Altering genes with the aid of light

May 8 2015

Scientists have been manipulating genes for a while. The University of Pittsburgh's Alexander Deiters just found a way to control the process with higher precision.

By using light.

Deiters and his group are the first to achieve this. The resulting paper was recently published in the *Journal of the American Chemical Society*.

Since 2013, scientists have used a gene-editing tool called CRISPR/Cas9. The method employs a bacterially derived protein (Cas9) and a synthetic guide RNA to induce a double-strand break at a specific location in the genome. This enables excision of a gene, alteration of its function, or introduction of desired mutations.

In practice, the CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats of DNA base sequences) method has shown tremendous promise to enable researchers to treat cystic fibrosis and sickle-cell anemia, create laboratory animals that mimic human disease, and create a strain of wheat resistant to powdery mildew.

Deiters, professor of chemistry in Pitt's Kenneth P. Dietrich School of Arts and Sciences, along with colleagues at the University of North Carolina at Chapel Hill, have, through a series of experiments, found a lysine residue (lysine is an amino acid) in Cas9 that can be replaced with a light-activated analog.

The approach developed by Deiters generates a Cas9 protein that is functionally inactive, so called "caged," until the cage is removed through light exposure, activating the enzyme and thereby activating gene editing.

"This method may allow people to engineer genes in cells or animals with better spatial and temporal control than ever before," Deiters says. "Previously, if you wanted to knock out a gene, you had limited control over where and when it would happen. Engineering a light switch into Cas9 provides a more precise editing tool. You can say, 'In this cell, at this time point, is where I want to modify the genome.'"

The improved control over the time and location at which a gene will be manipulated, Deiters says, may help eliminate "off-target effects" and could potentially enable genetic studies with unprecedented resolution.

Provided by University of Pittsburgh