# CRISPR technology in the Cancer field: Advantages, Limits, and Applications

Siyona Parkar

In 2024, there were 2.4 million cancer cases projected. This was the first time the estimated cases were above two million, and this number is expected to rise. All this can start with an accumulation of DNA mutations that can create cancer cells. Once these cancer cells start to grow uncontrollably, they become tumors which may be malignant and spread throughout the body. Since cancer starts with DNA mutations and cancer cases are growing, technology has been created that can manipulate DNA. CRISPR is a gene editing technology which uses guiding RNA to lead  Cas9 protein into a specific part of the genome, where a part of the DNA can be cut. Genes can be disabled or new material can be added. The first study in cancer treatment was in 2019 where the patient's immune cells, the T cells, were genetically modified to better detect and kill the cancer. The findings suggest that the treatment was safe, but needs improvement in efficiency. This review paper aims to uncover ways CRISPR can be used to treat cancer and whether it is an effective method to do so.

Cancer is one of the leading causes of death with approximately forty percent of people estimated to get cancer at some point in their lives. With rapidly developing technology, cancer can be tackled at the source: DNA mutations. In recent years, just in 2013, gene editing potential was realized in CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats). This technology allows scientists to replace, remove, or add genetic information. Genes may also be regulated by changing how much a gene is used. Not only that, but CRISPR has wide applications in the cancer field such as research, modeling, and therapeutics.

With CRISPR, as shown in figure 1, scientists are enabled to modify DNA sequences in living organisms by using a single guide RNA that guides DNA endonuclease Cas9 to cut a specific place in the DNA. Cas9 catalyzes a reaction that starts the cleavage of DNA, where the specific DNA sequence before the PAM (protospacer adjacent motif) sequence is cleaved. After it is cleaved, the cell starts a repair process which scientists use to change the gene. One of these repair processes is Non-Homologous End Joining (NHEJ) where the cell quickly fixes the DNA ends back together. This process is sloppy and often causes small insertions or deletions, otherwise known as indels, and usually causes the gene to be knocked out or disabled. The second repair process is Homology-Directed Repair (HDR). If scientists provide a repair template, a piece of DNA with the desired changes, the cell can use it to fix the break. Through these processes, DNA sequences have the ability to be precisely edited so mutations can be corrected or new genes can be inserted.

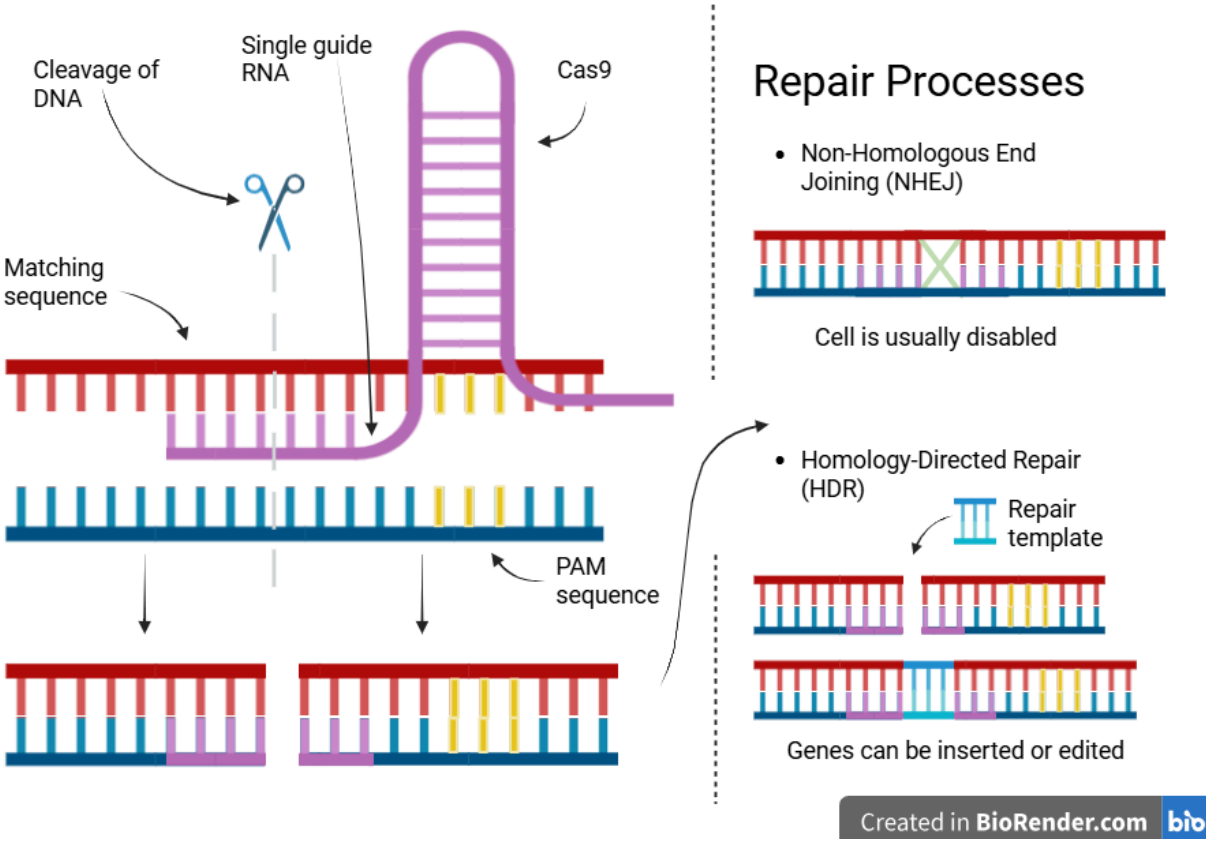


*Figure 1. How CRISPR-Cas9 is used to edit genes.Once DNA is cleaved, it can go through two different repair processes to remove, add or replace genetic information.*

By editing the cancer DNA or the immune system's DNA, CRISPR can be used in many ways in the cancer field. Some of which include cancer research to gain knowledge on genes, diagnostics, modelling, screening, treatment, and the list goes on. Gene-editing technology holds many new opportunities that have the capability to do tasks that could not be done before with as much ease or efficiency. Despite this, there are still problems that may stem from it as with any new technology. This review paper covers the benefits and harms of CRISPR, and how it may be used in cancer diagnostics and therapeutics.

First and foremost, even though CRISPR is a promising new technology, it has its strengths and limitations. Specifically in cancer-related work, its benefits include the ability to aid in studying cancer-causing genes, make multiple mutations in a gene at once, and correct mutations that lead to cancer. It has shown great precision and efficiency in manipulating cancer involved genes (Chen et al, 2019). However, it has limitations in delivery, off-target effects, safety, and ethical challenges. Cells modified by CRISPR have the potential to start the development of cancer, so using CRISPR for treatment could actually increase the risk of cancer (Radbakhsh and Moghaddam, 2024). This illustrates that CRISPR is not yet a perfect method to be applied in the cancer field, but it has great potential in cancer research and treatment. Its delivery methods and process has to be refined before people can start using it more, otherwise healthy cells can be killed, immune cells can be weakened, or there can be a risk of new cancers being triggered. Even now, it's only being used in vitro due to the ethical

challenges that happen with in vivo methods. All in all, CRISPR has the ability to be a powerful tool in a variety of uses in the cancer field.

On a related note, one use of CRISPR can be in cancer diagnosis. Besides CRISPR-Cas9, there are other enzymes that can be used alongside CRISPR such as Cas12 and Cas13 that work well in cancer diagnostics. These enzymes can activate trans-cleavage, also called collateral cleavage (Wang et al, 2023).The reporter molecules are tagged with a fluorophore and quencher, and once they are cleaved, they release a detectable fluorescence signal (Gong et al, 2021). Moreover, Cas12's ability to cleave collateral ssDNA is used in DETECTR to detect cancer-based mutations and it has a high sensitivity to circulating tumor DNA. Cas13 is the base for SHERLOCK, which is very sensitive and specific when detecting cancer-related RNA in liquid biopsies (Di Carlo and Sorrentino, 2024). This is powerful because the ability of trans-cleavage in these two enzymes allows cancer-related DNA/RNA to be detected through fluorescent or color changing signals quickly with a high level of sensitivity and specificity. So, it may be able to catch traces even before cancer symptoms appear. Also, this is beneficial in the use of cancer monitoring and research since no surgery is needed and can be done in vitro with liquid biopsies. This way, it is non-invasive and can be done multiple times. Considering everything, CRISPR Cas12 and Cas13 can improve the process of diagnosis in cancer.

Another key aspect of CRISPR is its ability to improve cancer therapeutics. Already, scientists have begun to test the use of CRISPR in immunotherapy. For example, as shown in figure 2, scientists have done a study on using CRISPR engineered T-cells in refractory cancer to test if gene editing with CRISPR is safe and feasible. It targeted NY-ESO-1, a cancer antigen, and in the study, T cells were edited at three genes: TRAC and TRBC to remove native TCRs, and PDCD1 to eliminate PD-1, a checkpoint inhibitor. The edited cells were called NYCE (NY-ESO-1 transduced CRISPR 3X edited cells), and were put back into the patient after editing. Out of the six patients, four patients had successfully engineered T cells. The results were that no serious adverse events related to gene editing were observed, edited T cells persisted for up to 9 months, and editing efficiency was high (Stadtmauer et al, 2020). Furthermore, there is another study focusing on using CRISPR for cancer/genome shredding to destroy glioblastoma cells. It targets highly repetitive DNA sequences from recurrent glioblastoma, and kills those cells, even the ones that have been resistant to TMZ chemotherapy. After repetitive treatment, tumor cells that haven't been killed after one round of cancer shredding can be removed (Tan et al, 2023). This shows feasibility and safety in CRISPR-Cas9 gene editing, and that CRISPR gene editing can be done in human immune cells while still having them function. In addition, the second study shows that CRISPR addresses tumor heterogeneity and therapeutic resistance in glioblastoma, a notoriously difficult-to-treat brain cancer. More importantly, it works in tumors that have shown resistant to other types of treatments. Still, more studies are needed that show higher editing efficiency and must be observed for a longer duration of  time to gain a complete understanding of the safety of treatment in real use. Certainly, the use of CRISPR in medical applications must be further studied to ensure its efficacy and safety.

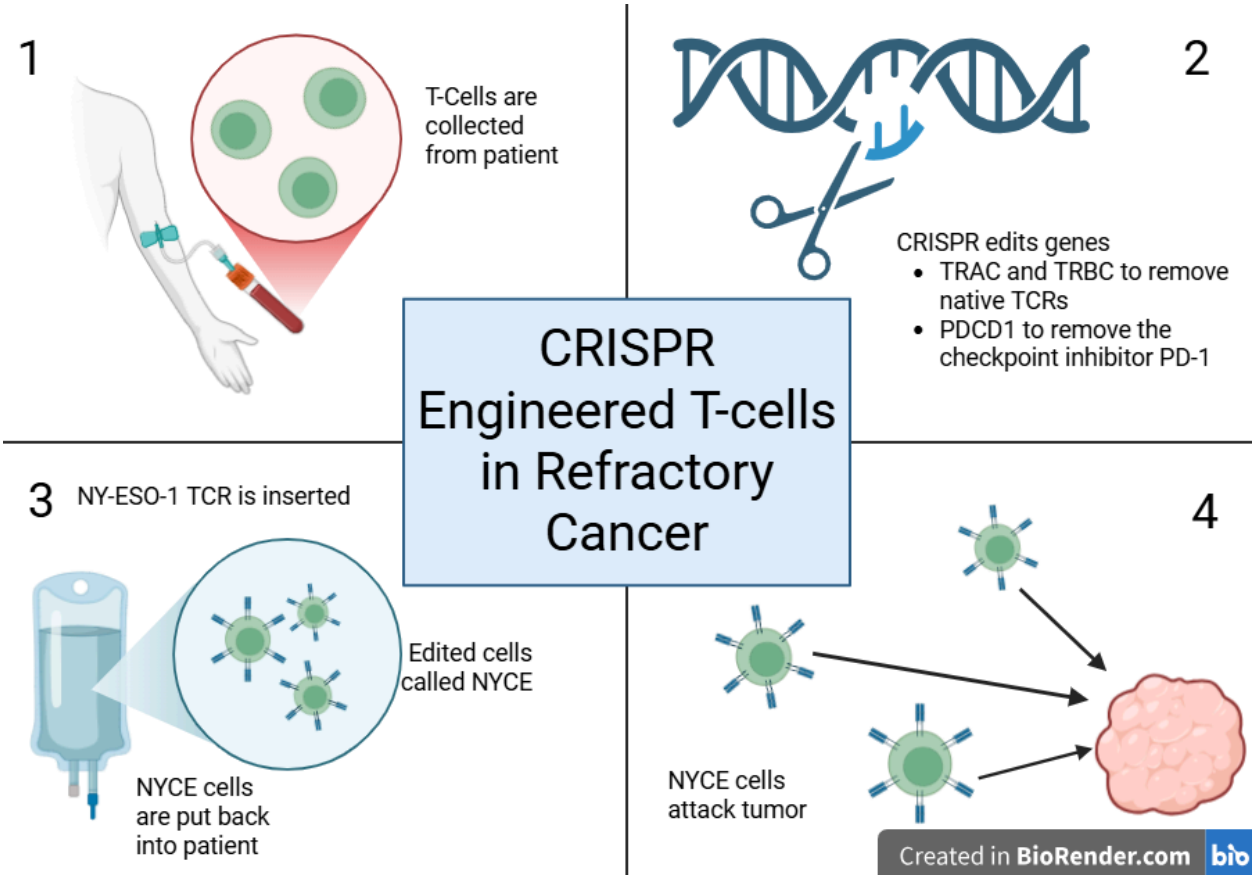


*Figure 2. CRISPR Engineered T-cells (NYCE) in Refractory Cancer. T-cells were collected from a patient then edited at three points: TRAC, TRBC, and PDCD1. NY-ESO-1 TCR was inserted, and after that, the edited cells called NYCE were reinfused into the patient. The study tested whether gene editing with CRISPR is safe and feasible.*

In summary, CRISPR gene editing technology has proven its worth to the cancer field in diagnostics and therapeutics with its ability to attack and detect cancer cells at the source. It is sensitive, efficient, and unparalleled by being able to help treat cancer when other methods cannot. Still, it has points of weakness that can harm non-cancerous cells and trigger new cancers. When actually being used in vivo, an ethical dilemma arises, so for now it is only used in vitro. Considering everything, CRISPR is a very promising, powerful tool that can be used in all sorts of genomic research, diagnostics, and therapeutics, especially being useful in cancer. In the future, with more clinical and non clinical studies, CRISPR will allow scientists to further learn about cancer-causing genes, quicken cancer diagnosis, and develop new therapies with highly personalized treatment.

Works Cited

The American Cancer Society and editorial content team. "Lifetime Risk of Developing or Dying from Cancer." *American Cancer Society*, 30 Jan. 2025,

www.cancer.org/cancer/risk-prevention/understanding-cancer-risk/lifetime-probability-of-developing-or-dying-from-cancer.html. Accessed 25 Aug. 2025.

Chen, Minjiang et al. "CRISPR-Cas9 for cancer therapy: Opportunities and challenges." *Cancer letters* vol. 447 (2019): 48-55. doi:10.1016/j.canlet.2019.01.017

"CRISPR applications in cancer diagnosis and treatment." *Cellular & molecular biology letters* 28.1 (2023): 73.

Di Carlo, E., Sorrentino, C. State of the art CRISPR-based strategies for cancer diagnostics and treatment. *Biomark Res* 12, 156 (2024).

Gong, Shaohua, et al. "CRISPR/Cas-based in vitro diagnostic platforms for cancer biomarker detection." (2021): 11899-11909.

Radbakhsh, Shabnam, and Hoda Namdari Moghaddam. "Advantages, Disadvantages and Risks of CRISPR/cas9 Technique for Gene Therapy." *Advanced Therapies Journal* 6.19 (2024): 36-42.

Stadtmauer, Edward A et al. "CRISPR-engineered T cells in patients with refractory cancer." *Science (New York, N.Y.)* vol. 367,6481 (2020): eaba7365. doi:10.1126/science.aba7365

Tan, I-Li, et al. "Targeting the non-coding genome and temozolomide signature enables CRISPR-mediated glioma oncolysis." *Cell reports* 42.11 (2023).