

## Case 2: You Want Those Genes CRISPR'd?

CRISPR-Cas9 is a gene correction system that is simpler to design, easier to use, less time-consuming and less costly than previous techniques. Applications of the technology are so broad "that the possibilities for using it to treat disease are virtually endless," according to E. Mullin at the *MIT Technology Review*.

Researchers across the globe are exploring the uses of CRISPR-Cas9. The Chinese ministry of health has approved all gene-therapy clinical trials in China. According to the *Wall Street Journal's* article, "China, Unhampered by Rules, Races Ahead in Gene-Editing Trials," so far, "scientists have genetically engineered the cells of at least 86 cancer and HIV patients in the country using CRISPER- Cas9 technology since 2015." Of these eighty-six, there have been fifteen deaths, seven of which were enrolled in the same clinical trials. The causes of the deaths are being attributed to the natural disease process, not to the CRISPR-Cas9 therapies.

CRISPR-Cas9 is a "gene correction" which focuses on replacing disease-causing DNA with healthy DNA. The gene editing process naturally activates the p53 gene, sometimes referred to as the "Guardian of the Genome," which is part of the body's natural defense. It works in one of two ways, either repairing cells with damaged DNA or telling the damaged cell to self-destruct. Herein lies the problem: p53 will also defend against genome edits made using CRISPR-Cas9, eventually causing the edited cells to be repaired (remove the edit) or self-destruct. Either way, the outcome is the same: some CRISPR-Cas9 therapies are largely ineffective. In order for CRISPR-Cas9 to reach maximum efficacy the p53 gene needs to be dysfunctional or deactivated. While a dysfunctional p53 may appear to be beneficial for CRISPR-Cas9 therapies there is a caveat: it is known to cause cancer.

Last year, two different biomedical labs published research on CRISPR-Cas9 effectiveness in *Nature Medicine*. They both came to the conclusion that there is an increased risk of cancer from the use of CRISPR-Cas9. As reported by *Scientific American*, researchers from Sweden's Karolinska Institute and from Switzerland's Novartis International AG have said that cells whose genomes are successfully edited by CRISPR-Cas9 "have the potential to seed tumors inside a patient. That could make some CRISPR'd cells ticking time bombs." More specifically, "The reason why that could be a problem is that p53 dysfunction can cause cancer. And not just occasionally. P53 mutations are responsible for nearly half of ovarian cancers; 43 percent of colorectal cancers; 38 percent of lung cancers; nearly one-third of pancreatic, stomach, and liver cancers; and one-quarter of breast cancers, among others."

Case from the 2019 National Intercollegiate Ethics Bowl



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