

# An “Asian variant” rather than the strains endemic to the main island of Japan : Clinical features of Scrub typhus at Ikema island in Okinawa, Japan

Shuichi Sugita, M.D.<sup>1</sup>, Sho Okano, Ph.D<sup>2</sup>, Jun Kudaka, Ph.D<sup>2</sup>, Katsuya Taira, Ph.D<sup>3</sup>, Masashi Narita, M.D.<sup>4</sup>, Masafumi Funato, M.D.<sup>1</sup>, Haruka Eda, M.D.<sup>1</sup>, Young Lee, M.D.<sup>1</sup>, Hiroyuki Tsuyuki, M.D.<sup>1</sup>, Yusuke Yamanaka, M.D.<sup>1</sup>, Akira Shimabukuro, M.D.<sup>1</sup>, Eiji Motonaga, M.D.<sup>1</sup>

(1)Okinawa Miyako Hospital, Miyakojima city Okinawa, Japan, (2)Okinawa Prefectural Institute of Health and Environment, Nanjo city, Okinawa, Japan, (3)Department of Public Health and Medical Care, Okinawa Prefectural Government, Naha city Okinawa, Japan, (4)Department of Medicine, Okinawa Chubu Hospital, Uruma, Okinawa, Japan

## Background

►Scrub typhus (ST) is a vector-borne diseases caused by *Orientia tsutsugamushi*, a major cause of febrile illness in Asia pacific region.

►Miyako island is south-west island in Okinawa, Japan, and has approximately 54,000 inhabitants.

►The details of epidemiology, clinical features and phylogenetic information of scrub typhus (ST) in Okinawa, where have not been described until this presentation.

►The field research at Ikema island from 2009 to 2010 revealed a number of *Leptotrombidium deliense*, known as a vector of ST in Southeast Asia.

## Method

►This is retrospective observational study on patients infected with ST at Okinawa Miyako Hospital, a core clinical hospital in Miyako island, Okinawa, Japan.

►We reviewed the clinical characteristics of 11 patients, who diagnosed with ST from 2008 to 2015.

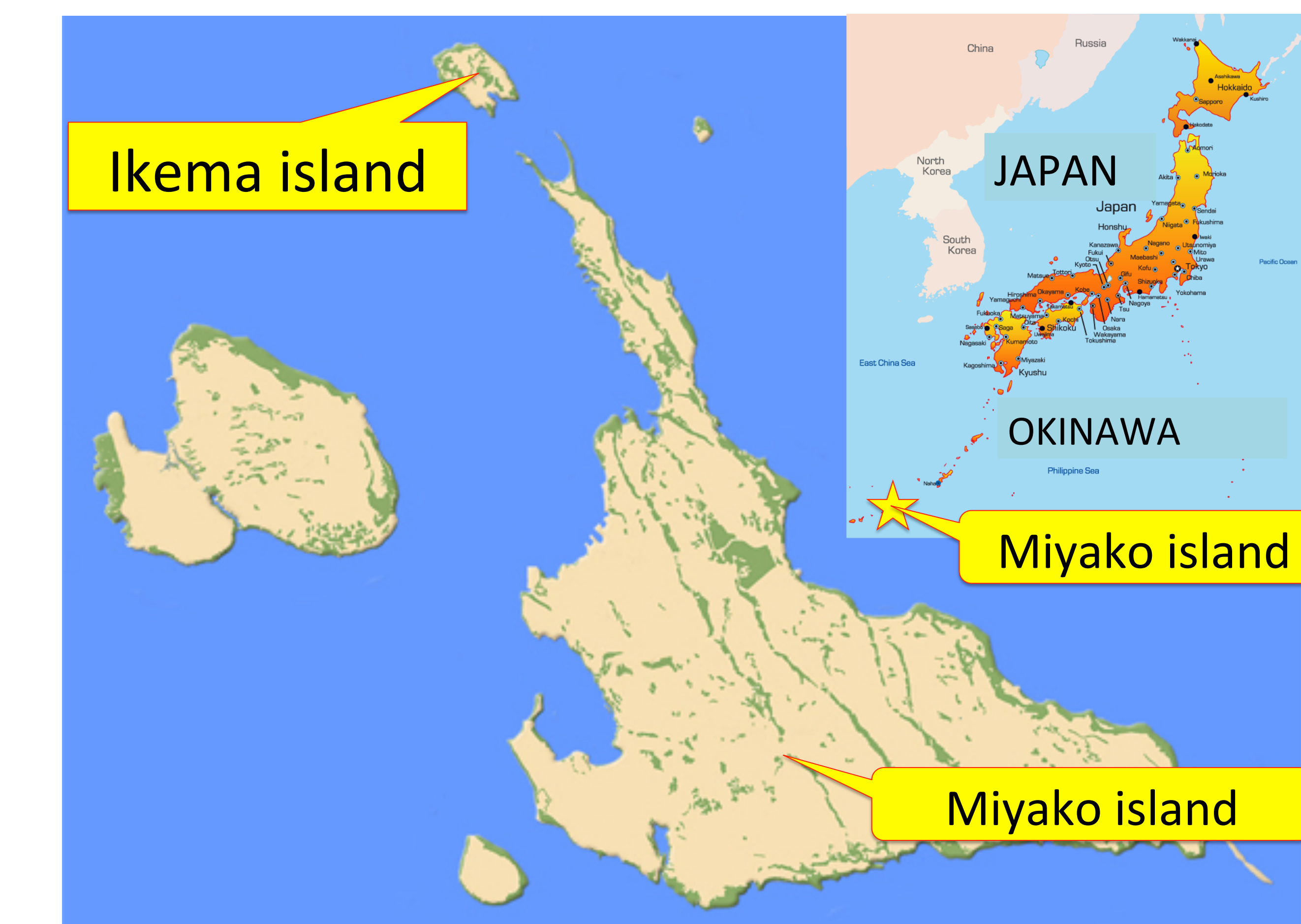


Figure 1. Geographic Location of Miyako island and Ikema island.

## Result

►The total 11 cases (Table 1.) are diagnosed by serological test and real-time PCR assays using eschars and blood specimens from the patients of ST.

►The 8 patients are residents in Ikema island, and the other 3 patients are in Miyako island, who had visited to Ikema island before the onset of symptoms.

►Average age of patients was 59.6 years old (range of 38 to 84), 7 of men and 4 of women, presented with aseptic meningitis in 18% (2/11), DIC in 18% (2/11), septic shock (qSOFA score 2>) in 4 cases. No case was died of ST.

►Bimodal seasonal distribution was described in “Summer” (from Apr. to Jul.) in 7 cases and in “Autumn/Winter” (Oct. to Dec.) in 4 cases.

►Case 2 is the offspring of Case 6, who are supposed to be infected around their house.

►Case 1 and 4 had history of fishing in Ikema island. Case 10, a shamanic women had walked around in the island via a sacred place for worship.

►Case 7 and Case 11 are very same person who infected twice times, representing the different (Yellow).

►Phylogenetic information by the gene sequences of the locus for the 56-kDa proteins revealed the 3 strains; 6 of Gilliam-variant, 3 of Saitama-variant and one of Karp-variant, which are also reported in Taiwan.

Table 1. Clinical features of scrub typhus in Ikema island

Case	1	2	3	4	5	6	7	8	9	10	11
Age•Sex	50•Male	53•Male	54•Male	38•Male	60•Male	84•Female	73•Female	61•Male	56•Male	54•Female	74•Female
Residential area	Miyako	Ikema	Ikema	Miyako	Ikema	Ikema	Ikema	Ikema	Ikema	Miyako	Ikema
Date of onset	Jun. 21.2008	Jun. 1.2010	Jul. 20.2011	Oct. 25.2011	May 29.2013	Jun. 6.2014	Dec. 5.2014	Apr. 27.2015	Jun.16.2015	Nov. 17.2015	Dec. 10.2015
Clinical triad	Fever	40.0°C	38.8°C	38.9°C	38.7°C	38°C	39.2°C	38.3°C	38.3°C	38.8°C	38.3°C
	Skin rash	+	+	+	+	+	+	+	+	+	+
	Site of eschar	Lt. popliteal	Rt.shin	Rt.hip	Rt.axillary	Lt.chest	Rt.thigh	Rt.Breast	Lt.knee	Scrotum	Rt.axillary
Complications	Meningitis	+			—				+		
	Liver disorder	+	+	+	+	+	+	+	+	—	+
	Lymphadenopathy	+	—	+	+	+	—	—	+	—	+
	qSOFA	1	2	3	0	0	1	0	3	1	2
	DIC	—	—	—	—	—	+	+	+	—	+
	Hyponatremia	—	+	+	+	—	—	+	+	+	+
	Urine:OB/Protein	+ / +	+ / +	+ / +			2+/3+	1+/1+	3+/2+	1+/2+	-/2+
Diagnostic test	PCR-serum	+	—		+	—	+	+	+	+	+
	PCR-eschar		+	+	+		+	+	+	+	+
	Serological test	+(Gilliam)	+(Gilliam)	+(Gilliam)	+(Gilliam)	+(Gilliam)	+(Gilliam)		+(Gilliam)	+(Gilliam)	
	Gene sequence	Gilliam-variant	Gilliam-variant	Gilliam-variant	Gilliam-variant			Saitama-variant	Gilliam-variant	Saitama-variant	Gilliam-variant

※1. qSOFA denotes quick SOFA is a bedside prompt that may identify patients with suspected infection who are at greater risk for a poor outcome outside the intensive care unit (ICU). ※2. DIC: Disseminated intravascular coagulation. ※3. OB: Occult blood. ※4. PCR: polymerase chain reaction.

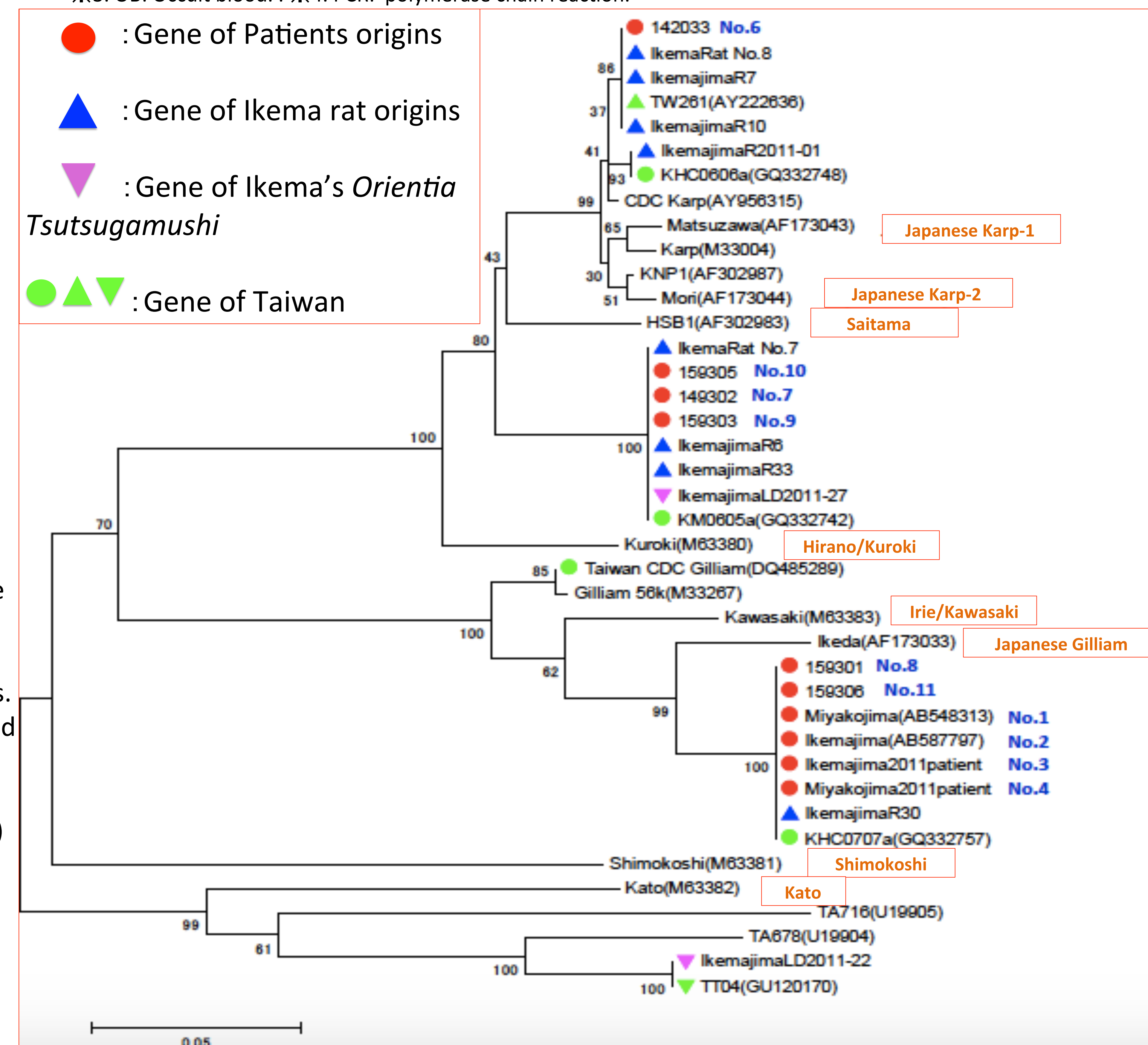


Figure 2. Phylogenetic tree.

This shows gene sequence of 11 case and relationships among major clades of *Orientia tsutsugamushi* as represented by the DNA sequences of the 56-kDa surface antigen gene. Most sequence groups are represented within Japan, with the exception of Gilliam (Myanmar, People's Republic of China), TA763 (Republic of China, Thai), and possibly JG-v (Republic of China, Thai).

## Discussion

►Scrub typhus is endemic to a 13,000,000 km<sup>2</sup> area of the Asia-Pacific rim, extending from Afghanistan to China, Korea, the islands of the southwestern Pacific, and northern Australia, including Okinawa Islands, Miyako island and Ikema island.

►*Leptotrombidium deliense*, a major vector of ST in Southeast Asia had captured in Ikema during the field work from 2009 to 2010, followed by isolating *Orientia tsutsugamushi* from rats and chiggers.

►Some hypothesis would be discussed the reason why the Asian-variant strains of ST found in Ikema island.

- 1) Historically, Ikema island had scaled up its relations with Taiwan and other Asian countries in the past.
- 2) Miyako island has been a landing zone for migratory birds from the southeast Asia to the mainland of Japan. “Ikema wetland” as a sanctuary for wildlife is located in the center of the Ikema island, which was designated a Wildlife Protection Area since 2011.
- 3) These cultural, economical and ecological exchange had seeded infected chiggers and chigger-infested wildlives, followed by growing the “mite islands” in the small island

►A recurrent ST case one year later would show the evidence that the vector (*L.deliense*) would carry several different genotypes of *Orientia tsutsugamushi*, under the diversity of genotypes (Japanese Gilliam, Saitama and Karp-variants) in this small island.

## Conclusion

►The clinical features and the gene sequences of ST at Ikema island in Okinawa are unique compared with the strains endemic to the main island of Japan. The single vector of *Leptotrombidium deliense* in Ikema island can do carry plural strains of *Orientia Tsutsugamushi*, which was demonstrated as recurrence of different strains in the same patient.

## References

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