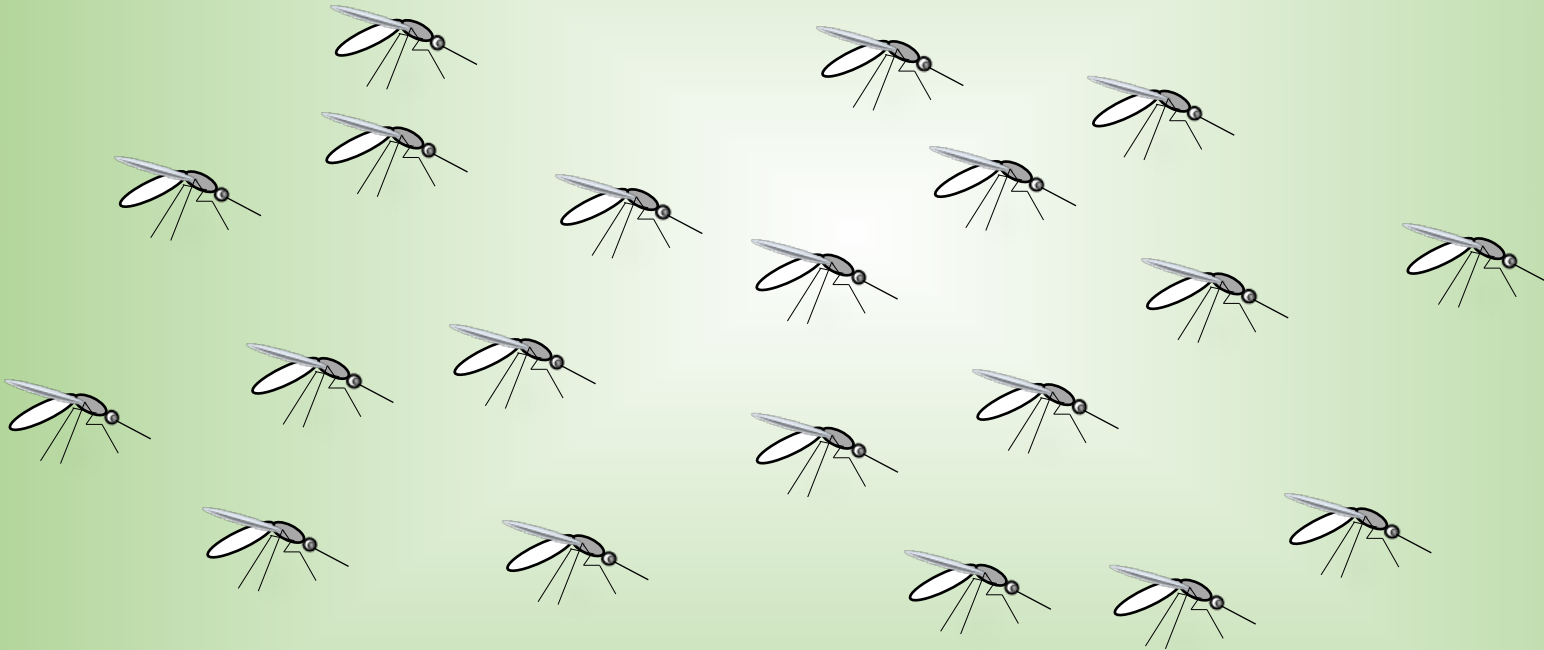


Gene Introduction

Virus-regulated mosquito gene

Suicidal Model (Double death model)

Natural Population



Gene Introduction

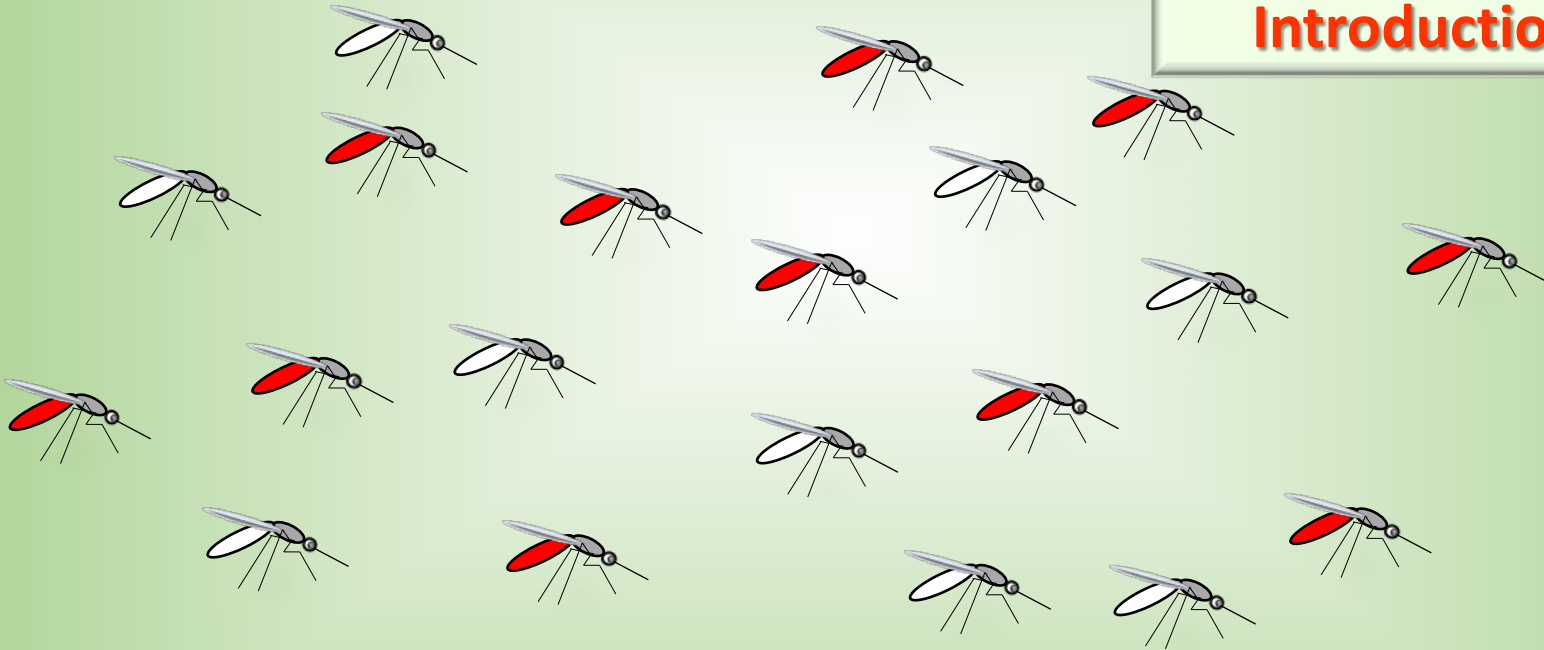
Virus-regulated mosquito gene

Suicidal Model (Double death model)

Natural Population

+

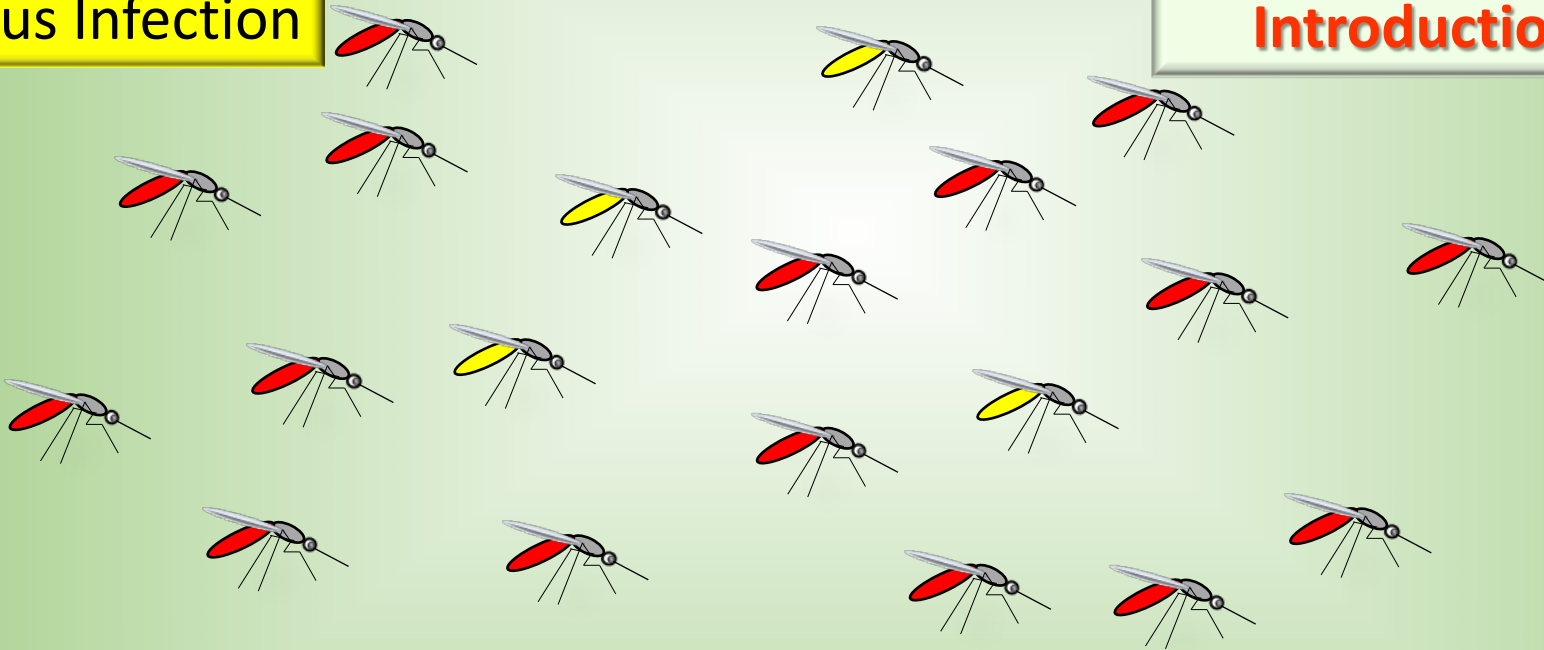
Introduction



Gene Introduction
Virus-regulated mosquito gene
Suicidal Model (Double death model)

Virus Infection

Natural Population
+
Introduction



Gene Introduction

Virus-regulated mosquito gene

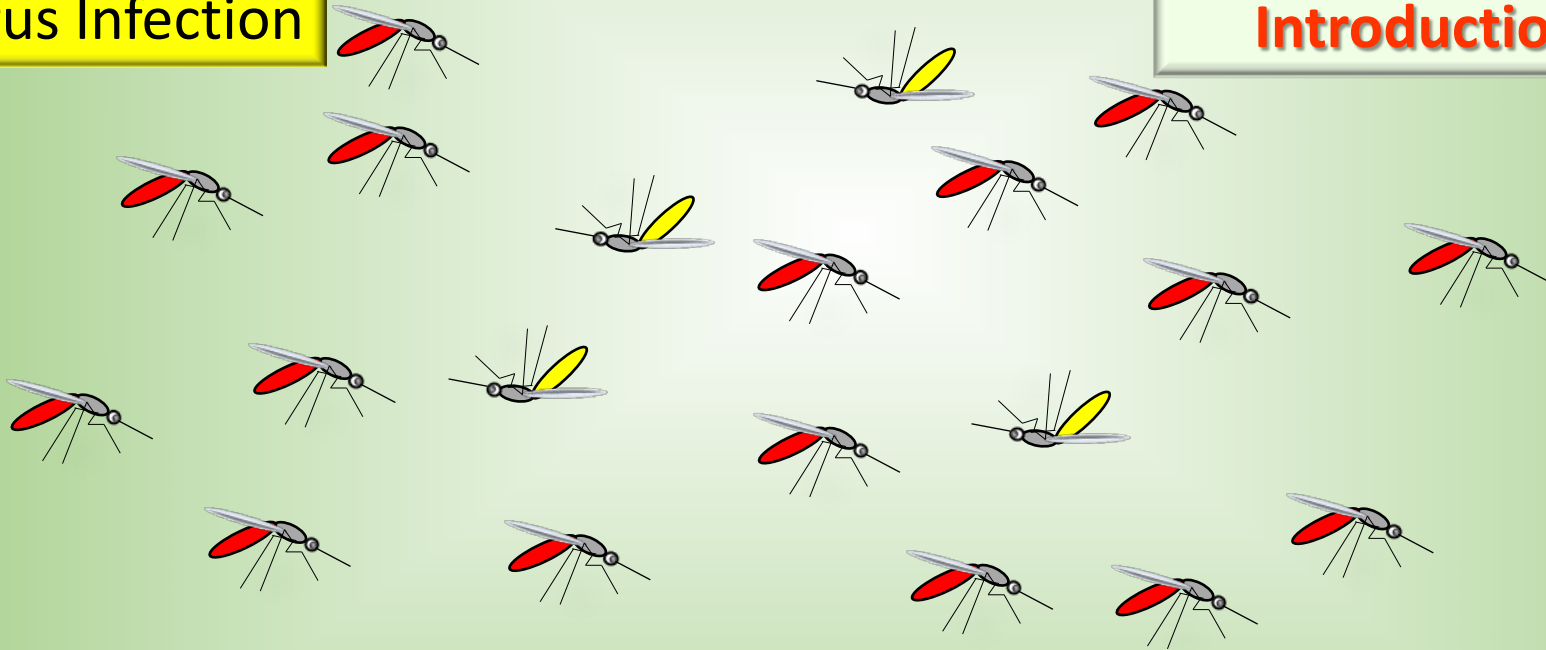
Suicidal Model (Double death model)

Virus Infection

Natural Population

+

Introduction



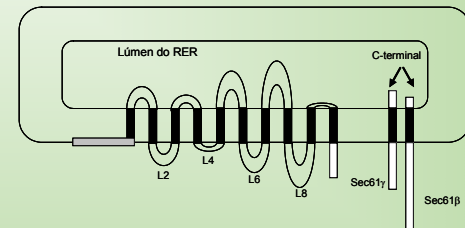
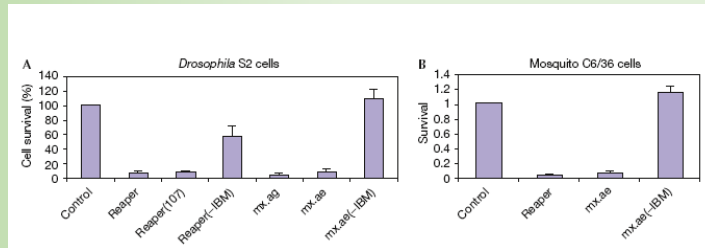
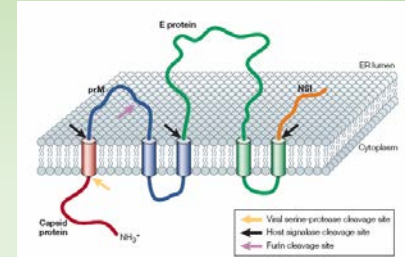
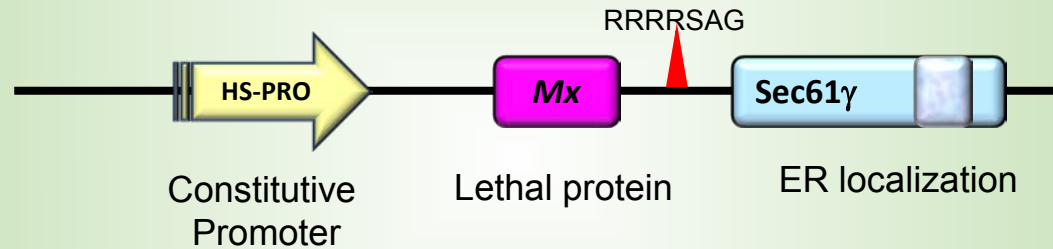
Gene Introduction

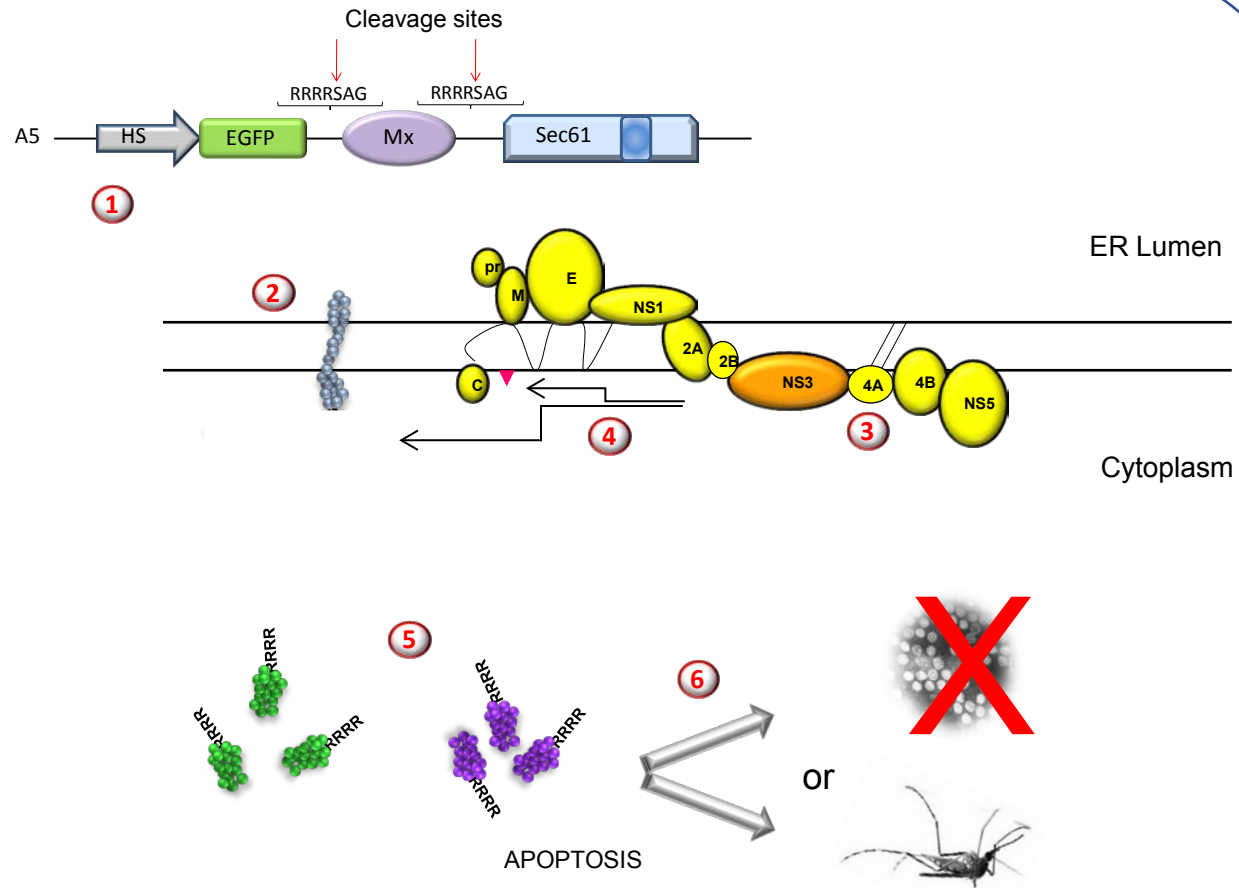
Virus-regulated mosquito gene

Suicidal Model (Double death model)

Step 2. Replacement

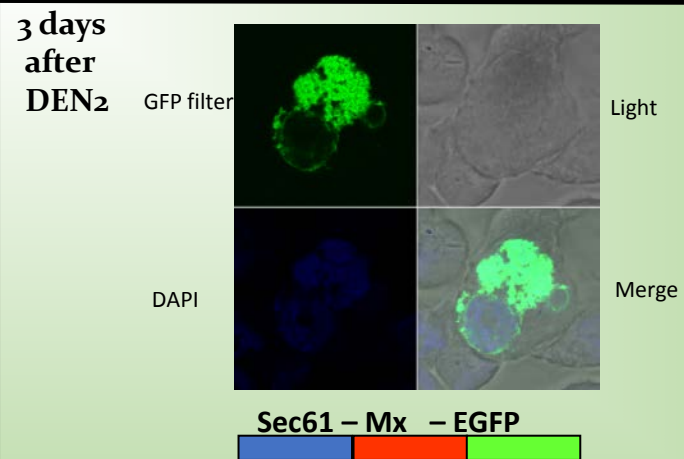
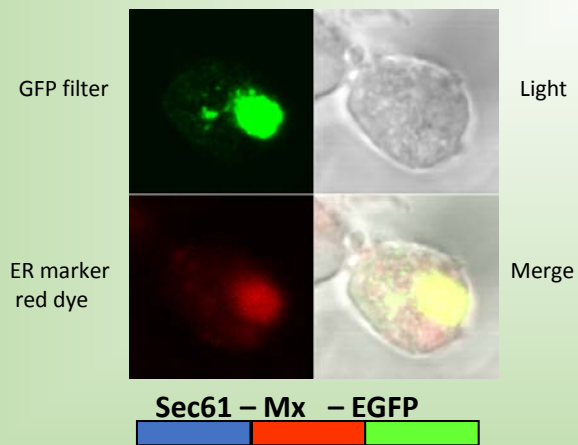
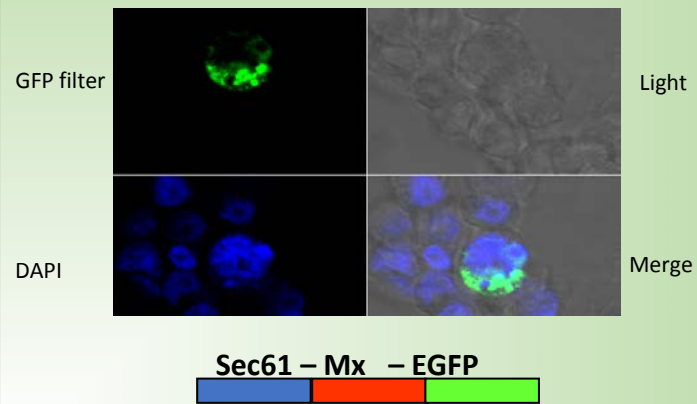
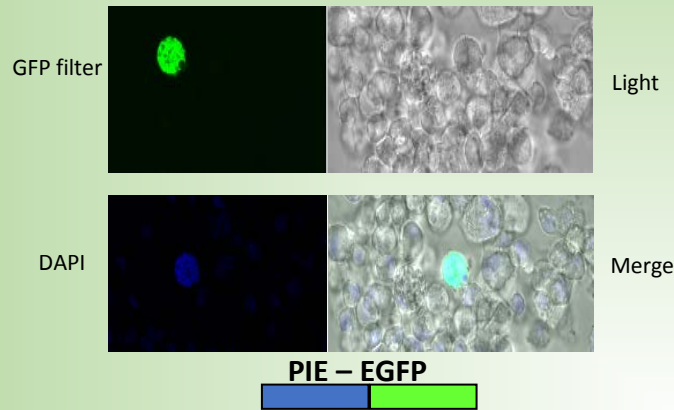
NS3 Cleavage site



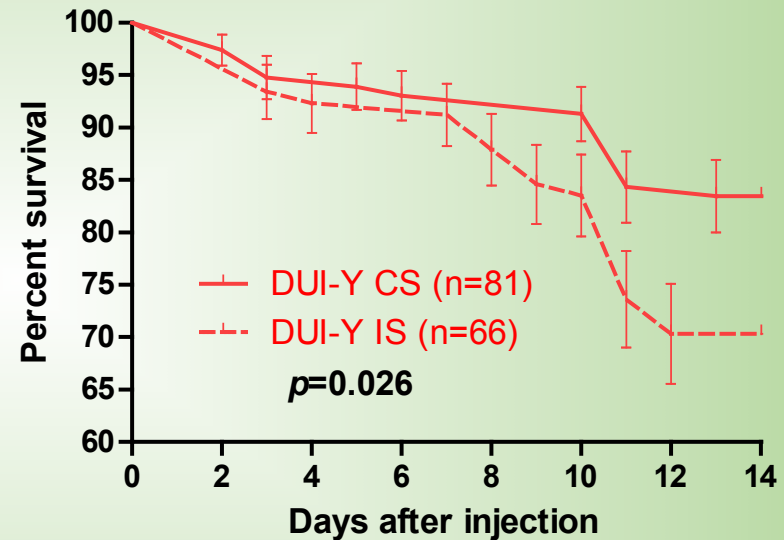
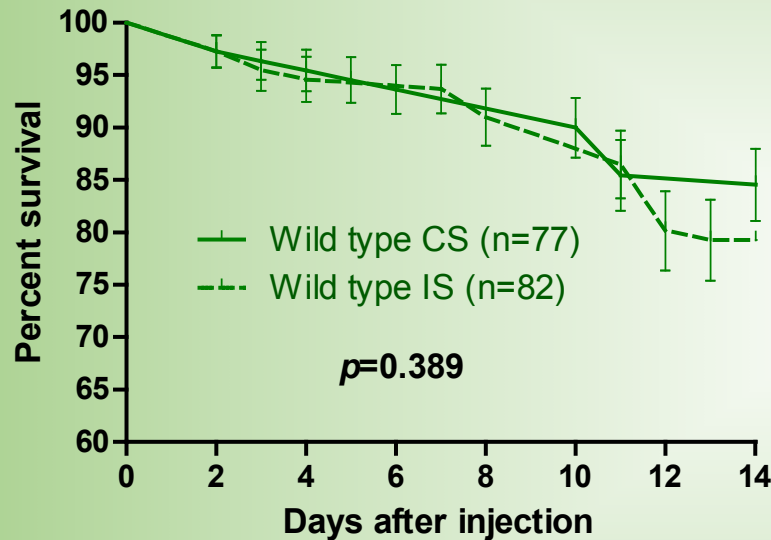


- **Double death model - Infection phenotypes in dengue challenged mosquito?**

- C6/36 cells - Transfection and D2 challenge:**

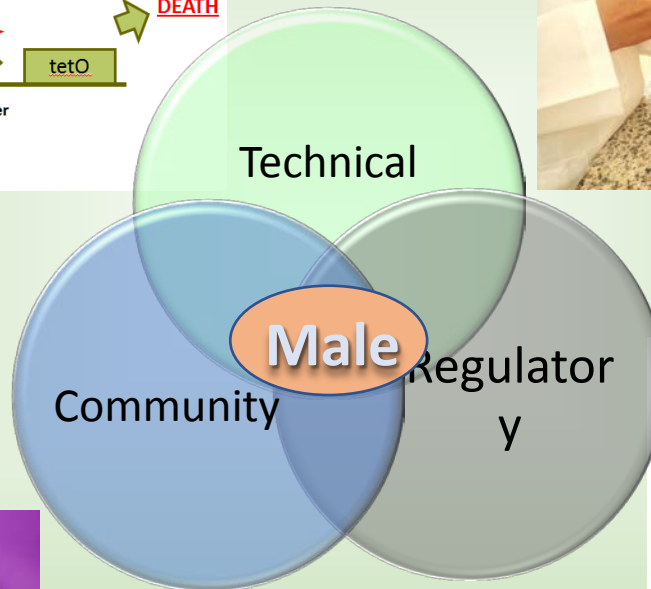
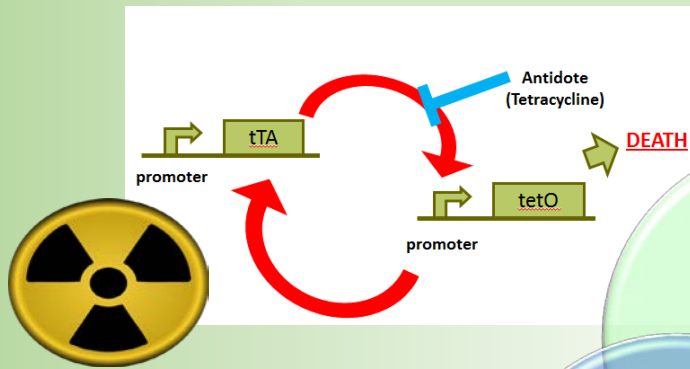


Intrathoracic injection - Survivorship



Survival rates of wild type (Higgs-strain) and DUI-Y transgenic line challenged with DENV-2 via intrathoracic injection. Five-to-seven day old females were injected with control supernatant (CS) and DENV-2 infected supernatant (IS) (vial load = 7.0×10^6 genomic copies). Females were recovered during 24hs after injection and survived females were maintained on 10% sucrose solution and censored during 14 days after injection (14DPI). Solid lines are showing survival curves of females injected with CS and dotted lines are showing survival curves of females injected with IS. Survival curves were statistically analyzed by Log-rank (Mantel-Cox) test.

Bringing new technology to the field

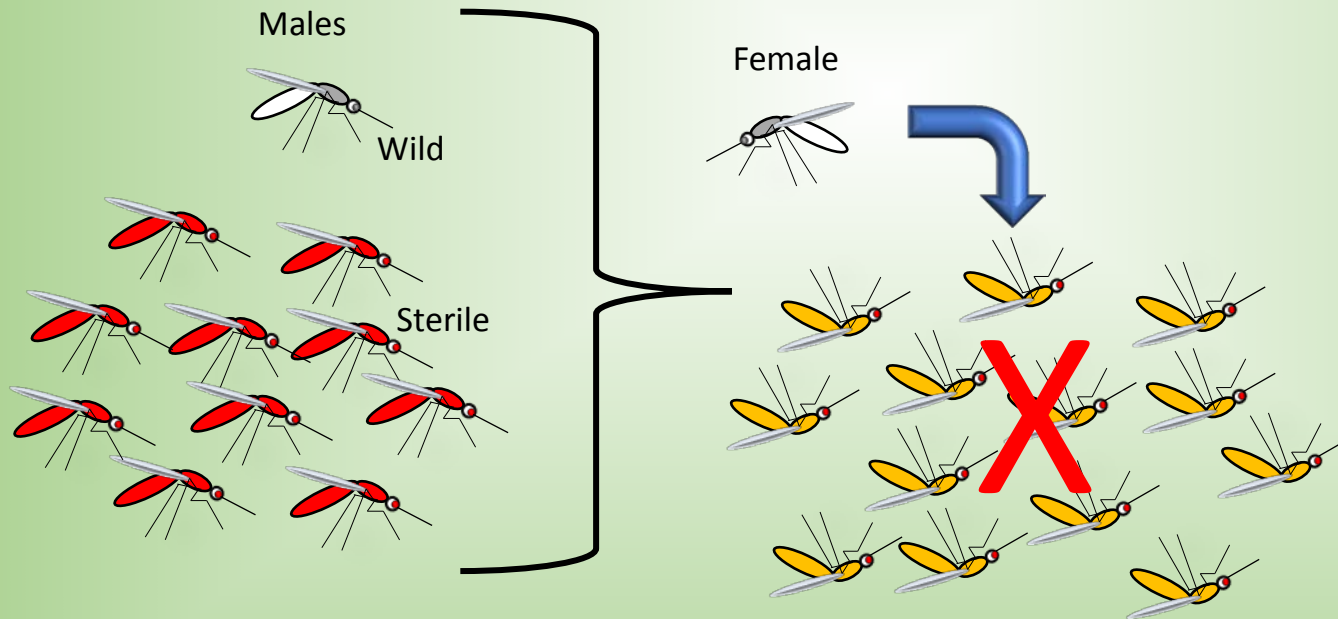


Nature

How the Sterility works?

How the Sterile Mosquito Works?

Why releasing male mosquitoes you kill mosquitoes?



Before releasing mosquitoes

- Site selection
 - Public Engagement:
 - Evolving Public Authorities (Government and agencies);
 - Local ones (community engagement);
 - Local people - explain what we are going to do in that area.



Community Engagement

Research Article

DESCRIPTION OF SOCIAL ASPECTS SURROUNDING RELEASES OF TRANSGENIC MOSQUITOES IN BRAZIL

Margareth Lara Capurro^{1,2}, Danilo Oliveira Carvalho^{1,2}, Luiza Garziera³, Michelle Cristine Pedrosa³, Itala Damasceno³, Iana Lima³, Brenna Duarte³, Jair Fernandes Virginio³, Rosemary Susan Lees⁴ and Aldo Malavasi³

Action		Period			
		Pre-release	Release		Post-release
		2010*	2011	2012	2013*
Domiciliary visit					
Internet	Social Network				
	Web site				
Interviews / appearances	TV				
	Radio				
	Newspaper				
	Magazines				
Jingle broadcast					
Leaflets distribution					
Meeting local leaders					
Questionnaires					
School presentations / lectures					
Monitoring system					
Truck loudspeakers					

* - In both years, the columns are representing the last two semesters and the first two respectively.



Community Engagement



Total people 17,101,269 in Brazil – Based on the Brazilian Institute of Public Opinion and Statistics (IBOPE) data

Talks and Lectures



City Hall Public Hearing

Leaflet distribution





PAT

Projeto Aedes Transgênico

Agente do PAT

Esse faz a diferença!

Você sabia que :

O Aedes aegypti

tem umas listras brancas no corpo e nas perninhas;	que machos não picam, logo não transmitem doenças;
somente a FÊMEA do mosquito quem pica, porque precisa de sangue para produzir os ovos;	que Aedes aegypti ataca de DIA e a muriçoca só a NOITE ;

A Dengue é transmitida através da picada da **FÊMEA** do mosquito infectado



FASE DO CICLO

1º passo
Pessoa doente
Pica, suga o sangue da pessoa infectada com a dengue, e o vírus leva de 7 a 14 dias para se desenvolver no mosquito.

2º passo
O mosquito (fêmea do Aedes aegypti)
A fêmea transmite o vírus pela saliva antes de sugar o sangue.

3º passo
Pessoa vulnerável
7 a 14 dias para aparecer os sintomas da dengue.

Realização:




Parcerias:







Este projeto está sendo realizado com o apoio do ESTADO DA BAHIA, através da SECRETARIA DE SAÚDE DO ESTADO DA BAHIA - SESAB

www.moscamed.org.br
 Av. Cl. 992 - Quadra D 13, lote 15
 Dist. Industrial do São Francisco - Juazeiro-BA
 CEP 48.908-000 - Tel/Fax: 74-3612-5399

PROJETO AEDES TRANSGÊNICO

4

NO LABORATÓRIO os machos são mantidos para **LIBERAÇÃO** e as fêmeas **ELIMINADAS**.

1

Os mosquitos transgênicos são produzidos em laboratório.



Modificados geneticamente

2

Eles contêm modificações específicas que o torna diferente do outro Aedes aegypti transmissor da dengue.

3

O macho transgênico ao cruzar com a fêmea selvagem, passa o gene mortal e os mosquitos gerados morrem ainda na fase de larva ou pupa.

CICLO DE VIDA



5

NA COMUNIDADE

- Colocadas as ovitrampas (armadilhas).
- é feita a identificação dos mosquitos capturados.
- a equipe faz a liberação dos mosquitos transgênicos.

6

Os agentes do PAT realizam o monitoramento para avaliação e análise da redução populacional dos insetos capturados.

Os machos transgênicos não picam. São mosquitos parceiros, que te protegem da dengue.

Mosquito Aedes \Dengue



Pica durante o dia (bite during the day)



Muriçoca (*Culex*)



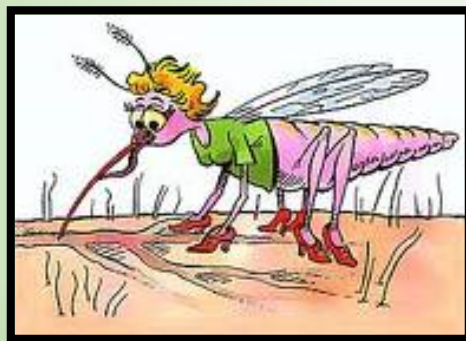
Pica durante a noite (bite during the night)



Bar – Blood for Sale!

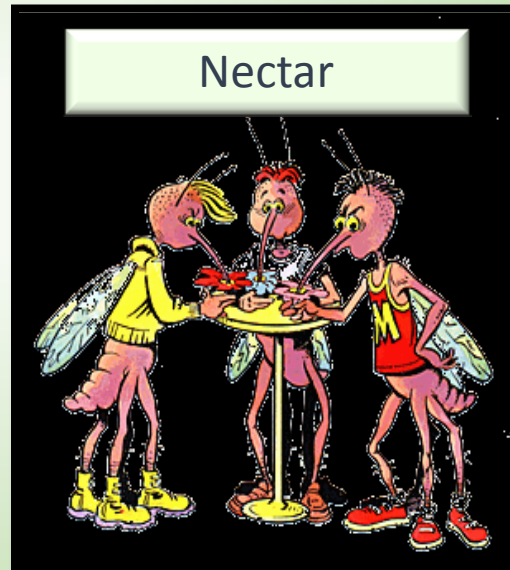


Only females (girls) bite



Fonte: Google

Nectar



ACTION	TARGET POPULATION LEVEL	# EVENTS	# PEOPLE
Presentations/Lectures	Local/Regional	10	962
Leaflets ⁽¹⁾	Local	-	10,000
Jingle ⁽¹⁾	Local	-	-
Meetings	National/ International	39	6,020
Interviews (radio)	Regional	15	1,500
Interviews (TV)	Regional/National	09	17,094,000 ⁽²⁾
Interviews (newspaper/magazine)	Local/Regional/ National	13	-
Internet (website / social network)	Regional/National	24	-(³)
Houses visited/interviewed with residents	Local	581	2,341
Meetings with local leaders, health agents	Local	16	820
Presentations at elementary and middle school	Local	08	452
Presentation at community center/city hall/others	Local	06	456
Driving truck with loudspeakers in the releasing area	Local	-	500
Spots, jingles and short messages broadcasted in local radio station	Local	52	1,200 ⁽⁴⁾
TOTAL			17,101,269

STRATEGIES		
Mandatory	Recommended	Suggested
- Visit/interview sample/every house in the target area	- Lectures at community centers/churches – targeting adults	- Action within a local event (parade, carnival, street fairs)
- Meetings with local leaders, school principals, district managers	- Radio spots, jingles and messages broadcasted	- Driving truck with loudspeakers in the targeting area – jingle and messages
- Lectures at schools – targeting kids/teens	- Press releases by Moscamed journalists	- Use of social media: Facebook and twitter
- Press coverage at local/regional level of PAT activities: production, releases	- PAT technical personnel interviewed by local/regional/(inter)national radio stations	- Press coverage at international level of PAT activities: releases
	- Press coverage at national level of PAT activities: production, releases	

Spot and Jingle



SPOT

To control dengue Moscamed is releasing in this community

A large amount of TRANSGENIC MOSQUITOES .

We would like to recall that this mosquitoes are not the well known *CULEX*

They are transgenic MALES and they DON'T BITE.

They are good fellows that will give you protection against dengue.

For more information call a health agent or get in touch with

MOSCAMED

By the phone

(74) 3612-5399

PAT –AEDES TRANSGENIC PROJECT

This one makes the difference.



Jingle Transgenic *Aedes*



Dr Peter Piermarini



Dr Jeff Powell



Dr Lincoln Suesdek



Institute of Molecular and Genomic Medicine
National Health Research Institutes

Dr Chun-Hong Chen



Instituto Nacional de Ciência e
Tecnologia em Entomologia Molecular

