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Consortium develops new method to manipulate genetic material

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A multi-institutional team of researchers, including scientists at the University of Minnesota Medical School, have developed a powerful tool for genomic research and medicine. The robust method will allow researchers to generate synthetic enzymes that can target and manipulate DNA sequences for inactivation or repair.

The potential for discovery is great, said Dan Voytas, Ph.D., director of the Arnold and Mabel Beckman Center for Transposon Research, and co-investigator on the research. In human therapeutics, researchers may aim to correct genetic disorders or diseases, and in plants, scientists may devise crops that are more resistant to pathogens, yield more product, and better combat stress.

In the July 25 issue of Molecular Cell, researchers including Voytas describe an efficient method to induce specific genomic modifications in many types of cells – including plants and humans. This is the first time the method will be publicly available and free to researchers.

"This method is going to be a turning point in the way we manipulate genomes," Voytas said. "It will allow any researcher to make a change to genetic material."

More specifically, the article shows researchers how to engineer customized zinc-finger nucleases (ZFNs), which can be used to induce specific genomic modifications in many types of cells.

"Recent work has shown that ZFNs can alter genes with high efficiency in cells from plants or model organisms like fruit flies, roundworms, and zebra fish, and in human cells," said J. Keith Joung, M.D., Ph.D., assistant professor of pathology at Harvard Medical School and director of the Molecular Pathology Unit at MGH, principal investigator of the study. "Our method will enable academic researchers to rapidly create high quality ZFNs for genes of interest and will stimulate use of this technology in biological research and potentially gene therapy."

Currently available methods for generating ZFNs are either inefficient or exceed the capabilities of all but a handful of laboratories in the world.

Morgan L. Maeder of the Joung lab led an effort by researchers from six institutions that demonstrated how this new method (termed OPEN, for Oligomerized Pool ENgineering) can rapidly generate ZFNs that induce alterations at sites in three biologically important human genes and a plant gene. ZFNs made by the new OPEN method – which utilizes a new archive of reagents that will be made publicly available by the Zinc Finger Consortium – were so efficient that they could modify as many as four copies of a gene in human cells and two copies in plant cells.

"Our study provides the first evidence that ZFNs can make specific changes in plant genes with high efficiency and opens a new avenue for plant genetic modification," Voytas said. At the University of Minnesota, Voytas and his team are interested in modifying plant genes for crop improvement.

"With the development of OPEN, many more academic labs will be able to construct, test and use ZFNs in their biological research projects," Joung said. "OPEN should also stimulate additional research into the potential application of ZFNs for gene therapy of single-gene disorders, such as sickle cell anemia and cystic fibrosis."

Source: University of Minnesota