Researchers develop hybrid protein tools for gene cutting and editing

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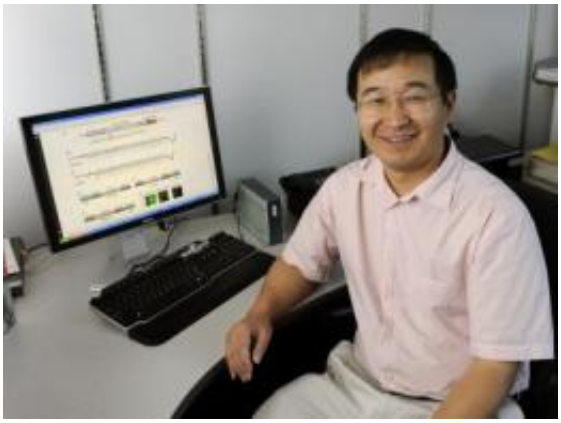

This is Bing Yang of Iowa State University. Credit: ISU photo by Bob Elbert

An Iowa State University team of researchers has developed a type of hybrid proteins that can make double-strand DNA breaks at specific sites in living cells, possibly leading to better gene replacement and gene editing therapies.

Bing Yang, assistant professor of genetics, development and cell biology, and his colleagues developed the hybrid protein by joining parts of two different bacterial proteins. One is called a TAL effector, which functions to find the specific site on the gene that needs to be cut, and the other is an enzyme called a nuclease that cuts the DNA strands.

Yang hopes the research will lead to the ability to modify genomes by

cutting out defective or undesirable parts of DNA, or by replacing defective or undesirable gene segments with a functioning piece of replacement DNA - a process called homologous recombination.

Yang says that his hybrid proteins can be constructed to locate specific segments of the DNA in any type of organism.

"This breakthrough could eventually make it possible to efficiently modify plant, animal and even human genomes," said Yang. "It should be effective in a range of organisms."

The proteins work by binding onto the specific segment of DNA the researcher wants to change. Yang's proteins do this by reading the DNA sequence and finding the specific area to be cut.

Once the protein binds onto the DNA at the correct spot, the other half of Yang's protein then cuts the double-stranded DNA.

Bad or undesirable DNA can be resected (removed) and good or more desirable DNA can be introduced. When the DNA heals, the good DNA is included in the gene.

Yang started his research about a year ago after seeing the results of research by Adam Bogdanove, ISU associate professor of plant pathology, showing that TAL effectors use a very straightforward code to bind to a specific DNA sequence.

This discovery allowed Yang to predict exactly where the TAL effector nuclease will bind on the DNA to make the cut.

Another study had similar results.

The concept has also been proven by Bogdanove and Dan Voytas,

collaborator in genetics, development and cell biology at Iowa State, and director of the Center for Genome Engineering at the University of Minnesota, Twin Cities.

The TAL effector-nuclease approach improves on tools currently available for genome modification. It should be faster and less expensive to make TAL effector nucleases, and easier to design them to recognize specific DAN sequences, according to Yang.

Yang's findings recently appeared in the online version of the journal *Nucleic Acids Research*. Voytas' and Bogdanove's study also appeared recently in the journal *Genetics*.

Voytas and Bogdanove were also able to show that the TAL effector part of the hybrid protein can be customized to target new DNA sequences.

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