



HAL
open science

Chikungunya Virus–Vector Interactions

Lark L Coffey, Anna-Bella Failloux, Scott Weaver

► **To cite this version:**

Lark L Coffey, Anna-Bella Failloux, Scott Weaver. Chikungunya Virus–Vector Interactions. *Viruses*, 2014, 6 (11), pp.4628 - 4663. 10.3390/v6114628 . pasteur-01680225

HAL Id: pasteur-01680225

<https://pasteur.hal.science/pasteur-01680225>

Submitted on 10 Jan 2018

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



Distributed under a Creative Commons Attribution 4.0 International License

Review

Chikungunya Virus–Vector Interactions

Lark L. Coffey ^{1,2}, Anna-Bella Failloux ³ and Scott C. Weaver ^{4,*}

¹ Center for Vectorborne Diseases, School of Veterinary Medicine, University of California, Davis, CA 95616, USA; E-Mail: lcoffey@ucdavis.edu

² Department of Pathology, Microbiology and Immunology, School of Veterinary Medicine, University of California, Davis, CA 95616, USA

³ Department of Virology, Arboviruses and Insect Vectors, Institut Pasteur, 25-28 rue du Dr. Roux, 75724 Paris cedex 15, France; E-Mail: anna-bella.failloux@pasteur.fr

⁴ Institute for Human Infections and Immunity, Center for Tropical Diseases and Department of Pathology, University of Texas Medical Branch, Galveston, TX 77555, USA

* Author to whom correspondence should be addressed; E-Mail: sweaver@utmb.edu; Tel.: +1-409-266-6500; Fax: +1-409-266-6810.

External Editor: Rollie Clem

Received: 3 September 2014; in revised form: 10 November 2014 / Accepted: 10 November 2014 / Published: 24 November 2014

Abstract: Chikungunya virus (CHIKV) is a mosquito-borne alphavirus that causes chikungunya fever, a severe, debilitating disease that often produces chronic arthralgia. Since 2004, CHIKV has emerged in Africa, Indian Ocean islands, Asia, Europe, and the Americas, causing millions of human infections. Central to understanding CHIKV emergence is knowledge of the natural ecology of transmission and vector infection dynamics. This review presents current understanding of CHIKV infection dynamics in mosquito vectors and its relationship to human disease emergence. The following topics are reviewed: CHIKV infection and vector life history traits including transmission cycles, genetic origins, distribution, emergence and spread, dispersal, vector competence, vector immunity and microbial interactions, and co-infection by CHIKV and other arboviruses. The genetics of vector susceptibility and host range changes, population heterogeneity and selection for the fittest viral genomes, dual host cycling and its impact on CHIKV adaptation, viral bottlenecks and intrahost diversity, and adaptive constraints on CHIKV evolution are also discussed. The potential for CHIKV re-emergence and expansion into new areas and prospects for prevention via vector control are also briefly reviewed.

Keywords: chikungunya; mosquito; vector; transmission; adaptation

1. Introduction

Emerging and re-emerging arthropod-borne viruses (arboviruses) represent a significant threat to human and veterinary health worldwide. Chikungunya virus (CHIKV), a mosquito-borne alphavirus that causes chikungunya fever (CHIK), a severe, debilitating and often chronic arthralgia, is a prime example; since it was first isolated in 1952, the virus has been detected as the etiologic agent of sporadic epidemics in Africa and Asia and, since 2004, has expanded its geographic range to circulate on Indian Ocean islands, and in Italy, France, and the Americas. CHIKV has also re-emerged in Southeast Asia since 2006, causing an estimated 1.3 million human cases [1]. CHIKV cycles in urban settings between humans and two mosquito species found in the U.S., suggesting a potential for endemic establishment there. As evidence of this, 11 autochthonous cases of CHIK were detected in south Florida as of November 2014 [2,3]. Emergence of arboviruses like CHIKV underscores the interconnectedness of humans with their environments, and highlights our vulnerabilities to new disease threats posed by spreading viruses. Understanding how arboviruses like CHIKV emerge is critical to predict and prevent or mitigate human disease. Central to understanding emergence is knowledge of the natural ecology of CHIKV transmission and the dynamics of vector infections. Here we discuss current knowledge of CHIKV infection dynamics in mosquito vectors and its relationship to human disease emergence.

2. Chikungunya Infection and Vector Life History Traits

2.1. Chikungunya Virus Transmission Cycles and Genetic Origins

Chikungunya virus is endemic in countries of Sub-Saharan Africa, India and Southeast Asia. The virus circulates in an enzootic cycle in Africa between forest-dwelling mosquitoes and non-human primates [4]. Phylogenetic studies reveal the existence of two major enzootic CHIKV lineages in Africa: Western, and East/Central/South African (ECSA) [5]. In Asia, where the first outbreak was reported in 1958 in Thailand, CHIKV has historically been maintained in an urban cycle transmitted to humans by the mosquito *Aedes (Stegomyia) aegypti* and, to a lesser extent, *Aedes (Stegomyia) albopictus* [6].

2.2. Chikungunya Distribution, Emergence and Spread

In 2004, CHIKV belonging to the ECSA lineage emerged from Lamu and Mombasa in coastal Kenya [7] and spread to Comoros and later, to other islands of the Indian Ocean including La Réunion (Figure 1). There, the predominant vector *A. albopictus* transmitted preferentially a CHIKV variant with a single amino acid change from an alanine (A) to valine (V) at E1 envelope glycoprotein amino acid 226 of the ECSA Indian Ocean lineage (IOL) genotype [8]. The E1-226V variant was more efficiently transmitted by *A. albopictus* [9,10], with roughly 40-fold more efficient initial infection of midgut epithelial cells [9–11]. The selection of the E1-226V variant occurs at the initial infection of the midgut of *A. albopictus*, leading to a higher viral dissemination and transmission of the IOL genotype by this mosquito [12]. A series of four additional adaptive mutations in the E2 gene have also been incriminated

more recently in enhancing transmission by *A. albopictus* [6,9,13]. During 2005–2006, the virus spread to neighboring Indian Ocean islands including Mayotte, Mauritius and Madagascar, where CHIKV E1-A226V was mainly transmitted by *A. albopictus* [12,14–16]. Subsequently, the CHIKV IOL was introduced to India [17,18] and the surrounding islands, Sri Lanka [19] and the Maldives. In Africa, the CHIKV E1-226V variant was also implicated outbreaks in Cameroon [20], Gabon [21,22] and Congo [23]. This variant also caused the first European CHIKV outbreak in Italy in 2007 [24]. Since 2008, IOL CHIKV strains were also imported into Southeast Asia: Malaysia [25], Singapore [26], Thailand [27], China [28], Cambodia [29] and Bhutan [30]. Remarkably, the E1-226V variant was found preferentially in rural areas where *A. albopictus* was more abundant than *A. aegypti*, and presumably was the primary vector [31,32]. In September 2010, autochthonous cases of CHIKV were reported in southeast of France [33,34], again with *A. albopictus* as the vector [34–36]. In Southeast France, this species appears to behave differently compared to its tropical counterpart, as it efficiently transmits the E1-226A IOL variant detected in local circulation [34,36]. *Aedes albopictus* has been found in 18 French departments [34,35,37] as well as 19 other countries in Europe [38,39].

Prior to December 2013, CHIKV transmission was not documented in the Americas, despite numerous introductions and the presence of conditions that are apparently suitable for its establishment [6]. In October 2013, two laboratory-confirmed, autochthonous CHIKV cases were detected in the French territory of Saint Martin Island, in the Caribbean Sea. Surprisingly, the CHIKV strain isolated belonged to the Asian genotype [40] rather than the IOL that emerged in 2004 in the Indian Ocean Basin and Asia [6]. This St. Martin strain was phylogenetically close to CHIKV identified in Indonesia in 2007, China in 2012 and Philippines in 2013 [40], but more distant from the Asian genotype that circulated in New Caledonia [41]. The only vector implicated in St. Martin, where *A. albopictus* has not been established, was *A. aegypti*. Very rapidly, an epidemic was established in the island and subsequently, CHIKV progressively spread throughout most of the Caribbean, and into Central and South America where human populations are mostly naïve to CHIKV [42].

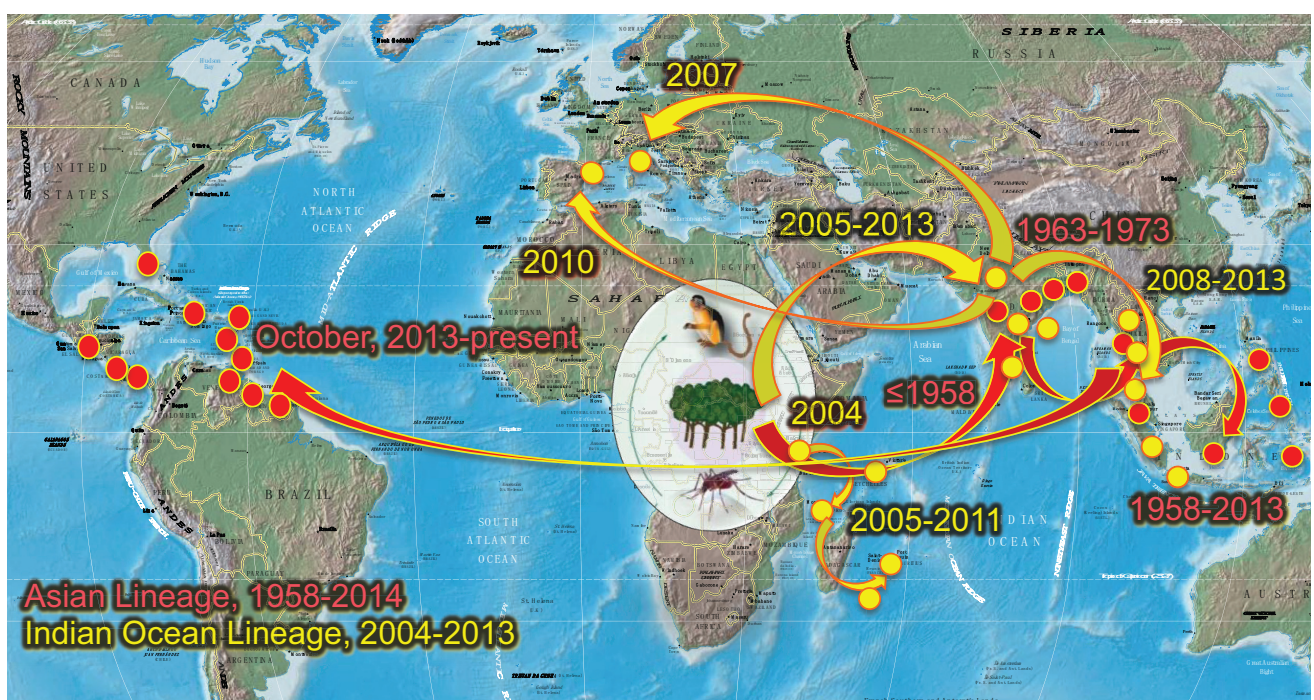


Figure 1. Geographic distribution and spread of Chikungunya virus (CHIKV) and its two urban vectors, *A. aegypti* and *A. albopictus*. Modified from reference [42], with permission.

American populations of *A. aegypti* and *A. albopictus* are susceptible to both ECSA/IOL and Asian genotypes of CHIKV with higher susceptibility observed for *A. aegypti* and the Asian CHIKV genotype, or *A. albopictus* and the ECSA/IOL genotype [43]. As of November 2014, 11 locally acquired cases of CHIKV have been documented in Florida, USA [44]. These recent findings and the history of CHIKV movement suggest that it will continue to spread throughout the Americas and other tropical and subtropical regions of the world wherever mosquito vectors occur.

3. Vectors

3.1. Chikungunya Vector Distribution

CHIKV is an African virus that circulates enzootically in sylvatic cycle between arboreal, canopy-dwelling mosquitoes and non-human primates. Enzootic strains from the West African and ECSA lineages have been isolated from diverse mosquito species in Senegal, Ivory Coast, Central African Republic, Uganda and South Africa [4,45–47]. In Senegal, CHIKV has been detected in vectors of yellow fever virus: *Aedes* (*Diceromyia*) *furcifer*, *A. (Diceromyia) taylori*, *A. (Stegomyia) luteocephalus*, *A. (Stegomyia) africanus* and *A. (Stegomyia) neoafricanus* [47]. In South Africa, *A. (Diceromyia) cordellieri*, was also involved in CHIKV transmission [48]. The urbanization of CHIKV, with epidemics occurring in peridomestic settings following the emergence of enzootic strains, coincides with the involvement of anthropophilic mosquitoes: *A. (Stegomyia) aegypti* (L.) and *A. (Stegomyia) albopictus* (Skuse), favoring inter-human transmission. *Aedes aegypti*, first described by Linné in 1862, originated in African forests and is today present in most tropical countries [49]. In Africa, *A. aegypti* is present in two genetic forms: (i) the dark and sylvatic *A. aegypti formosus*, found in forested habitats and using treeholes as larval development sites; and (ii) the pale and domestic *A. aegypti aegypti*, which is widespread in the tropics and subtropics and uses artificial larval habitats mainly in urban environments [50–52]. *Aedes aegypti aegypti* originated from the forest-dwelling *formosus* form, which may have spread from tropical African forests to North Africa where it probably became domesticated under pressure to use artificial water storage containers as larval habitats [53]. These mosquitoes progressively differentiated into domesticated populations known as *A. aegypti aegypti*. Human trading activities later introduced this subspecies globally throughout the most of the tropics and subtropics: the New World via the African slave trade from the 15th to 19th centuries, Asia in the 18th and 19th centuries, and the Pacific islands with troop movements during World War II.

Aedes aegypti can exist sympatrically with *A. albopictus* and also often shares larval habitats [16,54–56]. *Aedes albopictus*, originally described by Skuse in Calcutta, India in 1894 originated in forests of Southeast Asia [57], but is now commonly found in peri-urban, rural and forested areas on five continents [58]. *Aedes albopictus* has no particular ecological specialization, colonizing both temperate and tropical regions [59]. Two types of populations are described [60]: (1) temperate populations imported to the U.S. from Japan [61,62] and then from the U.S. to Europe [63,64], where they are now established in 20 European countries [58]; these temperate populations are characterized by diapausing, cold-resistant eggs [65]; and (2) tropical populations [60]. *Aedes albopictus* is a competent vector for at

least 26 arboviruses [66] and is implicated occasionally in DENV (e.g., on the Seychelles islands [67]; and more frequently in CHIKV transmission (e.g., on La Réunion Island [68]; see Table 1 of this review as well). Since the 2007 outbreak of CHIKV in Italy [24], Europe is considered vulnerable for transmission of several “tropical” arboviruses, particularly in regions where *A. albopictus* is present [34,69,70].

3.2. Vector Dispersal and Genetics

Aedes aegypti and *A. albopictus* have both spread beyond their native ranges via commercial trade and desiccation-resistant eggs [71]. *Aedes aegypti* largely replaced *A. albopictus* in Southeast Asian cities in the first half of the 20th century [65] while the introduction of *A. albopictus* into the Americas during the 1980s was associated with a decline in the abundance of *A. aegypti* in some regions such as occurred in the Americas in the 1980s [59,72,73] and is now ongoing in Central Africa [74,75] and on islands of the Indian Ocean region [16,76]. Long distance spread of CHIKV urban vectors beyond their natural flight ranges, typically a few hundred meters to a few kilometres [77], is usually achieved through transportation of immature stages (*i.e.*, larvae and eggs). From the 15th century onwards, successive waves of invasion by *A. aegypti* and, more recently, *A. albopictus*, have been facilitated by commercial transport.

Such mosquito invasions can be traced using molecular markers, which can now be developed from genome sequences. The *A. aegypti* genome sequence is complete [78] and genome annotations of *A. albopictus* are expected soon [79]. To assess mosquito phylogenetics, molecular markers used to define mosquito invasions have mainly been microsatellites (reviewed in [80]) and mtDNA [74,76,81–84]. Scenarios of invasions are more easily defined in island systems where mosquito populations have been geographically isolated with gene flow measurable through human displacements [85]. The involvement of human activities in reshuffling *A. albopictus* distributions has been demonstrated [86]. In Madagascar, *A. albopictus* dominant in the eastern coast and highland areas [87] are genetically distant from populations from South America and Southeast Asia [76]. This species continues to extend its geographic distribution in Madagascar, increasing its densities and progressively replacing *A. aegypti*, which is now present at residual levels in remote areas [76]. The decline in *A. aegypti* was also detected in the neighboring island of La Réunion [16,88].

The situation with these mosquitoes in Central Africa is slightly different. The invasion of *A. albopictus* occurred via several successive waves within a very short time frame. In the Central African Republic (CAR) *A. albopictus* first detected in 2008 [89], probably introduced from Cameroon where the species has been established since 2000 [90]. *Aedes albopictus* in Cameroon derives from multiple introductions from tropical sources that still need to be identified [74]. The polymorphism of mtDNA markers there is low, suggesting that *A. albopictus* were periodically introduced and that these events coincided with a decrease in *A. aegypti* densities [75].

3.3. Vector Competence

Vector competence, the ability of an arbovirus vector to acquire a pathogen and successfully transmit it to another susceptible host, is a complex process influenced by external factors including temperature, the availability of vertebrate hosts, vector population density and predation, as well as internal factors including mosquito survival and virus replication. For CHIKV, horizontal transmission through saliva that is injected when a mosquito probes or feeds on blood is the most common mechanism of transmission

(Figure 2), although vertical transmission via infected eggs may also occur at a low rate [91]. Vector competence is typically evaluated experimentally using static laboratory-based methods, where assessment of virus replication is the primary endpoint. For CHIKV, mosquitoes from endemic locations are usually presented artificial bloodmeals loaded with known titers of virus from sympatric settings. Mosquitoes that imbibe infectious bloodmeals are incubated at a constant temperature for at least seven days and then killed to assess replication. The fractions of mosquitoes that become infected, develop infections that have disseminated from the initial infection site in the midgut into the hemocoel, and excrete CHIKV in saliva are then measured to extrapolate vector competence for the population.

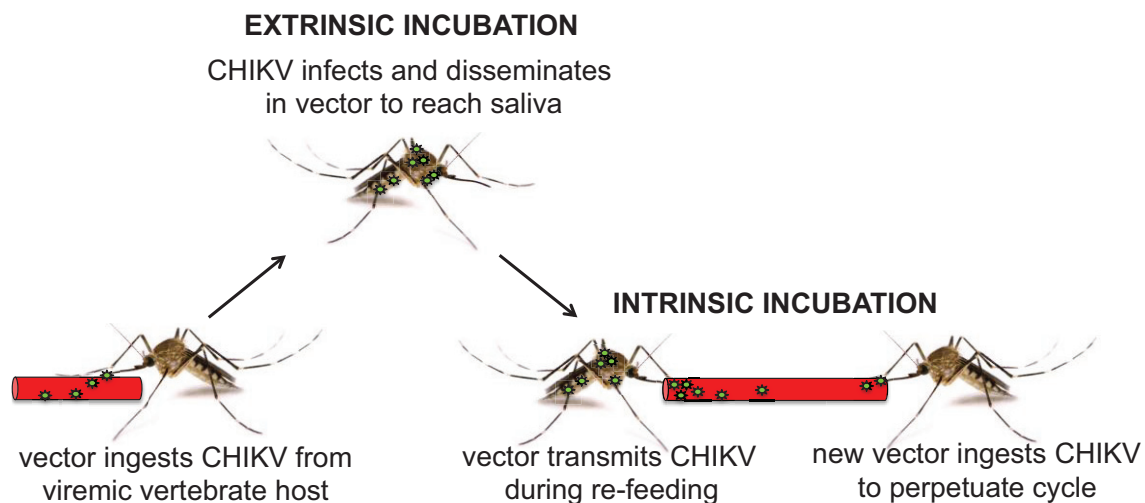


Figure 2. Process of infection and transmission of CHIKV by mosquito vectors. Vector mosquitoes ingest CHIKV from viremic vertebrate hosts during bloodfeeding. During the extrinsic incubation period that occurs in the vector, CHIKV infects the midgut and disseminates through the body cavity to infect salivary glands for secretion into saliva. Re-feeding vectors transmit CHIKV to vertebrate hosts by expectorating virus in saliva. New vectors perpetuate the CHIKV cycle by ingesting virus during intrinsic incubation, a period of viremia in the vertebrate host. Vector competence assays test infection, dissemination, and transmission of CHIKV after extrinsic incubation.

Table 1 summarizes experimental CHIKV vector competence estimates in arthropods from around the world. Most studies have focused on the two primary urban vectors, *A. aegypti* and *A. albopictus*, although other mosquitoes and one tick species have also been tested. Most studies have used relatively high bloodmeal titers exceeding $7 \log_{10}$ plaque forming units (PFU)/mL (but that are still below peaks in infected humans [92]) and mosquitoes were typically sampled more than seven days post-feed, experimental designs that maximize the chances of CHIKV infection and transmission. Infection, dissemination, and transmission rates of *A. aegypti* and *A. albopictus* vary according to the geographic sources of mosquitoes tested. At bloodmeal titers of $\geq 7 \log_{10}$ plaque-forming units (PFU)/mL, at least 80% of *A. aegypti* from all locations develop disseminated infections. More than half of *A. albopictus* that ingest bloodmeals $\geq 7 \log_{10}$ PFU/mL also became infected or develop disseminated infections, with several exceptions. Infection and dissemination rates in *A. albopictus* from the US are dose-dependent and increase with the titer of the ingested bloodmeal [9,93]; dose response studies have not been

published for mosquitoes from other regions. *Aedes albopictus* also exhibits strain-specific susceptibility; fewer mosquitoes from La Réunion Island, Mayotte, and colonized mosquitoes originally from Texas infected in parallel with a CHIKV isolate from early in the 2005–6 La Réunion Island outbreak developed disseminated infections than mosquitoes infected with strains isolated later in the outbreak (subsequent studies discussed below revealed that A to V substitution in amino acid 226 of the E1 protein (E1-A226V) mediates much of this differential infectivity [9,10,94]). In an attempt to exhaustively present CHIKV vector competence data, Table 1 shows all published data; however, comparing CHIKV vector competence over time in mosquitoes sampled from the same areas entails comparing data from experiments with unmatched bloodmeal titers. Differences could result from varied ingested doses rather than real differences in susceptibility to infection, dissemination and transmission. Despite this, studies from many locations worldwide show that *A. aegypti* and *A. albopictus* are generally highly susceptible to infection, dissemination and transmission of CHIKV. Alternate vector species, also represented in Table 1, may also serve as efficient CHIKV vectors in specific geographic settings; e.g., *Opifex fuscus* mosquitoes from New Zealand are highly competent at transmitting CHIKV from India.

3.4. Chikungunya Virus Vector Immunity and Microbial Interactions

While most arboviruses induce significant morbidity and/or mortality in some vertebrate hosts, infections of arthropod vectors are generally considered non-pathogenic. However, interactions between the replicating virus and the mosquito immune defense system produce an outcome that may influence subsequent viral dissemination or superinfection by other viruses (reviewed in [95]). Considerable progress has been achieved in understanding the innate defenses of the mosquito against arboviruses. The virus most intensively studied, DENV, triggers several immune pathways in *A. aegypti*: the Toll [96,97], JAK-STAT [98], and Imd/JNK pathways [99]. However, RNA interference (RNAi) appears to be the most significant innate antiviral immune response in mosquitoes [99–105]. So far, three major types of small RNA molecules have been identified in mosquito vectors: small interfering RNA (siRNA), microRNA (miRNA) and PIWI-interacting RNA (piRNA). These molecules have distinct roles in different cellular processes and virus-host interactions [106]. The antiviral siRNA pathway is triggered when long double-stranded RNA molecules are produced from secondary RNA structures and/or viral replication intermediates during infection of the vector. This leads to an activation of the RNA degradation machinery to the target viral RNA [100]. These pathways may act in a virus-specific manner.

Little is known about immune responses induced by CHIKV infection of mosquitoes. Viral replication is controlled *via* the exogenous RNAi pathway in mosquitoes [107]. The protein Ago-2 plays an important role in the antiviral RNAi response to CHIKV, similar to its role for other alphaviruses including, Sindbis (SINV) [102], Semliki Forest [108] and o'nyong-nyong viruses [101]. Viral replication under RNAi control may limit potential pathologic effects to favor mosquito survival [94].

The repeated use of insecticides to target mosquitoes as a means to control vector-borne diseases has found its limits due to the development of resistance [109], and alternative approaches are urgently needed. Recent strategies for controlling viral transmission have come from research on RNAi, such as the development of *A. aegypti* mosquitoes expressing small RNAs that render them resistant to viral infection; this approach is a promising mechanism for suppressing virus replication in mosquitoes [110–112]. Depending on the objectives, mosquito populations can also be reduced in density using various

strategies including the Sterile Insect Technique (SIT), a SIT-like system called Release of Insects carrying a Dominant Lethal (RIDL) [113], or replaced by transmission-refractory mosquitoes [114]. For this latter strategy, *Aedes* mosquitoes have been successfully transformed using transposon vectors [115] or infections with the intracellular bacterium *Wolbachia* [116]. However, a system is required to spread the refractory genes into mosquito populations as well as to maintain the expression of the refractory phenotype through generations. Several gene-driver systems have been proposed [117] including the Medea system, which shows promise by coupling genes conferring disease refractoriness with a genetic mechanism for driving them through wild populations [118].

In addition to their ability to shorten mosquito life span [119], certain strains of *Wolbachia* are also able to reduce arboviral transmission [120,121]. *Wolbachia* induce various distortions of host reproduction via a form of sterility known as cytoplasmic incompatibility (CI), thereby promoting its spread into populations [122]. Therefore, certain strains of *Wolbachia* provide the double role of a gene driver system and carrier of a refractory phenotype. While the mosquito *A. aegypti* is free of natural endosymbiotic bacteria *Wolbachia*, some *A. albopictus* populations are naturally super-infected with two *Wolbachia* strains, *wAlbA* and *wAlbB*. These *Wolbachia*, present in mosquito midguts and salivary glands [123], do not affect CHIKV replication [124]. In contrast, *Wolbachia* are able to limit DENV in *A. albopictus* [125] but cannot completely block transmission [126]. Moreover, *A. albopictus* transfected with a heterologous *Wolbachia* isolated from the fruit fly *Drosophila melanogaster* (*wMel*) inhibit the transmission of CHIKV [127] as in *A. aegypti* [121,128]. Several mechanisms have been proposed to explain the molecular basis of the pathogen-blocking *Wolbachia* infection phenotype: upregulation of immune genes, production of reactive oxygen species, or competition for a limited resource such as cholesterol [129–131].

In their digestive tracts, wild populations of *A. albopictus* and *A. aegypti* have been shown to house Proteobacteria and Firmicutes, including the genera *Acinetobacter*, *Asaia*, *Delftia*, *Pseudomonas*, *Wolbachia* and *Bacillus* as well as members of the family Enterobacteriaceae [132]. A higher diversity of bacteria can be occasionally found in wild *A. albopictus*; 27 genera of cultivable bacteria have been detected in this species from Madagascar, with *Pantoea* bacterium as the most prevalent [133]. Other bacterial members of the Alpha- and Gammaproteobacteria phyla, as well as Bacteroidetes, respond to CHIKV infection [132]. The abundance of bacteria belonging to the Enterobacteriaceae family increases with CHIKV infection [132], suggesting that cooperation or competition occurs within the host. Microbiota (including *Wolbachia*) endogenous to some mosquito species pre-activate the expression of basal genes in the immune response (*i.e.*, immune priming), allowing the vector to be prepared for infection by pathogens. In *A. aegypti* infected with DENV, the arthropod microbiota elicit basal immune responses that act against the virus, and this response reduces the density of the microbial load in the mosquito midgut [134]. Antiviral activities can be induced by secreting antiviral compounds; *Serratia odorifera* in *A. aegypti* enhances susceptibility to CHIKV by interaction of its P40 protein with the mitochondrial protein porin present on the midgut brush border membrane of the mosquito midgut, thereby downregulating mosquito immune responses [135].

3.5. Vector co-Infection by Chikungunya and Other Arboviruses

Mosquitoes may feed several times during their lifespan and can ingest genetically distinct variants of the same virus species or even viruses from different families. Once a virus has infected the mosquito salivary glands, the mosquito becomes competent for transmission to the next vertebrate host, usually for the remainder of its life [136,137]. The mosquito can therefore host a collection of diverse viruses, playing a role in selecting genotypes involved in epidemics [138].

Because CHIKV circulates in DENV-endemic regions where the anthropophilic mosquitoes *A. albopictus* and *A. aegypti* can transmit both viruses, reports of co-infection in humans are increasing. Since the first observation in 1964 in South India [139], co-infections have been reported since the 2004 re-emergence: Sri-Lanka [140], India [141–143], Malaysia [144], Gabon [145], Madagascar [14], Singapore [146], and Angola [147]. The increasing number of reports of co-infections seems to coincide with introductions of *A. albopictus* [145]. In Gabon, between 2007 and 2010, 0.9% of 4287 acutely febrile patients were positive for both CHIKV and DENV, and more unexpectedly, co-infected *A. albopictus* were also collected [148]. Patients were possibly co-infected with the two viruses through the bite of a single mosquito, as has been demonstrated experimentally [149]. Considering the nearly worldwide circulation of DENV and CHIKV, co-infections may become more frequent. Concurrent infections may make diagnosis more challenging and could also result in different disease syndromes. Concurrent epidemics of yellow fever virus and CHIKV were also reported in Africa [150–152] and patients infected with the two viruses were suspected [153]. In the same way, Zika virus (ZIKV), typically transmitted in urban settings by *A. aegypti*, is also transmitted by *A. albopictus*, whose expanding distribution may favor the cocirculation of CHIKV and ZIKV [154].

4. Chikungunya Virus

4.1. Genetics of Vector Susceptibility and Host Range Changes

As described above, CHIKV circulates in two distinct transmission cycles: (1) enzootic transmission among nonhuman primates and perhaps other vertebrates by arboreal *Aedes* spp. mosquitoes in sub-Saharan African sylvatic foci, and; (2) urban transmission among humans by *A. aegypti* and/or *A. albopictus*. Like interactions between other arboviruses and their arthropod vectors, susceptibility to CHIKV infection of mosquitoes and their ability to transmit depend on the genetics of both, and differences in these properties can affect circulation and human exposure as described above. Enzootic vector-CHIKV interactions have received little experimental study [47]. Although population-based differences in urban vector competence may occur, these have not been addressed in enough detail to be conclusive or to begin to assess genetic components of vector susceptibility. Following the detection of the *A. albopictus*-adaptive A226V substitution in the E1 envelope glycoprotein during the 2005–2006 Réunion Island epidemic [8–10], the impact of CHIKV genetics on urban vector infection and transmission has received considerable study. Vector-adaptive evolution had been previously described for DENV [155,156] and the alphavirus Venezuelan equine encephalitis virus (VEEV) [157], the latter also involving a substitution in an envelope glycoprotein, in this case E2. Surprisingly, neither vector-adaptive alphavirus mutations has been shown to have much effect on infection of the previous or donor vector, *A. aegypti* in the case of CHIKV [9,12] and *Culex (Melanoconion) taeniopus* in the case

of VEEV [158], challenging the hypothesis that most host-specific viral adaptations will have tradeoffs for fitness in other hosts. Further phylogenetic/reverse genetic studies of IOL CHIKV revealed an unprecedented series of four second-step, *A. albopictus*-adaptive mutations, each involving E2 substitutions, and one relying also on a synergistic effect of an E3 substitution [13,159]. Each of these mutations enhances initial infection of the mosquito midgut and has little or no effect on infection of *A. aegypti*. Furthermore, at least one combination of these independently acquired second-step mutations leads to an *A. albopictus* infection phenotype more efficient than that of any natural CHIKV strain studied to date, suggesting further vector-adaptive evolution and even more efficient circulation in regions where this mosquito is abundant. Structural modelling of these *A. albopictus*-adaptive envelope glycoprotein substitutions suggests that they alter the entry process in endosomes by affecting conformational changes required for E1 fusion with endosomes rather than directly affecting receptor binding [12,13].

4.2. Population Heterogeneity & Selection for Fittest Genomes

Alphaviruses like CHIKV exist as heterogeneous populations of viral RNAs called mutant swarms that arise from frequent nucleotide misincorporation during replication due to the inability of the viral RNA-dependent RNA polymerase (RdRp) to error correct. Given a ≈ 12 kb CHIKV genome and a mutation frequency of $\approx 10^{-4}$, each new RNA genome possesses one mutation on average. By comparison, double-stranded DNA virus mutation rates are several \log_{10} lower [160]. Most mutant genomes are detrimental and removed from the swarm via purifying negative selection. By contrast, positive selection of a fit phenotype results in increased abundance of a genotype. Therefore, a dynamic mutation-selection balance determines the size and genetic diversity of a mutant swarm. Genetic diversity renders a population less prone to the consequences of negative selection pressures that target certain genotypes and renders a population more likely to contain variants with potential phenotypic advantages; these features can enhance plasticity and adaptability. A high fidelity CHIKV variant with a point mutation at amino acid position 483, a fidelity-determining locus in the RdRp, that was discovered experimentally after treatment with chemical mutagens, generates 30% fewer mutants than wild-type (wt) virus and is less fit in vectors and a mouse model [161,162]. This reduced fitness may result from the less mutated population containing fewer genotypes that can resist evolutionary pressures including negative selection or population bottlenecks. Complementary studies with low fidelity variants of CHIKV generated by mutagenizing the amino acid at 483 produce more errors than wt variants and are also attenuated in mosquito cells and mice [138]. Together these studies indicate that CHIKV maintains an intermediate mutation frequency to avoid detriments to fitness resulting from populations with too few or too many mutant genomes.

4.3. Dual Host Cycling & Chikungunya Virus Adaptation

Strong purifying selection of alphaviruses that cycle between mosquitoes and vertebrates results in less genetic variation than predicted by their high mutation rates [138,163–165]. Work with other alphaviruses including eastern equine encephalitis virus (EEEV), SINV, and VEEV shows that alternating between hosts poses conflicting challenges to replication that can limit adaptation to either host alone by imposing fitness costs where adaptations are antagonistic ([166] reviewed in [167]). When

one host is artificially removed via experimental serial passage, the limitations of these trade-offs are evident; viruses serially passaged in a single host are more adaptable. CHIKV serially passaged in vertebrate or mosquito cells exhibits higher fitness when passaged in novel cell types and also showed enhanced neutralization escape and antiviral compound resistance. These changes are accompanied by increased genetic diversity. In contrast, alternating CHIKV passage between cell types restricts fitness and increases diversity, suggesting that only mutations beneficial or neutral in both host cells are maintained and that these variants retain fitness in alternating cycling [168].

4.4. Viral Bottlenecks and Intrahost Diversity

The ability to circumvent bottlenecks within and between dynamic environments including switching between vector and vertebrate hosts impacts CHIKV evolution and is important for understanding changing population dynamics that ultimately cause human disease. Bottlenecks that reduce arbovirus population size can influence viral fitness by restricting phenotypic plasticity that stems from having genetic diversity. The evolutionary theory Muller's ratchet asserts that asexual organisms with high mutation rates and small population sizes irreversibly accumulate deleterious mutations unless compensatory mutations restore mutation-free genomes to the population [169]. Studies with EEEV [170] validate this concept; fitness decreases after serial bottleneck passages can be rescued by subsequent large population passages, albeit with much replication needed to overcome the ratchet [171]. Anatomical barriers to productive alphavirus transmission by mosquito vectors are relatively well defined, although only one study has addressed CHIKV directly. As a first step, alphaviruses in a bloodmeal ingested by a mosquito must infect the midgut epithelium. Some VEEV studies suggest that only "portal" cells in the midgut epithelium are susceptible to infection [172]; other experiments show uniform susceptibility [173], possibly reflecting a longer virus-vector relationship for the latter. Secondary impediments to dissemination result in failure of the virus to escape from the midgut epithelium, infect salivary glands, and escape from salivary gland cells into saliva for transmission to vertebrates. The number of barcoded VEEV variants that successfully traverse these barriers is reduced at midgut escape and salivary gland infection compared to the ingested bloodmeal, and smaller initial bloodmeal populations are more prone to reductions in variant diversity [174], suggesting strong genetic bottlenecks that reduce diversity coincident with population size changes. These observed changes in genetic diversity of the mutant swarm in mosquitoes contrast with observations from other mosquito-borne arboviruses isolated from nature [175], as well as experimental *in vivo* passaging studies with VEEV that show the maintenance of genetic and phenotypic stability of the consensus (average sequence) [176]. The disparity in results between these studies may be explained by the re-establishment of genetic diversity after bottlenecks via subsequent replication. Studies with CHIKV support this idea; although population diversity in the midgut and salivary glands is reduced compared to the bloodmeal input or midgut population, respectively, it recovers downstream of each barrier and the consensus sequence remains unchanged [138].

Experimental studies showing that alternating hosts impose constraints on arboviruses including CHIKV indicate that inefficient transmission probably interrupts natural CHIKV cycling. However, the degree of natural extinction in vertebrate or vector hosts has not been directly addressed. Extinction in an individual mosquito-vertebrate-mosquito lineage is likely because most mosquitoes do not survive

long enough in nature to feed more than once. The maintenance of consensus genetic stability in nature in the presence of intense circulation may be due to the extinction of most individual lineages, possibly via vector bottlenecks in individual mosquitoes. However, these extinctions must not be widespread enough; otherwise CHIKV cycling would be interrupted. No studies published on CHIKV or other alphaviruses have examined mutant swarms in naturally infected mosquitoes, humans, or other vertebrate hosts. Artificially generated, barcoded VEEV variants in mosquitoes that transmitted to laboratory mice were also observed in the brains of animals [174], suggesting that mosquito-to-vertebrate transmission of alphaviruses does not present a major bottleneck (although few ($n = 3$) infected mice were sampled). Virus doses expectorated by mosquitoes vary greatly, and are probably overestimated by standard laboratory salivation assays where infected mosquitoes eject more virus into tubes than *in vivo* [177]. Therefore, variance in transmitted doses, especially when few particles are transmitted, likely impacts the outcome of vertebrate infection and maintenance of alphavirus cycling in natural foci. Interruptions in seasonal transmission may represent another significant bottleneck imposed on CHIKV, especially if the virus is introduced into temperate climates [178] where vector survival and competence would decrease in colder temperatures [179]; however this phenomenon is complex [180] and has not been studied extensively.

4.5. Adaptive Constraints on Chikungunya Virus Evolution

Although the 2004 IOL CHIK emergence underscores the adaptive potential of RNA viruses including most arboviruses, it also provides examples of constraints on adaptive evolution that remain difficult to predict. Although the E1-A226V substitution was selected convergently after IOL strains reached locations with abundant *A. albopictus*, it surprisingly was not found in any CHIKV strains of the Asian lineage despite their circulation in regions of Asia native to this vector for more than 60 years [5]. This lack of adaptation to *A. albopictus* in Asia resulted from an epistatic interaction with E1 residue 98; Asian CHIKV strains, which have a threonine residue at position 98, show no increase in *A. albopictus* infectivity when the E1-A226V substitution is engineered into a cDNA clone derived from the Asian strain, while ECSA and IOL strains with 98A show a dramatic increase in infection. The lack of sequenced enzootic CHIKV strains with 98T suggests that this residue, which by itself has no detectable effect on infection of urban vectors or models for human infection, resulted from a founder effect when CHIKV was introduced into Asia sometime before 1958 [181].

Although variation among Asian strain CHIKV infection of *A. aegypti* has received little study, no evidence has been produced to support adaptive evolution in Asia since the 1950s. The above evidence indicating an adaptive constraint on Asian strains, including those now circulating in the Americas, for enhanced transmission by *A. albopictus* suggests that *A. aegypti* will remain the principal vectors as spread into American regions inhabited by both vectors continues [13]. However, additional studies of the Asian lineage and its potential to increase transmissibility by either mosquito are needed.

5. Future Prospects

5.1. Potential for Re-Emergence and Expansion into New Areas

Due to the immunologically almost completely naïve status of human populations and the widespread and abundant *A. aegypti* nearly throughout the western hemisphere tropics, CHIKV is expected to continue to spread and ultimately recapitulate the distribution of DENV in the Americas. The lack of historical evidence for a major role of *A. albopictus* in transmission of Asian lineage CHIKV strains and the adaptive constraint described above suggest that temperate American regions inhabited by *A. albopictus* but not *A. aegypti* may not be at as high a level of risk as regions where IOL strains are circulating. However, IOL strains continue to circulate in Asia and have a history of many importations into the Americas [182], so their risk of introduction into the Americas continues. Should both Asian and IOL strains cocirculate, as they have in Southeast Asia since 2007, even more geographic regions of the Americas could be at risk for CHIK.

5.2. Prospects for Prevention via Vector Control

The poor history of DENV control since the 1970s suggests that mitigation of CHIKV transmission via vector control will be highly challenging. Due to its tight association with artificial larval habitats, endophily of adult females, and daytime biting patterns, control of *A. aegypti* and DENV transmission is difficult, and *A. albopictus* presents similar challenges. The development of resistance to commonly used insecticides further complicates the control of these vectors. Although some novel strategies for *A. aegypti* control discussed above such as RIDL offer promise, they remain in the early stages of field testing [183]. Interim measures including the application of persistent insecticides to the interior of houses may be needed in some situations to reduce CHIKV and DENV transmission.

The long-term prospects for CHIKV maintenance in the endemic, urban cycle are not entirely clear. Following introduction of the Asian lineage into South and Southeast Asia during the 1950s or earlier, it became extinct in India after 1973 for unknown reasons, but continues to circulate in Southeast Asia today [167,184]. The only major human immune cross-reactivity known to affect CHIKV to a major extent is that from Ross River and Mayaro viruses, which like CHIKV are members of the Semliki Forest complex of alphaviruses. Ross River virus only occurs in Australia and Indonesia, and Mayaro virus in South America where seroprevalence is generally low in urban settings. These data suggest that CHIKV will continue to circulate indefinitely in Asia and probably in the Americas as well.

Table 1. Chikungunya virus vector competence in arthropods. Infection was ascertained by detection of virus in bodies of bloodfed mosquitoes; dissemination was determined by detection of virus in legs or heads. Transmission was verified by detection of virus in saliva or by infection of vertebrates after re-feeding. CHIKV bloodmeal titers are expressed in \log_{10} cell culture infectious dose₅₀/mosquito, plaque forming units/mL, or suckling mouse infectious culture lethal dose₅₀/mL. Mosquitoes were held at 28 °C during the incubation period, except where noted: * indicates incubation at 24 °C and ** denotes incubation at 16 °C. For simplification, cohorts of the same species that fed on the same strain at similar bloodmeal titers are represented as one value and bloodmeal titers are shown as ranges.

Mosquito Species	Source	Generation Number	Source of CHIKV, Isolation Year	Strain Name	Bloodmeal Titer	Incubation Period (Days)	% Infected (n)	% Disseminated (n)	% Transmitted (n)	Reference
<i>Aedes aegypti</i>	Queensland, Australia	1	patient in Melbourne ex. Mauritius, March 2006	not stated	4	14-15	92 (23/25)	92 (23/25)	64 (16/25)	van den Hurk <i>et al.</i> , 2010 [128]
	New Caledonia	1	patient in New Caledonia ex. Indonesia, February 2011	NC 2011-568	7	14	n.d.	n.d.	27 (10/37)	Dupont-Rouzeyrol <i>et al.</i> , 2012 [41]
			patient in Reunion Island, 2006	6.21			n.d.	n.d.	75 (27/36)	
	Mayotte	3	patient in Reunion Island, 2005 (E1226V)	6.21	7.5	14	n.d.	87 (54/62)	n.d.	Martin <i>et al.</i> , 2010 [94]
			patient in Reunion Island, 2005 (E1226A)	6.115			n.d.	78 (43/55)	n.d.	
	Cameroon	1	patient in Reunion Island, 2005 (E1226V)	06.21	7	14	n.d.	89 (333/376)	n.d.	Paupy <i>et al.</i> , 2010 [185]
			patient in Reunion Island, 2005 (E1226A)	06.115			n.d.	97 (36/37)	n.d.	
			patient in Reunion Island, 2005 (E1226V)	06.21			n.d.	65 (70/107)	n.d.	Vazeille <i>et al.</i> , 2007 [10]
			patient in Mayotte, 2006	06.111			n.d.	82 (68/82)	n.d.	
			patient in Democratic Republic of Congo, 2000	06.117			n.d.	84 (56/66)	n.d.	
	Dakar, Senegal	4	patient in Thailand, 1962	15561	4.2–4.6	7	2 (1/45)	0 (0/45)	n.d.	Turell <i>et al.</i> , 1992 [186]
	Lagos, Nigeria	colony	patient in Calcutta, India, 1963	63-266	8	14	10 (2/20)	n.d.	50 (1/2)	Shah <i>et al.</i> , 1964 [187]
	French West Indies	1-2	patient in Reunion Island, 2006	06.21	7.5	14	98 (900/918)	n.d.	n.d.	Girod <i>et al.</i> , 2011 [188]
patient in Reunion Island, 2006			06.21	6	7	47 (301/634)	n.d.	n.d.		
Trinidad, West Indies	colony	patient in Calcutta, India, 1963	63-266	8	14	42 (3/7)	n.d.	100 (1/1)	Shah <i>et al.</i> , 1964	

Table 1. Cont.

Mosquito Species	Source	Generation Number	Source of CHIKV, Isolation Year	Strain Name	Bloodmeal Titer	Incubation Period (Days)	% Infected (n)	% Disseminated (n)	% Transmitted (n)	Reference
<i>Aedes aegypti</i>	Guadeloupe	1	patient in Reunion Island, 2005 (E1226V)	6.21	7.5	14	n.d.	96 (346/358)	n.d.	Girod <i>et al.</i> , 2011
	Martinique	1	patient in Reunion Island, 2005 (E1226V)	6.21	7.5	14	n.d.	98 (285/290)	n.d.	Girod <i>et al.</i> , 2011
	French Guyana	1	patient in Reunion Island, 2005 (E1226V)	6.21	7.5	14	n.d.	99 (269/270)	n.d.	Girod <i>et al.</i> , 2011
	Florida, USA	1	patient in France ex. Reunion Island, 2006	LR2006-OPY1	6.1	6	58 (15/26)	73 (11/15)	n.d.	Pesko <i>et al.</i> , 2009 [93]
			patients in Reunion Island, 2005	06.21 and/or 06.115	7.5	10	n.d.	100 (48/48)	n.d.	Vega-Rua <i>et al.</i> , 2014 [43]
	Louisiana, USA	4-5	patient in Thailand, 1962	15561	4.2–4.6	7	5 (3/60)	2 (1/60)	n.d.	Turell <i>et al.</i> , 1992
	Indiana, USA	7	patient in Thailand, 1962	15561	4.2–4.6	7	6 (2/35)	6 (2/35)	n.d.	Turell <i>et al.</i> , 1992
	Puerto Rico, USA	3	patient in Thailand, 1962	15561	4.2–4.6	7	55 (9/55)	11 (6/55)	n.d.	Turell <i>et al.</i> , 1992
		5	patient in Thailand, 1962	15561	5.3	7	33 (10/30)	10 (3/30)	n.d.	
	Mexico	1	patients in Reunion Island, 2005	06.21 and/or 06.115	7.5	10	n.d.	97 (58/60)	n.d.	Vega-Rua <i>et al.</i> , 2014
	Panama	1	patients in Reunion Island, 2005	06.21 and/or 06.115	7.5	10	n.d.	97 (58/60)	n.d.	Vega-Rua <i>et al.</i> , 2014
			patient in New Caledonia, 2011	NC/2011-568			n.d.	100 (30/30)	n.d.	
	Venezuela	1	patients in Reunion Island, 2005	06.21 and/or 06.115	7.5	10	n.d.	100 (51/51)	n.d.	Vega-Rua <i>et al.</i> , 2014
	Peru	1	patients in Reunion Island, 2005	06.21 and/or 06.115	7.5	10	n.d.	100 (89/89)	n.d.	Vega-Rua <i>et al.</i> , 2014
	Brazil	1	patients in Reunion Island, 2005	06.21 and/or 06.115	7.5	10	n.d.	98 (128/130)	n.d.	Vega-Rua <i>et al.</i> , 2014
patient in New Caledonia, 2011			NC/2011-568	n.d.			95 (57/60)	n.d.	Vega-Rua <i>et al.</i> , 2014	
Bolivia	1	patients in Reunion Island, 2005	06.21 and/or 06.115	7.5	10	n.d.	100 (60/60)	n.d.	Vega-Rua <i>et al.</i> , 2014	

Table 1. Cont.

Mosquito Species	Source	Generation Number	Source of CHIKV, Isolation Year	Strain Name	Bloodmeal Titer	Incubation Period (Days)	% Infected (n)	% Disseminated (n)	% Transmitted (n)	Reference
<i>Aedes aegypti</i>	Paraguay	1	patients in Reunion Island, 2005	06.21 and/or 06.115	7.5	10	n.d.	99 (89/90)	n.d.	Vega-Rua <i>et al.</i> , 2014
	Uruguay	1	patients in Reunion Island, 2005	06.21 and/or 06.115	7.5	10	n.d.	100 (60/60)	n.d.	Vega-Rua <i>et al.</i> , 2014
	Argentina	1	patients in Reunion Island, 2005	06.21 and/or 06.115	7.5	10	n.d.	99 (119/120)	n.d.	Vega-Rua <i>et al.</i> , 2014
	Bangkok, Thailand	2	patient in Thailand, 1962	15561	5.3	7	66 (20/30)	66 (20/30)	n.d.	Turell <i>et al.</i> , 1992
	Ho Chi Minh City, Vietnam	colony	patient in Reunion Island, 2005 (E1226A)	06.115	7	14	n.d.	66 (135/206)	n.d.	Vazeille <i>et al.</i> , 2007
			patient in Reunion Island, 2005 (E1226V)	06.21			n.d.	97 (227/234)	n.d.	
			patient in Mayotte, 2006	06.111			n.d.	92 (126/137)	n.d.	
			patient in Democratic Republic of Congo, 2000	06.117			n.d.	78 (108/138)	n.d.	
	Higgs variant, Renville D	colony	clone derived from patient in France ex. Reunion Island, 2006 E1226A	LR2006-OPY1 E1A226	5	7	20 (not stated)	n.d.	n.d.	Tssetsarkin <i>et al.</i> , 2007 [9]
			clone derived from patient in France ex. Reunion Island, 2006 E1226V	LR2006-OPY1 E1V226			5 (not stated)	n.d.	n.d.	
			infectious clone from patient in West Africa, E1226A	37997 E1A226			20 (not stated)	n.d.	n.d.	
			infectious clone from patient in West Africa, E1226V	37997 E1V226			10 (not stated)	n.d.	n.d.	
			<i>Aedes furcifer</i> , Kadougou, Senegal, 1983	37997			8	14	100 (7/7)	
not stated	colony	patient in Africa, not stated	not stated	8.6-9.2	14	53 (24/45)	n.d.	44 (20/45)	Mangiafico, 1971 [190]	
Rockefeller	colony	patient in Thailand, 1962	15561	4.2-4.6	7	18 (9/50)	12 (6/50)	n.d.	Turell <i>et al.</i> , 1992	
Madeira Island, Spain	1	patient in Reunion Island, 2005 (E1226V)	06.21	7	14	n.d.	100 (27/27)	40 (4/10)	Vazeille <i>et al.</i> , 2012 [191]	

Table 1. Cont.

Mosquito Species	Source	Generation Number	Source of CHIKV, Isolation Year	Strain Name	Bloodmeal Titer	Incubation Period (Days)	% Infected (n)	% Disseminated (n)	% Transmitted (n)	Reference
<i>Aedes albopictus</i>	Queensland, Australia	7	patient in Melbourne ex. Mauritius, March 2006	not stated	3.9	14-15	92 (23/25)	92 (23/25)	32 (8/25)	van den Hurk <i>et al.</i> , 2010
	Torres Strait, Australia	7	patient in Melbourne ex. Mauritius, March 2006	not stated	8	14	80 (4/5)	80 (4/5)	60 (3/5)	Nicholson <i>et al.</i> , 2014 [192]
	Mauritius	1	patient in India, 1973	Barsi, P0-731460	5.8	8-9	32 (13/41)	n.d.	n.d.	Tesh <i>et al.</i> , 1976 [193]
			patient in Tanzania, 1953	Ross, S-27	6.8	8-9	19 (13/67)	n.d.	n.d.	Tesh <i>et al.</i> , 1976
	Mayotte	1	patient in Reunion Island, 2005 (E1226A)	6.115	7	14	n.d.	25 (115/462)	n.d.	Vazeille <i>et al.</i> , 2007
		6	patient in Reunion Island, 2005 (E1226A)	6.115	7.5	14	n.d.	79 (45/57)	n.d.	Martin <i>et al.</i> , 2010 [94]
		1	patient in Reunion Island, 2005 (E1226V)	6.21	7	14	n.d.	91 (296/325)	n.d.	Vazeille <i>et al.</i> , 2007
		6	patient in Reunion Island, 2005 (E1226V)	6.21	7.5	14	n.d.	99 (64/65)	n.d.	Martin <i>et al.</i> , 2010
		1	patient in Mayotte, 2006	06.111	7	14	n.d.	98 (48/49)	n.d.	Vazeille <i>et al.</i> , 2007
		1	patient in Democratic Republic of Congo, 2000	06.117	7	14	n.d.	73 (41/56)	n.d.	Vazeille <i>et al.</i> , 2007
	Reunion Island	2	patient in Reunion Island, 2005 (E1226A)	6.115	7.5	14	n.d.	90 (26/29)	n.d.	Martin <i>et al.</i> , 2010
		1	patient in Reunion Island, 2005 (E1226A)	6.115	7	14	n.d.	25 (114/462)	n.d.	Vazeille <i>et al.</i> , 2007
		2	patient in Reunion Island, 2005 (E1226V)	6.21	7.5	14	n.d.	98 (55/56)	n.d.	Martin <i>et al.</i> , 2010
		1	patient in Reunion Island, 2005 (E1226V)	6.21	7	14	n.d.	96 (391/409)	n.d.	Vazeille <i>et al.</i> , 2007
		2	patient in Mayotte, 2006	6.111	7	14	n.d.	97 (91/94)	n.d.	Vazeille <i>et al.</i> , 2007
		2	patient in Democratic Republic of Congo, 2000	6.117	7	14	n.d.	80 (25/31)	n.d.	Vazeille <i>et al.</i> , 2007
	Madagascar	7	patient in Thailand, 1962	15561	5.3	7	95 (19/20)	35 (7/20)	n.d.	Turell <i>et al.</i> , 1992
		1	patient in India, 1973	Barsi, P0-731460	6.2	8-9	87 (33/38)	n.d.	n.d.	Tesh <i>et al.</i> , 1976
		1	patient in Tanzania, 1953	Ross, S-27	6.8	8-9	39 (19/49)	n.d.	n.d.	Tesh <i>et al.</i> , 1976
		2-5	patient in Reunion Island, 2006	not stated	7.5	14	n.d.	98 (497/503)	n.d.	Raharimalala <i>et al.</i> , 2012 [76]

Table 1. Cont.

Mosquito Species	Source	Generation Number	Source of CHIKV, Isolation Year	Strain Name	Bloodmeal Titer	Incubation Period (Days)	% Infected (n)	% Disseminated (n)	% Transmitted (n)	Reference
<i>Aedes albopictus</i>	Cameroon	1	patient in Reunion Island, 2006	06.21	7	14	n.d.	85 (187/218)	n.d.	Paupy <i>et al.</i> , 2010
			patient in Reunion Island, 2005 (E1226V)	06.21	7	14	n.d.	68 (41/60)	n.d.	Vazeille <i>et al.</i> , 2007
			patient in Mayotte, 2006	06.111	7	14	n.d.	44 (34/44)	n.d.	Vazeille <i>et al.</i> , 2007
			patient in Democratic Republic of Congo, 2000	06.117	7	14	n.d.	56 (22/39)	n.d.	Vazeille <i>et al.</i> , 2007
			patient in Reunion Island, 2005 (E1226A)	06.115	7	14	n.d.	12 (11/90)	n.d.	Vazeille <i>et al.</i> , 2007
	Virginia and Georgia, USA	1	mosquito pool, Comoros, 2005 strain COM125	COM125	4.9	7	73 (83/114)	n.d.	40 (33/83)	McTighe & Vaidyanathan, 2012
	Hawaii, USA	1	patient in Tanzania, 1953	Ross, S-27	7-7.5	8-9	69 (76/110)	n.d.	n.d.	Tesh <i>et al.</i> , 1976
		1	patient in India, 1973	Barsi, P0-731460	5.8	8-9	97 (120/124)	n.d.	n.d.	Tesh <i>et al.</i> , 1976
		colony	patient in Calcutta, India, 1963	63-266	8	14	100 (32/32)	n.d.	34 (8/22)	Shah <i>et al.</i> , 1964
		colony	patient in Thailand, 1962	15561	5.3	7	93 (28/30)	60 (18/30)	n.d.	Turell <i>et al.</i> , 1992
	Florida, USA	1	patient in France ex. Reunion Island, 2006	LR2006-OPY1	6.1	6	100 (22/22)	91 (20/22)	n.d.	Pesko <i>et al.</i> , 2009
			patients in Reunion Island, 2005	06.21 and/or 06.115	7.5	10	n.d.	83 (50/60)	n.d.	Vega-Rua <i>et al.</i> , 2014
		2	patient in Thailand, 1962	15561	5.3	7	97 (29/30)	37 (11/30)	n.d.	Turell <i>et al.</i> , 1992
	Missouri, USA	1	patients in Reunion Island, 2005	06.21 and/or 06.115	7.5	10	n.d.	90 (54/60)	n.d.	Vega-Rua <i>et al.</i> , 2014

Table 1. Cont.

Mosquito Species	Source	Generation Number	Source of CHIKV, Isolation Year	Strain Name	Bloodmeal Titer	Incubation Period (Days)	% Infected (n)	% Disseminated (n)	% Transmitted (n)	Reference
<i>Aedes albopictus</i>	Texas, USA	colony	clone derived from patient in France ex. Reunion Island, 2006 E1226A	LR2006-OPY1 E1A226	5	7	31 (61/194)	30 (not stated)		Tsetsarkin <i>et al.</i> , 2007
			clone derived from patient in France ex. Reunion Island, 2006 E1226V	LR2006-OPY1 E1V226	5	7	90 (241/269)	65 (not stated)		Tsetsarkin <i>et al.</i> , 2007
			infectious clone from patient in West Africa, E1226A	37997 E1A226	5	7	37 (97/226)	n.d.	n.d.	Tsetsarkin <i>et al.</i> , 2007
			infectious clone from patient in West Africa, E1226V	37997 E1V226	5	7	92 (253/274)	n.d.	n.d.	Tsetsarkin <i>et al.</i> , 2007
		9-10	patient in Thailand, 1962	15561	5.3	7	75 (15/20)	35 (7/20)	n.d.	Turell <i>et al.</i> , 1992
	Louisiana, USA	4-5	patient in Thailand, 1962	15561	5.3	7	97 (29/30)	80 (24/30)	n.d.	Turell <i>et al.</i> , 1992
	Mexico	1	patients in Reunion Island, 2005	06.21 and/or 06.115	7.5	10	n.d.	70 (42/60)	n.d.	Vega-Rua <i>et al.</i> , 2014
	Panama	1	patients in Reunion Island, 2005	06.21 and/or 06.115	7.5	10	n.d.	95 (57/60)	n.d.	Vega-Rua <i>et al.</i> , 2014
			patient in New Caledonia, 2011	NC/2011-568	7.5	10	n.d.	97 (29/30)	n.d.	Vega-Rua <i>et al.</i> , 2014
	Brazil	6-7	patient in Thailand, 1962	15561	5.3	7	73 (22/30)	50 (15/30)	n.d.	Turell <i>et al.</i> , 1992
		1	patients in Reunion Island, 2005	06.21 and/or 06.115	7.5	10	n.d.	94 (301/320)	n.d.	Vega-Rua <i>et al.</i> , 2014
	Argentina	1	patients in Reunion Island, 2005	06.21 and/or 06.115	7.5	10	n.d.	63 (35/56)	n.d.	Vega-Rua <i>et al.</i> , 2014
			patient in New Caledonia, 2011	06.21 and/or 06.115	7.5	10	n.d.	93 (28/30)	n.d.	Vega-Rua <i>et al.</i> , 2014
	Israel	1	patient in Tanzania, 1953	Ross, S-27	7.2	8-9	30 (14/47)	n.d.	n.d.	Tesh <i>et al.</i> , 1976
			patient in India, 1973	Barsi, P0-731460	5.8	8-9	67 (37/55)	n.d.	n.d.	Tesh <i>et al.</i> , 1976
	Lebanon	1	patient in Reunion Island, 2005 (E1226V)	6.21	8	14	n.d.	29 (12/42)	n.d.	Haddad <i>et al.</i> , 2012 [194]

Table 1. Cont.

Mosquito Species	Source	Generation Number	Source of CHIKV, Isolation Year	Strain Name	Bloodmeal Titer	Incubation Period (Days)	% Infected (n)	% Disseminated (n)	% Transmitted (n)	Reference
<i>Aedes albopictus</i>	Italy	0	patient in Reunion Island, 2005 (E1226V)	06.21	7	14	n.d.	83 (52/63)	n.d.	Talbalaghi <i>et al.</i> , 2010 [195]
	France	0	patient in Reunion Island, 2005 (E1226V)	6.21	7	14	n.d.	77.1 (27/35)	n.d.	Vazeille <i>et al.</i> , 2008 [196]
		13	patient in France, 2010 (E1226A)	1909	7.3	14	n.d.	96 (21/22)	14 (3/21)	Vega-Rua <i>et al.</i> , 2013 [36]
		13	patient in France, 2010 (E1226A)	1630	7.3	14	n.d.	90 (17/19)	12 (2/17)	Vega-Rua <i>et al.</i> , 2013
	Corsica, France	0	patient in Reunion Island, 2005 (E1226V)	6.21	7.5	14	n.d.	94 (377/401)	n.d.	Moutailler <i>et al.</i> , 2009 [197]
	Indonesia	1	patient in Tanzania, 1953	Ross, S-27	7.1	8–9	64 (34/53)	n.d.	n.d.	Tesh <i>et al.</i> , 1976
	Philippines	1	patient in Tanzania, 1953	Ross, S-27	7.2	8–9	55 (21/38)	n.d.	n.d.	Tesh <i>et al.</i> , 1976
	India	1	patient in Tanzania, 1953	Ross, S-27	7–7.2	8–9	38 (30/79)	n.d.	n.d.	Tesh <i>et al.</i> , 1976
			patient in India, 1973	Barsi, P0-731460	5.7–5.9	8–9	71 (74/104)	n.d.	n.d.	Tesh <i>et al.</i> , 1976
	Vietnam	1	patient in Tanzania, 1953	Ross, S-27	7.7	8–9	44 (29/66)	n.d.	n.d.	Tesh <i>et al.</i> , 1976
			patient in India, 1978	Barsi, P0-731460	5.7	8–9	49 (37/94)	n.d.	n.d.	Tesh <i>et al.</i> , 1976
	Thailand	1	patient in Tanzania, 1953	Ross, S-27	7.4	8–9	38 (12/32)	n.d.	n.d.	Tesh <i>et al.</i> , 1976
			patient in India, 1973	Barsi, P0-731460	6	8–9	73 (24/33)	n.d.	n.d.	Tesh <i>et al.</i> , 1976
	Malaysia	1	patient in Tanzania, 1953	Ross, S-27	6.9	8–9	29 (15/51)	n.d.	n.d.	Tesh <i>et al.</i> , 1976
			patient in India, 1973	Barsi, P0-731460	6	8–9	42 (27/64)	n.d.	n.d.	Tesh <i>et al.</i> , 1976
	Taipei	1	patient in Tanzania, 1953	Ross, S-27	7	8–9	25 (12/48)	n.d.	n.d.	Tesh <i>et al.</i> , 1976
			patient in India, 1973	Barsi, P0-731460	5.8	8–9	28 (14/50)	n.d.	n.d.	Tesh <i>et al.</i> , 1976
	Taiwan	2	patient in Thailand, 1962	15561	5.3	7	90 (27/30)	20 (6/30)	n.d.	Turell <i>et al.</i> , 1992
	Okinawa, Japan	5	patient in Thailand, 1962	15561	5.3	7	72 (18/25)	28 (7/25)	n.d.	Turell <i>et al.</i> , 1992
	Tokyo, Japan	5	patient in Thailand, 1962	15561	4.2–4.6	7	50 (14/28)	14 (7/50)	n.d.	Turell <i>et al.</i> , 1992
Jakarta	1	patient in India, 1975	Barsi, P0-731460	5.8	8–9	70 (23/33)	n.d.	n.d.	Tesh <i>et al.</i> , 1976	
Philippines	1	patient in India, 1976	Barsi, P0-731460	6	8–9	87 (33/38)	n.d.	n.d.	Tesh <i>et al.</i> , 1976	
Sabah, Malaysia	5	patient in Thailand, 1962	15561	4.2–4.6	7	43 (15/35)	6 (2/43)	n.d.	Turell <i>et al.</i> , 1992	

Table 1. Cont.

Mosquito Species	Source	Generation Number	Source of CHIKV, Isolation Year	Strain Name	Bloodmeal Titer	Incubation Period (Days)	% Infected (n)	% Disseminated (n)	% Transmitted (n)	Reference
<i>Aedes albopictus</i>	Hanoi, Vietnam	3	patient in Reunion Island, 2005 (E1226A)	6.115	7	14	n.d.	30 (16/54)	n.d.	Vazeille <i>et al.</i> , 2007
			patient in Reunion Island, 2005 (E1226V)	6.21	7	14	n.d.	84 (105/126)	n.d.	Vazeille <i>et al.</i> , 2007
			patient in Mayotte, 2006	6.111	7	14	n.d.	84 (105/126)	n.d.	Vazeille <i>et al.</i> , 2007
			patient in Democratic Republic of Congo, 2000	6.117	7	14	n.d.	47 (56/119)	n.d.	Vazeille <i>et al.</i> , 2007
	not stated	colony	patient in Africa, not stated	not stated	8.6–9.2	14	100 (50/50)	n.d.	80 (40/50)	Mangiafico, 1971
<i>Aedes antipodeus</i>	North Auckland, New Zealand	1	patient in India	91064A	7.8	21**	100 (15/15)	73 (11/15)	0 (0/15)	Kramer <i>et al.</i> , 2011 [198]
<i>Aedes caspius</i>	France	0	patient in Reunion Island, 2005 (E1226V)	06.21	7	14	n.d.	25 (4/16)	n.d.	Vazeille <i>et al.</i> , 2008
<i>Aedes detritus</i>	France	0	patient in Reunion Island, 2005 (E1226V)	06.21	7	14	n.d.	67.3 (33/49)	n.d.	Vazeille <i>et al.</i> , 2008
<i>Aedes fulgens</i>	South Africa	1	not stated	H817	5.7	9–12	88 (29/33)	n.d.	10 (3/29)	Jupp <i>et al.</i> , 1981 [199]
<i>Aedes furcifer</i>	South Africa	colony or 1-4	not stated	H817	5.7–6.9	8–29	71 (192/271)	n.d.	30 (8/27)	Jupp <i>et al.</i> , 1981
<i>Aedes hensilli</i>	Micronesia	12-15	Mosquito in Comoros, 2005	COM 125	5.7	8	63 (20/32)	80 (16/20)	n.d.	Ledermann <i>et al.</i> , 2014 [200]
<i>Aedes notoscriptus</i>	Auckland, New Zealand	1	patient in India	91064A	10.5	14*	36 (8/32)	75 (6/8)	0 (0/8)	Kramer <i>et al.</i> , 2011
<i>Aedes polynesiensis</i>	Samoa	colony	patient in Calcutta, India, 1963	63-266	8	14	40 (4/10)	n.d.	n.d.	Shah <i>et al.</i> , 1964
<i>Aedes togoi</i>	not stated	colony	patient in Africa, not stated	not stated	8.6–9.2	14	97 (42/43)	n.d.	12 (5/43)	Mangiafico, 1971
<i>Aedes triseriatus</i>	not stated	colony	patient in Africa, not stated	not stated	8.6–9.2	14	100 (50/50)	n.d.	84 (42/50)	Mangiafico, 1971
<i>Aedes vexans</i>	Italy	0	patient in Reunion Island, 2005 (E1226V)	06.21	7	14	n.d.	8 (2/26)	n.d.	Talbalaghi <i>et al.</i> , 2010
	France		patient in Reunion Island, 2005 (E1226V)	06.21	7	14	n.d.	0 (0/13)	n.d.	Vazeille <i>et al.</i> , 2008
<i>Aedes vittatus</i>	Senegal	1	mosquitoes, bats or humans in Senegal, 1962, '79 and '05	ArD30237, CS13-288 or HD 180738	6	10	89 (41/46)	54 (22/41)	18 (4/22)	Diagne <i>et al.</i> , 2014 [201]
					6-7	10	19 (19/98)	37 (7/19)	43 (3/7)	Diagne <i>et al.</i> , 2014

Table 1. Cont.

Mosquito Species	Source	Generation Number	Source of CHIKV, Isolation Year	Strain Name	Bloodmeal Titer	Incubation Period (Days)	% Infected (n)	% Disseminated (n)	% Transmitted (n)	Reference
<i>Anopheles gambiae</i>	G3	colony	<i>Aedes furcifer</i> , Kadoug ou, Senegal, 1983	37997	8	14	0 (0/8)	0 (0/8)	n.d.	Vanlandingham <i>et al.</i> , 2005
<i>Anopheles maculipennis</i>	Italy	0	patient in Reunion Island, 2005 (E1226V)	06.21	7	14	n.d.	0 (0/10)	n.d.	Talbalaghi <i>et al.</i> , 2010
<i>Culex fatigans</i>	Philippines	colony	patient in Calcutta, India, 1963	63-266	8	14	0 (0/10)	n.d.	n.d.	Shah <i>et al.</i> , 1964
<i>Culex horridus</i>	South Africa	1	not stated	H817	4.6–5.4	14–25	6 (1/17)	n.d.	n.d.	Jupp <i>et al.</i> , 1981
<i>Culex pipiens</i>	Italy	0	patient in Reunion Island, 2005 (E1226V)	06.21	7	14	n.d.	0 (0/45)	n.d.	Talbalaghi <i>et al.</i> , 2010
	France		patient in Reunion Island, 2005 (E1226V)	06.21	7	14	n.d.	0 (0/11)	n.d.	Vazeille <i>et al.</i> , 2008
<i>Culex quinquefasciatus</i>	Zimbabwe	1	not stated	H817	5.3	20–22	0 (0/19)	n.d.	0 (0/19)	Jupp <i>et al.</i> , 1981
<i>Eretmapodites chrysogaster</i>	not stated	colony	patient in Africa, not stated	not stated	8.6–9.2	14	80 (40/50)	n.d.	36 (18/50)	Mangiafico, 1971
<i>Mansonia africana</i>	Mozambique	0	not stated	H817	4.7–5.2	8–15	34 (23/67)	n.d.	n.d.	Jupp <i>et al.</i> , 1981
<i>Opifex fuscus</i>	Wellington, New Zealand	1	patient in India	91064A	6.2	11*	98 (46/47)	100 (46/46)	100 (46/46)	Kramer <i>et al.</i> , 2011
<i>Ornithodoros savignyi</i>	South Africa	0	not stated	H817	6.6	50-61	0 (0/11)	n.d.	n.d.	Jupp <i>et al.</i> , 1981

6. Conclusions

Chikungunya virus has caused explosive outbreaks of severe, debilitating and often chronic arthralgia since it emerged in the 1950s and later in 2004 from the enzootic ECSA lineage in Africa. The large populations of susceptible humans in many naïve regions and thriving populations of the two urban vectors, *A. aegypti* and *A. albopictus*, will probably facilitate endemicity throughout most regions of the tropics and subtropics for the foreseeable future, although the burden of disease is typically difficult to estimate because CHIKV and DENV infections are difficult to distinguish clinically. Further adaptation of CHIKV to these urban vectors is also suggested by recent findings [13]. Future emergences from enzootic African cycles will also remain a risk that is increasing with more and more air travel and international commerce. Although novel strategies to control vector populations and reduce transmission are in early stages of field testing, the deployment of one of several highly promising human vaccines probably offers the best hope for making a major impact in restricting CHIKV circulation and preventing human disease [184].

Conflicts of Interest

The authors declare no conflict of interest.

References and Notes

1. Powers, A.M.; Logue, C.H. Changing patterns of chikungunya virus: Re-emergence of a zoonotic arbovirus. *J. Gen. Virol.* **2007**, *88*, 2363–2377.
2. Kuehn, B.M. Chikungunya virus transmission found in the United States: US health authorities brace for wider spread. *JAMA* **2014**, *312*, 776–777.
3. CDC. Chikungunya virus in the United States. Available online: <http://www.cdc.gov/chikungunya/geo/united-states.html> (accessed on 8 November 2014).
4. Jupp, P.G.; McIntosh, B.M. *Aedes furcifer* and other mosquitoes as vectors of chikungunya virus at Mica, Northeastern Transvaal, South Africa. *J. Am. Mosq. Control. Assoc.* **1990**, *6*, 415–420.
5. Volk, S.M.; Chen, R.; Tsetsarkin, K.A.; Adams, A.P.; Garcia, T.I.; Sall, A.A.; Nasar, F.; Schuh, A.J.; Holmes, E.C.; Higgs, S.; *et al.* Genome-scale phylogenetic analyses of chikungunya virus reveal independent emergences of recent epidemics and various evolutionary rates. *J. Virol.* **2010**, *84*, 6497–6504.
6. Tsetsarkin, K.A.; Chen, R.; Sherman, M.B.; Weaver, S.C. Chikungunya virus: Evolution and genetic determinants of emergence. *Curr. Opin. Virol.* **2011**, *1*, 310–317.
7. Kariuki Njenga, M.; Nderitu, L.; Ledermann, J.P.; Ndirangu, A.; Logue, C.H.; Kelly, C.H.; Sang, R.; Sergon, K.; Breiman, R.; Powers, A.M. Tracking epidemic chikungunya virus into the Indian Ocean from East Africa. *J. Gen. Virol.* **2008**, *89*, 2754–2760.
8. Schuffenecker, I.; Itean, I.; Michault, A.; Murri, S.; Frangeul, L.; Vaney, M.C.; Lavenir, R.; Pardigon, N.; Reynes, J.M.; Pettinelli, F.; *et al.* Genome microevolution of chikungunya viruses causing the Indian Ocean outbreak. *PLoS Med.* **2006**, *3*, e263.
9. Tsetsarkin, K.A.; Vanlandingham, D.L.; McGee, C.E.; Higgs, S. A single mutation in chikungunya virus affects vector specificity and epidemic potential. *PLoS Pathog.* **2007**, *3*, e201.

10. Vazeille, M.; Moutailler, S.; Coudrier, D.; Rousseaux, C.; Khun, H.; Huerre, M.; Thiria, J.; Dehecq, J.S.; Fontenille, D.; Schuffenecker, I.; *et al.* Two chikungunya isolates from the outbreak of La Reunion (Indian Ocean) exhibit different patterns of infection in the mosquito, *Aedes albopictus*. *PLoS One* **2007**, *2*, e1168.
11. Tsetsarkin, K.A.; McGee, C.E.; Volk, S.M.; Vanlandingham, D.L.; Weaver, S.C.; Higgs, S. Epistatic roles of E2 glycoprotein mutations in adaption of chikungunya virus to *Aedes albopictus* and *Ae. aegypti* mosquitoes. *PLoS One* **2009**, *4*, e6835.
12. Arias-Goeta, C.; Mousson, L.; Rougeon, F.; Failloux, A.B. Dissemination and transmission of the E1–226V variant of chikungunya virus in *Aedes albopictus* are controlled at the midgut barrier level. *PLoS One* **2013**, *8*, e57548.
13. Tsetsarkin, K.A.; Chen, R.; Yun, R.; Rossi, S.L.; Plante, K.S.; Guerbois, M.; Forrester, N.; Perng, G.C.; Sreekumar, E.; Leal, G.; *et al.* Multi-peaked adaptive landscape for chikungunya virus evolution predicts continued fitness optimization in *Aedes albopictus* mosquitoes. *Nat. Commun.* **2014**, *5*, 4084.
14. Ratsitorahina, M.; Harisoa, J.; Ratovonjato, J.; Biacabe, S.; Reynes, J.M.; Zeller, H.; Raelina, Y.; Talarmin, A.; Richard, V.; Louis Soares, J. Outbreak of dengue and chikungunya fevers, toamasina, Madagascar, 2006. *Emerg. Infect. Dis.* **2008**, *14*, 1135–1137.
15. De Lamballerie, X.; Leroy, E.; Charrel, R.N.; Tsetsarkin, K.; Higgs, S.; Gould, E.A. Chikungunya virus adapts to tiger mosquito via evolutionary convergence: A sign of things to come? *Viol. J.* **2008**, *5*, 33.
16. Bagny, L.; Delatte, H.; Quilici, S.; Fontenille, D. Progressive decrease in *Aedes aegypti* distribution in reunion island since the 1900s. *J. Med. Entomol.* **2009**, *46*, 1541–1545.
17. Kumar, N.P.; Joseph, R.; Kamaraj, T.; Jambulingam, P. A226V mutation in virus during the 2007 chikungunya outbreak in Kerala, India. *J. Gen. Virol.* **2008**, *89*, 1945–1948.
18. Yergolkar, P.N.; Tandale, B.V.; Arankalle, V.A.; Sathe, P.S.; Sudeep, A.B.; Gandhe, S.S.; Gokhle, M.D.; Jacob, G.P.; Hundekar, S.L.; Mishra, A.C. Chikungunya outbreaks caused by African genotype, India. *Emerg. Infect. Dis.* **2006**, *12*, 1580–1583.
19. Kularatne, S.A.; Gihan, M.C.; Weerasinghe, S.C.; Gunasena, S. Concurrent outbreaks of chikungunya and dengue fever in Kandy, Sri Lanka, 2006–07: A comparative analysis of clinical and laboratory features. *Postgrad. Med. J.* **2009**, *85*, 342–346.
20. Peyrefitte, C.N.; Rousset, D.; Pastorino, B.A.; Pouillot, R.; Bessaud, M.; Tock, F.; Mansaray, H.; Merle, O.L.; Pascual, A.M.; Paupy, C.; *et al.* Chikungunya virus, Cameroon, 2006. *Emerg. Infect. Dis.* **2007**, *13*, 768–771.
21. Peyrefitte, C.N.; Bessaud, M.; Pastorino, B.A.; Gravier, P.; Plumet, S.; Merle, O.L.; Moltini, I.; Coppin, E.; Tock, F.; Daries, W.; *et al.* Circulation of chikungunya virus in Gabon, 2006–2007. *J. Med. Virol.* **2008**, *80*, 430–433.
22. Paupy, C.; Kassa Kassa, F.; Caron, M.; Nkoghe, D.; Leroy, E.M. A chikungunya outbreak associated with the vector *Aedes albopictus* in remote villages of Gabon. *Vector Borne Zoonotic Dis.* **2012**, *12*, 167–169.
23. Mombouli, J.V.; Bitsindou, P.; Elion, D.O.; Grolla, A.; Feldmann, H.; Niama, F.R.; Parra, H.J.; Munster, V.J. Chikungunya virus infection, Brazzaville, Republic of Congo, 2011. *Emerg. Infect. Dis.* **2013**, *19*, 1542–1543.

24. Rezza, G.; Nicoletti, L.; Angelini, R.; Romi, R.; Finarelli, A.C.; Panning, M.; Cordioli, P.; Fortuna, C.; Boros, S.; Magurano, F.; *et al.* Infection with chikungunya virus in Italy: An outbreak in a temperate region. *Lancet* **2007**, *370*, 1840–1846.
25. Sam, I.C.; Chan, Y.F.; Chan, S.Y.; Loong, S.K.; Chin, H.K.; Hooi, P.S.; Ganeswrie, R.; Abubakar, S. Chikungunya virus of Asian and Central/East African genotypes in Malaysia. *J. Clin. Virol.* **2009**, *46*, 180–183.
26. Ng, L.C.; Tan, L.K.; Tan, C.H.; Tan, S.S.; Hapuarachchi, H.C.; Pok, K.Y.; Lai, Y.L.; Lam-Phua, S.G.; Bucht, G.; Lin, R.T., *et al.* Entomologic and virologic investigation of chikungunya, Singapore. *Emerg. Infect. Dis.* **2009**, *15*, 1243–1249.
27. Theamboonlers, A.; Rianthavorn, P.; Praianantathavorn, K.; Wuttirattanakowit, N.; Poovorawan, Y. Clinical and molecular characterization of chikungunya virus in South Thailand. *Jpn. J. Infect. Dis.* **2009**, *62*, 303–305.
28. Wu, D.; Wu, J.; Zhang, Q.; Zhong, H.; Ke, C.; Deng, X.; Guan, D.; Li, H.; Zhang, Y.; Zhou, H.; *et al.* Chikungunya outbreak in Guangdong Province, China, 2010. *Emerg. Infect. Dis.* **2012**, *18*, 493–495.
29. Duong, V.; Andries, A.C.; Ngan, C.; Sok, T.; Richner, B.; Asgari-Jirhandeh, N.; Bjorge, S.; Huy, R.; Ly, S.; Laurent, D.; *et al.* Reemergence of chikungunya virus in Cambodia. *Emerg. Infect. Dis.* **2012**, *18*, 2066–2069.
30. Wangchuk, S.; Chinnawirotpisan, P.; Dorji, T.; Tobgay, T.; Dorji, T.; Yoon, I.K.; Fernandez, S. Chikungunya fever outbreak, Bhutan, 2012. *Emerg. Infect. Dis.* **2013**, *19*, 1681–1684.
31. Hapuarachchi, H.C.; Bandara, K.B.; Sumanadasa, S.D.; Hapugoda, M.D.; Lai, Y.L.; Lee, K.S.; Tan, L.K.; Lin, R.T.; Ng, L.F.; Bucht, G.; *et al.* Re-emergence of chikungunya virus in south-east Asia: Virological evidence from Sri Lanka and Singapore. *J. Gen. Virol.* **2010**, *91*, 1067–1076.
32. Rianthavorn, P.; Prianantathavorn, K.; Wuttirattanakowit, N.; Theamboonlers, A.; Poovorawan, Y. An outbreak of chikungunya in Southern Thailand from 2008 to 2009 caused by African strains with A226V mutation. *Int. J. Infect. Dis.* **2010**, *14*, e161–e165.
33. Gould, E.A.; Gallian, P.; De Lamballerie, X.; Charrel, R.N. First cases of autochthonous dengue fever and chikungunya fever in France: From bad dream to reality! *Clin. Microbiol. Infect.* **2010**, *16*, 1702–1704.
34. Grandadam, M.; Caro, V.; Plumet, S.; Thiberge, J.M.; Souares, Y.; Failloux, A.B.; Tolou, H.J.; Budelot, M.; Cosserat, D.; Leparç-Goffart, I.; *et al.* Chikungunya virus, Southeastern France. *Emerg. Infect. Dis.* **2011**, *17*, 910–913.
35. Delaunay, P.; Jeannin, C.; Schaffner, F.; Marty, P. News on the presence of the tiger mosquito *Aedes albopictus* in metropolitan France. *Arch. Pediatr.* **2009**, *16*, S66–S71.
36. Vega-Rua, A.; Zouache, K.; Caro, V.; Diancourt, L.; Delaunay, P.; Grandadam, M.; Failloux, A.B. High efficiency of temperate *Aedes albopictus* to transmit chikungunya and dengue viruses in the Southeast of France. *PLoS One* **2013**, *8*, e59716.
37. Paty, M.; Six, C.; Charlet, F.; Heuze, G.; Cochet, A.; Wiegandt, A.; Chappert, J.; Dejour-Salamanca, D.; Guinard, A.; Soler, P.; *et al.* Large number of imported chikungunya cases in mainland France, 2014: A challenge for surveillance and response. *Euro Surveill.* **2014**, *19*, 20856.
38. Tomasello, D.; Schlagenhauf, P. Chikungunya and dengue autochthonous cases in Europe, 2007–2012. *Travel Med. Infect. Dis.* **2013**, *11*, 274–284.

39. Napoli, C.; Salcuni, P.; Pompa, M.G.; Declich, S.; Rizzo, C. Estimated imported infections of chikungunya and dengue in Italy, 2008 to 2011. *J. Travel Med.* **2012**, *19*, 294–297.
40. Leparc-Goffart, I.; Nougairede, A.; Cassadou, S.; Prat, C.; de Lamballerie, X. Chikungunya in the Americas. *Lancet* **2014**, *383*, 514.
41. Dupont-Rouzeyrol, M.; Caro, V.; Guillaumot, L.; Vazeille, M.; D’Ortenzio, E.; Thiberge, J.M.; Baroux, N.; Gourinat, A.C.; Grandadam, M.; Failloux, A.B. Chikungunya virus and the mosquito vector *Aedes aegypti* in New Caledonia (South Pacific region). *Vector borne and Zoonotic Dis.* **2012**, *12*, 1036–1041.
42. Weaver, S.C. Arrival of chikungunya virus in the new world: Prospects for spread and impact on public health. *PLoS Negl. Trop. Dis.* **2014**, *8*, e2921.
43. Vega-Rua, A.; Zouache, K.; Girod, R.; Failloux, A.B.; Lourenco-de-Oliveira, R. High level of vector competence of *Aedes aegypti* and *Aedes albopictus* from ten American countries as a crucial factor in the spread of chikungunya virus. *J. Virol.* **2014**, *88*, 6294–6306.
44. ARBONet. *Chikungunya Virus Disease—United States, 2014 Provisional Data Reported to Arbonet*; Centers for Disease Control Arboviral Diseases Branch: Fort Collins, CO, USA, 2014.
45. Weinbren, M.P.; Haddow, A.J.; Williams, M.C. The occurrence of chikungunya virus in Uganda. I. Isolation from mosquitoes. *Trans. R. Soc. Trop. Med. Hygiene* **1958**, *52*, 253–257.
46. McCarthy, M.C.; Haberberger, R.L.; Salib, A.W.; Soliman, B.A.; El-Tigani, A.; Khalid, I.O.; Watts, D.M. Evaluation of arthropod-borne viruses and other infectious disease pathogens as the causes of febrile illnesses in the Khartoum Province of Sudan. *J. Med. Virol.* **1996**, *48*, 141–146.
47. Diallo, M.; Thonnon, J.; Traore-Lamizana, M.; Fontenille, D. Vectors of chikungunya virus in Senegal: Current data and transmission cycles. *The American journal of tropical medicine and hygiene* **1999**, *60*, 281–286.
48. Jupp, P.G.; Kemp, A. What is the potential for future outbreaks of chikungunya, dengue and yellow fever in Southern Africa? *South. Afr. Med. J.* **1996**, *86*, 35–37.
49. Gubler, D.J. Epidemic dengue/dengue hemorrhagic fever as a public health, social and economic problem in the 21st century. *Trends Microbiol.* **2002**, *10*, 100–103.
50. McClelland, G.A.H. A worldwide survey of variation in scale pattern of the abdominal tergum of *Aedes aegypti* (L.) (diptera: Culicidae). *Trans. R. Entomol. Soc. Lond.* **1974**, *126*, 239–259.
51. Tabachnick, W.J.; Powell, J.R. A world-wide survey of genetic variation in the yellow fever mosquito, *Aedes Aegypti*. *Genet. Res.* **1979**, *34*, 215–229.
52. Failloux, A.B.; Vazeille, M.; Rodhain, F. Geographic genetic variation in populations of the dengue virus vector *Aedes aegypti*. *J. Mol. Evolut.* **2002**, *55*, 653–663.
53. Powell, J.R.; Tabachnick, W.J. History of domestication and spread of *Aedes aegypti*—A review. *Memorias do Instituto Oswaldo Cruz* **2013**, *108*, 11–17.
54. Juliano, S.A.; Lounibos, L.P.; O’Meara, G.F. A field test for competitive effects of *Aedes albopictus* on *Aedes aegypti* in South Florida: Differences between sites of coexistence and exclusion? *Oecologia* **2004**, *139*, 583–593.
55. Braks, M.A.; Honorio, N.A.; Lourencqo-De-Oliveira, R.; Juliano, S.A.; Lounibos, L.P. Convergent habitat segregation of *Aedes aegypti* and *Aedes albopictus* (diptera: Culicidae) in Southeastern Brazil and Florida. *J. Med. Entomol.* **2003**, *40*, 785–794.

56. Simard, F.; Nchoutpouen, E.; Toto, J.C.; Fontenille, D. Geographic distribution and breeding site preference of *Aedes albopictus* and *Aedes aegypti* (diptera: Culicidae) in Cameroon, Central Africa. *J. Med. Entomol.* **2005**, *42*, 726–731.
57. Smith, C.E. The history of dengue in tropical Asia and its probable relationship to the mosquito *Aedes aegypti*. *J. Trop. Med. Hygiene* **1956**, *59*, 243–251.
58. Medlock, J.M.; Hansford, K.M.; Schaffner, F.; Versteirt, V.; Hendrickx, G.; Zeller, H.; Van Bortel, W. A review of the invasive mosquitoes in Europe: Ecology, public health risks, and control options. *Vector borne Zoonotic Dis.* **2012**, *12*, 435–447.
59. Lounibos, L.P. Invasions by insect vectors of human disease. *Annu. Rev. Entomol.* **2002**, *47*, 233–266.
60. Rai, K.S. *Aedes albopictus* in the Americas. *Annu. Rev. Entomol.* **1991**, *36*, 459–484.
61. Hawley, W.A.; Reiter, P.; Copeland, R.S.; Pumpuni, C.B.; Craig, G.B., Jr. *Aedes albopictus* in North America: Probable introduction in used tires from Northern Asia. *Science* **1987**, *236*, 1114–1116.
62. Sprenger, D.; Wuithiranyagool, T. The discovery and distribution of *Aedes albopictus* in Harris County, Texas. *J. Am. Mosq. Control Assoc.* **1986**, *2*, 217–219.
63. Adhami, J.; Reiter, P. Introduction and establishment of *Aedes (Stegomyia) albopictus skuse* (diptera: Culicidae) in Albania. *J. Am. Mosq. Control Assoc.* **1998**, *14*, 340–343.
64. Sabatini, A.; Raineri, V.; Trovato, G.; Coluzzi, M. *Aedes albopictus* in Italy and possible diffusion of the species into the Mediterranean area. *Parassitologia* **1990**, *32*, 301–304.
65. Hawley, W.A. The biology of *Aedes albopictus*. *J. Am. Mosq. Control Association. Suppl.* **1988**, *1*, 1–39.
66. Paupy, C.; Delatte, H.; Bagny, L.; Corbel, V.; Fontenille, D. *Aedes albopictus*, an arbovirus vector: From the darkness to the light. *Microbes Infect.* **2009**, *11*, 1177–1185.
67. Metselaar, D.; Grainger, C.R.; Oei, K.G.; Reynolds, D.G.; Pudney, M.; Leake, C.J.; Tukei, P.M.; D’Offay, R.M.; Simpson, D.I. An outbreak of type 2 dengue fever in the Seychelles, probably transmitted by *Aedes albopictus (skuse)*. *Bull. World Health Organ.* **1980**, *58*, 937–943.
68. Delatte, H.; Dehecq, J.S.; Thiria, J.; Domerg, C.; Paupy, C.; Fontenille, D. Geographic distribution and developmental sites of *Aedes albopictus* (diptera: Culicidae) during a chikungunya epidemic event. *Vector Borne Zoonotic Dis.* **2008**, *8*, 25–34.
69. Gjenero-Margan, I.; Aleraj, B.; Krajcar, D.; Lesnikar, V.; Klobucar, A.; Pem-Novosel, I.; Kurecic-Filipovic, S.; Komparak, S.; Martic, R.; Duricic, S.; *et al.* Autochthonous dengue fever in Croatia, August–September 2010. *Euro Surveill.* **2011**, *16*, 9.
70. La Ruche, G.; Souares, Y.; Armengaud, A.; Peloux-Petiot, F.; Delaunay, P.; Despres, P.; Lenglet, A.; Jourdain, F.; Leparac-Goffart, I.; Charlet, F.; *et al.* First two autochthonous dengue virus infections in metropolitan France, September 2010. *Euro Surveill.* **2010**, *15*, 19676.
71. Juliano, S.A.; O’Meara, G.F.; Morrill, J.R.; Cutwa, M.M. Desiccation and thermal tolerance of eggs and the coexistence of competing mosquitoes. *Oecologia* **2002**, *130*, 458–469.
72. O’Meara, G.F.; Evans, L.F., Jr.; Gettman, A.D.; Cuda, J.P. Spread of *Aedes albopictus* and decline of *Ae. aegypti* (diptera: Culicidae) in Florida. *J. Med. Entomol.* **1995**, *32*, 554–562.
73. Juliano, S.A.; Lounibos, L.P. Ecology of invasive mosquitoes: Effects on resident species and on human health. *Ecol. Lett.* **2005**, *8*, 558–574.
74. Kamgang, B.; Brengues, C.; Fontenille, D.; Njiokou, F.; Simard, F.; Paupy, C. Genetic structure of the tiger mosquito, *Aedes albopictus*, in Cameroon (Central Africa). *PLoS One* **2011**, *6*, e20257.

75. Kamgang, B.; Ngoagouni, C.; Manirakiza, A.; Nakoune, E.; Paupy, C.; Kazanji, M. Temporal patterns of abundance of *Aedes aegypti* and *Aedes albopictus* (diptera: Culicidae) and mitochondrial DNA analysis of *Ae. albopictus* in the Central African Republic. *PLoS Negl. Trop. Dis.* **2013**, *7*, e2590.
76. Raharimalala, F.N.; Ravaomanarivo, L.H.; Ravelonandro, P.; Rafaraso, L.S.; Zouache, K.; Tran-Van, V.; Mousson, L.; Failloux, A.B.; Hellard, E.; Moro, C.V.; *et al.* Biogeography of the two major arbovirus mosquito vectors, *Aedes aegypti* and *Aedes albopictus* (diptera, culicidae), in Madagascar. *Parasites Vectors* **2012**, *5*, 56.
77. Reiter, P.; Sprenger, D. The used tire trade: A mechanism for the worldwide dispersal of container breeding mosquitoes. *J. Am. Mosq. Control Assoc.* **1987**, *3*, 494–501.
78. Nene, V.; Wortman, J.R.; Lawson, D.; Haas, B.; Kodira, C.; Tu, Z.J.; Loftus, B.; Xi, Z.; Megy, K.; Grabherr, M.; *et al.* Genome sequence of *Aedes aegypti*, a major arbovirus vector. *Science* **2007**, *316*, 1718–1723.
79. Bonizzoni, M.; Gasperi, G.; Chen, X.; James, A.A. The invasive mosquito species *Aedes albopictus*: Current knowledge and future perspectives. *Trends Parasitol.* **2013**, *29*, 460–468.
80. Urdaneta-Marquez, L.; Failloux, A.B. Population genetic structure of *Aedes aegypti*, the principal vector of dengue viruses. *Infect. Genetics Evol.* **2011**, *11*, 253–261.
81. Birungi, J.; Munstermann, L.E. Genetic structure of *Aedes albopictus* (diptera: Culicidae) populations based on mitochondrial nd5 sequences: Evidence for an independent invasion into Brazil and United States. *Ann. Entomol. Soc. Am.* **2002**, *95*, 125–132.
82. Maia, R.T.; Scarpassa, V.M.; Maciel-Litaiff, L.H.; Tadei, W.P. Reduced levels of genetic variation in *Aedes albopictus* (diptera: Culicidae) from Manaus, Amazonas State, Brazil, based on analysis of the mitochondrial DNA nd5 gene. *Genetics Mol. Res.* **2009**, *8*, 998–1007.
83. Mousson, L.; Dauga, C.; Garrigues, T.; Schaffner, F.; Vazeille, M.; Failloux, A.B. Phylogeography of *Aedes (stegomyia) aegypti* (l.) and *Aedes (stegomyia) albopictus* (skuse) (diptera: Culicidae) based on mitochondrial DNA variations. *Genet. Res.* **2005**, *86*, 1–11.
84. Usmani-Brown, S.; Cohnstaedt, L.; Munstermann, L.E. Population genetics of *Aedes albopictus* (diptera: Culicidae) invading populations, using mitochondrial nicotinamide adenine dinucleotide dehydrogenase subunit 5 sequences. *Ann. Entomol. Soc. Am.* **2009**, *102*, 144–150.
85. Gillespie, R.G.; Roderick, G.K. Arthropods on islands: Colonization, speciation, and conservation. *Annu. Rev. Entomol.* **2002**, *47*, 595–632.
86. Beebe, N.W.; Ambrose, L.; Hill, L.A.; Davis, J.B.; Hapgood, G.; Cooper, R.D.; Russell, R.C.; Ritchie, S.A.; Reimer, L.J.; Lobo, N.F.; *et al.* Tracing the tiger: Population genetics provides valuable insights into the *Aedes (stegomyia) albopictus* invasion of the Australasian region. *PLoS Negl. Trop. Dis.* **2013**, *7*, e2361.
87. Fontenille, D.; Rodhain, F. Biology and distribution of *Aedes albopictus* and *Aedes aegypti* in Madagascar. *J. Am. Mosq. Control Assoc.* **1989**, *5*, 219–225.
88. Bagny, L.; Arnoux, S.; Delatte, H.; Lajoie, G.; Fontenille, D. Spread of invasive *Aedes albopictus* and decline of resident *Aedes aegypti* in urban areas of Mayotte 2007–2010. *Biol. Invasions* **2012**, *14*, 1623–1633.
89. Diallo, M.; Laganier, R.; Nangouma, A. First record of *Ae. albopictus* (skuse 1894), in Central African Republic. *Trop. Med. Int. Health* **2010**, *15*, 1185–1189.

90. Fontenille, D.; Toto, J.C. *Aedes (stegomyia) albopictus (skuse)*, a potential new dengue vector in Southern Cameroon. *Emerg. Infect. Dis.* **2001**, *7*, 1066–1067.
91. Agarwal, A.; Dash, P.K.; Singh, A.K.; Sharma, S.; Gopalan, N.; Rao, P.V.; Parida, M.M.; Reiter, P. Evidence of experimental vertical transmission of emerging novel ECSA genotype of chikungunya virus in *Aedes aegypti*. *PLoS Negl. Trop. Dis.* **2014**, *8*, e2990.
92. Thiberville, S.D.; Boisson, V.; Gaudart, J.; Simon, F.; Flahault, A.; de Lamballerie, X. Chikungunya fever: A clinical and virological investigation of outpatients on Reunion Island, South-West Indian Ocean. *PLoS Negl. Trop. Dis.* **2013**, *7*, e2004.
93. Pesko, K.; Westbrook, C.J.; Mores, C.N.; Lounibos, L.P.; Reiskind, M.H. Effects of infectious virus dose and bloodmeal delivery method on susceptibility of *Aedes aegypti* and *Aedes albopictus* to chikungunya virus. *J. Med. Entomol.* **2009**, *46*, 395–399.
94. Martin, E.; Moutailler, S.; Madec, Y.; Failloux, A.B. Differential responses of the mosquito *Aedes albopictus* from the Indian Ocean region to two chikungunya isolates. *BMC Ecol.* **2010**, *10*, 8.
95. Sanchez-Vargas, I.; Travanty, E.A.; Keene, K.M.; Franz, A.W.; Beaty, B.J.; Blair, C.D.; Olson, K.E. RNA interference, arthropod-borne viruses, and mosquitoes. *Virus Res.* **2004**, *102*, 65–74.
96. Xi, Z.; Ramirez, J.L.; Dimopoulos, G. The *Aedes aegypti* toll pathway controls dengue virus infection. *PLoS Pathog.* **2008**, *4*, e1000098.
97. Ramirez, J.L.; Dimopoulos, G. The toll immune signaling pathway control conserved anti-dengue defenses across diverse *Ae. aegypti* strains and against multiple dengue virus serotypes. *Dev. Compar. Immunol.* **2010**, *34*, 625–629.
98. Souza-Neto, J.A.; Sim, S.; Dimopoulos, G. An evolutionary conserved function of the jak-stat pathway in anti-dengue defense. *Proc. Natl. Acad. Sci. USA* **2009**, *106*, 17841–17846.
99. Sanders, H.R.; Foy, B.D.; Evans, A.M.; Ross, L.S.; Beaty, B.J.; Olson, K.E.; Gill, S.S. Sindbis virus induces transport processes and alters expression of innate immunity pathway genes in the midgut of the disease vector, *Aedes aegypti*. *Insect Biochem. Mol. Biol.* **2005**, *35*, 1293–1307.
100. Sanchez-Vargas, I.; Scott, J.C.; Poole-Smith, B.K.; Franz, A.W.; Barbosa-Solomieu, V.; Wilusz, J.; Olson, K.E.; Blair, C.D. Dengue virus type 2 infections of *Aedes aegypti* are modulated by the mosquito's RNA interference pathway. *PLoS Pathog.* **2009**, *5*, e1000299.
101. Keene, K.M.; Foy, B.D.; Sanchez-Vargas, I.; Beaty, B.J.; Blair, C.D.; Olson, K.E. RNA interference acts as a natural antiviral response to o'nyong-nyong virus (alphavirus; *Togaviridae*) infection of *Anopheles gambiae*. *Proc. Natl. Acad. Sci. USA* **2004**, *101*, 17240–17245.
102. Campbell, C.L.; Keene, K.M.; Brackney, D.E.; Olson, K.E.; Blair, C.D.; Wilusz, J.; Foy, B.D. *Aedes aegypti* uses RNA interference in defense against sindbis virus infection. *BMC Microbiol.* **2008**, *8*, 47.
103. Myles, K.M.; Wiley, M.R.; Morazzani, E.M.; Adelman, Z.N. Alphavirus-derived small RNAs modulate pathogenesis in disease vector mosquitoes. *Proc. Natl. Acad. Sci. USA* **2008**, *105*, 19938–19943.
104. Cirimotich, C.M.; Scott, J.C.; Phillips, A.T.; Geiss, B.J.; Olson, K.E. Suppression of RNA interference increases alphavirus replication and virus-associated mortality in *Aedes aegypti* mosquitoes. *BMC Microbiol.* **2009**, *9*, 49.

105. Khoo, C.C.; Piper, J.; Sanchez-Vargas, I.; Olson, K.E.; Franz, A.W. The RNA interference pathway affects midgut infection- and escape barriers for sindbis virus in *Aedes aegypti*. *BMC Microbiol.* **2010**, *10*, 130.
106. Donald, C.L.; Kohl, A.; Schnettler, E. New insights into control of arbovirus replication and spread by insect RNA interference pathways. *Insects* **2012**, *3*, 511–531.
107. McFarlane, M.; Arias-Goeta, C.; Martin, E.; O’Hara, Z.; Lulla, A.; Mousson, L.; Rainey, S.M.; Misbah, S.; Schnettler, E.; Donald, C.L.; *et al.* Characterization of *Aedes aegypti* innate-immune pathways that limit chikungunya virus replication. *PLoS Negl. Trop. Dis.* **2014**, *8*, e2994.
108. Schnettler, E.; Donald, C.L.; Human, S.; Watson, M.; Siu, R.W.; McFarlane, M.; Fazakerley, J.K.; Kohl, A.; Frangkoudis, R. Knockdown of piRNA pathway proteins results in enhanced semliki forest virus production in mosquito cells. *J. Gen. Virol.* **2013**, *94*, 1680–1689.
109. McGraw, E.A.; O’Neill, S.L. Beyond insecticides: New thinking on an ancient problem. *Nat. Rev. Microbiol.* **2013**, *11*, 181–193.
110. Franz, A.W.; Sanchez-Vargas, I.; Adelman, Z.N.; Blair, C.D.; Beaty, B.J.; James, A.A.; Olson, K.E. Engineering RNA interference-based resistance to dengue virus type 2 in genetically modified *Aedes aegypti*. *Proc. Natl. Acad. Sci. USA* **2006**, *103*, 4198–4203.
111. Mathur, G.; Sanchez-Vargas, I.; Alvarez, D.; Olson, K.E.; Marinotti, O.; James, A.A. Transgene-mediated suppression of dengue viruses in the salivary glands of the yellow fever mosquito, *Aedes aegypti*. *Insect Mol. Biol.* **2010**, *19*, 753–763.
112. Travanty, E.A.; Adelman, Z.N.; Franz, A.W.; Keene, K.M.; Beaty, B.J.; Blair, C.D.; James, A.A.; Olson, K.E. Using RNA interference to develop dengue virus resistance in genetically modified *Aedes aegypti*. *Insect Biochem. Mol. Biol.* **2004**, *34*, 607–613.
113. Alphey, L.; McKemey, A.; Nimmo, D.; Neira Oviedo, M.; Lacroix, R.; Matzen, K.; Beech, C. Genetic control of *Aedes* mosquitoes. *Pathog. Glob. Health* **2013**, *107*, 170–179.
114. Alphey, L. Natural and engineered mosquito immunity. *J. Biol.* **2009**, *8*, 40.
115. Fraser, M.J., Jr. Insect transgenesis: Current applications and future prospects. *Annu. Rev. Entomol.* **2012**, *57*, 267–289.
116. Walker, T.; Johnson, P.H.; Moreira, L.A.; Iturbe-Ormaetxe, I.; Frentiu, F.D.; McMeniman, C.J.; Leong, Y.S.; Dong, Y.; Axford, J.; Kriesner, P.; *et al.* The wMel wolbachia strain blocks dengue and invades caged *Aedes aegypti* populations. *Nature* **2011**, *476*, 450–453.
117. Sinkins, S.P.; Gould, F. Gene drive systems for insect disease vectors. *Nat. Rev. Genet.* **2006**, *7*, 427–435.
118. Chen, C.H.; Huang, H.; Ward, C.M.; Su, J.T.; Schaeffer, L.V.; Guo, M.; Hay, B.A. A synthetic maternal-effect selfish genetic element drives population replacement in *Drosophila*. *Science* **2007**, *316*, 597–600.
119. McMeniman, C.J.; Lane, R.V.; Cass, B.N.; Fong, A.W.; Sidhu, M.; Wang, Y.F.; O’Neill, S.L. Stable introduction of a life-shortening wolbachia infection into the mosquito *Aedes aegypti*. *Science* **2009**, *323*, 141–144.
120. Hedges, L.M.; Brownlie, J.C.; O’Neill, S.L.; Johnson, K.N. Wolbachia and virus protection in insects. *Science* **2008**, *322*, 702.

121. Moreira, L.A.; Iturbe-Ormaetxe, I.; Jeffery, J.A.; Lu, G.; Pyke, A.T.; Hedges, L.M.; Rocha, B.C.; Hall-Mendelin, S.; Day, A.; Riegler, M.; *et al.* A wolbachia symbiont in *Aedes aegypti* limits infection with dengue, chikungunya, and plasmodium. *Cell* **2009**, *139*, 1268–1278.
122. Hancock, P.A.; Sinkins, S.P.; Godfray, H.C. Strategies for introducing wolbachia to reduce transmission of mosquito-borne diseases. *PLoS Negl. Trop. Dis.* **2011**, *5*, e1024.
123. Zouache, K.; Voronin, D.; Tran-Van, V.; Mousson, L.; Failloux, A.B.; Mavingui, P. Persistent wolbachia and cultivable bacteria infection in the reproductive and somatic tissues of the mosquito vector *Aedes albopictus*. *PLoS One* **2009**, *4*, e6388.
124. Mousson, L.; Martin, E.; Zouache, K.; Madec, Y.; Mavingui, P.; Failloux, A.B. Wolbachia modulates chikungunya replication in *Aedes albopictus*. *Mol. Ecol.* **2010**, *19*, 1953–1964.
125. Mousson, L.; Zouache, K.; Arias-Goeta, C.; Raquin, V.; Mavingui, P.; Failloux, A.B. The native wolbachia symbionts limit transmission of dengue virus in *Aedes albopictus*. *PLoS Negl. Trop. Dis.* **2012**, *6*, e1989.
126. Lu, P.; Bian, G.; Pan, X.; Xi, Z. Wolbachia induces density-dependent inhibition to dengue virus in mosquito cells. *PLoS Negl. Trop. Dis.* **2012**, *6*, e1754.
127. Blagrove, M.S.; Arias-Goeta, C.; Di Genua, C.; Failloux, A.B.; Sinkins, S.P. A wolbachia wMel transinfection in *Aedes albopictus* is not detrimental to host fitness and inhibits chikungunya virus. *PLoS Negl. Trop. Dis.* **2013**, *7*, e2152.
128. van den Hurk, A.F.; Hall-Mendelin, S.; Pyke, A.T.; Frentiu, F.D.; McElroy, K.; Day, A.; Higgs, S.; O’Neill, S.L. Impact of wolbachia on infection with chikungunya and yellow fever viruses in the mosquito vector *Aedes aegypti*. *PLoS Negl. Trop. Dis.* **2012**, *6*, e1892.
129. Rances, E.; Ye, Y.H.; Woolfit, M.; McGraw, E.A.; O’Neill, S.L. The relative importance of innate immune priming in wolbachia-mediated dengue interference. *PLoS Pathog.* **2012**, *8*, e1002548.
130. Pan, X.; Zhou, G.; Wu, J.; Bian, G.; Lu, P.; Raikhel, A.S.; Xi, Z. Wolbachia induces reactive oxygen species (ros)-dependent activation of the toll pathway to control dengue virus in the mosquito *Aedes aegypti*. *Proc. Natl. Acad. Sci. USA* **2012**, *109*, E23–E31.
131. Caragata, E.P.; Rances, E.; Hedges, L.M.; Gofton, A.W.; Johnson, K.N.; O’Neill, S.L.; McGraw, E.A. Dietary cholesterol modulates pathogen blocking by wolbachia. *PLoS Pathog.* **2013**, *9*, e1003459.
132. Zouache, K.; Raharimalala, F.N.; Raquin, V.; Tran-Van, V.; Raveloson, L.H.; Ravelonandro, P.; Mavingui, P. Bacterial diversity of field-caught mosquitoes, *Aedes albopictus* and *Aedes aegypti*, from different geographic regions of Madagascar. *FEMS Microbiol. Ecol.* **2011**, *75*, 377–389.
133. Minard, G.; Tran, F.H.; Raharimalala, F.N.; Hellard, E.; Ravelonandro, P.; Mavingui, P.; Valiente Moro, C. Prevalence, genomic and metabolic profiles of acinetobacter and asaia associated with field-caught *Aedes albopictus* from Madagascar. *FEMS Microbiol. Ecol.* **2013**, *83*, 63–73.
134. Ramirez, J.L.; Souza-Neto, J.; Torres Cosme, R.; Rovira, J.; Ortiz, A.; Pascale, J.M.; Dimopoulos, G. Reciprocal tripartite interactions between the *Aedes aegypti* midgut microbiota, innate immune system and dengue virus influences vector competence. *PLoS Negl. Trop. Dis.* **2012**, *6*, e1561.
135. Apte-Deshpande, A.D.; Paingankar, M.S.; Gokhale, M.D.; Deobagkar, D.N. *Serratia odorifera* mediated enhancement in susceptibility of *Aedes aegypti* for chikungunya virus. *Indian J. Med. Res.* **2014**, *139*, 762–768.

136. Black, W.C.; Bennett, K.E.; Gorrochotegui-Escalante, N.; Barillas-Mury, C.V.; Fernandez-Salas, I.; de Lourdes Munoz, M.; Farfan-Ale, J.A.; Olson, K.E.; Beaty, B.J. Flavivirus susceptibility in *Aedes aegypti*. *Arch. Med. Res.* **2002**, *33*, 379–388.
137. Bennett, K.E.; Flick, D.; Fleming, K.H.; Jochim, R.; Beaty, B.J.; Black, W.C.T. Quantitative trait loci that control dengue-2 virus dissemination in the mosquito *Aedes aegypti*. *Genetics* **2005**, *170*, 185–194.
138. Stapleford, K.A.; Coffey, L.L.; Lay, S.; Borderia, A.V.; Duong, V.; Isakov, O.; Rozen-Gagnon, K.; Arias-Goeta, C.; Blanc, H.; Beaucourt, S.; *et al.* Emergence and transmission of arbovirus evolutionary intermediates with epidemic potential. *Cell. Host Microbe* **2014**, *15*, 706–716.
139. Myers, R.M.; Carey, D.E. Concurrent isolation from patient of two arboviruses, chikungunya and dengue type 2. *Science* **1967**, *157*, 1307–1308.
140. Hapuarachchi, H.A.; Bandara, K.B.; Hapugoda, M.D.; Williams, S.; Abeyewickreme, W. Laboratory confirmation of dengue and chikungunya co-infection. *Ceylon Med. J.* **2008**, *53*, 104–105.
141. Ezzedine, K.; Cazanave, C.; Pistone, T.; Receveur, M.C.; Neau, D.; Ragnaud, J.M.; Malvy, D. Dual infection by chikungunya virus and other imported infectious agent in a traveller returning from India. *Travel Med. Infect. Dis.* **2008**, *6*, 152–154.
142. Chahar, H.S.; Bharaj, P.; Dar, L.; Guleria, R.; Kabra, S.K.; Broor, S. Co-infections with chikungunya virus and dengue virus in Delhi, India. *Emerg. Infect. Dis.* **2009**, *15*, 1077–1080.
143. Schilling, S.; Emmerich, P.; Gunther, S.; Schmidt-Chanasit, J. Dengue and chikungunya virus co-infection in a German traveller. *J. Clin. Virol.* **2009**, *45*, 163–164.
144. Nayar, S.K.; Noridah, O.; Paranthaman, V.; Ranjit, K.; Norizah, I.; Chem, Y.K.; Mustafa, B.; Chua, K.B. Co-infection of dengue virus and chikungunya virus in two patients with acute febrile illness. *Med. J. Malays.* **2007**, *62*, 335–336.
145. Leroy, E.M.; Nkoghe, D.; Ollomo, B.; Nze-Nkogue, C.; Becquart, P.; Grard, G.; Pourrut, X.; Charrel, R.; Moureau, G.; Ndjoyi-Mbiguino, A.; *et al.* Concurrent chikungunya and dengue virus infections during simultaneous outbreaks, Gabon, 2007. *Emerg. Infect. Dis.* **2009**, *15*, 591–593.
146. Chang, S.F.; Su, C.L.; Shu, P.Y.; Yang, C.F.; Liao, T.L.; Cheng, C.H.; Hu, H.C.; Huang, J.H. Concurrent isolation of chikungunya virus and dengue virus from a patient with coinfection resulting from a trip to Singapore. *J. Clin. Microbiol.* **2010**, *48*, 4586–4589.
147. Parreira, R.; Centeno-Lima, S.; Lopes, A.; Portugal-Calisto, D.; Constantino, A.; Nina, J. Dengue virus serotype 4 and chikungunya virus coinfection in a traveller returning from Luanda, Angola, January 2014. *Euro Surveill.* **2014**, *19*, 10.
148. Caron, M.; Paupy, C.; Grard, G.; Becquart, P.; Mombo, I.; Nso, B.B.; Kassa Kassa, F.; Nkoghe, D.; Leroy, E.M. Recent introduction and rapid dissemination of chikungunya virus and dengue virus serotype 2 associated with human and mosquito coinfections in Gabon, Central Africa. *Clin. Infect. Dis.* **2012**, *55*, e45–e53.
149. Vazeille, M.; Mousson, L.; Martin, E.; Failloux, A.B. Orally co-infected *Aedes albopictus* from La Reunion Island, Indian Ocean, can deliver both dengue and chikungunya infectious viral particles in their saliva. *PLoS Negl. Trop. Dis.* **2010**, *4*, e706.
150. Courtois, G.; Osterrieth, P.; Blanes Ridaura, G. Isolation of the yellow fever virus in the Belgian Congo. *Ann. Soc. Belge Med. Tropicale* **1960**, *40*, 29–60.

151. Osterrieth, P.; Rathe, E.; Deleplanque-Liegeois, P. Simultaneous isolation of the yellow fever and chikungunya viruses at Bili (Haut-Uele, Belgian Congo). *Ann. Soc. Belge Med. Tropicale* **1961**, *41*, 207–212.
152. Filipe, A.F.; Pinto, M.R. Arbovirus studies in Luanda, Angola. 2. Virological and serological studies during an outbreak of dengue-like disease caused by the chikungunya virus. *Bull. World Health Organ.* **1973**, *49*, 37–40.
153. Gould, L.H.; Osman, M.S.; Farnon, E.C.; Griffith, K.S.; Godsey, M.S.; Karch, S.; Mulenda, B.; El Kholly, A.; Grandesso, F.; de Radigues, X.; *et al.* An outbreak of yellow fever with concurrent chikungunya virus transmission in South Kordofan, Sudan, 2005. *Trans. R. Soc. Trop. Med. Hygiene* **2008**, *102*, 1247–1254.
154. Grard, G.; Caron, M.; Mombo, I.M.; Nkoghe, D.; Mboui Ondo, S.; Jiolle, D.; Fontenille, D.; Paupy, C.; Leroy, E.M. Zika virus in Gabon (Central Africa)—2007: A new threat from *Aedes albopictus*? *PLoS Negl. Trop. Dis.* **2014**, *8*, e2681.
155. Armstrong, P.M.; Rico-Hesse, R. Differential susceptibility of *Aedes aegypti* to infection by the American and Southeast Asian genotypes of dengue type 2 virus. *Vector Borne Zoonotic Dis.* **2001**, *1*, 159–168.
156. Cologna, R.; Armstrong, P.M.; Rico-Hesse, R. Selection for virulent dengue viruses occurs in humans and mosquitoes. *J. Virol.* **2005**, *79*, 853–859.
157. Brault, A.C.; Powers, A.M.; Ortiz, D.; Estrada-Franco, J.G.; Navarro-Lopez, R.; Weaver, S.C. Venezuelan equine encephalitis emergence: Enhanced vector infection from a single amino acid substitution in the envelope glycoprotein. *Proc. Natl. Acad. Sci. USA* **2004**, *101*, 11344–11349.
158. Deardorff, E.R.; Weaver, S.C. Vector competence of *Culex (Melanoconion) taeniopus* for equine-virulent subtype ie strains of venezuelan equine encephalitis virus. *Am. J. Trop. Med. Hygiene* **2010**, *82*, 1047–1052.
159. Tsetsarkin, K.A.; Weaver, S.C. Sequential adaptive mutations enhance efficient vector switching by chikungunya virus and its epidemic emergence. *PLoS Pathog.* **2011**, *7*, e1002412.
160. Holmes, E.C. *The Evolution and Emergence of RNA Viruses*; Oxford University Press: New York, NY, USA, 2009.
161. Rozen-Gagnon, K.; Stapleford, K.A.; Mongelli, V.; Blanc, H.; Failloux, A.B.; Saleh, M.C.; Vignuzzi, M. Alphavirus mutator variants present host-specific defects and attenuation in mammalian and insect models. *PLoS Pathog.* **2014**, *10*, e1003877.
162. Coffey, L.L.; Beeharry, Y.; Borderia, A.V.; Blanc, H.; Vignuzzi, M. Arbovirus high fidelity variant loses fitness in mosquitoes and mice. *Proc. Natl. Acad. Sci. USA* **2011**, *108*, 16038–16043.
163. Davis, C.T.; Ebel, G.D.; Lanciotti, R.S.; Brault, A.C.; Guzman, H.; Siirin, M.; Lambert, A.; Parsons, R.E.; Beasley, D.W.; Novak, R.J.; *et al.* Phylogenetic analysis of North American West Nile virus isolates, 2001–2004: Evidence for the emergence of a dominant genotype. *Virology* **2005**, *342*, 252–265.
164. Ebel, G.D.; Carricaburu, J.; Young, D.; Bernard, K.A.; Kramer, L.D. Genetic and phenotypic variation of West Nile virus in New York, 2000–2003. *Am. J. Trop. Med. Hygiene* **2004**, *71*, 493–500.

165. Parameswaran, P.; Charlebois, P.; Tellez, Y.; Nunez, A.; Ryan, E.M.; Malboeuf, C.M.; Levin, J.Z.; Lennon, N.J.; Balmaseda, A.; Harris, E.; *et al.* Genome-wide patterns of intrahuman dengue virus diversity reveal associations with viral phylogenetic clade and interhost diversity. *J. Virol.* **2012**, *86*, 8546–8558.
166. Turner, P.E.; Morales, N.M.; Alto, B.W.; Remold, S.K. Role of evolved host breadth in the initial emergence of an RNA virus. *Evolution* **2010**, *64*, 3273–3286.
167. Coffey, L.L.; Forrester, N.; Tsetsarkin, K.; Vasilakis, N.; Weaver, S.C. Factors shaping the adaptive landscape for arboviruses: Implications for the emergence of disease. *Future Microbiol.* **2013**, *8*, 155–176.
168. Coffey, L.L.; Vignuzzi, M. Host alternation of chikungunya virus increases fitness while restricting population diversity and adaptability to novel selective pressures. *J. Virol.* **2011**, *85*, 1025–1035.
169. Muller, H.J. The relation of recombination to mutational advance. *Mutat. Res.* **1964**, *1*, 2–9.
170. Weaver, S.C.; Brault, A.C.; Kang, W.; Holland, J.J. Genetic and fitness changes accompanying adaptation of an arbovirus to vertebrate and invertebrate cells. *J. Virol.* **1999**, *73*, 4316–4326.
171. Duarte, E.A.; Clarke, D.K.; Moya, A.; Elena, S.F.; Domingo, E.; Holland, J. Many-trillionfold amplification of single RNA virus particles fails to overcome the Muller’s ratchet effect. *J. Virol.* **1993**, *67*, 3620–3623.
172. Smith, D.R.; Adams, A.P.; Kenney, J.L.; Wang, E.; Weaver, S.C. Venezuelan equine encephalitis virus in the mosquito vector *Aedes taeniorhynchus*: Infection initiated by a small number of susceptible epithelial cells and a population bottleneck. *Virology* **2008**, *372*, 176–186.
173. Kenney, J.L.; Adams, A.P.; Gorchakov, R.; Leal, G.; Weaver, S.C. Genetic and anatomic determinants of enzootic venezuelan equine encephalitis virus infection of *Culex (Melanoconion) taeniopus*. *PLoS Negl. Trop. Dis.* **2012**, *6*, e1606.
174. Forrester, N.L.; Guerbois, M.; Seymour, R.L.; Spratt, H.; Weaver, S.C. Vector-borne transmission imposes a severe bottleneck on an RNA virus population. *PLoS Pathog.* **2012**, *8*, e1002897.
175. Brackney, D.E.; Pesko, K.N.; Brown, I.K.; Deardorff, E.R.; Kawatachi, J.; Ebel, G.D. West Nile virus genetic diversity is maintained during transmission by *Culex pipiens quinquefasciatus* mosquitoes. *PLoS One* **2011**, *6*, e24466.
176. Coffey, L.L.; Vasilakis, N.; Brault, A.C.; Powers, A.M.; Tripet, F.; Weaver, S.C. Arbovirus evolution *in vivo* is constrained by host alternation. *Proc. Natl. Acad. Sci. USA* **2008**, *105*, 6970–6975.
177. Smith, D.R.; Aguilar, P.V.; Coffey, L.L.; Gromowski, G.D.; Wang, E.; Weaver, S.C. Venezuelan equine encephalitis virus transmission and effect on pathogenesis. *Emerg. Infect. Dis.* **2006**, *12*, 1190–1196.
178. Ruiz-Moreno, D.; Vargas, I.S.; Olson, K.E.; Harrington, L.C. Modeling dynamic introduction of chikungunya virus in the United States. *PLoS Negl. Trop. Dis.* **2012**, *6*, e1918.
179. Eisen, L.; Monaghan, A.J.; Lozano-Fuentes, S.; Steinhoff, D.F.; Hayden, M.H.; Bieringer, P.E. The impact of temperature on the bionomics of *Aedes (stegomyia) aegypti*, with special reference to the cool geographic range margins. *J. Med. Entomol.* **2014**, *51*, 496–516.
180. Zouache, K.; Fontaine, A.; Vega-Rua, A.; Mousson, L.; Thiberge, J.M.; Lourenco-De-Oliveira, R.; Caro, V.; Lambrechts, L.; Failloux, A.B. Three-way interactions between mosquito population, viral strain and temperature underlying chikungunya virus transmission potential. *Proc. Biol. Sci.* **2014**, *281*, 1–8.

181. Tsetsarkin, K.A.; Chen, R.; Leal, G.; Forrester, N.; Higgs, S.; Huang, J.; Weaver, S.C. Chikungunya virus emergence is constrained in Asia by lineage-specific adaptive landscapes. *Proc. Natl. Acad. Sci. USA* **2011**, *108*, 7872–7877.
182. Lanciotti, R.S.; Kosoy, O.L.; Laven, J.J.; Panella, A.J.; Velez, J.O.; Lambert, A.J.; Campbell, G.L. Chikungunya virus in US travelers returning from India, 2006. *Emerg. Infect. Dis.* **2007**, *13*, 764–767.
183. Wilke, A.B.; Marrelli, M.T. Genetic control of mosquitoes: Population suppression strategies. *Rev. Inst. Med. Trop. Sao Paulo* **2012**, *54*, 287–292.
184. Weaver, S.C.; Osorio, J.E.; Livengood, J.A.; Chen, R.; Stinchcomb, D.T. Chikungunya virus and prospects for a vaccine. *Expert Rev. Vaccines* **2012**, *11*, 1087–1101.
185. Paupy, C.; Ollomo, B.; Kamgang, B.; Moutailler, S.; Rousset, D.; Demanou, M.; Herve, J.P.; Leroy, E.; Simard, F. Comparative role of *Aedes albopictus* and *Aedes aegypti* in the emergence of dengue and chikungunya in Central Africa. *Vector Borne Zoonotic Dis.* **2010**, *10*, 259–266.
186. Turell, M.J.; Beaman, J.R.; Tammariello, R.F. Susceptibility of selected strains of *Aedes aegypti* and *Aedes albopictus* (diptera: Culicidae) to chikungunya virus. *J. Med. Entomol.* **1992**, *29*, 49–53.
187. Shah, K.V.; Gilotra, S.K.; Gibbs, C.J., Jr.; Rozeboom, L.E. Laboratory studies of transmission of chikungunya virus by mosquitoes: A preliminary report. *Indian J. Med. Res.* **1964**, *52*, 703–709.
188. Girod, R.; Gaborit, P.; Marrama, L.; Etienne, M.; Ramdini, C.; Rakotoarivony, I.; Dollin, C.; Carinci, R.; Issaly, J.; Dusfour, I.; *et al.* High susceptibility to chikungunya virus of *Aedes aegypti* from the French West Indies and French Guiana. *Trop. Med. Int. Health* **2011**, *16*, 134–139.
189. Vanlandingham, D.L.; Hong, C.; Klingler, K.; Tsetsarkin, K.; McElroy, K.L.; Powers, A.M.; Lehane, M.J.; Higgs, S. Differential infectivities of o'nyong-nyong and chikungunya virus isolates in *Anopheles gambiae* and *Aedes aegypti* mosquitoes. *Am. J. Trop. Med. Hygiene* **2005**, *72*, 616–621.
190. Mangiafico, J.A. Chikungunya virus infection and transmission in five species of mosquito. *Am. J. Trop. Med. Hygiene* **1971**, *20*, 642–645.
191. Vazeille, M.; Yebakima, A.; Lourenco-de-Oliveira, R.; Andriamahefazafy, B.; Correia, A.; Rodrigues, J.M.; Veiga, A.; Moreira, A.; Leparc-Goffart, I.; Grandadam, M.; *et al.* Oral receptivity of *Aedes aegypti* from Cape Verde for yellow fever, dengue, and chikungunya viruses. *Vector Borne Zoonotic Dis.* **2013**, *13*, 37–40.
192. Nicholson, J.; Ritchie, S.A.; van den Hurk, A.F. *Aedes albopictus* (diptera: Culicidae) as a potential vector of endemic and exotic arboviruses in Australia. *J. Med. Entomol.* **2014**, *51*, 661–669.
193. Tesh, R.B.; Gubler, D.J.; Rosen, L. Variation among geographic strains of *Aedes albopictus* in susceptibility to infection with chikungunya virus. *Am. J. Trop. Med. Hygiene* **1976**, *25*, 326–335.
194. Haddad, N.; Mousson, L.; Vazeille, M.; Chamat, S.; Tayeh, J.; Osta, M.A.; Failloux, A.B. *Aedes albopictus* in Lebanon, a potential risk of arboviruses outbreak. *BMC Infect. Dis.* **2012**, *12*, 300.
195. Talbalaghi, A.; Moutailler, S.; Vazeille, M.; Failloux, A.B. Are *Aedes albopictus* or other mosquito species from Northern Italy competent to sustain new arboviral outbreaks? *Med. Vet. Entomol.* **2010**, *24*, 83–87.
196. Vazeille, M.; Jeannin, C.; Martin, E.; Schaffner, F.; Failloux, A.B. Chikungunya: A risk for Mediterranean countries? *Acta Trop.* **2008**, *105*, 200–202.

197. Moutailler, S.; Barre, H.; Vazeille, M.; Failloux, A.B. Recently introduced *Aedes albopictus* in Corsica is competent to chikungunya virus and in a lesser extent to dengue virus. *Trop. Med. Int. Health* **2009**, *14*, 1105–1109.
198. Kramer, L.D.; Chin, P.; Cane, R.P.; Kauffman, E.B.; Mackereth, G. Vector competence of New Zealand mosquitoes for selected arboviruses. *Am. J. Trop. Med. Hygiene* **2011**, *85*, 182–189.
199. Jupp, P.G.; McIntosh, B.M.; Dos Santos, I.; DeMoor, P. Laboratory vector studies on six mosquito and one tick species with chikungunya virus. *Trans. R. Soc. Trop. Med. Hygiene* **1981**, *75*, 15–19.
200. Ledermann, J.P.; Guillaumot, L.; Yug, L.; Saweyog, S.C.; Tided, M.; Machieng, P.; Pretrick, M.; Marfel, M.; Griggs, A.; Bel, M.; *et al.* *Aedes hensilli* as a potential vector of chikungunya and zika viruses. *PLoS Negl. Trop. Dis.* **2014**, *8*, e3188.
201. Diagne, C.T.; Faye, O.; Guerbois, M.; Knight, R.; Diallo, D.; Faye, O.; Ba, Y.; Dia, I.; Faye, O.; Weaver, S.C.; *et al.* Vector competence of *Aedes aegypti* and *Aedes vittatus* (diptera: Culicidae) from Senegal and Cape Verde archipelago for West African lineages of chikungunya virus. *Am. J. Trop. Med. Hygiene* **2014**, *91*, 635–641.

© 2014 by the authors; licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution license (<http://creativecommons.org/licenses/by/4.0/>).