NEWS

Computer program guides molecular scissors on where to snip

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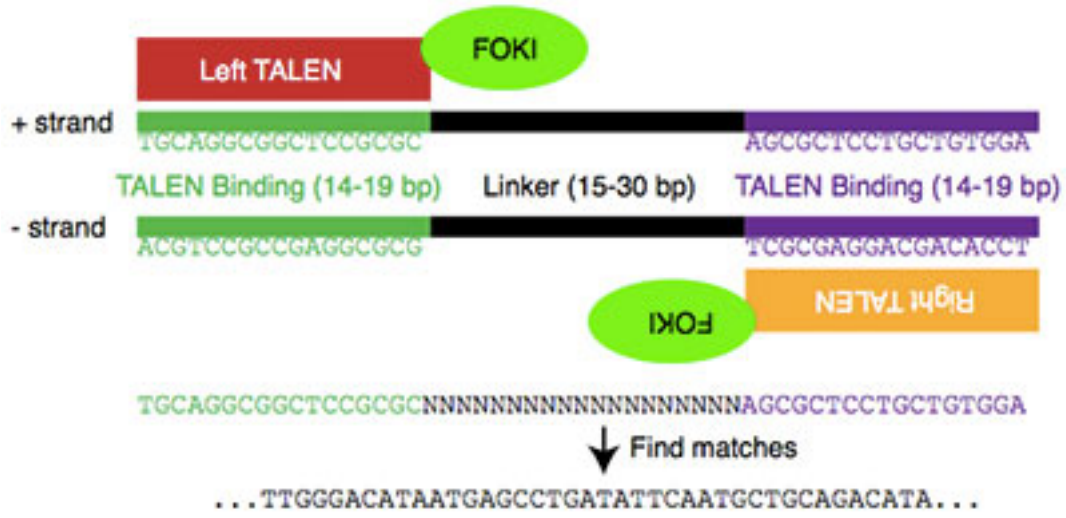

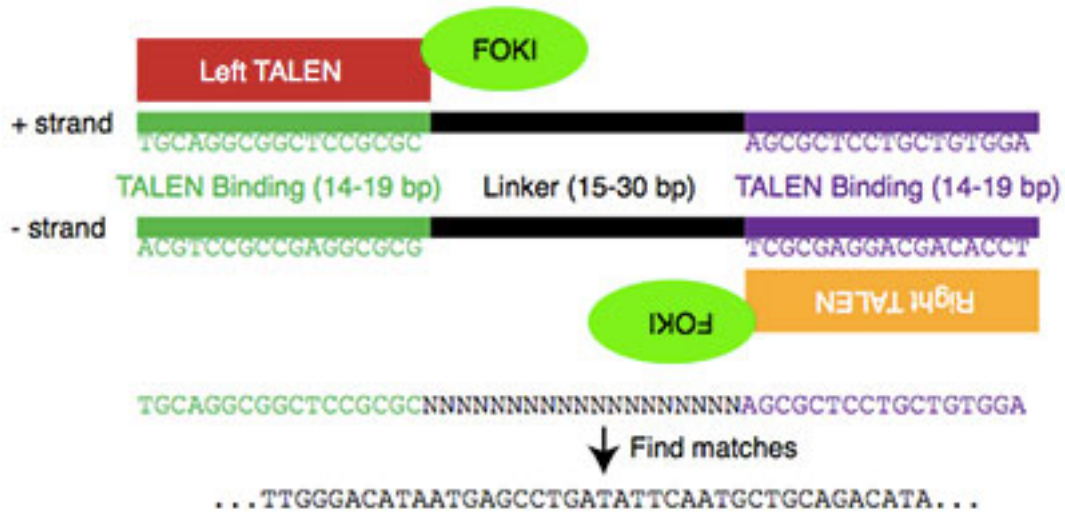

TALENted editors: Certain proteins can bind to precise sites on a DNA strand and snip out the code.

Researchers have created software that can design customized molecular scissors to edit the genomes of living cells. The program, called **TALENSeek**, was presented in a poster Saturday afternoon at the **2013 Society for Neuroscience annual meeting** in San Diego.

In the past few years, a suite of new genome-editing tools has galvanized the biology field, allowing researchers to precisely manipulate DNA and RNA in living cells.

Proteins known as transcription activator-like effector nucleases (TALENs) and clustered regularly interspaced short palindromic repeats (CRISPRs) attach to precise locations on the genome, snip out both strands of DNA, and can even replace it with new code. Several groups are using this technology to **make new models of autism-related disorders**.

“These proteins we can design to any region we want in the genome with very few restrictions,” says **Jason Stein**, a postdoctoral fellow in **Daniel Geschwind**’s laboratory at the University of California, Los Angeles. The proteins can introduce specific single-letter variations, for example, knock out a gene or boost a gene’s expression.

Stein initially created TALENSeek as a way to help his collaborators at the Allen Institute for Brain Science in Seattle. Researchers at the institute are **generating hundreds of lines of human neurons** derived from reprogrammed stem cells and intend to use genome-editing tools on these cells. The new software program can quickly identify binding sites for TALENs and CRISPRs that

would target particular genes.

Identifying the binding sites can be tricky. A gene encompasses hundreds to thousands of DNA base pairs, and a binding site typically has fewer than 20 of them. The best molecular scissors are specific, meaning that they bind to the gene of interest and nowhere else in the genome. “So they don’t have any off-target cutting,” Stein says.

Other groups have created similar software programs, such as **E-TALEN**. But Stein says his program is unique because it identifies sites that exist in both human and mouse cells, so the same scissors can be used for both sets of experiments.

So far, Stein and his colleagues have used the software to find binding sites within several genes, including PAX6, which is a marker for neural progenitor cells. Using genome editing they attached a fluorescent protein to the gene, effectively making a line of labeled progenitor cells.

The lab is planning to do similar experiments with autism-linked genes, including **CNTNAP2**, Stein says.

TALENSeek — which Stein had wanted to name TALENSwift, after the pop star — is available to anyone for free at the **Geschwind lab website**.

*For more reports from the 2013 Society for Neuroscience annual meeting, please **click here**.*