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Unintended Effects of Genetic Manipulation
A Project of The Nature Institute
Project Director: Craig Holdrege
Email: nontarget@natureinstitute.org

20 May Hill Road • Ghent, NY 12075 USA • Tel: (518) 672-0116 • http://natureinstitute.org

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Using CRISPR-Cas9 to Engineer Resistance to Virus in Cassava Plants Backfires

Colleen Cordes

An attempt to develop a virus-resistant cassava plant with CRISPR-Cas9, the popular new genetic engineering tool, backfired, according to a new study. Instead of ending up with a virus-resistant variant of cassava, the experiment generated a mutant form of the targeted virus that resists being disabled by CRISPR — a mutant that could be, the researchers reported, "an intermediate step towards the development of a truly pathogenic novel virus."

"We urge caution in the application of CRISPR-Cas9 for virus resistance in plants, both in glasshouse and field settings, to avoid inducing the evolution of resistant viruses," the researchers added.

The study was conducted under controlled greenhouse conditions by plant biologists at the University of Alberta, the University of Liège in Belgium, and ETH Zurich, which is part of the Swiss Federal Institutes of Technology Domain. It was published in the April 25, 2019 issue of *Genome Biology.*

The authors were trying to engineer resistance to the African cassava mosaic virus, a member of a widespread family of DNA viruses that cause disease in plants — in this case, in cassava, a root vegetable that is high in starch and an important food crop in tropical regions.

The researchers inserted a bacteria-derived CRISPR-Cas9 system into the plant – an attempt at "anti-viral CRISPR transgenics." In nature, the CRISPR system is a bacterial immune response, helping bacteria defend against viruses by acting as a kind of "molecular scissors", damaging a virus by cutting through its DNA. So the inserted material here was expected to help cassava plants resist the targeted virus in a similar way.

But the engineering did not confer to the transgenic lines of cassava plants any significant resistance to the targeted virus. Instead, the researchers found that between 33% and 48% of virus genomes that had been exposed to the CRISPR-Cas9 material in the transgenic plants evolved a "novel, conserved mutant virus that cannot be cleaved by CRISPR-Cas9."

The researchers encouraged others who are interested in developing anti-viral CRISPR transgenics to conduct the kind of careful genetic analyses done here to make sure they also do not generate such unintended effects. "This is especially important," they noted, "for informing regulation of such actively mutagenic applications of CRISPR-Cas9 technology in agriculture."

Over time, research into how the CRISPR system in bacterial cells can adapt to mutant viruses may shed light on how to safely engineer anti-viral CRISPR transgenic plants that could also adapt to mutations in the viruses that attack them, the researchers suggested.

"In the meantime," they cautioned, "the implementation of technologies with the potential to speed up virus evolution should be carefully assessed as they pose significant biosafety risks."

Sources

Mehta, Devang, Alessandra Stürchler, Ravi B. Anjanappa et al. (2019). "Linking CRISPR-Cas9 Interference in Cassava to the Evolution of Editing-Resistant Geminiviruses," *Genome Biology* vol. 20, no. 80 (April 25). https://doi.org/10.1186/s13059-019-1678-3

Willis, Katie (2019). "Gene-Editing Technology to Create Virus-Resistant Cassava Plant Has Opposite Effect, Researchers Find," University of Alberta (April 25). https://www.ualberta.ca/science/science-news/2019/april/virus-resistance-cassava