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Gene-editing tools pave way for new Alzheimer's treatments

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Two new studies using CRISPR gene editing offer potential new

treatments for Alzheimer's disease.

"A pipeline of potential new treatments offers hope for the Alzheimer's and dementia community," said Maria Carrillo, chief science officer for the Alzheimer's Association. "The progress and approvals we've seen, as well as the diversification of potential new therapies over the past few years, provides hope to those impacted by this devastating disease.

"The anti-amyloid drugs newly approved by the U.S. Food and Drug Administration are an important first step in Alzheimer's treatment, but there is so much more to be done," she said in an association news release.

One study targets the most common Alzheimer's risk gene, APOE-e4. The other aims to decrease production of beta amyloid, a toxic protein in the brain.

CRISPR is shorthand for the Clustered Regularly Interspaced Short Palindromic Repeats system. Gene editing using this system is considered a powerful tool for identifying new potential medications.

"Studies such as these two that focus the most advanced technologies—in this case, CRISPR—on moving Alzheimer's treatment and prevention forward are enthusiastically welcomed, and need to be multiplied many times over," Carrillo said. "We envision a future where multiple treatments address every aspect of this most complex disease. And that, once proven, the treatments can be combined in ways that complement and enhance each other to reduce risk, treat effectively, stop the progression and eventually cure Alzheimer's disease and all other dementia."

Inheriting the APOE-e4 gene doesn't guarantee a person will develop Alzheimer's, but having one copy of APOE-e4 increases the risk two- to

threefold. Having two of these genes increase the risk by as much as 12 times.

The study targeting this gene found levels of APOE-e4 could be significantly reduced in both miniature brains derived from an Alzheimer's patient as well as in humanized mouse models. It could do this without changing levels of other APOE variants that are thought to be neutral or protective.

"The findings are incredibly exciting," said Boris Kantor, associate research professor of neurobiology at the Duke University Center for Advanced Genomic Technologies in Durham, N.C. "They provide proof-of-concept evidence supporting our approach as a high potential new strategy to treat and possibly even prevent Alzheimer's disease, which currently has no cure."

Ornit Chiba-Falek, division chief of translational brain sciences at Duke, said the goal is to move towards precision medicine.

"We believe the results are very promising," she said.

In the other study, researchers developed a gene-editing strategy that targets the amyloid precursor protein (APP). Study author Brent Aulston of the Subhojit Roy lab at University of California, San Diego calls APP "a gene with a central and indisputable role" in Alzheimer's.

APP can create byproducts that are either protective (sAPPa) or pathologic (beta amyloid), depending on how it is cut by various enzymes in the brain, according to the study. Researchers hope to reduce the production of beta amyloid while increasing neuroprotective actions.

They found that CRISPR treatment led to reduction of beta amyloid plaques and associated markers of brain inflammation. It also prompted

an increase in neuroprotective APP products, and correction of behavioral and nervous system function deficits when testing the process in an Alzheimer's disease mouse model.

This CRISPR-editing did not lead to undesirable side effects in normal mice.

"We believe this demonstrates that, in mice, our potential treatment strategy is both safe and efficacious," Aulston said. "These results justify future studies aimed at getting APP CRISPR editing into human testing."

Their findings were presented Sunday at the Alzheimer's Association International Conference, in Amsterdam. Such research is considered preliminary until published in a peer-reviewed journal.

More information: The U.S. Centers for Disease Control and Prevention has more on Alzheimer's disease.