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Origin of the dengue virus outbreak in Martin County, Florida, USA 2013

Frank D. Teets [a], Moti N. Ramgopal [b], Kristen D. Sweeney [b], Amanda S. Graham [a], Scott F. Michael [a], Sharon Isern [a,*]

[a] Department of Biological Sciences, College of Arts and Sciences, Florida Gulf Coast University, 10501 FGCU Boulevard South, Fort Myers, FL 33965, United States
[b] Martin Health System Center for Clinical Research, 10000 SW Innovation Way, Port St. Lucie, FL 34987, United States

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ABSTRACT

After a 75-year absence from Florida, substantial local transmission of dengue virus (DENV) occurred in Key West, Monroe County, Florida in 2009 and continued in 2010. The outbreak culminated in 85 reported cases. In 2011 and 2012, only isolated cases of local DENV transmission were reported in Florida; none were reported in Key West. In 2013, a new outbreak occurred, but this time in Martin County about 275 miles north of Key West with 22 reported cases. As the Key West and Martin County outbreaks involved DENV serotype 1 (DENV-1), we wanted to investigate whether the same strain or a different strain of DENV was responsible for the outbreaks. In this study, we report the sequence and phylogenetic analysis of the E gene region from a patient diagnosed with dengue in Martin County. Our results indicate that the 2013 Martin County DENV-1 strain is distinct from the 2009–2010 Key West DENV-1 and that it is most closely related to viruses from a recent expansion of South American DENV-1 strains into the Caribbean. We conclude that the 2013 Martin County outbreak was the result of a new introduction of DENV-1 in Florida.

1. Introduction

Currently, about 40% of the world's population lives in areas at risk of dengue infection (World Health Organization, 2009) and the incidence of dengue is increasing in range and intensity worldwide. A recent meta-analysis estimated 390 million dengue infections per year, more than three times the burden

* Corresponding author.
E-mail address: sisern@fgcu.edu (S. Isern).

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previously estimated by the World Health Organization (World Health Organization, 2009; Bhatt et al., 2013). Dengue is caused by a mosquito-transmitted flavivirus, dengue virus (DENV). DENV infection typically manifests as an acute febrile illness with highly variable outcomes ranging from inapparent symptoms to hemorrhagic fever, shock syndrome or even death. There are four distinct serotypes of DENV (DENV-1, -2, -3, and -4). Infection with one serotype typically provides lifetime protection against the same serotype, but the resulting immune response can lead to increased disease severity during a secondary infection with a different serotype. There are currently no commercially available vaccines to prevent DENV infection or specific drugs to inhibit viral replication. The primary means of disease prevention and spread is vector control.

DENV is primarily transmitted by peridomestic *Aedes aegypti* and *Aedes albopictus* mosquito vectors. Both of these species are typically found in tropical and subtropical regions. However, in recent years, the range of these mosquito vectors has increased, leading to a subsequent expansion of the range of DENV transmission (Benedict et al., 2007; Enserink, 2008). Global travel and commerce have played key roles in range expansion and increasing transmission. Transported mosquito adults and larvae, as well as DENV infected travelers returning from regions where DENV is endemic, can initiate de novo local DENV transmission if the mosquito vectors are present. As a result, sporadic outbreaks of locally transmitted DENV have occurred in numerous temperate regions including France, Croatia, and the United States (US) (La Ruche et al., 2010; Schmidt-Chanasit et al., 2010; Centers for Disease Control and Prevention, 2010). According to the US Geological Survey, in 2013, there were 773 laboratory-confirmed imported DENV cases in 41 states (http://diseasemaps.usgs.gov/dep_us_human.html). Given the variable symptoms and lack of clinical experience with DENV in the US, this is almost certainly an underestimate of the true number of imported cases. *A. aegypti* is found in 19 of these states with its range stretching across the southeastern US, up the east coast to New York and west to Kentucky and Indiana, and *A. albopictus* is now established on the Atlantic seaboard from Florida to southern New York (Darsie and Ward, 2005).

In 2009, after a 75-year absence from Florida, a substantial outbreak of locally transmitted DENV occurred in Key West, Monroe County, Florida. According to the Florida Department of Health, twenty-two cases of locally transmitted DENV were confirmed that year (http://www.floridahealth.gov/diseases-and-conditions/mosquito-borne-diseases/surveillance.html). In 2010, an additional sixty-three cases of locally acquired DENV were reported in Monroe County and one case each in Miami-Dade and Broward Counties. The same strain of DENV serotype 1 (DENV-1) was isolated from both mosquitoes and patients in Monroe County, confirming local transmission (Graham et al., 2011; Munoz-Jordan et al., 2013). No further cases of locally acquired DENV have been reported in Monroe County since 2010, suggesting that DENV had been extirpated from the local vector population in that location. However, small numbers of sporadic cases with no travel history have continued in Florida. In 2011, seven additional cases of locally acquired DENV were reported: three cases in Miami-Dade, two in Palm Beach, and one each in Martin and Hillsborough Counties. In 2012, four more cases were reported: two in Miami-Dade and one each in Osceola and Seminole Counties. Most recently, in 2013, another substantial outbreak occurred where twenty-three cases of locally acquired DENV were reported: twenty-two in Martin County and one in Miami-Dade County. The Florida counties with reported cases of locally acquired DENV are shown in Fig. 1.

In this study, we set out to determine whether the locally transmitted DENV strain from Martin County in 2013 is the same as or different from the locally transmitted DENV from Key West in 2009–2010. The answer to this question has major implications for control efforts and epidemiological surveillance. If the two viruses are similar, then that would suggest that a single introduction had spread to multiple areas in Florida due to movement of people and/or mosquitoes within the state. The distance between the neighborhoods of Old Town Key West and Jensen Beach and Rio in Martin County is about 275 miles (Fig. 1), linked much of the way by direct interstate highways. If the two viruses are distinct, that would suggest a new introduction of DENV in Florida from outside the US. Control and surveillance measures to address these two distinct scenarios would differ in focusing on local versus international transport.

Here we report the sequence and phylogenetic analyses of the E protein region of DENV amplified from a single patient diagnosed in Martin County in 2013. Our results indicate that the Martin County and Key West DENV are both DENV-1, but that the two strains are distinct. While the Key West DENV-1 was most closely related to viruses from Nicaragua, the Martin County DENV-1 is most closely related to viruses from a recent expansion of South American DENV-1 viruses into the Caribbean.