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Limited geographic distribution of the novel cyclovirus CyCV-VN

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A novel cyclovirus, CyCV-VN, was recently identified in cerebrospinal fluid (CSF) from patients with central nervous system (CNS) infections in central and southern Vietnam. To explore the geographic distribution of this novel virus, more than 600 CSF specimens from patients with suspected CNS infections in northern Vietnam, Cambodia, Nepal and The Netherlands were screened for the presence of CyCV-VN but all were negative. Sequence comparison and phylogenetic analysis between CyCV-VN and another novel cyclovirus recently identified in CSF from Malawian patients indicated that these represent distinct cycloviral species, albeit phylogenetically closely related. The data suggest that CyCV-VN has a limited geographic distribution within southern and central Vietnam. Further research is needed to determine the global distribution and diversity of cycloviruses and importantly their possible association with human disease.

Cycloviruses (CyCVs) belong to the *Circoviridae* family and have recently been found in different sample types from different hosts, including mammals and insects^{1–5}. Recently, we reported a new cyclovirus species, tentatively named cyclovirus-Vietnam (CyCV-VN), in cerebrospinal fluid (CSF) of two Vietnamese patients⁶. The virus was subsequently detected in 4% of 642 CSF samples of patients with central nervous system (CNS) infections from 7 different provinces in southern and central Vietnam, but in none of 122 CSF samples from patients with noninfectious CNS conditions⁶. Almost simultaneously, another novel CyCV (CyCV-VS5700009) was reported in CSF and serum from patients with paraplegia in Malawi⁷, while other CyCVs have previously been reported in stool samples of patients with acute flaccid paralysis from Tunisia, Pakistan and Nigeria³. Together, these data suggest that cycloviruses may have a wide geographic distribution, and that specific CyCV species might be associated with specific clinical phenotypes, although it should be noted that associated pathology of cycloviruses has yet to be proven.

Results

To explore whether CyCV-VN is circulating beyond central and southern Vietnam, we screened a total of 615 CSF specimens from patients with acute CNS infections from northern Vietnam (n = 233), Cambodia (n = 123), Nepal (n = 80) and The Netherlands (n = 179) for the presence of CyCV-VN DNA (Table 1).

CyCV-VN DNA, however, was absent from all 615 CSF specimens tested, suggesting a confined geographical distribution of this virus.

To determine whether CyCV-VN represents a cycloviral species distinct from CyCV-VS5700009, the novel cyclovirus recently detected in CSF from Malawian patients⁷, we conducted sequence comparisons and phylogenetic analyses to examine the genetic relationship between CyCV-VN and CyCV-VS5700009. Pairwise comparisons showed that the degree of sequence similarity between CyCV-VN and CyCV-VS5700009 was 60% at the nucleotide level of the complete genome sequence and 36% and 76% at the amino acid level of the capsid protein



Table 1 | Patient cohorts from which samples were used in this study to detect CyCV-VN

	Number of samples		Population	City*	Country	References	Time frame	P value [#]
	total	positive						
Previous study	642	26			southern and central Vietnam	6	1999–2009	
Present study	233	0	adults	Ha Noi	northern Vietnam	11	2007–2008	0.0004
	123	0	children	Siem Reap	Cambodia	12	2009–2010	0.01
	80	0	all ages	Kathmandu	Nepal	13	2009–2011	0.1
	179	0	all ages	nationwide	The Netherlands	unpublished	2010–2011	0.003
All	615	0						<0.0001

*Name of the city indicates the location of the hospital where the patients were admitted.

[#]Fischer exact; compared with results from the study in reference #6.

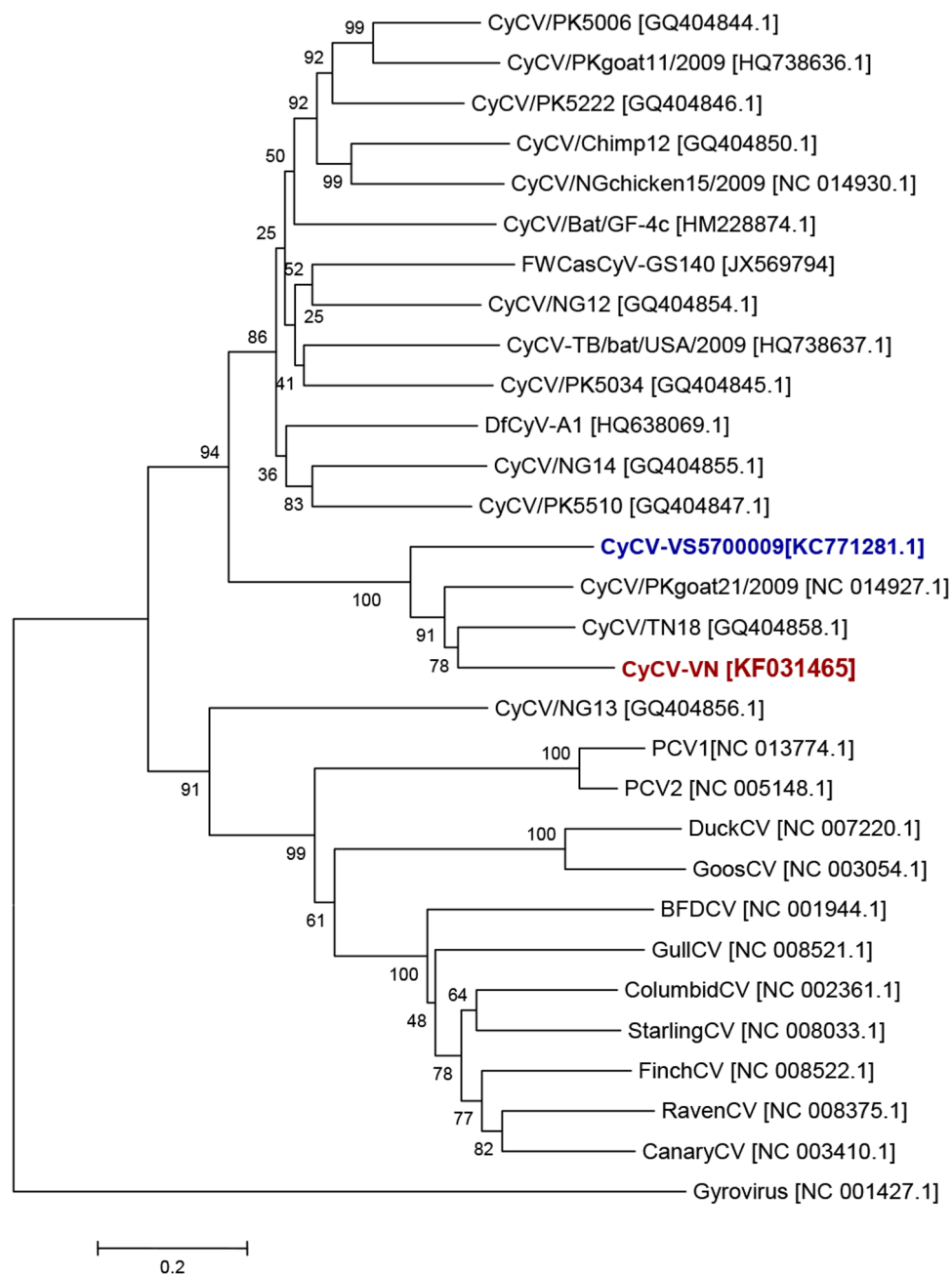


Figure 1 | Reconstructed phylogeny tree of complete genome sequences of cycloviruses, CyCV-VN (red) and CyCV-VS700009 (blue); circoviruses and a gyrovirus were used as outliers. CV: circovirus, Sequence accession number are in square brackets.



Author contributions

H.D.T.N., N.V.V.C., N.V.K., W.T., H.F.L.W., A.v.d.E., A.G., S.S. and T.T.H. collected CSF specimens. M.C., N.V.T., N.H.U., M.C., J.B. and N.T.T.C.B. conducted laboratory experiments. L.V.T. did sequence analyses. L.V.T., H.R.v.D., J.F., L.v.d.H., J.B. and M.D.d.J. designed the study. L.V.T., H.R.v.D. and M.D.d.J. drafted the manuscript. All authors were involved in subsequent reviewing and editing the manuscript.

Additional information

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