



BOLETÍN BIBLIOGRÁFICO BIBLIOTECA DE SALUD

DR. BOGOSLAV JURICIC TURINA

Boletín Bibliográfico N°1 Marzo 2014

La Biblioteca de Salud "Dr. Bogoslav Juricic Turina, dependiente de la División de Planificación Sanitaria del Ministerio de Salud, tiene el agrado de enviar a usted, el Boletín Bibliográfico N°1/2014. (Incluye vínculo al texto completo)

VIRUS ZIKA

1. Wong PS; Li MZ; Chong CS; Ng LC; Tan CH

Environmental Health Institute, National Environment Agency, Singapore, Singapore.

Aedes (Stegomyia) albopictus (Skuse): a potential vector of Zika virus in Singapore.

PLoS Negl Trop Dis;7(8):e2348, 2013.

BACKGROUND: Zika virus (ZIKV) is a little known arbovirus until it caused a major outbreak in the Pacific Island of Yap in 2007. Although the virus has a wide geographic distribution, most of the known vectors are sylvatic *Aedes* mosquitoes from Africa where the virus was first isolated. Presently, *Ae. aegypti* is the only known vector to transmit the virus outside the African continent, though *Ae. albopictus* has long been a suspected vector. Currently, *Ae. albopictus* has been shown capable of transmitting more than 20 arboviruses and its notoriety as an important vector came to light during the recent chikungunya pandemic. The vulnerability of Singapore to emerging infectious arboviruses has stimulated our interest to determine the competence of local *Ae. albopictus* to transmit ZIKV. **METHODOLOGY/PRINCIPAL FINDINGS:** To determine the competence of *Ae. albopictus* to ZIKV, we orally infected local mosquito strains to a Ugandan strain virus. Fully engorged mosquitoes were maintained in an environmental chamber set at 29°C and 80-85%RH. Twelve mosquitoes were then sampled daily from day one to seven and on day 10 and 14 post infection (pi). Zika virus titre in the midgut and salivary glands of each mosquito were determined using tissue culture infectious dose₅₀ assay, while transmissibility of the virus was determined by detecting viral antigen in the mosquito saliva by qRT-PCR. High dissemination and transmission rate of

ZIKV were observed. By day 7-pi, all mosquitoes have disseminated infection and 73% of these mosquitoes have ZIKV in their saliva. By day 10-pi, all mosquitoes were potentially infectious. CONCLUSIONS/SIGNIFICANCE: The study highlighted the potential of *Ae. albopictus* to transmit ZIKV and the possibility that the virus could be established locally. Nonetheless, the threat of ZIKV can be mitigated by existing dengue and chikungunya control program being implemented in Singapore.

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3731215/pdf/pntd.0002348.pdf>

2. Faye O; Faye O; Diallo D; Diallo M; Weidmann M; Sall AA

Quantitative real-time PCR detection of Zika virus and evaluation with field-caught mosquitoes.

Virology 510:311, 2013.

BACKGROUND: Zika virus (ZIKV), a mosquito borne flavivirus is a pathogen affecting humans in Asia and Africa. ZIKV infection diagnosis relies on serology-which is challenging due to cross-reactions with other flaviviruses and/or absence or low titer of IgM and IgG antibodies at early phase of infection- virus isolation, which is labor intensive, time consuming and requires appropriate containment. Therefore, real-time RT-PCR (rRT-PCR) is an appealing option as a rapid, sensitive and specific method for detection of ZIKV in the early stage of infection. So far, only one rRT-PCR assay has been described in the context of the outbreak in Micronesia in 2007. In this study, we described a one step rRT-PCR for ZIKV which can detect a wider genetic diversity of ZIKV isolates from Asia and Africa. **RESULTS:** The NS5 protein coding regions of African ZIKV isolates were sequenced and aligned with representative flaviviruses sequences from GenBank to design primers and probe from conserved regions. The analytical sensitivity of the assay was evaluated to be 32 genome-equivalents and 0.05 plaque forming unit (pfu). The assay was shown to detect 37 ZIKV isolates covering a wide geographic in Africa and Asia over 36 years but none of the 31 other flaviviruses tested showing high analytical specificity. The rRT-PCR could be performed in less than 3 hours. This method was used successfully to detect ZIKV strains from field-caught mosquitoes. **CONCLUSION:** We have developed a rapid, sensitive and specific rRT-PCR for detection of ZIKV. This assay is a useful tool for detection of ZIKV infection in regions where a number of other clinically indistinguishable arboviruses like dengue or chikungunya co-circulate. Further studies are needed to validate this assay in clinical positive samples collected during acute ZIKV infection.

<http://www.virologyj.com/content/pdf/1743-422X-10-311.pdf>

3. Faye O; Freire CC; Iamarino A; Faye O; de Oliveira JV; Diallo M; Zanotto PM; Sall AA

Institut Pasteur de Dakar, Dakar, Senegal....

Molecular evolution of Zika virus during its emergence in the 20 (th) centuries.

PLoS Negl Trop Dis; 8(1):e2636, 2014 Jan.

Zika virus (ZIKV) is a mosquito-borne flavivirus first isolated in Uganda in 1947. Although entomological and virologic surveillance have reported ZIKV enzootic activity in diverse countries of Africa and Asia, few human cases were reported until 2007, when a Zika fever epidemic took place in Micronesia. In the context of West Africa, the WHO Collaborating Centre for Arboviruses and Hemorrhagic Fever at Institut Pasteur of Dakar. Despite several reports on ZIKV, the genetic relationships among viral strains from West Africa remain poorly understood. To evaluate the viral spread and its molecular epidemiology, we investigated 37 ZIKV isolates collected from 1968 to 2002 in six localities in Senegal and Côte d'Ivoire. In addition, we included strains from six other countries. Our results suggested that these two countries in West Africa experienced at least two independent introductions of ZIKV during the 20 (th) centuries, and that apparently these viral lineages were not restricted by mosquito vector species. Moreover, we present evidence that ZIKV has possibly undergone recombination in nature and that a loss of the N154 glycosylation site in the envelope protein was a possible adaptive response to the *Aedes dalzieli* vector.

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3888466/pdf/pntd.0002636.pdf>

4. Grard G; Caron M; Mombo IM; Nkoghe D; Mboui Ondo S; Jiolle D; Fontenille D; Paupy C; Leroy EM

UMVE, Centre International de Recherches Médicales de Franceville, Franceville, Gabon....

Zika Virus in Gabon (Central Africa) - 2007: A New Threat from *Aedes albopictus*?

PLoS Negl Trop Dis; 8(2):e2681, 2014 Feb.

BACKGROUND: Chikungunya and dengue viruses emerged in Gabon in 2007, with large outbreaks primarily affecting the capital Libreville and several northern towns. Both viruses subsequently spread to the south-east of the country, with new outbreaks occurring in 2010. The mosquito species *Aedes albopictus*, that was known as a secondary vector for both viruses, recently invaded the country and was the primary vector involved in the Gabonese outbreaks. We conducted a retrospective study of human sera and mosquitoes collected in Gabon from 2007 to 2010, in order to identify other circulating arboviruses. **METHODOLOGY/PRINCIPAL FINDINGS:** Sample collections, including 4312 sera from patients presenting with painful febrile disease, and 4665 mosquitoes belonging to 9 species, split into 247 pools (including 137 pools of *Aedes albopictus*), were screened with molecular biology methods. Five human sera and two *Aedes albopictus* pools, all sampled in an urban setting during the 2007 outbreak, were positive for the flavivirus Zika (ZIKV). The ratio of *Aedes albopictus* pools positive for ZIKV was similar to that positive for dengue virus during the concomitant dengue

outbreak suggesting similar mosquito infection rates and, presumably, underlying a human ZIKV outbreak. ZIKV sequences from the envelope and NS3 genes were amplified from a human serum sample. Phylogenetic analysis placed the Gabonese ZIKV at a basal position in the African lineage, pointing to ancestral genetic diversification and spread. CONCLUSIONS/SIGNIFICANCE: We provide the first direct evidence of human ZIKV infections in Gabon, and its first occurrence in the Asian tiger mosquito, *Aedes albopictus*. These data reveal an unusual natural life cycle for this virus, occurring in an urban environment, and potentially representing a new emerging threat due to this novel association with a highly invasive vector whose geographic range is still expanding across the globe.

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3916288/pdf/pntd.0002681.pdf>

5. Li MI; Wong PS; Ng LC; Tan CH

Environmental Health Institute, National Environment Agency, Singapore, Singapore.

Oral susceptibility of Singapore *Aedes (Stegomyia) aegypti* (Linnaeus) to Zika virus.

PLoS Negl Trop Dis; 6(8):e1792, 2012.

BACKGROUND: Zika virus (ZIKV) is a little known flavivirus that caused a major outbreak in 2007, in the South-western Pacific Island of Yap. It causes dengue-like syndromes but with milder symptoms. In Africa, where it was first isolated, ZIKV is mainly transmitted by sylvatic *Aedes* mosquitoes. The virus has also been isolated from *Ae. aegypti* and it is considered to be the vector involved in the urban transmission of the virus. Transmission of the virus by an African strain of *Ae. aegypti* has also been demonstrated under laboratory conditions. The aim of the present study is to describe the oral susceptibility of a Singapore strain of *Ae. aegypti* to ZIKV, under conditions that simulate local climate. METHODOLOGY/PRINCIPAL FINDINGS: To assess the receptivity of Singapore's *Ae. aegypti* to the virus, we orally exposed a local mosquito strain to a Ugandan strain of ZIKV. Upon exposure, fully engorged mosquitoes were maintained in an environmental chamber set at 29 °C and 70-75% RH. Eight mosquitoes were then sampled daily from day 1 to day 7, and subsequently on days 10 and 14 post exposure (pe). The virus titer of the midgut and salivary glands of each mosquito were determined using a tissue culture infectious dose (50) (TCID₅₀) assay. High midgut infection and salivary gland dissemination rates were observed. By day 5 after the infectious blood meal, ZIKV was found in the salivary glands of more than half of the mosquitoes tested (62%); and by day 10, all mosquitoes were potentially infective. CONCLUSIONS/SIGNIFICANCE: This study showed that Singapore's urban *Ae. aegypti* are susceptible and are potentially capable of transmitting ZIKV. The virus could be established in Singapore should it be introduced. Nevertheless, Singapore's current dengue control strategy is applicable to control ZIKV.

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3429392/pdf/pntd.0001792.pdf>

6. Haddow AD; Schuh AJ; Yasuda CY; Kasper MR; Heang V; Huy R; Guzman H; Tesh RB; Weaver SC

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

Genetic characterization of Zika virus strains: geographic expansion of the Asian lineage. PLoS Negl Trop Dis; 6(2):e1477, 2012.

BACKGROUND: Zika virus (ZIKV) is a mosquito-borne flavivirus distributed throughout much of Africa and Asia. Infection with the virus may cause acute febrile illness that clinically resembles dengue fever. A recent study indicated the existence of three geographically distinct viral lineages; however this analysis utilized only a single viral gene. Although ZIKV has been known to circulate in both Africa and Asia since at least the 1950s, little is known about the genetic relationships between geographically distinct virus strains. Moreover, the geographic origin of the strains responsible for the epidemic that occurred on Yap Island, Federated States of Micronesia in 2007, and a 2010 pediatric case in Cambodia, has not been determined. **METHODOLOGY/PRINCIPAL FINDINGS:** To elucidate the genetic relationships of geographically distinct ZIKV strains and the origin of the strains responsible for the 2007 outbreak on Yap Island and a 2010 Cambodian pediatric case of ZIKV infection, the nucleotide sequences of the open reading frame of five isolates from Cambodia, Malaysia, Nigeria, Uganda, and Senegal collected between 1947 and 2010 were determined. Phylogenetic analyses of these and previously published ZIKV sequences revealed the existence of two main virus lineages (African and Asian) and that the strain responsible for the Yap epidemic and the Cambodian case most likely originated in Southeast Asia. Examination of the nucleotide and amino acid sequence alignments revealed the loss of a potential glycosylation site in some of the virus strains, which may correlate with the passage history of the virus. **CONCLUSIONS/SIGNIFICANCE:** The basal position of the ZIKV strain isolated in Malaysia in 1966 suggests that the recent outbreak in Micronesia was initiated by a strain from Southeast Asia. Because ZIKV infection in humans produces an illness clinically similar to dengue fever and many other tropical infectious diseases, it is likely greatly misdiagnosed and underreported.

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3289602/pdf/pntd.0001477.pdf>

7. Heang V; Yasuda CY; Sovann L; Haddow AD; Travassos da Rosa AP; Tesh RB; Kasper MR

Zika virus infection, Cambodia, 2010.

Emerg Infect Dis; 18(2):349-51, 2012 Feb.

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3310457/pdf/11-1224_finalL.pdf

8. Foy BD; Kobylinski KC; Chilson Foy JL; Blitvich BJ; Travassos da Rosa A; Haddow AD; Lanciotti RS; Tesh RB

Department of Microbiology, Immunology and Pathology, Colorado State University, Fort Collins, Colorado 80523-1692, USA.

Probable non-vector-borne transmission of Zika virus, Colorado, USA.

Emerg Infect Dis; 17(5):880-2, 2011 May.

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3321795/?report=printable>

9. Hayes EB

Barcelona Centre for International Health Research, Barcelona, Spain.

Zika virus outside Africa.

Emerg Infect Dis; 15(9):1347-50, 2009 Sep.

Zika virus (ZIKV) is a flavivirus related to yellow fever, dengue, West Nile, and Japanese encephalitis viruses. In 2007 ZIKV caused an outbreak of relatively mild disease characterized by rash, arthralgia, and conjunctivitis on Yap Island in the southwestern Pacific Ocean. This was the first time that ZIKV was detected outside of Africa and Asia. The history, transmission dynamics, virology, and clinical manifestations of ZIKV disease are discussed, along with the possibility for diagnostic confusion between ZIKV illness and dengue. The emergence of ZIKV outside of its previously known geographic range should prompt awareness of the potential for ZIKV to spread to other Pacific islands and the Americas.

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2819875/pdf/09-0442_finalS.pdf

10. Duffy MR; Chen TH; Hancock WT; Powers AM; Kool JL; Lanciotti RS; Pretrick M; Marfel M; Holzbauer S; Dubray C; Guillaumot L; Griggs A; Bel M; Lambert AJ; Laven J; Kosoy O; Panella A; Biggerstaff BJ; Fischer M; Hayes EB

Zika virus outbreak on Yap Island, Federated States of Micronesia.

N Engl J Med; 360(24):2536-43, 2009 Jun 11.

BACKGROUND: In 2007, physicians on Yap Island reported an outbreak of illness characterized by rash, conjunctivitis, and arthralgia. Although serum from some patients had IgM antibody against dengue virus, the illness seemed clinically distinct from previously detected dengue. Subsequent testing with the use of consensus primers detected Zika virus RNA in the serum of the patients but no dengue virus or other arboviral RNA. No previous outbreaks and only 14 cases of Zika virus disease have been previously documented. **METHODS:** We obtained serum samples from patients and interviewed patients for information on clinical signs and symptoms. Zika virus disease was confirmed by a finding of Zika virus RNA or a specific neutralizing antibody response to Zika virus in the serum. Patients with IgM antibody against Zika virus who had a

potentially cross-reactive neutralizing-antibody response were classified as having probable Zika virus disease. We conducted a household survey to estimate the proportion of Yap residents with IgM antibody against Zika virus and to identify possible mosquito vectors of Zika virus. RESULTS: We identified 49 confirmed and 59 probable cases of Zika virus disease. The patients resided in 9 of the 10 municipalities on Yap. Rash, fever, arthralgia, and conjunctivitis were common symptoms. No hospitalizations, hemorrhagic manifestations, or deaths due to Zika virus were reported. We estimated that 73% (95% confidence interval, 68 to 77) of Yap residents 3 years of age or older had been recently infected with Zika virus. *Aedes hensilli* was the predominant mosquito species identified. CONCLUSIONS: This outbreak of Zika virus illness in Micronesia represents transmission of Zika virus outside Africa and Asia. Although most patients had mild illness, clinicians and public health officials should be aware of the risk of further expansion of Zika virus transmission.

<http://www.nejm.org/doi/pdf/10.1056/NEJMoa0805715>