CRISPR-Cas9 gene editing shows very low risk of mistakes

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Along with the promise that CRISPR-Cas9 gene editing technology can offer new human therapies is the need to ensure its safety. A recent study showed that CRISPR-Cas9 did not produce off-target gene mutations in zebrafish. These results, published in *Frontiers in Genetics*, confirm previous data in animal models that the risk to the rest of the

genome from gene editing is minimal.

"Our data add to a growing and important body of work from the scientific community that unintended mutations from gene editing with CRISPR-Cas9 are extremely rare," says senior author Nico Katsanis, Ph.D., Director of the Advanced Center for Translational and Genetic Medicine, Stanley Manne Children's Research Institute, at Ann & Robert H. Lurie Children's Hospital of Chicago. Dr. Katsanis also is Professor of Pediatrics and Cell and Molecular Biology at Northwestern University Feinberg School of Medicine. "These findings help to alleviate concerns about harmful errors when gene editing is used in humans. Our results provide reassurance that this technology is a valuable and valid tool with great promise for the treatment of genetic disorders."

CRISPR-Cas9 already is used in early stage clinical trials for cancer, sickle cell disease and childhood blindness. Currently, researchers remove cells from the body, edit the target gene and return it to the body.

Dr. Katsanis and colleagues performed whole exome sequencing (WES) in over 50 individual organisms from three generations of zebrafish, which allowed robust testing of gene editing effects. Zebrafish are a commonly used laboratory animal that share approximately 70 percent of its genome with humans. WES is used to identify genetic variants in portion of the genome that codes for proteins, and makes up the building blocks of cells, tissues and organs of the body.

"Although our study is just one of many recent reports, it is unique because we studied a large group of related animals that allowed us to screen for off-target effects in an unbiased way," says co-author Erica Davis, Ph.D., from the Advanced Center for Translational and Genetic Medicine, Manne Research Institute at Lurie Children's. Dr. Davis is Associate Professor of Pediatrics and Cell and Molecular Biology at

Northwestern University Feinberg School of Medicine. "In addition to clinical implications, our results indicate that CRISPR-Cas9 is also a powerful research tool, helping us create new models of genetic disease with confidence."

More information: Marie R. Mooney et al, Analysis of Single Nucleotide Variants in CRISPR-Cas9 Edited Zebrafish Exomes Shows No Evidence of Off-Target Inflation, *Frontiers in Genetics* (2019). DOI: 10.3389/fgene.2019.00949

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