





Complete Genome Sequence of a Divergent Human Rhinovirus C Isolate from an Infant with Severe Community-Acquired Pneumonia in Colorado, USA

Charles Langelier, a Corin V. White, b Marci K. Sontag, c Peter M. Mourani, d Joseph L. DeRisib,e

Division of Infectious Diseases, Department of Medicine, University of California San Francisco, San Francisco, California, USA^a; Department of Biochemistry and Biophysics, University of California San Francisco, San Francisco, California, USAb; Department of Epidemiology, Colorado School of Public Health, University of Colorado Denver Anschutz Medical Campus, Aurora, Colorado, USAc; Section of Critical Care Medicine, Department of Pediatrics, University of Colorado School of Medicine and Children's Hospital Colorado, Aurora, Colorado, USAd; Chan-Zuckerberg Biohub, San Francisco, California, USAe

ABSTRACT Here, we report the genome sequence of a divergent human rhinovirus C isolate identified from an infant with a severe community-acquired respiratory infection. RNA sequencing performed on an Illumina platform identified reads aligning to human rhinovirus species, which were de novo assembled to produce a coding-complete genome sequence.

uman rhinoviruses can induce a diverse spectrum of clinical outcomes, ranging from mild disease to fulminant pneumonia (1–3). The factors governing the severity of rhinoviral infection are not well understood, but species- and type-specific differences are suspected to be influential (1-3). The genomic study of rhinovirus isolates associated with distinctly severe clinical syndromes may illuminate such connections. As such, we report the coding-complete genome sequence of a divergent human rhinovirus species C isolate recovered in March 2015 from the tracheal aspirate of a 15-month-old infant with a severe community-acquired lower respiratory tract infection. The previously healthy infant developed progressively worsening cough and congestion that advanced to acute respiratory failure and septic shock. A clinical respiratory virus PCR assay returned positive for rhinovirus, but all other testing, including bacterial cultures from tracheal aspirate and blood, returned negative. Following 8 days of intensive care unit support involving mechanical ventilation, vasopressors, and empiric broad-spectrum antibiotics, he fully recovered.

Following enrollment in a research study investigating factors predisposing to ventilator-associated pneumonia (IRB 14-1530), excess tracheal aspirate from the day of intubation was collected. RNA extraction and subsequent reverse transcription were carried out followed by sequencing library construction using the Illumina Nextera library preparation kit according to previously described methods (4-6). Paired-end sequencing on an Illumina instrument generated 9.9 \times 10 6 raw reads which were parsed through a recently described pathogen detection computational pipeline that incorporates iterative filtration to remove the human genome and low-quality and low-complexity sequences (4-6). From this, 58,922 unique reads aligning to human rhinovirus species were identified. Paired-read iterative contig extension (PRICE) (7) software was subsequently employed for de novo assembly to generate a 7,056-bp contiguous sequence, which was found to be most phylogenetically related to human rhinovirus C isolate LZ269 (GenBank accession number JF317013). The Picornavirus Working Group has established that novel human rhinovirus C types should exhibit at

Received 16 October 2017 Accepted 26 October 2017 Published 30 November 2017

Citation Langelier C, White CV, Sontag MK, Mourani PM, DeRisi JL. 2017. Complete genome sequence of a divergent human rhinovirus C isolate from an infant with severe community-acquired pneumonia in Colorado, USA. Genome Announc 5:e01245-17. https:// doi.org/10.1128/genomeA.01245-17

Copyright © 2017 Langelier et al. This is an open-access article distributed under the terms of the Creative Commons Attribution 4.0 International license

Address correspondence to Charles Langelier, chaz.langelier@ucsf.edu.

least 13% nucleotide sequence divergence in the VP1 protein. This isolate is 23% divergent in VP1 and 21% divergent when compared across the entire genome (8).

Accession number(s). The rhinovirus C isolate described here has been deposited at DDBJ/EMBL/GenBank under the accession number MG148341.

REFERENCES

- 1. Langelier C, Christenson SA. 2016. An expression of clinical significance: exploring the human genome to understand the variable response to rhinovirus. Am J Respir Crit Care Med 193:710-712. https://doi.org/10 .1164/rccm.201511-2272ED.
- 2. Kistler A, Avila PC, Rouskin S, Wang D, Ward T, Yagi S, Schnurr D, Ganem D, DeRisi JL, Boushey HA. 2007. Pan-viral screening of respiratory tract infections in adults with and without asthma reveals unexpected human coronavirus and human rhinovirus diversity. J Infect Dis 196:817-825. https://doi.org/10.1086/520816.
- 3. Lee WM, Lemanske RF, Evans MD, Vang F, Pappas T, Gangnon R, Jackson DJ, Gern JE. 2012. Human rhinovirus species and season of infection determine illness severity. Am J Respir Crit Care Med 186:886-891. https://doi .org/10.1164/rccm.201202-0330OC.
- 4. Langelier C, Zinter MS, Kalantar K, Yanik GA, Christenson S, O'Donovan B, White C, Wilson M, Sapru A, Dvorak CC, Miller S, Chiu CY, DeRisi JL. 7 July 2017. Metagenomic sequencing detects respiratory pathogens in hematopoietic cellular transplant patients. Am J Respir Crit Care Med https:// doi.org/10.1164/rccm.201706-1097LE.
- 5. Doan T, Wilson MR, Crawford ED, Chow ED, Khan LM, Knopp KA, O'Donovan BD, Xia D, Hacker JK, Stewart JM, Gonzales JA, Acharya NR, DeRisi JL. 2016. Illuminating uveitis: metagenomic deep sequencing identifies common and rare pathogens. Genome Med 8:90. https://doi.org/10 .1186/s13073-016-0344-6.
- 6. Gu W, Crawford ED, O'Donovan BD, Wilson MR, Chow ED, Retallack H, DeRisi JL. 2016. Depletion of abundant sequences by hybridization (DASH): using Cas9 to remove unwanted high-abundance species in sequencing libraries and molecular counting applications. Genome Biol 17:41. https://doi.org/10.1186/s13059-016-0904-5.
- 7. Ruby JG, Bellare P, Derisi JL. 2013. PRICE: software for the targeted assembly of components of (meta) genomic sequence data. G3 3:865-880. https://doi .org/10.1534/q3.113.005967.
- 8. Simmonds P, McIntyre C, Savolainen-Kopra C, Tapparel C, Mackay IM, Hovi T. 2010. Proposals for the classification of human rhinovirus species C into genotypically assigned types. J Gen Virol 91:2409-2419. https://doi.org/ 10.1099/vir.0.023994-0.