

AGGIORNAMENTI IN TEMA DI MEDICINA DEI VIAGGI E DELLE MIGRAZIONI  
ZIKA VIRUS E ALTRE ARBOVIROSI

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**SOLO AEDES?**  
**IL RUOLO POTENZIALE DI *AEDES***  
***ALBOPICTUS***



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Laboratorio di Parassitologia

Venezia, 09 giugno 2016

- Il virus circolava prevalentemente fra i primati selvatici e alcune zanzare arboree quali *Aedes africanus*
- raramente è stato riconosciuto causa di infezioni "spillover" negli esseri umani, anche in aree altamente enzootiche
- Cosa è successo?

# Cosa è successo?

bioRxiv preprint first posted online Nov. 25, 2015; doi: <http://dx.doi.org/10.1101/032839>. The copyright holder for this preprint (which was not peer-reviewed) is the author/funder. It is made available under a [CC-BY 4.0 International license](#).

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## Spread of the pandemic Zika virus lineage is associated with NS1 codon usage adaptation in humans

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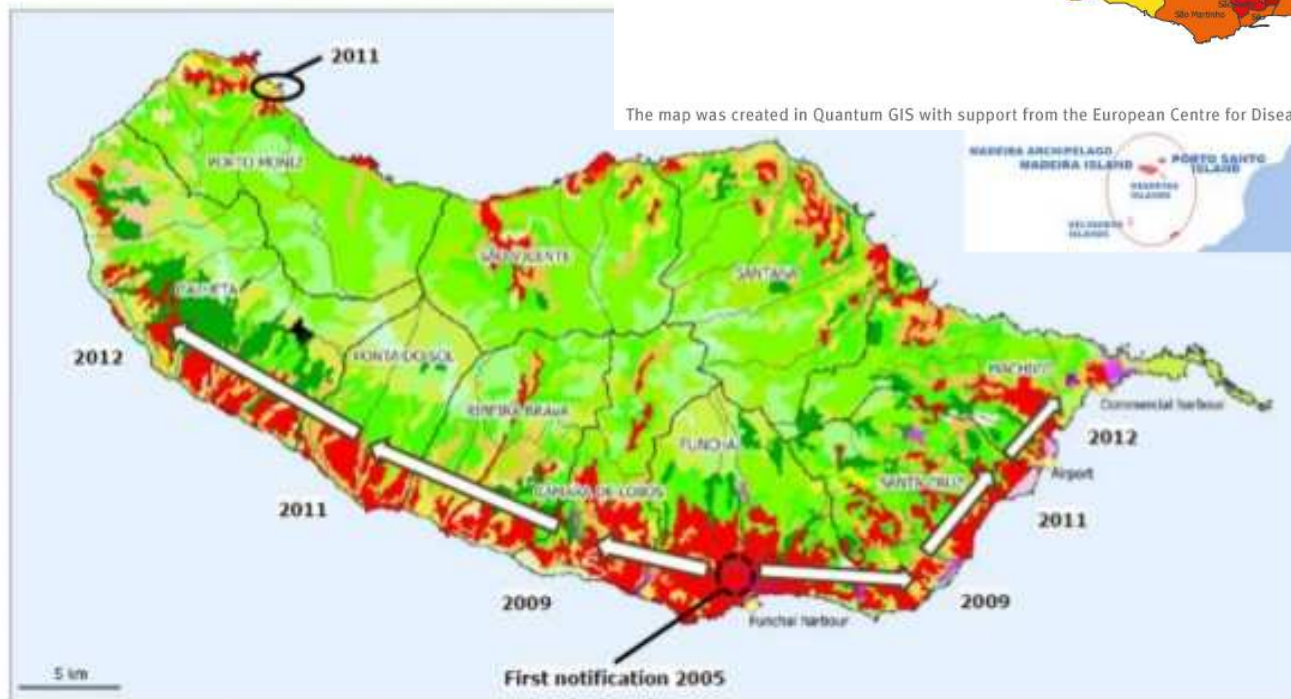
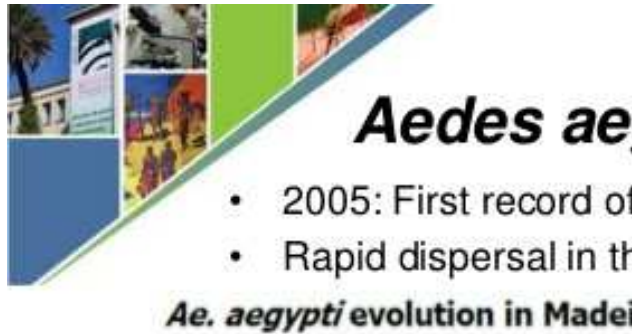
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### ABSTRACT

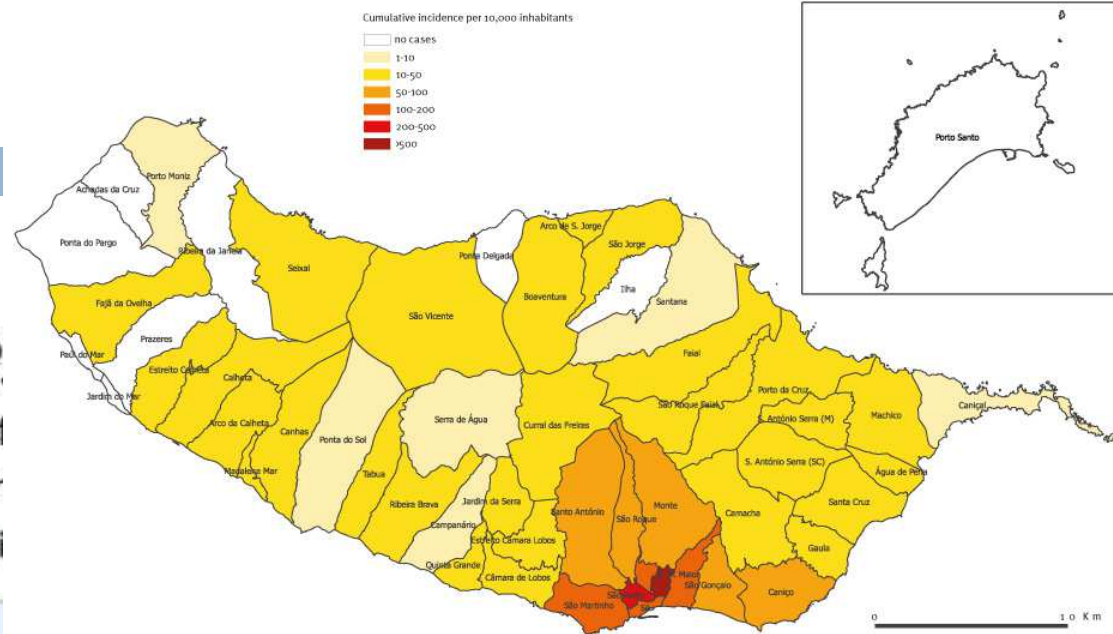
Zika virus (ZIKV) infections were more common in the zoonotic cycle until the end of the 20<sup>th</sup> century with few human cases in Africa and Southeastern Asia. Recently, the Asian lineage of ZIKV is spreading along human-to-human chains of transmission in the Pacific Islands and in South America. To better understand its recent urban expansion, we compared genetic differences among the lineages. Herein we show that the recent Asian lineage spread is associated with significant NS1 codon usage adaptation to human housekeeping genes, which could facilitate viral replication and increase viral titers. These findings were supported by a significant correlation with growth in Malthusian fitness. Furthermore, we predicted several epitopes in the NS1 protein that are shared between ZIKV and Dengue. Our results imply in a significant dependence of the recent human ZIKV spread on NS1 translational selection.

# Aedes aegypti

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**FIGURE 2**  
Cumulative incidence of dengue cases by parish, outbreak on Madeira, Portugal, 3 October–25 November 2012



The map was created in Quantum GIS with support from the European Centre for Disease Prevention and Control.

# *Aedes aegypti*

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POLICY PLATFORM

## First International Workshop on Zika Virus Held by Oswaldo Cruz Foundation FIOCRUZ in Northeast Brazil March 2016 – A Meeting Report

Rafael F. O. Franca , Maria Helena L. Neves, Constancia F. Junqueira Ayres, Osvaldo P. Melo-Neto, Sinval P. Brandão Filho

Published: June 3, 2016 • <http://dx.doi.org/10.1371/>

Mosquitoes from the genus *Aedes* (*Ae. albopictus* and *Ae. aegypti*) are the main species responsible for Zika virus transmission in Brazil [12,13].

# The vector/s?

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- .....in only two of the 11 outbreaks of the past decade have the vector(s) been identified: *Ae. albopictus* was incriminated as the primary vector in Gabon and *Aedes hensilii* in the Island of Yap outbreak;
- *Aedes aegypti* **has been implicated** in the ongoing transmission in the Americas.
- Still, mosquito population diversity does play an important role in transmission potential.

Christofferson RC. Zika Virus Emergence and Expansion: Lessons Learned from Dengue and Chikungunya May Not Provide All the Answers. *Am J Trop Med Hyg.* 2016 Feb 22. pii: 15-0866.



# *Aedes aegypti*

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Health & Medicine

## Nobody is completely sure which mosquito spreads Zika in Brazil

globalpost

April 06, 2016 · 8:30 AM EDT

By Will Carless ([follow](#))

68 shares



Comment



*Aedes aegypti* mosquitoes inside Oxitec laboratory in Campinas, Brazil.

Credit: Paulo Whitaker/Reuters

.....nobody has yet managed to identify the virus in a single *Aedes aegypti* mosquito — or any other species — captured in Brazil, where authorities estimate 1.5 million people have contracted Zika

# Aedes aegypti

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.....non dimentichiamo

## *Aedes aegypti*: segnalazioni in Italia



Istituto Superiore di Sanità  
Dipart. MIPI

Dr R.Romi - ISS

### □ Air temperature changes until now

#### ▣ Mean temperature trends

Different estimates of mean temperature trend in Italy over more than 100 years have been reported: a total temperature increase from 1850–1899 to 2001–2005 of  $0.76^{\circ}\text{C} (\pm 0.19^{\circ}\text{C})$  (1), and a temperature increase from 1865 to 2003 of  $1.0 \pm 0.1^{\circ}\text{C}$  per century (2)

These results also show that **minimum temperature has increased more than maximum temperature (particularly in the north)** (2). Similar temperature trends for all seasons were confirmed for Sicily (20)

# Condizioni necessarie alla trasmissione

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- La zanzara deve essere competente
- La zanzara deve trovare nell'ambiente degli ospiti viremici
- Gli ospiti devono essere quelli «preferiti» da quella specie di zanzara
- La zanzara deve sopravvivere più a lungo del «periodo di incubazione estrinseca» del patogeno
- Per la trasmissione all'uomo la zanzara deve avere un certo grado di antropofilia

# Esempi di diversa competenza

12

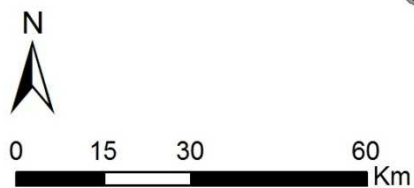
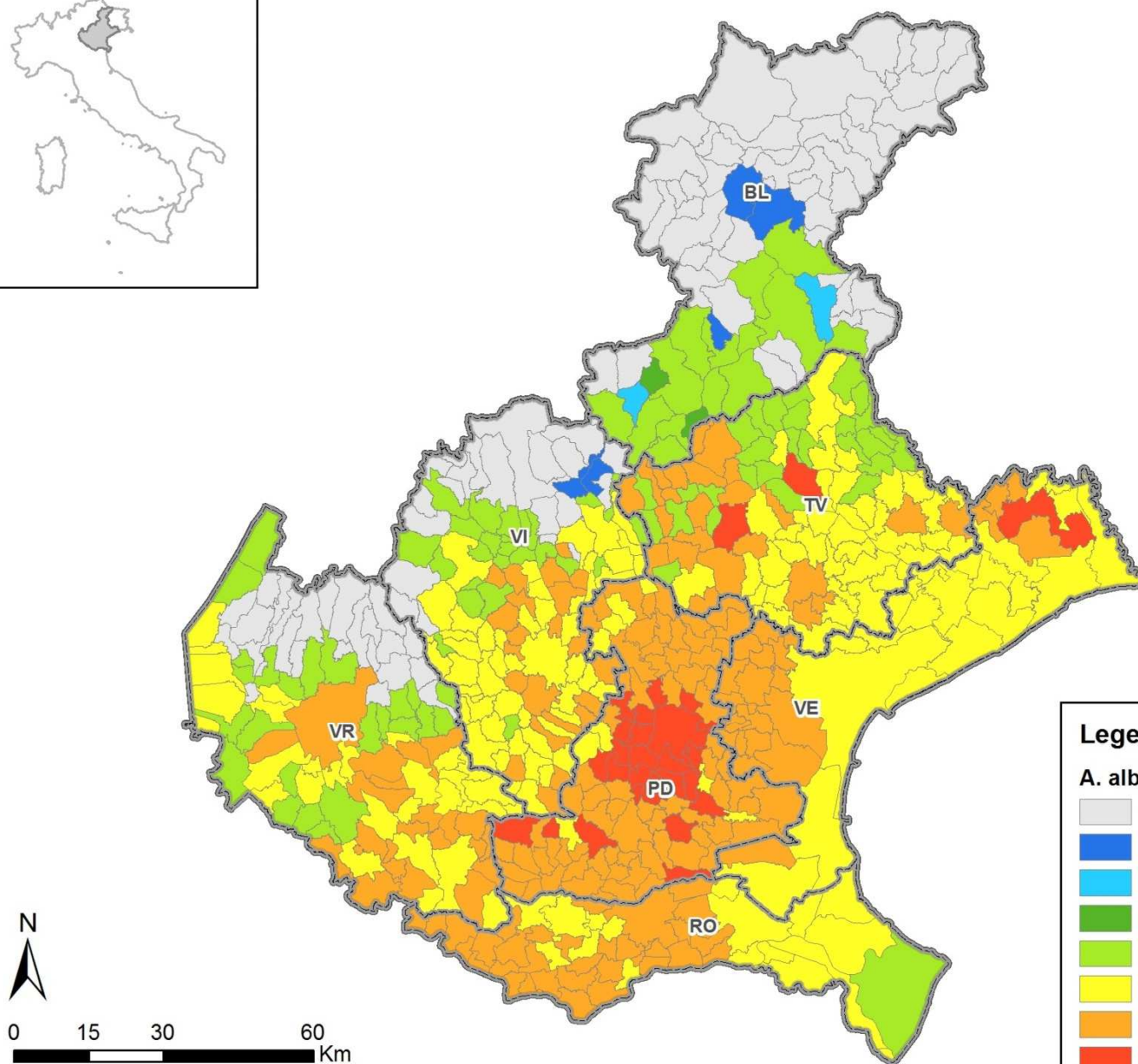


## Competenza vettoriale

- CHIKV non mutato 24%
- CHIKV mutato **80%**
- DENV I 47%
- DENV II 72%
- DENV III 64%
- DENV IV 38%

*Mitchell, 1991, Carrieri et al., 2012*

# *Aedes albopictus*



## Legend

### *A. albopictus* presence (year of detection)

- NOT present
- from 2012
- from 2011
- from 2010
- from 2005
- from 2000
- from 1995
- from 1990



# Competenza *Aedes albopictus* italiane x CHIKV e DENV

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## CHIK mutato

- 75-90%
- periodo di incubazione estrinseca nella zanzara di 2 giorni!!

## DENV

- 14-38,5%

# Veneto 2015

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Specie	tot	% sul tot	siti pos	media/sito	
<i>Culex pipiens</i>	81004	76,251	49	1653,14	
<i>Ochlerotatus caspius</i>	8875	8,354	47	188,83	
<i>Aedes albopictus</i>	2288	2,154	45	50,84	
<i>Anopheles maculipennis s.l.</i>	877	0,826	23	38,13	
<i>Aedes vexans</i>	305	0,287	28	10,89	
<i>Culiseta annulata</i>	93	0,088	23	4,04	
<i>Ochlerotatus detritus</i>	28	0,026	3	9,33	
<i>Culex modestus</i>	25	0,024	8	3,13	
<i>Anopheles plumbeus</i>	19	0,018	7	2,71	
<i>Coquillettidia richiardii</i>	10	0,009	5	2,00	
<i>Aedes/Ochlerotatus spp.</i>	7	0,007	4	1,75	
<i>Ochlerotatus annulipes</i>	4	0,004	2	2,00	
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<i>Aedes koreicus</i>	3	0,003	2	1,50	
<i>Culiseta longiareolata</i>	2	0,002	2	1,00	
<i>Culex hortensis</i>	1	0,001	1	1,00	
<i>Anopheles spp.</i>	1	0,001	1	1,00	
<b>TOTALE</b>	106.233	100,00			

- Competenza vettoriale
  - ▣ Ceppo virus: Uganda strain
  - ▣ Ceppo zanzare: *Aedes albopictus* locali di Singapore
- DIR: 7 dpi 100% (all mosquitoes have disseminated infection)
- TR: 73% of these mosquitoes have ZIKV in their saliva
- TR: 10 dpi 100% (all mosquitoes were potentially infectious)
- PIE: 4-7 gg

Wong P-SJ, Li MI, Chong C-S, Ng L-C, Tan C-H (2013) *Aedes (Stegomyia) albopictus* (Skuse): A Potential Vector of Zika Virus in Singapore. *PLoS Negl Trop Dis* 7(8): e2348.

## □ Conclusioni degli AA:

### **Conclusions/Significance:**

The study highlighted the potential of *Ae. albopictus* to transmit ZIKV and the possibility that the virus could be established locally

Nonetheless, the threat of ZIKV can be mitigated by existing dengue and chikungunya control program being implemented in Singapore.

# ZIKA e tigre

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- Competenza vettoriale
  - ▣ ceppo virale Asian genotype of ZIKV (NC-2014-5132)
  - ▣ ceppo tigre: 7 popolazioni (5 di *Ae. aegypti* e 2 di *Ae. albopictus*) dai Caraibi (Martinica, Guadalupa) e America continentale (sud Stati Uniti, Guiana francese, Brasile)
- IR: 14 dpi: *Ae. aegypti* 76.7% vs *Ae. albopictus* 50%
- DIR: *Ae. aegypti* 60.7% vs *Ae. albopictus* 13.3%
- TR: *Ae. albopictus* 50% vs *Ae. aegypti* 21.4%
- **TE: 3.3% per *Ae. albopictus* vs 10% per *Ae. aegypti***
- **PIE: > 7 days with a blood-meal at 10(7) TCID<sub>50</sub>/mL to *Ae.***
- *aegypti* and *Ae. albopictus* from the Americas.

Chouin-Carneiro et al. (2016) Differential Susceptibilities of *Aedes aegypti* and *Aedes albopictus* from the Americas to Zika Virus. *PLoS Negl Trop Dis* 10(3): e0004543.



## Conclusioni degli AA

- *Aedes aegypti* and *Aedes albopictus* exhibit similar transmission potential for ZIKV
- *Ae. aegypti* in the French overseas territories of America disseminate ZIKV more efficiently
- Differenze significative in DIR fra le varie popolazioni di zanzare

## Conclusions/Significance

This study suggests that although susceptible to infection, *Ae. aegypti* and *Ae. albopictus* were **unexpectedly low competent vectors for ZIKV**. This may suggest that other factors such as the large naïve population for ZIKV and the high densities of human-biting mosquitoes contribute to the rapid spread of ZIKV during the current outbreak

*Chouin-Carneiro et al., 2016*

# ZIKA e tigre italiana

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- Competenza vettoriale
  - ▣ Ceppo virale: Asian genotype (patient from French Polinesia)
  - ▣ Ceppo zanzare: Scalea, Calabria (late summer of 2015) and a long-established colony of *Ae. aegypti* (Reynosa, Mexico, 1998)

Cumulative infection, dissemination, transmission and population transmission rates of *Aedes albopictus* and *Ae. aegypti* experimentally infected with Zika virus, Italy, 2016

	<i>Aedes aegypti</i>	<i>Aedes albopictus</i>
Infection rate	43%	10%
Dissemination rate	73%	29%
Transmission rate	60%	29%
Population transmission rate	26%	3%

Infection rate: number of positive bodies/number of tested fed females; dissemination rate: number of positive legs plus wings/number of positive bodies; transmission rate: number of positive saliva/number of positive bodies; population transmission rate: number of positive saliva/number of tested fed females.

Periodo di  
incubazione  
estrinseca: 11 giorni!!

Di Luca M, Severini F, Toma L, Boccolini D, Romi R, Remoli ME, Sabbatucci M, Rizzo C, Venturi G, Rezza G, Fortuna C. Experimental studies of susceptibility of Italian *Aedes albopictus* to Zika virus. *Euro Surveill.* 2016;21(18):pii=30223.

## RAPID COMMUNICATIONS

### Assessing the potential risk of Zika virus epidemics in temperate areas with established *Aedes albopictus* populations

G Guzzetta<sup>1</sup>, P Poletti<sup>1,2</sup>, F Montarsi<sup>3</sup>, F Baldacchino<sup>4</sup>, G Capelli<sup>3</sup>, A Rizzoli<sup>4</sup>, R Rosà<sup>4</sup>, S Merler<sup>1</sup>

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2. Dondena Centre for Research on Social Dynamics and Public Policy, Bocconi University, Milan, Italy
3. Istituto Zooprofilattico Sperimentale delle Venezie, Padova, Italy
4. Department of Biodiversity and Molecular Ecology, Research and Innovation Centre, Fondazione Edmund Mach, San Michele all'Adige (Trento), Italy

Correspondence: Stefano Merler (merler@fbk.eu)

#### Citation style for this article:

Guzzetta G, Poletti P, Montarsi F, Baldacchino F, Capelli G, Rizzoli A, Rosà R, Merler S. Assessing the potential risk of Zika virus epidemics in temperate areas with established *Aedes albopictus* populations. *Euro Surveill*. 2016;21(15):pii=30199. DOI: <http://dx.doi.org/10.2807/1560-7917.ES.2016.21.15.30199>

Attenzione!!! stima effettuata con le densità di  
*Ae. albopictus* della provincia di BL e TN

n 14 April 2016

Based on 2015 abundance of *Aedes albopictus* in nine northern Italian municipalities with temperate continental/oceanic climate, we estimated the basic reproductive number  $R_0$  for Zika virus (ZIKV) to be systematically below the epidemic threshold in most scenarios. Results were sensitive to the value of the probability of mosquito infection after biting a viraemic host. Therefore, further studies are required to improve models and predictions, namely evaluating vector competence and potential non-vector transmissions.

temperature satellite data with a resolution of 250 m [2] (Figure 2).

#### Mosquito population dynamics

We developed a population model representing the developmental cycle of mosquitoes by means of temperature-dependent parameters (Figure 3) and fitted it to capture data in order to estimate the density of female adult mosquitoes per hectare over time at each municipality. For two towns (Belluno and Feltre), human landing captures were carried out (seven and five sessions, respectively) where BG traps were positioned

# Solo Aedes?

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Life | Thu Mar 3, 2016 4:08pm EST

Related: HEALTH, BRAZIL

## Research indicates another common mosquito may be able to carry Zika

RIO DE JANEIRO | BY PAULO PRADA



REUTERS VIDEO

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# Altre zanzare?

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During the Biology of the Virus Vector Interaction session, researchers from IAM reviewed the evidence regarding Zika virus transmission and presented results derived from laboratory experiments

Using mosquitos artificially fed with Zika virus infected blood, they **were able to detect the virus in the salivary glands of *Culex quinquefasciatus* 7 and 15 days post-feeding, confirming a high infection rate of 100% and 67%, respectively.**

She also tested the viral load in their salivary glands and found the ***Culex* mosquitoes were reproducing it at an especially high level.**

In Brazil, *Culex quinquefasciatus* is 20 times more common than *Aedes aegypti*

Constancia Ayres alla TV brasiliana

<http://www.reuters.com/article/us-health-zika-brazil-idUSKCN0W52AW>



# *Culex quinquefasciatus*

24

- non presente in Italia
- praticamente indistinguibile morfologicamente da *Culex pipiens*
- presenza di ibridi



Molecular identification provides the first evidence of the presence of hybrids between *Cx. quinquefasciatus* and *Cx. pipiens* as well as cytoplasmic introgression of *Cx. quinquefasciatus* into *Cx. pipiens* as a result of hybridization events in **coastal regions of Southern Europe and Mediterranean region**. Together with observed hybrids between *pipiens* and *molestus* forms, these findings point to the presence of hybrids in these areas, **with consequent higher potential for disease transmission**.

# Veneto 2015

25

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<b>TOTALE</b>	<b>106.233</b>	<b>100,00</b>			

...non solo tigre.....

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*Aedes atropalpus* 1996 in Veneto

- eradicata

*Aedes koreicus* 2011 in Veneto

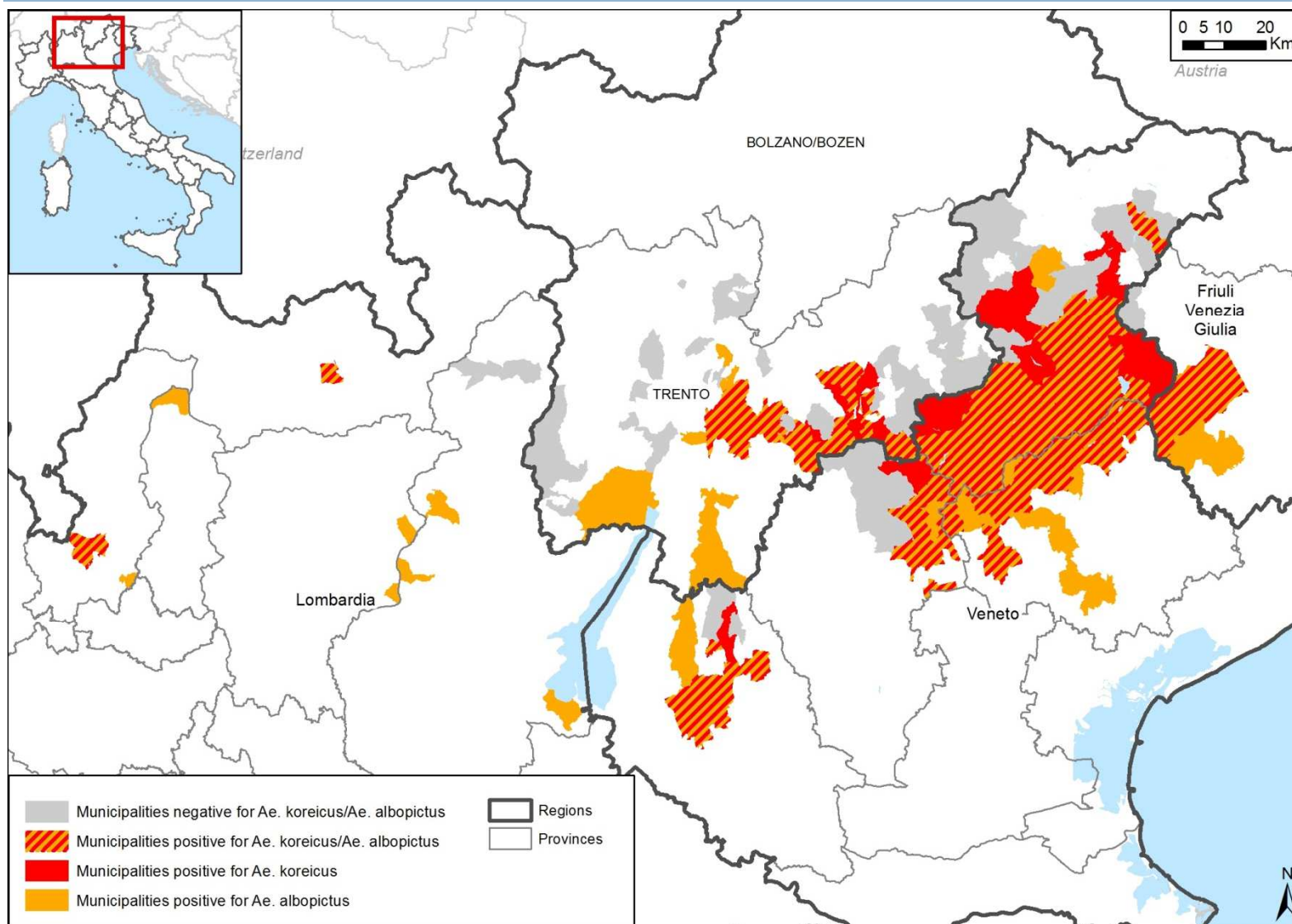
- stabilita ed in espansione

*Aedes japonicus* 2015 in FVG

- .....

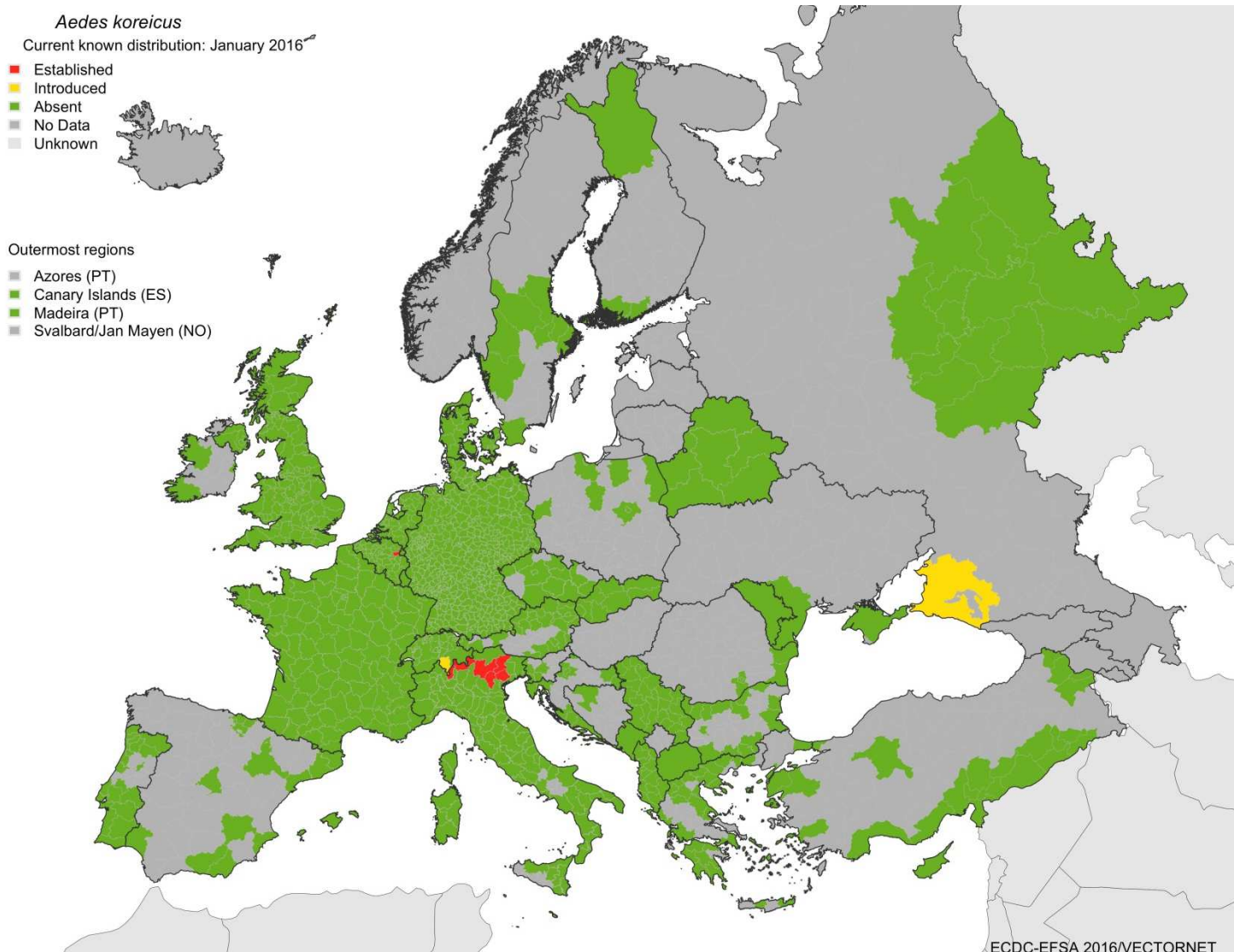
# *Aedes koreicus* – distribuzione (2015)

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# *Aedes koreicus* – distribuzione Europa

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# *Aedes koreicus* – patogeni trasmessi

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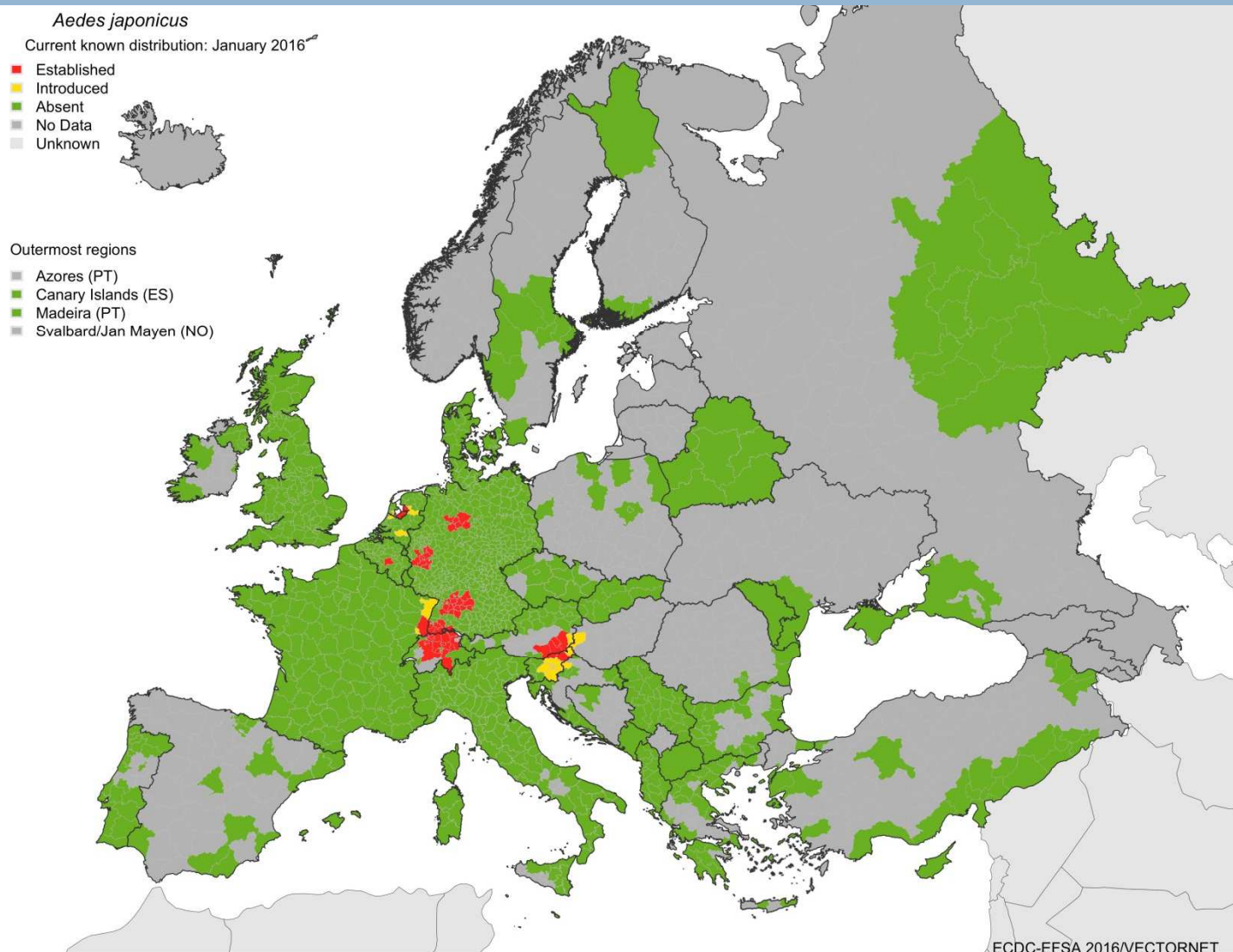
## *Aedes koreicus*

- encefalite giapponese (sperimentale + in campo)
- *Dirofilaria immitis* (sperimentale)
- per il resto completamente sconosciuta, tutto da provare



# *Aedes japonicus* - distribuzione

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# *Aedes japonicus* – patogeni trasmessi

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## *Aedes japonicus*

- EEE (sperimentale)
- La Crosse (sperimentale)
- EJ (sperimentale)
- SLE (sperimentale)
- WNV (sperimentale + in campo)



## Summary specie invasive- patogeni trasmessi

TABLE 2. OVERVIEW OF THE VECTOR STATUS OF THE EXOTIC AEDINE MOSQUITO SPECIES INTERCEPTED OR ESTABLISHED IN EUROPE

pathogen			aegypti	albopictus	atropalpus	japonicus	koreicus	triseriatus
Viruses	<i>Alphavirus</i>	Chikungunya	■	■				
		Eastern Equine encephalitis		▨		■		■
		La Crosse		▨	■	■		■
		Venezuelan Equine encephalitis		▨				■
		Western equine encephalitis						■
	<i>Flavivirus</i>	Dengue	■	■				■
		Japanese encephalitis		▨		■	▨	
		St Louis encephalitis				■		■
		West Nile		▨	▨	▨		▨
		Yellow fever	■					■
		Zika	■	■				
	<i>Bunyavirus</i>	Jamestown Canyon						▨
Nematodes	<i>Dirofilaria</i>	<i>D. immitis</i> and <i>D. repens</i>		■			■	

■	Proven vector in the field
▨	Found infected in field and laboratory competence studies having potential role as vector, but no proven vector in the field
■	Only laboratory competence studies having showed potential involvement in transmission
□	No vector or not known



# Grazie dell'attenzione

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*fatto e cucinato da Fabrizio Montarsi*