Open Access
Check for updates
International Journal of Medical Science and Dental Health (ISSN: 2454-4191)
Volume 11, Issue 07, July 2025,
Doi https://doi.org/10.55640/ijmsdh-11-07-15

Genetic Engineering in Medicine: New Tools and Medical Applications

Anwar Madlool Al-janabi
Department of Biochemistry, Faculty of Medicine, University of Kufa, Iraq

Ibtihal Alshamarti
Basic Science Department, Faculty of Dentistry, University of Kufa, Baghdad, Iraq

Corresponding Author - Ali A. Al-fahham
Faculty of nursing, University of Kufa, Iraq

Received: 24 June 2025, **accepted:** 09 July 2025, **Published Date:** 28 July 2025

Abstract

Genetic engineering is the main reason for radical transformation of modern medicine by allowing molecular level accurate manipulations for prevention, treatment and possible cure from numerous diseases. Recently developed technologies include CRISPR-Cas9 plus newly created systems delivering genes that facilitate the rapid evolution of gene-based therapies on infections, malignant tumors, and hereditary disorders. This review article investigates new approaches to fight pathogens come with GE involving immune cell engineering and therapeutic vaccine design while tools for tumor microenvironment modulation and immune recognition enhancement as well as direct editing of mutations driving cancer are opened up in oncology through GE. Besides, genetic engineering promises treatment of hereditary diseases through correction of pathogenic variants within autosomal dominant, autosomal recessive, and X-linked disorders which vastly improves patient quality of life and survival possibilities. Beneath all this great advancement lies substantial problems in delivery efficiency, ethical considerations, much needed long-term safety data as well others. Further study and careful clinical translation will be required to unleash the total therapeutic potential that GE can provide. Jointly, these advances put genetic engineering right at the cutting edge of precision medicine by offering new hope for conditions that were previously considered unamenable to treatment and rewriting the future landscape of medical treatment.

Keywords

ncRNA; microRNAs; long non-coding RNAs; circular RNAs.

Introduction

Over the past several decades, genetic engineering has evolved from a theoretical concept to a transformative force in modern medicine. The ability to precisely modify, insert, delete, or regulate genetic material within living cells has revolutionized biological research and opened new horizons for diagnosing, treating, and preventing disease (Niemann et al., 2021). With the advent of sophisticated tools such as CRISPR-Cas systems, base editors, and epigenetic modulators, the medical applications of genetic engineering have expanded rapidly—offering solutions to previously intractable conditions ranging from single-gene disorders to complex cancers and viral infections (Barrangou & Doudna, 2016).

The concept of manipulating genetic information is not at all new; milestones as early as the development of

recombinant DNA technology in the 1970s set a foundation for modern genetic engineering (Cohen et al., 1973). It is this innovation that made gene cloning possible, and production of recombinant proteins such as insulin, and initiations of first-generation trials on gene therapy (Naldini, 2015). However, earlier approaches have been described as inefficient, imprecise, and eliciting immune responses more than anticipated. Recent technological innovations have addressed most of these limitations in that there is now available even greater editing specificity with accessibility to it typified by CRISPR-Cas9 brought to the market by Jinek et al., (2012)

Clustered regularly interspaced short palindromic repeats (CRISPR) systems belong to the arsenal of tools that have been extremely transformative. CRISPR-Cas9 was originally discovered as bacterial adaptive immunity against viruses, but soon after its discovery, it was rapidly adopted and implemented as a genome editing tool capable of introducing site-specific double-strand breaks in DNA to be repaired by the cell's endogenous mechanisms (Doudna & Charpentier, 2014). The said tool together with its newer versions in the forms of base editors and prime editors has already been used by scientists and medical practitioners for correcting pathogenic mutations, deactivating harmful genes, and modulating gene expression (Anzalone et al., 2020).

Other genetic engineering techniques have impacted the medical field. ZFNs and TALENs were used before CRISPR in the area of targeted genome editing and although more technically intensive, can still be used in selected therapeutic applications (Gaj et al., 2013). On the other hand, RNA interference (RNAi) methodologies have brought a silent revolution in functional genomics and are translated into clinically approved therapeutics such as patisiran for hereditary transthyretin amyloidosis (Adams et al., 2018). From these tools, genetic engineering has evolved as a general strategy to modify gene sequences, regulate gene activity, and correct or compensate for disease-causing mutations.

The medical application of these tools is broad and evolving. The most immediate applications were gene therapy: delivering copies of genes to replace defective ones—for example, treatments available for SCID and retinal dystrophies (Mendell et al., 2017). More recently described are applications involving ex vivo editing of patient-derived cells that have purported curative promises for sickle cell disease and β-thalassemia by reactivating fetal hemoglobin production (Frangoul et al., 2021). In oncology, genetically engineered immune cells such as CAR-T cells provide a striking illustration of the potential for genetic engineering within the translation of immune system retargeting towards highly specific recognition and elimination of malignancy (June & Sadelain, 2018).

Equally valuable, genetic engineering has facilitated the achievements of personalized medicine. The sequencing of the human genome and genomics revealed that disease mechanisms are different in various individuals; thus, approaches must be varied for every individual. Gene editing and regulation tools provide for the variation of intervention methods, which soon may target mutations specific to a single patient's disease (Kim et al., 2022). This level of individualization is currently very applicable to rare genetic diseases and specific categories of cancers when standard treatments do not address the problem.

Another emerging field in the medical application is synthetic biology and genetic engineering by which biological systems can be developed with new functionalities. Engineered probiotics are being developed, which, for example, sense harmful metabolites and neutralize them within the gut (Mimee et al., 2016). Modified bacteria and viruses are currently under exploration as safe targeted delivery vehicles of therapeutics to cancer sites (Yazawa et al., 2020) Genetic engineering was also at the very heart of enabling the fast development of mRNA vaccines against COVID-19 disease - proof that impacts stretch well beyond any traditional notions regarding gene therapy (Polack et al., 2020)

The challenge though is how to translate such genetic engineering advances from bench to bedside. Among the delivery method challenges, especially for in vivo applications, is the need to develop methods that will ensure accurate targeting while reducing off-target effects. Other obstacles include immunogenicity-immune reactions against components of editing and also against the edited cells. Ethical considerations are especially important in germline editing since this raises social concerns about unintended consequences across generations. Another requirement is a robust regulatory framework and long-term studies in order to assess risks but still allow innovation.

The promise of genetic engineering for the future of medicine thus goes hand-in-hand with a renewed

commitment to balance innovation against considerations of safety and responsible ethics. As these tools develop further, there is a growing imperative for informed conversation between all aspects of the researcher, clinician, policymaker, and general public as to what scope and limitations are most appropriate to impose upon such powerful methodologies (Daley et al., 2019). Education and transparent communication can help align scientific progress with societal values and patient needs.

Essentially, genetic engineering has developed impressively from rudimentary cloning experiments in the 1970s to genome editing technologies that would be quite accurate and involved drastic medical applications. CRISPR, base editing, and synthetic biology platforms are newly discovered tools opening further perspectives for treatment and offering hope for conditions considered as irreversible maladies. Considerable hurdles in technology development as well as ethical issues notwithstanding, laboratories around the globe continue their work to bring us ever closer to this future of highly targeted and personalized treatment. The paper is devoted to the discussed changes in the practice of modern healthcare due to genetic engineering, its potential and existing barriers..

Genetic engineering in combating infectious diseases

Infectious diseases have always been among the most persistent maladies assaulting human health across the globe, taking millions of lives annually even amidst significant victories in vaccination and antimicrobial therapy. Genetic engineering has evolved over the recent decades into a revolutionary approach for both prevention and treatment by way of tools introduced for pathogen modification, host immune potentiation, and new therapeutic strategies to leaapfrog limitations imposed by traditional means (Barrangou & Doudna, 2016.

One of the most remarkable applications is the genetic engineering approach to vaccines of a new generation. Genetic engineering creates subunit and DNA-based vaccines and in the very recent past, mRNA-based vaccines that now express specific antigens—rushing pathogen inactivated or weakened for conventional vaccines (Pardi et al., 2018). Previously unused pathogenic material is not required for inactivated or attenuated genetic engineering design subunit, DNA, and recently mRNA vaccines that encode specific antigens. It was the rapid development that brought home dramatically the flexibility allowed by this method. The viral spike protein only will be encoded by those vaccines (Polack et al., 2020).

Outside vaccines, gene editing technologies such as CRISPR-Cas9 present means of directly disrupting viral genomes. In the case of chronic infections like HIV, where latent viral reservoirs are left even after the application of antiretroviral therapy, CRISPR systems have been explored to excise integrated proviral DNA from host genomes (Kaminski et al., 2016). Although still confined mainly within laboratories and clinical trials, these strategies promise real cures that go way beyond simple suppression. Meanwhile, genetically engineered immune cells have been studied for their ability to target infectious agents. For example, T cells could be engineered to express chimeric antigen receptors that recognize viral proteins hence possibly eliciting strong immune responses against chronic viral infections (Leibman et al., 2017). In a related approach, the production of broadly neutralizing antibodies may be enhanced by genetic engineering either delivered via viral vectors or directly in vivo using gene transfer techniques (Balazs et al., 2014).

Yet another frontier includes vector control by way of genetic modification of disease-carrying insects. For instance, scientists have engineered Aedes aegypti mosquitoes with gene drives that propagate genes either for population suppression or making them incapable of carrying any viruses such as dengue, Zika, and chikungunya (Gantz et al., 2015). Though ecological and ethical concerns still exist regarding this technology, it places the versatility scale high for genetic engineering when applied to issues of vector-borne diseases. Synthetic biology, a discipline intimately associated with genetic engineering permits the creation of living therapeutics- microbes programmed to seek and destroy pathogens within the human host. As an illustration, engineered probiotic bacteria have already been constructed so that they may eventually be able to sense molecules associated with infection in their host and secrete antimicrobial peptides or other immune modulators (Mimee et al., 2016).

Altogether, this speaks to the transformative role that genetic engineering could play in the prophylaxis and management of infectious diseases. Even though technical challenges related to delivery efficiency as well as off-target effects and immune responses need to be

solved through further research to perfect these tools, this constitutes not mere progress but rather a conceptual shift toward precision and adaptability that would prepare global health systems better for new pathogens (Lino et al., 2018).

Role in the management of malignant tumors

GE has radically shifted the whole paradigm of treating cancer toward highly accurate strains and sometimes patient-specific approaches, which are leaps beyond standard chemotherapy and radiotherapy. Tumors were typically heterogeneous; they could maneuver immune surveillance and treatment but the novelty in GE led to newly established methodologies for direct editing of tumor cells, harnessing the immune system, and creating potent therapies with reduced toxicity (Rosenberg & Restifo, 2015).

Chimeric antigen receptor T cell, or CAR-T therapy, is one of the most transformational GE-based approaches. It works by taking out a patient's T cells and then actively modifying them ex vivo so that they can express synthetic receptors capable of recognizing tumor-specific antigens. These modified cells are then infused back into the patient (June et al., 2018). The CAR-T cells have demonstrated outstanding efficacy in some selected hematological malignancies like B-cell acute lymphoblastic leukemia with more than 80% complete remission rates reported from some clinical trials (Maude et al., 2018). Even though major obstacles have restricted the application of CAR-T in solid tumors—mainly due to accessibility issues related to antigens and an immunosuppressive tumor microenvironment—scientists across different domains are simultaneously working on engineering next-generation CAR-T cells with improved homing abilities, resistance against inhibitory signals, and "armored" functions that will be able to secrete cytokines enhancing anti-tumor immunity (Fesnak et al., 2016).

Another emerging application of GE is gene editing of tumor cells or stromal cells to return normal behavior or sensitize them to treatment. CRISPR-Cas9 is the most popular gene editing tool being explored to inactivate oncogenes, repair tumor suppressor genes, and knock out genes causing resistance to therapy (Jinek et al., 2012; Doudna & Charpentier, 2014). For example, preclinical models have already indicated that knocking out PD-1 by CRISPR in T cells will make these cells more persistent and enhance their anti-tumor activity (Rupp et al., 2017). Another GE-based strategy is represented by oncolytic viruses. These are viruses genetically engineered to selectively infect and lyse cancer cells while sparing normal healthy cells. Some of them also carry immune-stimulatory genes, such as the gene for GM-CSF, which enhance anti-tumor immune responses further. Approved by FDA, herpes simplex virus genetically engineered for use against advanced melanoma is known as talimogene laherparepvec (T-VEC) which under the brand (Imlygic™)

Personalized cancer vaccines is also based on GE. Tumor neoantigens– unique mutations specific to the cancer of an individual can be identified through sequencing and synthetic mRNA vaccines encoding these neoantigens may be produced to teach the immune system what it should attack. Early phase clinical studies have established that such personalized neoantigen vaccines are capable of inducing strong and specific T cell responses which might assist in controlling tumor growth. Also, it can send suicide genes to the tumor cells or healthy genes that will make the cells sensitive to a certain prodrug. Another plan includes sending genes for cytokines straight into the tumor site so they can help immune responses fight and destroy cancer cells. These methods may be used with normal treatments for stronger results. Much progress notwithstanding, major challenges include the safe and efficient delivery of gene-editing tools to avoid off-target effects as well as tumor immune evasion mechanisms which are currently under study. However, what cannot be denied is the fact that genetic engineering has ushered in a new era in oncology, with hope for even more effective treatments bearing much less toxicity to be directed at each patient's tumor biology (Ott et al., 2017).

Role in the treatment of hereditary disease

The entry of genetic engineering (GE) into the stage has transformed approaches to the treatment of hereditary diseases, particularly those that were considered untreatable before. Most single-gene mutations causing disease follow Mendelian patterns of inheritance; that is, through autosomal dominant, autosomal recessive, and X-linked recessive conditions. GE offers possibilities for correction, silencing, or compensation regarding these mutations— in essence providing means of treatment at the etiological level rather than at symptomatic levels (High & Roncarolo, 2019). In autosomal dominant diseases, that is, conditions elicited by a single faulty

allele, approaches essentially involve the silencing or editing of the mutant allele and leave the normal copy untouched. Huntington's disease is an autosomal dominant disorder brought about by expanded CAG repeats in one gene, referred to as HTT. Recent preclinical studies have thus far applied RNA interference (RNAi) and antisense oligonucleotides (ASOs) to selectively express suppression of mutant HTT expression so as to lower levels of toxic protein and bring improvement in neuron health (Tabrizi et al., 2019). A pathogenic allele can also be specifically targeted for disruption by CRISPR-Cas9; hence, disease-causing protein production will be suppressed without affecting the healthy allele (Yang et al., 2017).

All autosomal recessive diseases will require the expression of two defective alleles and most often, the therapy involves restoring function or replacement of a protein that is missing or defective. Therapeutic gene delivery to SMN1 and mutations have been discovered with spinal muscular atrophy (SMA) helped demonstrate success in gene therapy. The approach practically approved by the FDA includes Onasemnogene abeparvovec that applies an adeno-associated virus (AAV) vector to deliver a functional copy of SMN1-missing motor proteins considerably improve survival in infants (Mendell et al., 2017). Beta-thalassemia together with sickle cell disease can be clinically approached in much similar ways due to their pathology as autosomal recessive hemoglobinopathies. In clinical trials, ex vivo editing on hematopoietic stem cells using the CRISPR-Cas has been applied for beta-thalassemia. Editing BCL11A enhancer reactivates fetal hemoglobin (HbF) proves transfusion independency among significant several patients (Frangoul et al., 2021).

Hemophilia A and Duchenne muscular dystrophy represent X-linked recessive diseases that have also been the object of GE-oriented interventions. AAV-mediated gene therapy in hemophilia A, presenting mutations at the F8 gene, has already developed stable expression of clotting factor VIII that dramatically increases the period before bleeding episodes return to normal levels. Gene editing strategies toward DMD include exon skipping through ASOs or CRISPR-mediated excision of specific exons to restore the dystrophin reading frame so that a partially functional dystrophin protein can be produced (Pasi et al., 2020). Beyond those inheritance patterns, genetic engineering is being applied to mitochondrial diseases. Mitochondrial diseases are caused by mutations in mitochondrial DNA. Even though direct editing of mitochondrial DNA has not yet been enabled, recently developed base editing tools and mitoTALENs do provide a proof-of-concept for selective removal of mutant mitochondrial genomes (Bacman et al., 2018).

Such breakthroughs were facilitated by the development of delivery vectors (for example, AAV and lipid nanoparticles), improved specificity for editing, and a better understanding of disease genetics. Challenges include immune responses against viral vectors and off-target effects related to gene editing which are compounded when germline editing is involved due to the ethical considerations that it raises (Cyranoski & Ledford, 2018). Targeted genetic engineering, disease-modifying therapy is offered by hereditary maladies where toxic allele(s) can be turned off in autosomal dominant diseases and gene function can be restored for recessive disorders. As technologies come of age, GE holds an unprecedented promise to change the clinical management of genetic diseases that have long been considered beyond the reach of a cure.

Conclusion

Genetic engineering completely transformed modern medicine in its way to targeted and potentially curative approaches regarding infectious diseases, malignancies, and genetic disorders. New techniques of gene editing CRISPR-Cas9, viral and non-viral delivery systems, and RNA-based therapies are now available to correct disease-causing mutations and enhance immunological responses as well as restore the function of many important proteins that were lost. Meanwhile though great challenges Delivery efficiency safety ethics etc remain hindered by barriers the pace of redefinition of the therapeutic landscape through advancing genetic engineering keeps getting ever closer to becoming a clinical reality in precision medicine thereby offering new hope where all others had failed.

References

1. Adams, D., Gonzalez-Duarte, A., O'Riordan, W. D., Yang, C.-C., Ueda, M., Kristen, A. V., ... & Suhr, O. B. (2018). Patisiran, an RNAi therapeutic, for hereditary transthyretin amyloidosis. New England Journal of Medicine, 379(1), 11–21. https://doi.org/10.1056/NEJMoa1716153

2. 2.Andtbacka, R. H. I., Kaufman, H. L., Collichio, F., Amatruda, T., Senzer, N., Chesney, J., Delman, K. A., Spitler, L. E., Puzanov, I., Agarwala, S. S., Milhem, M. M., Cranmer, L. D., Curti, B. D., Lewis, K. D., Ross, M., Guthrie, T., Linette, G. P., Daniels, G. A., Harrington, K., ... Coffin, R. S. (2015). Talimogene laherparepvec improves durable response rate in patients with advanced melanoma. Journal of Clinical Oncology, 33(25), 2780–2788. https://doi.org/10.1200/JCO.2014.58.3377
3. Anzalone, A. V., Randolph, P. B., Davis, J. R., Sousa, A. A., Koblan, L. W., Levy, J. M., ... & Liu, D. R. (2020). Search-and-replace genome editing without double-strand breaks or donor DNA. Nature, 576(7785), 149–157. https://doi.org/10.1038/s41586-019-1711-4
4. Bacman, S. R., Kauppila, J. H. K., Pereira, C. V., Nissanka, N., Miranda, M., Pinto, M., ... & Moraes, C. T. (2018). MitoTALEN reduces mutant mtDNA load and restores tRNALys levels in a mouse model of mitochondrial disease. Nature Medicine, 24(11), 1696–1700. https://doi.org/10.1038/s41591-018-0165-7
5. Balazs, A. B., et al. (2014). Vectored antibody gene delivery protects against lethal influenza challenge in mice. Nature Biotechnology, 32(4), 384–388. https://doi.org/10.1038/nbt.2851
6. Barrangou, R., & Doudna, J. A. (2016). Applications of CRISPR technologies in research and beyond. Nature Biotechnology, 34(9), 933–941. https://doi.org/10.1038/nbt.3659
7. Cohen, S. N., Chang, A. C. Y., & Hsu, L. (1973). Nonchromosomal antibiotic resistance in bacteria: Genetic transformation of Escherichia coli by R-factor DNA. Proceedings of the National Academy of Sciences, 69(8), 2110–2114. https://doi.org/10.1073/pnas.69.8.2110
8. Cyranoski, D., & Ledford, H. (2018). Genome-edited baby claim provokes international outcry. Nature, 563(7733), 607–608. https://doi.org/10.1038/d41586-018-07545-0
9. Daley, G. Q., Lovell-Badge, R., & Steffann, J. (2019). After the storm—a responsible path for genome editing. New England Journal of Medicine, 380(10), 897–899. https://doi.org/10.1056/NEJMp1900504
10. Doudna, J. A., & Charpentier, E. (2014). Genome editing: The new frontier of genome engineering with CRISPR-Cas9. Science, 346(6213). https://doi.org/10.1126/science.1258096
11. Fesnak, A. D., June, C. H., & Levine, B. L. (2016). Engineered T cells: the promise and challenges of cancer immunotherapy. Nature Reviews Cancer, 16(9), 566–581. https://doi.org/10.1038/nrc.2016.97
12. Frangoul, H., Altshuler, D., Cappellini, M. D., Chen, Y. S., Domm, J., Eustace, B. K., ... & Corbacioglu, S. (2021). CRISPR–Cas9 gene editing for sickle cell disease and β-thalassemia. New England Journal of Medicine, 384(3), 252–260. https://doi.org/10.1056/NEJMoa2031054
13. Gaj, T., Gersbach, C. A., & Barbas, C. F. (2013). ZFN, TALEN, and CRISPR/Cas-based methods for genome engineering. Trends in Biotechnology, 31(7), 397–405. https://doi.org/10.1016/j.tibtech.2013.04.004
14. Gantz, V. M., Jasinskiene, N., Tatarenkova, O., Fazekas, A., Macias, V. M., Bier, E., & James, A. A. (2015). Highly efficient Cas9-mediated gene drive for population modification of the malaria vector mosquito Anopheles stephensi. Proceedings of the National Academy of Sciences, 112(49), E6736–E6743. https://doi.org/10.1073/pnas.1521077112
15. Gyngell, C., Douglas, T., & Savulescu, J. (2017). The ethics of germline gene editing. Journal of Applied Philosophy, 34(4), 498–513. https://doi.org/10.1111/japp.12249
16. High, K. A., & Roncarolo, M. G. (2019). Gene therapy. New England Journal of Medicine, 381(5), 455–464. https://doi.org/10.1056/NEJMra1706910
17. Jinek, M., Chylinski, K., Fonfara, I., Hauer, M., Doudna, J. A., & Charpentier, E. (2012). A programmable dual-RNA–guided DNA endonuclease in adaptive bacterial immunity. Science, 337(6096), 816–821. https://doi.org/10.1126/science.1225829
18. June, C. H., O'Connor, R. S., Kawalekar, O. U., Ghassemi, S., & Milone, M. C. (2018). CAR T cell immunotherapy for human cancer. Science, 359(6382), 1361–1365. https://doi.org/10.1126/science.aar6711
19. Kaminski, R., Bella, R., Yin, C., Otte, J., Ferrante, P., Gendelman, H. E., Li, H., Burdo, T. H., McMillan, J., Afonso, P. V., Chaudhry, A., Beilman, G. J., Hu, W., & Khalili, K. (2016). Excision of HIV-1 DNA by CRISPR-Cas9: A proof-of-concept in vivo study. Gene Therapy, 23(8–9), 690–695. https://doi.org/10.1038/gt.2016.41

20. Kim, J. H., Kim, M., Kim, S., & Kim, J. S. (2022). Genomic editing tools and their medical applications. Experimental & Molecular Medicine, 54(5), 689–703. https://doi.org/10.1038/s12276-022-00767-7

21. Leibman, R. S., Richardson, M. W., Ellebrecht, C. T., Maldini, C. R., Glover, J. A., Secreto, A. J., Kulikovskaya, I., Lacey, S. F., Akkina, R., Yi, Y., Collman, R. G., Riley, J. L., Ruella, M., Barrett, D. M., Grupp, S. A., June, C. H., Gill, S., Porter, D. L., Jacobson, J. M., … Riley, J. L. (2017). Supraphysiologic control over HIV-1 replication mediated by CD8+ T cells expressing a re-engineered CD4-based chimeric antigen receptor. Journal of Virology, 91(4), e01937–16. https://doi.org/10.1128/JVI.01937-16

22. Lino, C. A., Harper, J. C., Carney, J. P., & Timlin, J. A. (2018). Delivering CRISPR: a review of the challenges and approaches. Drug Delivery, 25(1), 1234–1257. https://doi.org/10.1080/10717544.2018.1474964

23. Maude, S. L., Laetsch, T. W., Buechner, J., Rives, S., Boyer, M., Bittencourt, H., Bader, P., Verneris, M. R., Stefanski, H. E., Myers, G. D., De Moerloose, B., Hiramatsu, H., Schlis, K., Davis, K. L., Martin, P. L., Nemecek, E. R., Yanik, G. A., Peters, C., Baruchel, A., … Grupp, S. A. (2018). Tisagenlecleucel in children and young adults with B-cell lymphoblastic leukemia. New England Journal of Medicine, 378(5), 439–448. https://doi.org/10.1056/NEJMoa1709866

24. Mendell, J. R., Al-Zaidy, S., Shell, R., Arnold, W. D., Rodino-Klapac, L. R., Prior, T. W., ... & Kissel, J. T. (2017). Single-dose gene-replacement therapy for spinal muscular atrophy. New England Journal of Medicine, 377(18), 1713–1722. https://doi.org/10.1056/NEJMoa1706198

25. Mimee, M., Tucker, A. C., Voigt, C. A., & Lu, T. K. (2016). Programming a human commensal bacterium, Bacteroides thetaiotaomicron, to sense and respond to stimuli in the murine gut microbiota. Cell Systems, 1(1), 62–71. https://doi.org/10.1016/j.cels.2015.06.001

26. Mullard, A. (2020). Gene-editing therapies head into clinic. Nature Reviews Drug Discovery, 19(6), 351–352. https://doi.org/10.1038/d41573-020-00074-9

27. Naldini, L. (2015). Gene therapy returns to centre stage. Nature, 526(7573), 351–360. https://doi.org/10.1038/nature15818

28. Nelson, C. E., Hakim, C. H., Ousterout, D. G., Thakore, P. I., Moreb, E. A., Castellanos Rivera, R. M., ... & Gersbach, C. A. (2016). In vivo genome editing improves muscle function in a mouse model of Duchenne muscular dystrophy. Science, 351(6271), 403–407. https://doi.org/10.1126/science.aad5143

29. Niemann, H. H., Liu, Y., & Timmis, K. N. (2021). Genetic engineering: Past achievements and future prospects. Current Opinion in Biotechnology, 70, 1–8. https://doi.org/10.1016/j.copbio.2020.09.001

30. Ott, P. A., Hu, Z., Keskin, D. B., Shukla, S. A., Sun, J., Bozym, D. J., Zhang, W., Luoma, A., Giobbie-Hurder, A., Peter, L., Chen, C., Olive, O., Carter, T. A., Li, S., Lieb, D. J., Eisenhaure, T., Gjini, E., Stevens, J., Lane, W. J., … Wu, C. J. (2017). An immunogenic personal neoantigen vaccine for patients with melanoma. Nature, 547(7662), 217–221. https://doi.org/10.1038/nature22991

31. Pardi, N., Hogan, M. J., Porter, F. W., & Weissman, D. (2018). mRNA vaccines — a new era in vaccinology. Nature Reviews Drug Discovery, 17(4), 261–279. https://doi.org/10.1038/nrd.2017.243

32. Pasi, K. J., Rangarajan, S., Mitchell, N., Lester, W., Symington, E., Madan, B., ... & Pierce, G. F. (2020). Multiyear follow-up of AAV5-hFVIII-SQ gene therapy for hemophilia A. New England Journal of Medicine, 382(1), 29–40. https://doi.org/10.1056/NEJMoa1908490

33. Polack, F. P., Thomas, S. J., Kitchin, N., Absalon, J., Gurtman, A., Lockhart, S., ... & Gruber, W. C. (2020). Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine. New England Journal of Medicine, 383(27), 2603–2615. https://doi.org/10.1056/NEJMoa2034577

34. Rainov, N. G. (2000). A phase III clinical evaluation of herpes simplex virus type 1 thymidine kinase and ganciclovir gene therapy as an adjuvant to surgical resection and radiation in adults with previously untreated glioblastoma multiforme. Human Gene Therapy, 11(17), 2389–2401. https://doi.org/10.1089/104303400750035611

35. Rosenberg, S. A., & Restifo, N. P. (2015). Adoptive cell transfer as personalized immunotherapy for human cancer. Science, 348(6230), 62–68. https://doi.org/10.1126/science.aaa4967

36. Rupp, L. J., Schumann, K., Roybal, K. T., Gate, R. E., Ye, C. J., Lim, W. A., & Marson, A. (2017). CRISPR/Cas9-mediated PD-1 disruption enhances anti-tumor efficacy of human chimeric antigen

receptor T cells. Scientific Reports, 7(1), 737. https://doi.org/10.1038/s41598-017-00462-8

37. Russell, S. J., Peng, K. W., & Bell, J. C. (2012). Oncolytic virotherapy. Nature Biotechnology, 30(7), 658–670. https://doi.org/10.1038/nbt.2287

38. Tabrizi, S. J., Leavitt, B. R., Landwehrmeyer, G. B., Wild, E. J., Saft, C., Barker, R. A., ... & Lane, R. M. (2019). Targeting huntingtin expression in patients with Huntington's disease. New England Journal of Medicine, 380(24), 2307–2316. https://doi.org/10.1056/NEJMoa1900907

39. Yang, S., Chang, R., Yang, H., Zhao, T., Hong, Y., Kong, H. E., ... & Li, S. (2017). CRISPR/Cas9-mediated gene editing ameliorates neurotoxicity in mouse model of Huntington's disease. Journal of Clinical Investigation, 127(7), 2719–2724. https://doi.org/10.1172/JCI92087

40. Yazawa, K., Fujimura, K., Koyama, Y., Nishikawa, S., & Shibata, H. (2020). Bacterial cancer therapy: engineering bacteria as anti-cancer agents. Frontiers in Oncology, 10, 297.https://doi.org/10.3389/fonc.2020.00297