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Advancements in Genetic Engineering

Perspective

Clustered Regularly Interspaced Short Palindromic Repeats in Treating Cancer

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DESCRIPTION

CRISPR and CRISPR-associated protein 9 (Cas9), which were discovered in bacteria and archaea as an adaptive immune response to foreign genetic materials, have been widely used as a precise genome editing tool for basic research and therapeutic purposes in cancer. Cancer is caused by gene mutations, complex chromosomal alterations, translocations, losses, and gains. Because the CRISPR-Cas9 system can recognize specific genomic loci *via* single guide RNAs (sgRNAs) and effectively edit the loci *via* the Cas9 protein, its accuracy and versatility have been applied in biomedical research, opening up new avenues for cancer research and treatment. Furthermore, the CRISPR-Cas9 system has the potential to accelerate cancer research by performing functional genomics/epigenomics, modelling cancer genesis and progression *in vitro* and *in vivo*, targeting non-coding RNA, screening for novel therapeutic targets, or developing targeted cancer therapies and immunotherapies.

The CRISPR-Cas9 system can mediate precise genetic corrections or disruptions in *in vitro* and *in vivo* environments, depending on the delivery of viral or non-viral vectors, and the CRISPR-Cas9 technology shows promise for improving gene therapy outcomes. The CRISPR-Cas9 system has sparked tremendous interest in cancer therapeutic applications and has demonstrated therapeutic potential in virally driven cancers. CRISPR-based gene activation (CRISPRa) is a powerful tool for screening for function gain, whereas CRISPR-based gene inhibition (CRISPRi) is a more powerful tool for screening for function loss. Cancer survival-essential genes can be identified using CRISPR libraries, making them promising candidates for molecularly targeted drugs.

Cancer genomes frequently contain multiple genetic aberrations, which are the primary factors that drive cancer genesis and progression, and the CRISPR-Cas9 system has been used to edit cancer-causing gene mutations and deletions as well as to engineer immune cells, such as Chimeric Antigen Receptor T (CAR T) cells, for cancer immunotherapy. CRISPR-Cas9 translational therapeutics are also used in cancer therapy.

The CRISPR-Cas9 technique is used to treat various types of cancers, including cervical cancer, multiple myeloma, melanoma, synovial sarcoma, myxoid/round cell liposarcoma, B cell leukaemia, esophageal cancer, neurofibromatosis type 1, tumours of the central nervous system, bladder cancer, prostate cancer, renal cell carcinoma, non-small cell lung cancer, gastric carcinoma. The CRISPR-Cas9 plasmids, mRNA, Cas9 protein, and sgRNAs are delivered for cancer gene therapy. Furthermore, almost all *in vivo* studies using non-viral vectors for cancer gene therapy did not address the CRISPR-Cas9 system's off-target effects. As a result, advanced delivery systems for the CRISPR-Cas9 system must be developed further, and off-target effects for cancer gene therapy should be investigated.

CONCLUSION

CRISPR-Cas9 technology is a potent tool for cancer research and treatment. Virtual or computational high-throughput screens using various CRISPR-Cas9 libraries and databases can target some essential genes for carcinogenesis, progression, metastasis, and tolerance. Gene functions are also identified in CRISPRa or CRISPRi-created cell or animal models, and gene medicines or small molecule drugs are then designed and tested for advanced cancer therapy. Although the CRISPR-Cas9 system has discovered some new druggable targets, the majority of them are still in the preclinical stage. The CRISPR-Cas9 system edits immune cells for cancer immunotherapies, which is the most promising approach for clinical-based genome editing therapeutics. Cancer therapy based on the CRISPR-Cas9 system may offer a new option for patients who have exhausted all other options.

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