

## Aggiornamenti in tema di medicina dei viaggi e delle migrazioni: 1° Evento

# Principali arbovirosi trasmesse da culicidi in Italia: endemiche e a rischio di introduzione

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# Fattori che contribuiscono all'emergenza

- Ambientali
  - cambiamenti climatici
- Globalizzazione
  - persone, animali, cose
- Urbanizzazione
  - persone, vettori
- Mutazioni virali
- Adattamenti vettori

## BOX WO-1

### Drivers of Emergence for Vector-Borne Pathogens

- Globalization
  - Pathogen introduction
  - Vector introduction
  - Host introduction
- Land use change
  - Agriculture and urbanization
  - Community ecology and transmission dynamics
- Climate and climate change
- Evolution
  - Pathogens, vectors, hosts

SOURCE: As presented by Marm Kilpatrick on September 17, 2014.

# CHIK mutazioni

PLoS Pathog. 2011 Dec;7(12):e1002412. doi: 10.1371/journal.ppat.1002412. Epub 2011 Dec 8.

## **Sequential adaptive mutations enhance efficient vector switching by Chikungunya virus and its epidemic emergence.**

Tsetsarkin KA<sup>1</sup>, Weaver SC.

### Author information

#### **Abstract**

The adaptation of Chikungunya virus (CHIKV) to a new vector, the *Aedes albopictus* mosquito, is a major factor contributing to its ongoing re-emergence in a series of large-scale epidemics of arthritic disease in many parts of the world since 2004. Although the initial step of CHIKV adaptation to *A. albopictus* was determined to involve an A226V amino acid substitution in the E1 envelope glycoprotein that first arose in 2005, little attention has been paid to subsequent CHIKV evolution after this adaptive mutation was convergently selected in several geographic locations. To determine whether selection of second-step adaptive mutations in CHIKV or other arthropod-borne viruses occurs in nature, we tested the effect of an additional envelope glycoprotein amino acid change identified in Kerala, India in 2009. This substitution, E2-L210Q, caused a significant increase in the ability of CHIKV to develop a disseminated infection in *A. albopictus*, but had no effect on CHIKV fitness in the alternative mosquito vector, *A. aegypti*, or in vertebrate cell lines. Using infectious viruses or virus-like replicon particles expressing the E2-210Q and E2-210L residues, we determined that E2-L210Q acts primarily at the level of infection of *A. albopictus* midgut epithelial cells. In addition, we observed that the initial adaptive substitution, E1-A226V, had a significantly stronger effect on CHIKV fitness in *A. albopictus* than E2-L210Q, thus explaining the observed time differences required for selective sweeps of these mutations in nature. These results indicate that the continuous CHIKV circulation in an *A. albopictus*-human cycle since 2005 has resulted in the selection of an additional, second-step mutation that may facilitate even more efficient virus circulation and persistence in endemic areas, further increasing the risk of more severe and expanded CHIK epidemics.



.....e ancora

[Virol J.](#) 2013 Jun 2;10:174. doi: 10.1186/1743-422X-10-174.

## **Chikungunya virus with E1-A226V mutation causing two outbreaks in 2010, Guangdong, China.**

[Wu D<sup>1</sup>](#), [Zhang Y](#), [Zhouhui Q](#), [Kou J](#), [Liang W](#), [Zhang H](#), [Monagin C](#), [Zhang Q](#), [Li W](#), [Zhong H](#), [He J](#), [Li H](#), [Cai S](#), [Ke C](#), [Lin J](#).

### Author information

#### **Abstract**

**BACKGROUND:** CHIKV is a mosquito-borne emerging pathogen that has a major health impact in humans in tropical zones around the globe. A new variant of the virus, E1-A226V caused a large outbreak in the Indian Ocean islands and India from 2004-2007. CHIKV outbreak was initially reported in Dongguan region of Guangdong in 2010 in China, another smaller CHIKV outbreak was found in Yangjiang region of Guangdong two weeks later. The viral agent causing the two outbreaks was inferred to be the new E1-A226V variant and Yangjiang CHIKV might be introduced from Dongguan. To confirm the hypothesis and determine the origin of CHIKV causing the outbreaks, we described Yangjiang outbreak in this study, and the molecular characterization of CHIKV from Yangjiang and Dongguan outbreaks were analyzed.

**RESULTS:** 27 clinical cases of CHIK fever were reported in outbreak in Yangjiang region. Sera sample from 12 clinical cases were collected from the outbreak, and nucleic acid and antibody tests for CHIKV were performed using Real-time RT-PCR and indirect immunofluorescence. Positive samples of Real-time RT-PCR were subjected to viral isolation. The results showed 3/12 samples positive for Real-time RT-PCR. 7/12 and 4/12 samples were positive for IgM and IgG against CHIKV respectively, two virus strains were isolated. Four viral genomes from Dongguan and Yangjiang were sequenced, characterized and phylogenetically analyzed. Phylogenetic analysis revealed that the four sequenced viruses had the closest relationship (99.4~99.6% identity) with the Singapore 2008 isolate belonging to the Indian ocean clade. A common mutation at the site of the E1-A226V was observed among four viruses. Four and three aa substitutions were detected in the CHIKV sequence from the Dongguan and Yangjiang outbreak strains respectively.

**CONCLUSION:** CHIKV with an E1-A226V mutation that originated from Southeast Asia isolates caused two outbreaks in China in 2010, and originated from two different infectious sources.

# .....ruolo della tigre appena confermato

[PLoS Negl Trop Dis](#). 2018 Apr 19;12(4):e0006435. doi: 10.1371/journal.pntd.0006435. eCollection 2018 Apr.

## **Vector competence of Italian *Aedes albopictus* populations for the chikungunya virus (E1-226V).**

[Severini F](#)<sup>1</sup>, [Boccolini D](#)<sup>1</sup>, [Fortuna C](#)<sup>2</sup>, [Di Luca M](#)<sup>1</sup>, [Toma L](#)<sup>1</sup>, [Amendola A](#)<sup>2</sup>, [Benedetti E](#)<sup>2</sup>, [Minelli G](#)<sup>3</sup>, [Romi R](#)<sup>1</sup>, [Venturi G](#)<sup>2</sup>, [Rezza G](#)<sup>2</sup>, [Remoli ME](#)<sup>2</sup>.

### Author information

#### **Abstract**

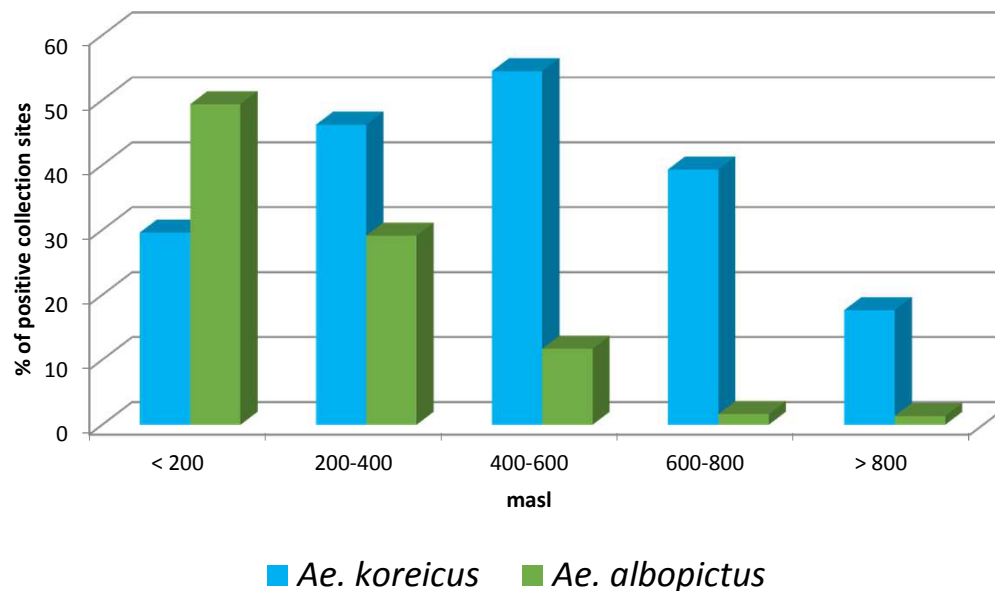
**BACKGROUND:** Chikungunya virus (CHIKV) is an emerging arbovirus, belonging to the Togaviridae family, Alphavirus genus, transmitted by *Aedes* spp. mosquitoes. Since 2007, two different CHIKV strains (E1-226A and E1-226V) have been responsible for outbreaks in European countries, including Italy, sustained by *Ae. albopictus* mosquitoes.

**FINDINGS:** In this study, we assessed the susceptibility to the CHIKV E1-226V, strain responsible for the Italian 2007 outbreak, of eight *Ae. albopictus* populations collected in Northern, Central, Southern, and Island Italy, by experimental infections. Vector competence was evaluated by estimating infection, dissemination, and transmission rates (IR, DR, TR), through detection of the virus in the bodies, legs plus wings, and saliva, respectively. Additionally, vertical transmission was evaluated by the detection of the virus in the offspring. The results of our study demonstrated that the Italian populations of *Ae. albopictus* tested were susceptible to CHIKV infection, and can disseminate the virus outside the midgut barrier with high values of IR and DR. Viral infectious RNA was detected in the saliva of three populations from Central, Southern, and Island Italy, also tested for TR and population transmission rate (PTR) values. No progeny of the first and second gonotrophic cycle were positive for CHIKV.

**CONCLUSIONS:** This study strongly confirms the role of *Ae. albopictus* as a potential CHIKV vector in Italy. This may represent a threat, especially considering both the high density of this species, which is widespread throughout the country, and the increasing number of cases of imported arboviruses.

# L'adattamento della zanzara tigre

- esofila
- diurna
- tropicale
- anche endofila
- moderatamente notturna
- sempre più tollerante al «fresco»



# Patogeni trasmessi presenti in Italia

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## *Culex pipiens*

- WNV
- USUV



- protozoi (*malaria volatili*)
- elminti (*Dirofilaria immitis* e *D. repens*)

## *Aedes albopictus*

- WNV?
- USUV?



- protozoi (*malaria volatili*)?
- elminti (*Dirofilaria immitis* e *D. repens*)



## Transmission of vector-borne diseases (VBD)

**Table A:** Important mosquito-borne pathogens that cause disease in humans

Pathogen	Disease	Case fatality rate (%)	Important vectors to human
<b>Togaviridae arboviruses</b>			
Chikungunya	Febrile to severe illness	Very low	<i>Ae. aegypti</i> , <i>Ae. albopictus</i>
Eastern equine encephalitis	Encephalitis	50–75	<i>Coquillettidia perturbans</i> , <i>Ae. vexans</i>
Ross River	Febrile	0	<i>Culex annulirostris</i>
Sindbis	Febrile	0	<i>Ae. cinereus</i> , <i>Cx. pipiens</i>
Venezuelan equine encephalitis	Encephalitis	0.1–20	<i>Cx. pipiens</i>
Western equine encephalitis	Encephalitis	5–10	<i>Cx. tarsalis</i>
<b>Flaviviridae arboviruses</b>			
Dengue 1–4	Febrile to haemorrhagic	3–12	<i>Ae. aegypti</i> , <i>Ae. albopictus</i>
West Nile	Febrile to encephalitis	3–15	<i>Culex</i> spp. ( <i>Cx. pipiens</i> , <i>Cx. modestus</i> )
Japanese encephalitis	Encephalitis	30–40	<i>Cx. tritaeniorhynchus</i>
Murray Valley encephalitis	Encephalitis	20–70	<i>Cx. annulirostris</i>
St. Louis encephalitis	Encephalitis	4–20	<i>Cx. pipiens</i> , <i>Cx. nigripalpus</i>
Yellow fever	Haemorrhagic	5–20	<i>Ae. aegypti</i> , <i>Ae. africanus</i> , <i>Haemagogus</i> spp.
<b>Bunyaviridae arboviruses</b>			
La Crosse encephalitis	Encephalitis	<1	<i>Ae. triseriatus</i>
Rift Valley fever	Febrile	<1	<i>Aedes</i> spp., <i>Cx. pipiens</i>
<b>Plasmodium protozoa</b>			
Malaria	Febrile to renal failure	1–7 (< 5 years)	<i>Anopheles</i> spp.

Source: Beaty & Marquardt 1996; Schaffner 2003



# La lista.....

Virus genus	Virus name
<i>Alphavirus</i>	Babanki (AF), <b>Barmah Forest</b> (AU), <b>Chikungunya</b> (AF, AS, AM, PPH, and HV), <b>Eastern equine encephalitis</b> (AM), Everglades (AM), <b>Igbo Ora</b> (AF), <b>Mayaro</b> (AM, PPH, and HV), <b>O'nyon-nyong</b> (AF, PPH, and HV), <b>Ross River</b> (AU), <b>Semliki Forest</b> (AF, AS, and PPH), <b>Sindbis</b> (EU, AF, and AU), Tonate (AM), <b>Venezuelan equine encephalomyelitis</b> (AM and HV), <b>Western equine encephalitis</b> (AM)
<i>Flavivirus</i>	Banji (AF), Bussuquara (AM and PPH), Cacipacore (AM), <b>Dengue</b> (4 serotypes; AS, AM, AF, PPH, and HV), Edge hill (AU), Ilheus (AM), <b>Japanese encephalitis</b> (AS), Kedougou (AF), Kokobera (AU), Koutango (AF), <b>Murray Valley encephalitis</b> (Alfuy; AU), <b>Rocio encephalitis</b> (AM), Sepik (AU), Sponsweni (AF), St Louis encephalitis (AM), Usutu (EU and AF), Wesselsbron (AF), <b>West Nile fever (Kunjin)</b> (AF, AS, AM, AU, and EU), <b>Yellow fever</b> (AF, AM, PPH, and HV), <b>Zika</b> (AF, AS, AU, PPH, and HV)
<i>Orthobunyavirus</i>	Bunyawera* (Bunyamwera [AF], Germiston [AF], Guaroa [AM], Batai [Calovo; EU, AF, and AS], Ilesha [AF], Tensaw [AM], Maguari [AM], Shokwe [AF], Fort Sherman [AM], Ngari [AF]), Bwaba* (Bwamba [AF and PPH], Pongola [AF]), California encephalitis* (Jamestown Canyon [AM], Inkoo [EU], <b>La Crosse*</b> [AM], <b>Tahyna</b> [EU, AS, and AF], Snowshoe hare encephalitis [EU and AM], Trivittatus [AM]), Caraparu* (Apeu [AM], Caraparu [AM and PPH], Ossa [AM]), Catu* (AM and PPH), Guama* (AM and PPH), Madrid* (AM), Marituba* (Marituba [AM and PPH], Murutucu [AM], Nepuyo [AM], Restan [AM]), Nyando* (AF), Oriboca* (Oriboca [AM and PPH], Itaquí [AM]), Shuni* (AM), Tacaiuma* (AM and PPH), ungrouped (Gan Gan [AU], Tataguine [AF], Tanga [AF], Bangui [AF]), Wyeomyia* (AM)
<i>Phlebovirus</i>	<b>Rift Valley fever</b> (AF), Arumowot (AF)
<i>Orbivirus</i>	Lebombo (AF), Orungo (AF and PPH)
<i>Seadornavirus</i>	Banna (AS)
<i>Vesiculovirus</i>	Piry (AM)

# Altri vettori

Calzolari M, 2015

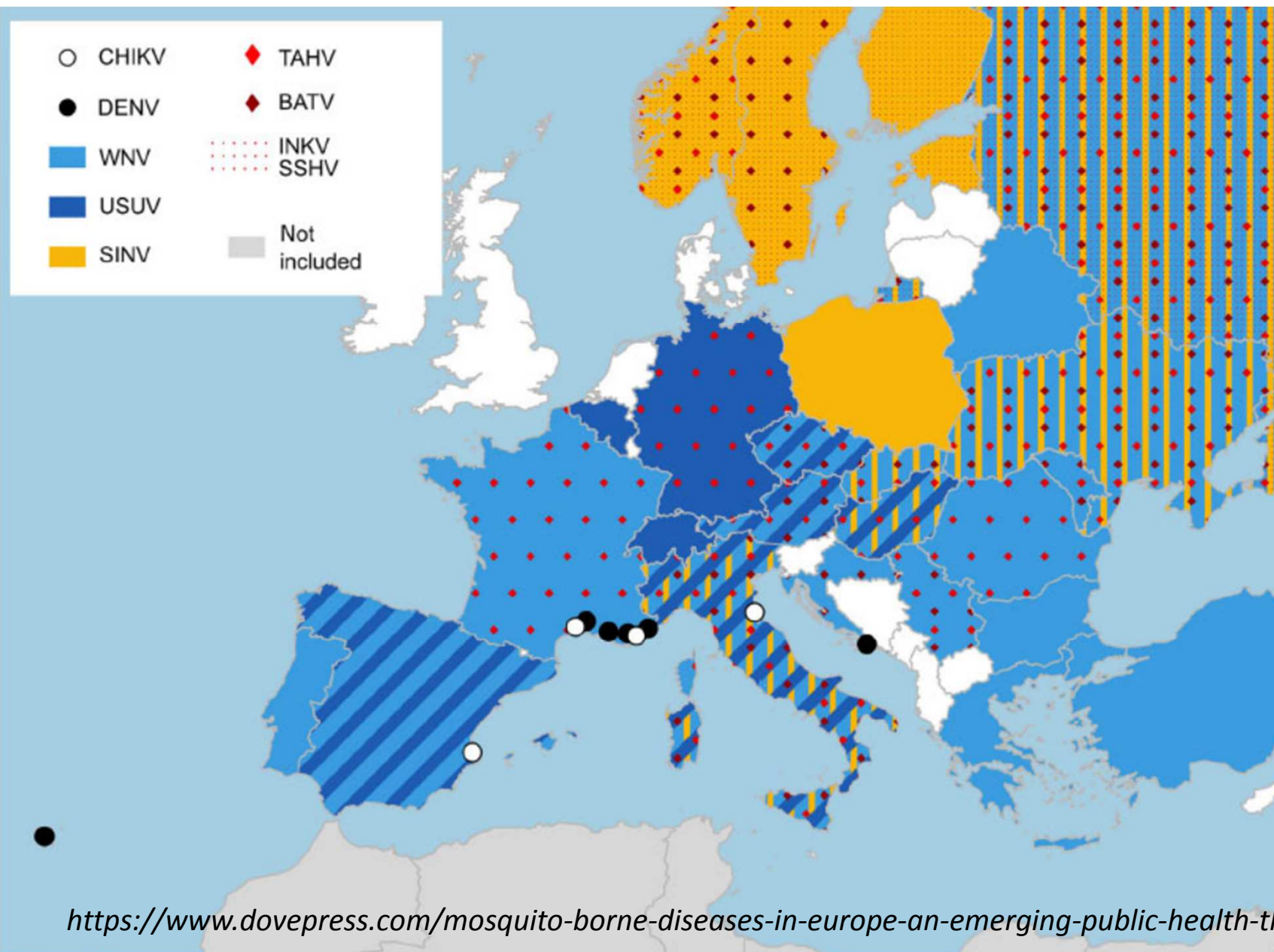
Species	Distribution	Pathogens transmitted in Europe
<i>Aedes caspius</i>	All of Europe	Tahyna virus and <i>Dirofilaria repens</i>
<i>Aedes vexans</i>	All of Europe	Tahyna virus
<i>Aedes albopictus</i>	Signaled in 1991 in Italy and now established in Southern Europe	Dengue virus and Chikungunya virus
<i>Aedes communis</i>	Eastern Europe (rare in Western Europe)	Inkoo virus and Sindbis virus
<i>Culiseta morsitans</i>	All of Europe	Sindbis virus
<i>Culex pipiens</i> complex		
<i>Cx. pipiens</i>	All of Europe and more spread in Southern Europe	West Nile virus and <i>Dirofilaria repens</i>
<i>Cx. torrentium</i>	All of Europe and more spread in Northern-Central Europe	Sindbis virus
<i>Anopheles maculipennis</i> complex <sup>a</sup>		
<i>An. labranchiae</i>	Southeastern Europe	<i>Plasmodium</i> spp.
<i>An. atroparvus</i>	Mainly Continental Europe	
<i>An. sacharovi</i>	Southern Europe (Mediterranean)	
<i>An. maculipennis</i> s.l.		Batai virus

# L'impatto a livello mondiale

	<b>DALYs 2013</b>	<b>95% confidence interval</b>
Malaria	65493.1	53064.9–79960.7
Lymphatic filariasis	2022.1	1096.3–3294.4
Dengue	1142.7	727.6–1978.2
Yellow fever	30.7	25.3–37.1
Other neglected tropical diseases* (including other mosquito-borne viral fevers)	3132.7	2328.1–4208.7
Encephalitis** (including mosquito- borne viral encephalitis)	4804.2	4022.4–5926.9

*Calzolari M, 2015*





<https://www.dovepress.com/mosquito-borne-diseases-in-europe-an-emerging-public-health-threat-peer-reviewed-article-RIP>



## Mosquito-borne arboviruses of African origin: review of key viruses and vectors

[Leo Braack](#)<sup>1</sup>, [A. Paulo Gouveia de Almeida](#)<sup>2,3</sup>, [Anthony J. Cornel](#)<sup>1,4</sup>, [Robert Swanepoel](#)<sup>5</sup> and [Christiaan de Jager](#)<sup>6</sup>

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### Abstract

Go to: 

Key aspects of 36 mosquito-borne arboviruses indigenous to Africa are summarized, including lesser or poorly-known viruses which, like Zika, may have the potential to escape current sylvatic cycling to achieve greater geographical distribution and medical importance. Major vectors are indicated as well as reservoir hosts, where known. A series of current and future risk factors is addressed. It is apparent that Africa has been the source of most of the major mosquito-borne viruses of medical importance that currently constitute serious global public health threats, but that there are several other viruses with potential for international challenge. The conclusion reached is that increased human population growth in decades ahead coupled with increased international travel and trade is likely to sustain and increase the threat of further geographical spread of current and new arboviral disease.

# A rischio introduzione

Culex  
pipiens



- Sindbis
- RVF(?)
- SLE (?)

Aedes  
albopictus



- DENV
- CHIK
- ZIKA
- e almeno  
altri 20

# RFV

- In a major study to determine vectors of RVFV in Kenya, some 164,626 identified mosquitoes (of 297,000 collected) were sorted in pools of which the following species tested positive, in descending order of frequency:
  - *Aedes mcintoshi/circumluteolus* (26 pools),
  - *Aedes ochraceus* (23 pools),
  - *Mansonia uniformis* (15 pools);
  - *Culex poicilipes*, *Culex bitaeniorhynchus* (3 pools each);
  - *Anopheles squamosus*, *Mansonia africana* (2 pools each);
  - *Culex quinquefasciatus*, *Culex univittatus*, *Aedes pembaensis*

# *Aedes koreicus* – patogeni trasmessi

## *Aedes koreicus*

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





# Transmission is possible....

[Pathog Glob Health](#). 2018 May 8:1-8. doi: 10.1080/20477724.2018.1464780. [Epub ahead of print]

## **The new European invader *Aedes (Finlaya) koreicus*: a potential vector of chikungunya virus.**

[Ciocchetta S](#)<sup>1,2</sup>, [Prow NA](#)<sup>1</sup>, [Darbro JM](#)<sup>1</sup>, [Frentiu FD](#)<sup>2</sup>, [Savino S](#)<sup>3</sup>, [Montarsi F](#)<sup>4</sup>, [Capelli G](#)<sup>4</sup>, [Aaskov JG](#)<sup>2</sup>, [Devine GJ](#)<sup>1</sup>.

### Author information

### **Abstract**

Arthropod-borne disease outbreaks, facilitated by the introduction of exotic mosquitoes, pose a significant public health threat. Recent chikungunya virus (CHIKV) epidemics in Europe highlight the importance of understanding the vector potential of invading mosquitoes. In this paper we explore the potential of *Aedes koreicus*, a mosquito new to Europe, to transmit CHIKV. Mosquitoes were challenged with CHIKV and maintained at two temperatures: 23 °C and a fluctuating temperature. Total CHIKV infection rates at 3, 10 and 14 days post-feeding were low for both temperature treatments (13.8% at 23 °C; 6.2% at fluctuating T). A low percentage (6.1%, n = 65) of mosquitoes maintained at a constant 23 °C showed dissemination of the virus to the wings and legs. Infection of mosquito saliva, with live virus, occurred in 2 mosquitoes. No dissemination was noted under the fluctuating temperature regime. Based on these results we conclude that CHIKV transmission by this species is possible.

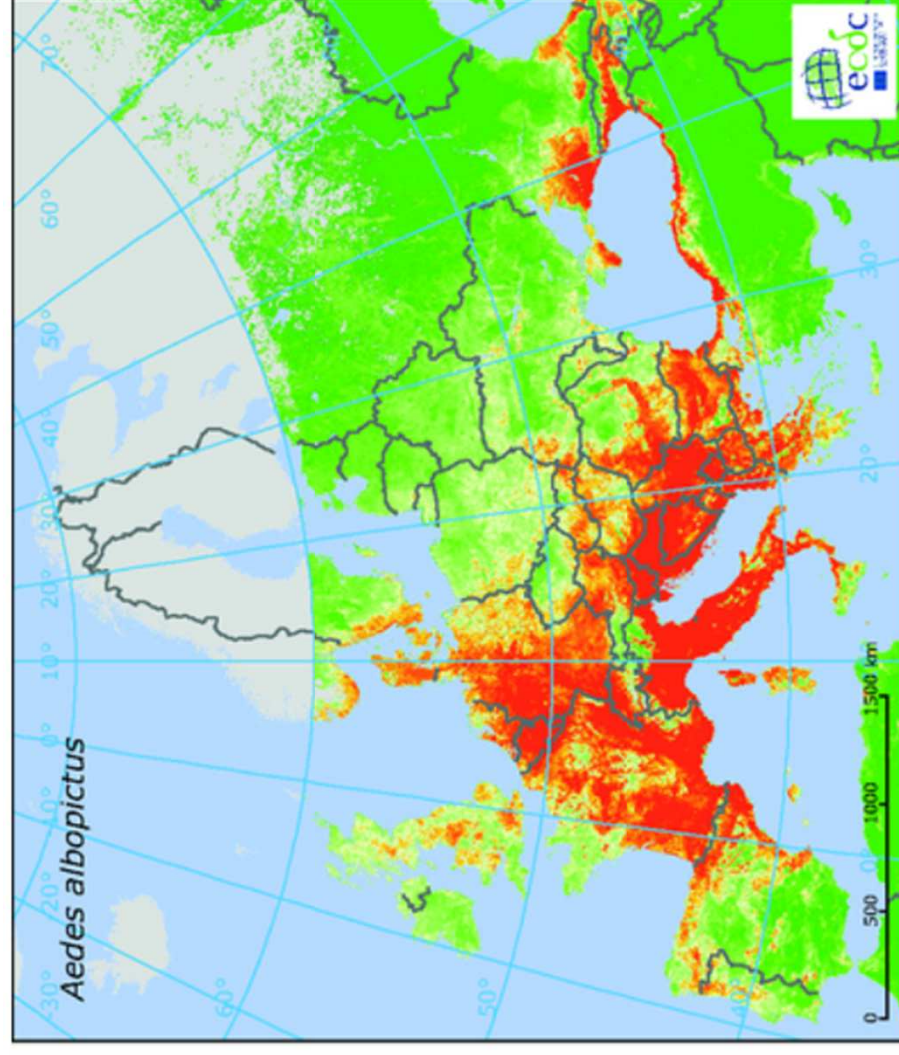
# *Aedes japonicus* – patogeni trasmessi

## *Aedes japonicus*

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



Photo by Ary Farajollahi, Bugwood.org



### Climatic suitability for *Aedes aegypti* and *Aedes albopictus* (Asian tiger mosquito) in Europe

Suitability (%)





## Summary specie invasive- patogeni trasmessi

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

pathogen			<i>aegypti</i>	<i>albopictus</i>	<i>atropalpus</i>	<i>japonicus</i>	<i>koreicus</i>	<i>triseriatus</i>
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	■					■
	<i>Bunyavirus</i>	Zika	■	■				
		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

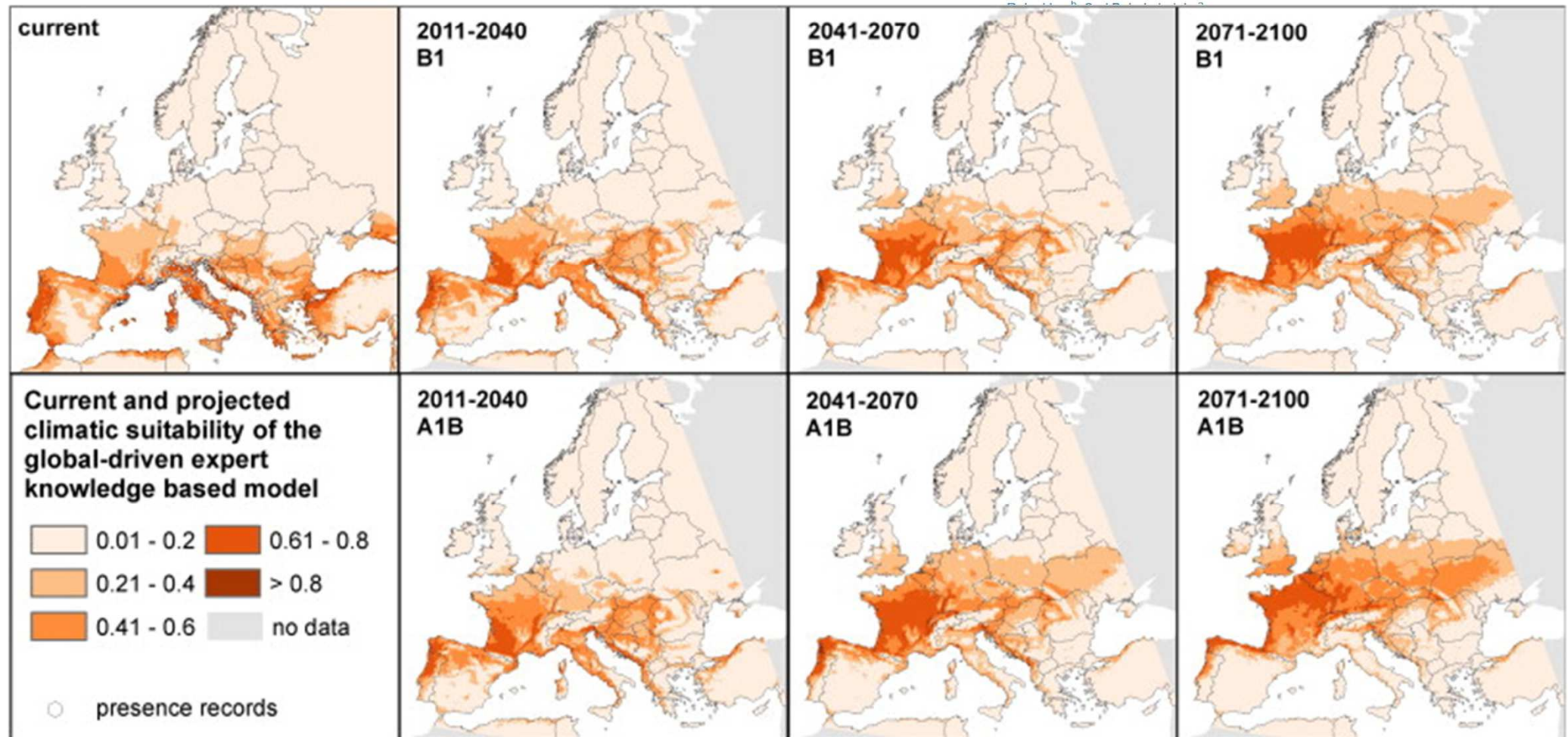
Medlock et al., 2012



.....basta aspettare

Projection of climatic suitability for *Aedes albopictus* Skuse (Culicidae) in Europe under climate change conditions

Dominik Fischer <sup>a,\*,</sup> Stephanie Margarete Thomas <sup>a,</sup> Franziska Niemitz <sup>a,</sup> Björn



# Usutu virus prima e dopo 2017

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- Patogeno per i volatili
  - Non considerato una zoonosi (potenziale)
  - Pochi casi umani segnalati in persone non immunocompetenti o con altre patologie
  - Tuttavia risposta anticorpale nell'uomo
    - 1,1% in ER 2009 (Gaibani et al., 2012)
    - 0,23% in ER 2010-2011 (Pierro et al, 2013)
- Patogeno per i volatili
  - considerato una zoonosi (anche se non tutti sono d'accordo)
  - un caso di USUV in un donatore sano in Germania (Cadar et al., 2017)
  - liquor cefalo-rachidiano di numerosi casi neuro-invasivi retrospettivi in Emilia Romagna (Grottola et al., 2017)

# USUV



Saiz & Blázquez, 2017

## Il risk assessment della massaia....

	DENV	CHIK	ZIKA	YFV
epidemia nel mondo	++	+++	+	+
asintomatici in grado di trasmettere al vettore	++	+++	+	+
trasmesso da zanzara locale	+	+	-/+	-/+
grado antropofilia	+++	+++	+++	+++
competenza zanzara locale	+	+++	-/+	
trasmissione verticale zanzara	+	+	-/+	+
esiste un vaccino	no	no	no	si
tot	10	14	7	-



# Grazie per l'attenzione

- Regione Veneto
- Regione FVG
- Ministero della Salute
  
- Lo staff del laboratorio di Parassitologia