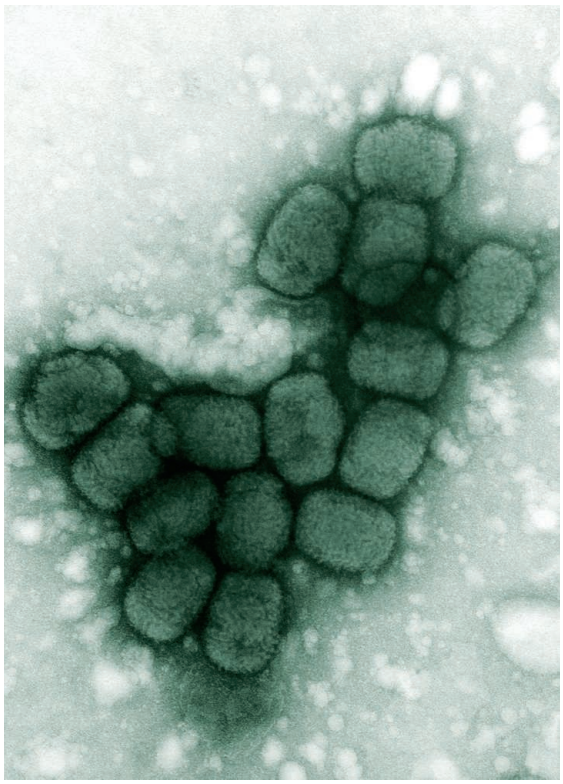
LETTERS

Edited by **Jennifer Sills**

Is it time to destroy the smallpox virus?



THE LAST CASES of smallpox occurred more than 37 years ago. Should we now destroy the variola virus samples that remain in the two World Health Organization (WHO)–designated smallpox laboratories, located in the United States (Centers for Disease Control and Prevention) and Russia (Koltsobo, Siberia)? In May, the 67th World Health Assembly in Geneva decided that the previously agreed-upon decision to destroy the smallpox virus stocks would, once again, be postponed for an additional 3 years until the 70th World Health Assembly in 2017. We support the decision not to destroy the virus.

Although true eradication and protection from bioterrorist smallpox attacks will only be assured once the causative agent is eliminated from all laboratories, there is no way to guarantee that all stocks have been destroyed. During the last search for residual variola, all nations collaborated and responded to a special WHO letter addressed to the heads of health service of each country. Sixteen smallpox isolates were reported (*1*). Given these results, more stocks likely exist in unknown places. The recent discovery of variola in old specimens at the National Institutes of Health (NIH) in Bethesda, Maryland, highlights this risk (*2*–*4*). Furthermore, from the late 1980s to the early 1990s, the former USSR biowarfare laboratory produced huge amounts of variola virus. Much like the recent NIH situation, it would not be surprising to find that, in some dark corner of this or a similar facility, viable tubes of variola virus were still resting comfortably.

The destruction of official government stocks could serve to increase, rather than decrease, risk in the event that adversarial groups gain access to the virus. Moreover, synthesis of smallpox virus could be accomplished by a well-trained laboratory technician. Lack of access to the original strain could also impede research should a new strain emerge.

Given the likely continuing need to have viable variola virus to conduct required research, the security and the political threats in today's world, and historical efforts to use variola as a biologic weapon, we support the establishment of a secure system to maintain live smallpox virus under the supervision of the United Nations. We recommend that the WHO establish a special commission to implement this system.

Isao Arita*[1] *and Donald Francis*[2]

[1]Director Emeritus, National Hospital Organization, Kumamoto Medical Center, Kumamoto 861–8068, Japan. [2]Executive Director, Global Solutions for Infectious Diseases, South San Francisco, CA 94080, USA.

*Corresponding author. E-mail: dfrancis@gsid.org

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3. S. Reardon, *Sci. Am.* (2014); www.scientificamerican.com/article/vials-of-smallpox-virus-found-unsecured-at-nih/.
4. J. Kaiser, *Science Insider* (2014); http://news.sciencemag.org/health/2014/07/six-vials-smallpox-discovered-u-s-lab.

Gene drives raise dual-use concerns

THERE IS NO doubt that clear regulations are required before gene drives can be released into the environment, as K. A. Oye *et al.* point out in their Policy Forum "Regulating gene drives" (8 August, p. 626; published online 17 July). However, they do not address a more pressing concern. Regulations are effective only for legitimate organizations and nations, whereas gene drive technologies can, in the wrong hands, potentially be used for malicious purposes. For example, just as gene drives can make mosquitoes unfit for hosting and spreading the malaria parasite, they could conceivably be designed with gene drives carrying cargo for delivering lethal bacteria toxins to humans. Other scary scenarios, such as targeted attacks on major crop plants, could also be envisaged.

Fortunately, learning how to insert a gene drive into the germline and optimize its function will have to be done anew for each species, and may be far trickier in organisms with larger genomes (*1*). It is therefore timely to call upon the scientific research community to prevent the disclosure of exact instructions on making specific gene drives in scientific manuscripts or patent applications. Just as the exact technical instructions for making nuclear weapons remain classified 70 years after the Manhattan Project—as they rightfully should—the gene drive methodological details do not belong in the scientific literature.

David Gurwitz

Department of Human Molecular Genetics and Biochemistry, Sackler Faculty of Medicine, and Sagol School of Neuroscience, Tel Aviv University, Tel Aviv, 69978, Israel.
E-mail: gurwitz@post.tau.ac.il

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Response

WE RESPECT GURWITZ'S concern over potential misuse of gene drives but disagree with his proposal to restrict information access. Treating information related to gene drives as classified would be technically ineffective and politically counterproductive.

Gene drives incorporate CRISPR genome editing machinery such that editing occurs anew in each organism that inherits a copy (*1*). Building standard gene drives in a new species will involve adapting the widely available CRISPR technology to that species. At best, classifying information would force agents intent on misuse to adapt CRISPR on their own. This is unlikely to impede any agent able to overcome the formidable challenge of introducing entirely new traits intended for misuse.

Even if withholding information on CRISPR adaptation or gene drives did

PHOTO: DR. FRED MURPHY/CDC

impede attempts at misuse, it could also backfire by delaying the construction of time-sensitive reversal and immunization drives useful for defense. Classifying details would also fuel suspicion, retard development of technological safeguards, and vitiate informed debate on risks. Given that the vast majority of species will not represent biosecurity threats, acting as if the risk of misuse outweighs the benefits of transparency would be shortsighted.

The analogy to classifying instructions on making nuclear weapons does not hold. Classification in the nuclear domain differentiates between methods needed to develop weapons, which cannot be defended against, and methods used in nuclear power and medicine (*2*). By contrast, classifying information required to build gene drives cannot target potential misuses without also impeding development of defenses, as well as environmental, health, agricultural, and safety applications of CRISPR technology.

We encourage scientists to consider the possibility of eventual misuse and to consult with biosecurity experts before initiating development of gene drives in a new species, but suggest that banning release of technical information would reduce rather than enhance biosecurity.

Kenneth A. Oye[1] and Kevin M. Esvelt[2]

[1]Center for International Studies, Massachusetts Institute of Technology, Cambridge, MA 02139, USA. [2]Wyss Institute for Biologically Inspired Engineering, Harvard Medical School, Boston, MA 02115, USA.

*Corresponding author. E-mail: oye@mit.edu

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TECHNICAL COMMENT ABSTRACTS

Comment on "The hologenomic basis of speciation: Gut bacteria cause hybrid lethality in the genus *Nasonia*"

James Angus Chandler and Michael Turelli

■ Brucker and Bordenstein (Reports, 9 August 2013, p. 667) claim that adaptive codivergence of gut bacteria with hosts contributes to hybrid lethality. Yet, they provide no evidence for coadaptation of bacteria and *Nasonia* hosts. Their data on hybrid viability suggest that bacteria contribute to inviability only because intrinsic hybrid dysfunction increases susceptibility to free-living bacteria. Hologenomic speciation remains testable speculation without experimental support.

Full text at http://dx.doi.org/10.1126/science.1251997

Response to Comment on "The hologenomic basis of speciation: Gut bacteria cause hybrid lethality in the genus *Nasonia*"

Robert M. Brucker and Seth R. Bordenstein

■ Chandler and Turelli postulate that intrinsic hybrid dysfunction underscores hybrid lethality in *Nasonia*. Although it is a suitable conception for examining hybrid incompatibilities, their account of the evidence is factually inaccurate and leaves out the evolutionary process for why lethality became conditional on nuclear-microbe interactions. Hybrid incompatibilities in the context of phylosymbiosis are resolved by hologenomic principles and exemplify this emerging postmodern synthesis.

Full text at http://dx.doi.org/10.1126/science.1256708