

## Non-O1 *Vibrio cholerae* unlinked to cholera in Haiti

Beginning with the observations of John Snow, many formal epidemiologic and molecular studies have corroborated the idea that cholera toxin-producing *Vibrio cholerae* (the agent of cholera) can move great distances via human activity. Recently “shoe leather”-based epidemiologic and whole genome-based molecular approaches have provided compelling evidence that the devastating ongoing cholera epidemic in Haiti was caused by a toxigenic strain of *V. cholerae* O1 that was inadvertently introduced into Haiti by United Nations (UN) security forces from Nepal, a South Asian country that suffered cholera outbreaks only weeks before the UN troops’ deployment (1–4). Hence, we were shocked to read the statement that “...assignment of attribution [for cholera in Haiti] remains controversial...” in the recent article, “Genomic diversity of 2010 Haiti cholera outbreak strains” by Colwell and colleagues (5). This article suggested that the cholera epidemic in Haiti is caused not only by a toxigenic *V. cholerae* O1 strain but also by strains belonging to a diverse group of non-O1 *V. cholerae* that lack the genes for cholera toxin and other important virulence factors. The authors concluded that the Haitian O1 strains they characterized were “...clonal, resembling epidemic isolates from South Asia and Africa,” but claim that non-O1 *V. cholerae* also had a role, because they cultured only nontoxigenic non-O1 *V. cholerae* from 21% of clinical samples from diarrhea patients. However, the methods used to culture *V. cholerae* O1 are notoriously unreliable, particularly under makeshift conditions. Furthermore, because the cholera case definition is not articulated, there is a strong possibility that some samples were not cholera/outbreak-associated. Notably, nontoxigenic non-O1 *V. cholerae* can be diarrheagenic, as can the non-*Vibrio* species that Colwell and colleagues (5) isolated from 31% of putative cholera cases tested, but neither causes cholera, a diarrheal disease that can be reproduced by oral ingestion of purified cholera toxin. Furthermore, in regard to the claim that non-O1 *V. cholerae* “serve as a reservoir for genomic and pathogenicity islands,” we cannot identify any genomic regions or sequence variants in the

Haitian toxigenic O1 isolates that are present in Colwell and colleagues’ non-O1 isolates but absent from Nepalese isolates. The sequences that are claimed to enable distinction between Haitian O1 *V. cholerae* and other variant El Tor strains (e.g., in CTX $\phi$ , *gyrA*, and *parC*) do not differ between Haitian O1 *V. cholerae* and Nepalese O1 *V. cholerae*, which were inexplicably omitted from the analyses by the Colwell group. Thus, we find no evidence that indigenous non-O1 *V. cholerae* contributed any genetic material to the toxigenic Haitian O1 outbreak strain.

Colwell and colleagues’ assertion that the role of non-O1 strains in the epidemic “cannot be dismissed” (5) is worthy of rebuttal because such statements obscure the true origin of the 2010 Haitian cholera epidemic. Genetic analysis of the causative O1 strain and solid epidemiologic investigations of the outbreak clearly indicate that human activity brought toxigenic *V. cholerae* O1 to Haiti (1–4). Research efforts should focus on learning more about how cholera is spread by humans and how we might prevent that with appropriate interventions that include vaccination, antibiotics, and other public health strategies during times of crisis.

**John J. Mekalanos<sup>a,1</sup>, William Robins<sup>a</sup>, David W. Ussery<sup>b</sup>, Brigid M. Davis<sup>c</sup>, Eric Schadt<sup>d</sup>, and Matthew K. Waldor<sup>c</sup>**

<sup>a</sup>Department of Microbiology and Immunobiology, Harvard Medical School, Boston, MA 02115; <sup>b</sup>Center for Biological Sequence Analysis, Department of Systems Biology, The Technical University of Denmark, 2800 Kgs. Lyngby, Denmark; <sup>c</sup>Department of Medicine, Brigham and Women’s Hospital, Boston, MA 02115; and <sup>d</sup>Department of Genetics and Genomic Sciences, Mount Sinai School of Medicine, New York, NY 10029

1. Chin CS, et al. (2011) The origin of the Haitian cholera outbreak strain. *N Engl J Med* 364:33–42.
2. Piarroux R, et al. (2011) Understanding the cholera epidemic, Haiti. *Emerg Infect Dis* 17: 1161–1168.
3. Hendriksen RS, et al. (2011) Population genetics of *Vibrio cholerae* from Nepal in 2010: evidence on the origin of the Haitian outbreak. *MBio* 2:e00157-11.
4. United Nations (2011) *Final Report of the Independent Panel of Experts on the Cholera Outbreak in Haiti*. Available at: <http://www.un.org/News/dh/infocus/haiti/UN-cholera-report-final.pdf>. Accessed May 1, 2011.
5. Hasan NA, et al. (2012) Genomic diversity of 2010 Haitian cholera outbreak strains. *Proc Natl Acad Sci USA* 102:E2010–E2017.

Author contributions: J.J.M. and M.K.W. designed research; W.R., D.W.U., B.M.D., and E.S. performed research; and J.J.M. and M.K.W. wrote the paper.

The authors declare no conflict of interest.

<sup>1</sup>To whom correspondence should be addressed. E-mail: john\_mekalanos@hms.harvard.edu.