

Expanding Access to Cell and Gene Therapies

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Abstract: Cell and gene therapies have become very effective for treating patients with hematologic malignancies, hemoglobinopathies, and immune deficiencies, but most patients are being treated at academic medical centers. It's important to make these therapies available to more patients. For hospitals without specialized cell processing facilities the blood bank or hospital pharmacy is well suited to handle these products. The administration of *in vivo* gene therapies which does not involve the infusion of cells and is similar to the intravenous administration of drugs, can be handled by pharmacies. Providing cellular therapies is more difficult since most are cryopreserved. To provide these therapies a hospital must have access to -80°C or liquid nitrogen freezers for storage of the cellular therapy, the ability to thaw and quickly administer the therapy, and a system to document their administration. The difficulties associated with providing these therapies at more medical centers and how to overcome these issues are discussed.

Keywords: cell therapy; gene therapy; chimeric antigen receptor T-cells; hematopoietic stem cells

1. Introduction

Cell and gene therapies have been used at academic medical centers for over thirty years. Patients with congenital immune deficiencies were the first to be treated with gene therapies. These treatments which began in the 1990's involved the transduction of the patients' own lymphocytes with vectors encoding the gene to be corrected [1]. While they showed promise, patients benefited only for a short period of time. As hematopoietic stem cell (HSC) transplant therapy improved, clinical investigators began to treat patients with congenital immune deficiencies with gene modified autologous hematopoietic stem cells [2].

Although gene modification of HSCs successfully treated immune deficiencies, the rarity of these diseases meant that few patients were treated. The development of gene-modified T-cells to treat cancer, especially hematologic malignancies, greatly increased the application of gene therapy. In the 1990s Steve Rosenberg and colleagues showed that some cancers could be treated with cellular immunotherapies. They used autologous tumor-infiltrating lymphocytes (TILs) to treat patients with melanoma and other malignancies [3]. In 2006 and 2009, they used T-cells genetically engineered to express T-cell receptor (TCR) specific for tumor antigens to treat patients with metastatic melanoma [4,5]. In 2010 Jim Kochenderfer and colleagues showed that T-cells genetically modified to express chimeric antigen receptor (CAR) targeting CD19 could be used to treat patients with advanced follicular lymphoma [6] and in 2011 Kalos and colleagues showed that they could be used to treat patients with chronic lymphocytic leukemia [7,8]. Since then, the use of CAR T-cells and other genetically modified T-cells to treat cancer has grown rapidly. The clinical success of these CAR-T therapies has led to the licensure of cellular therapies to treat patients with B-cell hematological malignancies [9].

Most current clinical gene therapies are *ex vivo*, meaning they are produced in a laboratory. Typically, the cells used to manufacture cellular therapies are collected from the patient undergoing the therapy. The cells may



undergo selection for specific types, stimulation, gene transduction, culture and expansion. The final cell therapy product must undergo quality control testing before it is released and administered. The final product may be administered fresh, or it may be cryopreserved and later thawed and infused.

Some gene therapies involve the direct administration of genes or genes to patients via viral vectors or nanoparticles and are known as *in vivo* gene therapies [10]. The genes may be delivered intravenously or directly into the tumor. Recently, preclinical and first-in-human studies have shown that CAR T-cells can be generated using *in vivo* gene editing [11].

Despite the clinical success of cell and gene therapies they are primarily used at large medical centers involved in teaching and research limiting the number of patients who can be treated. Although the field has grown, for these therapies to reach their full potential they must be available to even more patients and be provided at widely accessible healthcare facilities. This review covers the types of cell and gene therapies used clinically, how they are produced, and how they are administered. In addition, how to make these therapies more available is discussed.

2. Types of Therapy

Several types of cell and gene therapies (CGTs) are currently in clinical use, and the nature of each therapy determines how it is manufactured and administered to patients. Broadly, these therapies can be classified as cell therapies, which rely on cells processed *ex vivo* in a laboratory, and gene therapies, which introduce, modify, or regulate genetic material within target cells. Gene therapies may be delivered either *ex vivo*, in which a patient's cells are genetically modified outside the body before reinfusion, or *in vivo*, in which the genetic material is administered directly to the patient without the use of laboratory-processed cells.

2.1. Cellular Therapies

These therapies are made from cells and their production and delivery are complex. They are typically autologous therapies, those that are made for a specific patient using their own blood cells. Cellular therapies can also be made from cells that are derived from family-related or unrelated donor whose Human Leukocyte Antigen (HLA) antigens match the patient's. These are known as allogeneic cellular therapies.

The starting material for cellular therapies may come from several different cell most often hematopoietic stem cells (HSCs) or peripheral blood mononuclear cells. HSCs can be used for transplantation or gene therapy for hemoglobinopathies and immunodeficiencies.

The highest concentration of HSCs is in the bone marrow, from which an individual's HSCs can be collected. For cell therapies HSCs can be collected by aspiration from the bone marrow typically from the posterior iliac crests.

HSCs are also present in the peripheral blood for collection, but their concentration is very low. This concentration can be increased by administering a drug that "mobilizes" HSCs from the bone marrow into the blood. The drugs most often used to mobilize HSCs include G-CSF and plerixafor [12]. However, even after mobilization, the HSC concentration in the blood remains low. Even a unit of whole blood (e.g., 500 mL), collected from a donor still does not contain enough HSCs for successful HSC gene therapies or transplants. As such, collecting enough HSCs required for these therapies typically requires enriching for peripheral blood mononuclear cells by processing many liters of whole blood via apheresis.

Apheresis involves the collection of venous blood from the patient using a blood cell separator. The process separates and removes HSC- or T-cell rich-leukocytes from the blood before returning RBCs, plasma, and other leukocytes back to the patient. Blood cell separators use disposable collection kits that are closed to the environment in order to collect a sterile product. Cell collection by apheresis requires a highly trained staff following rigorous procedures.

Mononuclear cells in the blood are also used to produce many cellular therapies. Most cellular cancer immunotherapies are made from T-cells; however, some are made from NK cells and monocytes. T cells are used to make TCR engineered T-cells and CAR T-cells. Although T-cells are among the most abundant leukocytes in the blood, obtaining enough T-cells to produce these cellular therapies also requires apheresis to collect T-cell rich mononuclear leukocytes from the patient. Monocytes are used to make dendritic cell therapies, and they can also be collected from the blood by apheresis as can NK cells.

2.2. Cellular Gene Therapies

Cellular gene therapies involve genetic modification of cells collected from a patient or donor in a clinical cell processing laboratory. Cellular gene therapies can be used to treat patients with congenital immune deficiencies or cancer.

To treat a patient with an immune deficiency such as chronic granulomatous disease (CGD) or severe combined immune deficiency (SCID), their HSCs must be collected for manufacturing. The collected cells are sent to a clinical cell processing laboratory which isolates the CD34+ cells. The cell processing laboratory then genetically modifies the cells to correct the defect causing the clinical immune deficiency.

To treat patients with cellular cancer immunotherapies that involve genetic modification of T-cells, their peripheral blood mononuclear cells are collected and sent to a clinical cell processing laboratory. Typically, T-cells are isolated, and genetically modified to specifically target cancer cells.

2.3. In Vivo Gene Therapies

In Vivo gene therapies involve the delivery of genes through viral vectors or liquid nanoparticles. In some cases, the genes may be injected directly into tumors, but they can also be injected into the blood. Following injection into the blood they can enter blood cells or organs such as the liver or lungs. Recent studies have shown that the intravenous injection of CAR construct genes encapsulated in lipid nanoparticles can target T-cells produced circulating CAR T-cells [13].

While the use of *in vivo* gene therapy is early and current clinical use is limited to small phase 1 cohorts, its clinical application is likely to grow. The use of therapies such as CAR T-cells produced *in vivo* has many advantages over the CAR T-cells produced *ex vivo*. *Ex vivo* gene therapies, most commonly autologous therapies, are typically produced in a cell processing laboratory in small, patient-specific lots. Enough cells are produced only to treat a single patient. In addition, the cells used to manufacture cellular gene therapy must be collected from the patient or a suitable donor. In contrast, *in vivo* gene therapies are produced in centralized manufacturing facilities in lots large enough to treat many patients. In addition, *in vivo* therapies do not require collecting a patient's cells. The gene commonly carried by a viral vector or liquid nanoparticle, is injected directly into the blood, central nervous system, tissue, or other parts of the body with the expectation that they will enter cells for modification.

3. Current System for Providing Cell and Gene Therapies to Patients

Currently most cell and gene therapies are provided to patients at academic medical centers. Most academic medical centers have the resources in place to collect starting materials, manufacture and/or supply these therapies (Table 1). They have laboratories to process HSCs and produce cellular therapies. In addition, they have nursing staff who are experienced in administering HSCs. Many cellular therapies including commercial cell and gene therapies are cryopreserved. Laboratories at medical centers that process HSCs and/or cellular therapies have the equipment and skills necessary to cryopreserve, thaw and infuse cellular therapies. In addition, some medical centers without cell processing laboratories have these resources.

Table 1. Activities required to produce and supply cellular therapies and groups responsible for providing these services.

Activity	Group
Evaluate People Donating the Cells used to Begin the Manufacturing Process	Nurses and Physicians
Collection of the Donor's Cells	Collection Medical Center, Blood Center or Specialized Collection Center
Manufacturing the Cell Therapy	Medical Center Cell Processing laboratory or Company
Shipping the Cell Therapy	Courier under the oversight of sponsor

Manufacturing cellular therapies is complicated and many medical centers that provide these therapies to patients lack the capacity and capability to manufacture these therapies. The cell therapies provided by these centers are manufactured at external facilities, often by companies. These medical centers have in place mechanisms to receive, store, thaw and infuse cell therapies. Since many cell therapies are made using a patient's own HSCs or mononuclear cells, these medical centers have mechanisms to collect these cells from their patients. The medical centers may provide the collection services, or they may have arrangements with other groups to provide these services. Since many cellular therapy products are cryopreserved, medical centers providing *ex vivo* cellular therapies must also have equipment and procedures to store, thaw and infuse cryopreserved products.

Autologous leukocytes used to manufacture cellular and gene therapies are usually collected by apheresis which requires specialized equipment and highly trained staff. The manufacturing process also requires specialized equipment and highly trained staff. In addition, the manufacturing process requires highly controlled cell processing facilities. Specialized quality control laboratories are also needed. Depending on center-specific practices and donor type (autologous or allogeneic), donors of the cells used to manufacture the cellular therapy are tested for transfusion-transmitted diseases, including hepatitis B virus (HBV), hepatitis C virus (HCV), and human immunodeficiency virus (HIV). The cellular therapy product being manufactured must undergo in-process

and lot release quality control testing. Typically, the final cellular product is cryopreserved until lot release testing is complete. If the product test results satisfy all lot release criteria and quality assurance requirements, it can then be thawed and infused into the patient.

Centers that infuse cell therapies must have knowledge and expertise about the toxicities and complications that can arise with the provision of cellular therapies. Many cell and gene therapies require that patients undergo lymphocyte depleting chemotherapy prior to their administration which may result in thrombocytopenia and or neutropenia. The infusion of some cell therapy products is associated with toxicities which can be either predictable or unexpected. The infusion of cell therapies can be associated with fevers especially for products that have been cryopreserved. In addition, CAR T-cells can cause cytokine release syndrome (CRS), immune effector cell-associated neurotoxicity syndrome (ICANS), or immune effector cell-associated hemophagocytic lymphohistocytosis-like syndrome (IEC-HS), however, the severity is highly variable. Some patients experience no CRS, IEC-HS or ICANS while others can have severe toxicities. Centers providing these therapies to patients must be aware of both the common and uncommon toxicities and complications that are associated with their infusion. They must have knowledge concerning the management and treatment of these toxicities and complications.

The quality and clinical performance of final cell therapy products can also vary greatly among patients. This variety is due to some degree of variability in the autologous cells used to begin the manufacturing process. For products made from T-cells the presence of monocytes and granulocytes among the T-cells used to begin the manufacturing process can affect the final product [14]. In addition, differences in the patient T-cells used to begin manufacturing can cause differences in the final product potency and toxicity [15].

4. Making Cell and Gene Therapies More Widely Available

Currently the number of groups involved with cell and gene therapies is limited. These groups include biotechnology companies that manufacture cell and gene therapies as well as select academic medical centers. Academic medical centers are also involved with the administration of these products to patients. Blood centers may also be involved with collecting the starting cellular materials used to manufacture cell therapies. The limited number of centers involved in the *ex vivo* cell therapy pathway creates a major geographic constraint for patients, who must live near or be able to travel to specialized centers that can provide apheresis, manufacturing, infusion, and toxicity management, which can worsen access for patient populations lacking the necessary resources [16,17]. Therapies that forgo the additional collection and manufacturing steps, such as *in vivo* cell therapies, may help with this issue.

In order to make cell and gene therapies more widely available, more hospitals need to become involved in providing these therapies. Hospitals that do not currently produce cell therapies will need to establish mechanisms to receive, store, issue, and administer these therapies (Table 2). Typically, *ex vivo* cellular therapies are stored in a liquid nitrogen or -80°C freezer. Freezer temperatures must be monitored, and if they go out of range, products should be moved to another freezer. Administering cryopreserved cell therapies is complicated because the cryoprotectants used to freeze the cells such as dimethyl sulfoxide (DMSO) are toxic to thawed cells and the thawing process can damage the cells. Consequently, although cryopreserved cellular products may have defined post-thaw expiration or stability timeframes lasting up to a few hours, they should ideally be infused as soon as possible after thawing. The thawed cellular products must be infused within a defined time window to ensure stability and quality of the product. In addition to performing these activities, hospitals also need a method to document them. This could be done manually, but electronic cell processing record keeping systems are available.

Table 2. Activities involved with providing patients with cellular therapies and groups performing these activities.

Activity	Responsible Group
Receiving the Cell Therapy Products	Blood Bank, Pharmacy, or Cell Processing Lab
Storing the Cell Therapy Products	Blood Bank, Pharmacy, or Cell Processing Lab
Releasing the Cell Therapy Product for Administration	Blood Bank, Pharmacy, or Cell Processing Lab
Administering the Cell Therapy Products to the Patient	Clinic or Hospital Medical and Nursing Staff
Monitoring Patients for Toxicities	Clinic or Hospital Medical and Nursing Staff

Beyond the infrastructure for receiving, storing, and dispensing cell and gene therapy (CGT) products, centers and hospitals providing these services must establish a solid and product-specific knowledge base covering product handling protocols, point-of-care workflows, and personnel competency. Storage and handling requirements differ across CGT modalities, and risks of product deterioration must be identified and mitigated to ensure product quality and patient safety [18]. Most CGT products require storage and transport at ultra-low cryogenic temperatures; however, handling details between product packaging, transportation, and storage equipment may

introduce temperature excursions. For example, while thawing protocols are broadly similar in that most autologous CAR T-cell products are cryopreserved and thawed at bedside or at a location close enough to bedside prior to infusion, individual protocols must account for procedural variables, such as thaw duration, wash-out, and equilibration conditions. This complexity is further compounded by the biological activities of autologous products: the quality of patient cells collected via apheresis can vary significantly from patient to patient. This heterogeneity of product quality has direct operational implications at the point of care: thaw-to-infusion time, thawing location, delivery device, etc. Training requirements for CGT personnel are extensive and must be tailored to the treatment center's practice with adequate competency assessment.

In hospitals that transfuse a significant amount of blood but do not have a cell processing laboratory, the blood bank may be able to handle cell and gene therapies. In hospitals without large blood banks, the pharmacy may be able to handle cell and gene therapies. Under different regulatory jurisdictions such as in Europe, the hospital pharmacy department may be responsible for reception, storage, reconstitution (thawing), and final dispensation. Accordingly, hospital pharmacists bear responsibility for these processes and treatment centers must maintain qualified personnel and the relevant specialized equipment [19]. This may be another avenue to expand access to cellular products for more patients.

While handling *ex vivo* cell and gene therapies is complicated, handling *in vivo* therapies is simpler and more akin to that of a drug. They are stored, issued and infused like a drug. The administration of *in vivo* gene therapies is relatively free of acute infusion related complications (e.g., DMSO toxicity seen with cryopreserved *ex vivo* products). Early clinical studies of *in vivo* CAR-T therapy show the same common toxicities as *ex vivo* therapies (e.g., CRS, ICANS), but the severity depends on the delivery platform. Non-viral (e.g., mRNA via LNP) approaches showed low-grade CRS, while a viral vector approach showed high-grade CRS [20–23]. The same concerns about using viral vectors in *ex vivo* therapies also apply to lentiviral vector-based *in vivo* CAR-T therapy, as they can increase the risk of off-target gene insertions and insertional mutagenesis. Furthermore, several questions unique to *in vivo* therapies remain, such as the degree of T-cell targeting without off-target transduction, delivery and redosing efficacy challenges due to anti-vector immunogenicity, the lack of pre-infusion quality control with *ex vivo* therapies, and a regulatory framework that remains to be developed. That said, as experience with *in vivo* therapies matures and the use of *in vivo* therapies grows experience with *in vivo* therapies matures and the use of *ex vivo* therapies decrease providing these therapies will become easier.

5. Conclusions

Cellular therapies have been used for many years and have been very clinically effective; however, they have been primarily *ex vivo* gene therapies and their use have been limited because they are complicated and expensive to produce. While some therapies such as HSC for transplantation will remain dependent on the collection, processing, and infusion of cells, the field of gene therapy will likely move toward non-cell-based *in vivo* therapies which will be less expensive to produce and easier to provide.

All patients will need to have access to these therapies. This will require providing these therapies to patients at more hospitals. To do this the knowledge that has been gained at academic centers must be shared widely and processes and procedures must be simplified. While the provision of *ex vivo* cellular therapies to patients involves several steps, most large medical centers will likely be able to provide this service with proper training of staff and the acquisition of appropriate equipment. The hospital blood bank or pharmacy should be able to receive, store and issue these products, particularly *in vivo* gene therapies. Professional societies involved with pharmacies, cell therapies, blood banks, and transfusion medicine services should increase their involvement with training professionals in these fields to help them develop the skills needed to lead the implementation of policies and procedures required to administer cell and gene therapies at medical centers everywhere.

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Use of AI and AI-Assisted Technologies

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References

1. Blaese, R.M.; Culver, K.W.; Miller, A.D.; et al. T Lymphocyte-Directed Gene Therapy for ADA-SCID: Initial Trial Results after 4 Years. *Science* **1995**, *270*, 475–480. <https://doi.org/10.1126/science.270.5235.475>.
2. Malech, H.L.; Garabedian, E.K.; Hsieh, M.M. Evolution of Gene Therapy, Historical Perspective. *Hematol. Oncol. Clin. North Am.* **2022**, *36*, 627–645. <https://doi.org/10.1016/j.hoc.2022.05.001>.
3. Rosenberg, S.A.; Yang, J.C.; Sherry, R.M.; et al. Durable Complete Responses in Heavily Pretreated Patients with Metastatic Melanoma Using T-Cell Transfer Immunotherapy. *Clin. Cancer Res.* **2011**, *17*, 4550–4557. <https://doi.org/10.1158/1078-0432.ccr-11-0116>.
4. Morgan, R.A.; Dudley, M.E.; Wunderlich, J.R.; et al. Cancer Regression in Patients after Transfer of Genetically Engineered Lymphocytes. *Science* **2006**, *314*, 126–129. <https://doi.org/10.1126/science.1129003>.
5. Johnson, L.A.; Morgan, R.A.; Dudley, M.E.; et al. Gene Therapy with Human and Mouse T-Cell Receptors Mediates Cancer Regression and Targets Normal Tissues Expressing Cognate Antigen. *Blood* **2009**, *114*, 535–546. <https://doi.org/10.1182/blood-2009-03-211714>.
6. Kochenderfer, J.N.; Wilson, W.H.; Janik, J.E.; et al. Eradication of B-Lineage Cells and Regression of Lymphoma in a Patient Treated with Autologous T Cells Genetically Engineered to Recognize CD19. *Blood* **2010**, *116*, 4099–4102. <https://doi.org/10.1182/blood-2010-04-281931>.
7. Kalos, M.; Levine, B.L.; Porter, D.L.; et al. T Cells with Chimeric Antigen Receptors Have Potent Antitumor Effects and Can Establish Memory in Patients with Advanced Leukemia. *Sci. Transl. Med.* **2011**, *3*, 95ra73. <https://doi.org/10.1126/scitranslmed.3002842>.
8. Koehler, P.; Schmidt, P.; Hombach, A.A.; et al. Engineered T Cells for the Adoptive Therapy of B-Cell Chronic Lymphocytic Leukaemia. *Adv Hematol.* **2012**, *2012*, 595060. <https://doi.org/10.1155/2012/595060>.
9. Cappell, K.M.; Kochenderfer, J.N. Long-Term Outcomes Following CAR T Cell Therapy: What We Know So Far. *Nat Rev Clin Oncol.* **2023**, *20*, 359–371. <https://doi.org/10.1038/s41571-023-00754-1>.
10. Raguram, A.; Banskota, S.; Liu, D.R. Therapeutic *in Vivo* Delivery of Gene Editing Agents. *Cell* **2022**, *185*, 2806–2827. <https://doi.org/10.1016/j.cell.2022.03.045>.
11. Bimbo, J.F.; van Diest, E.; Murphy, D.E.; et al. T Cell-Specific Non-Viral DNA Delivery and *in Vivo* CAR-T Generation Using Targeted Lipid Nanoparticles. *J. Immunother. Cancer* **2025**, *13*, e011759. <https://doi.org/10.1136/jitc-2025-011759>.
12. Allen, E.S.; Conry-Cantilena, C. Mobilization and Collection of Cells in the Hematologic Compartment for Cellular Therapies: Stem Cell Collection with G-CSF/Plerixafor, Collecting Lymphocytes/Monocytes. *Semin. Hematol.* **2019**, *56*, 248–256. <https://doi.org/10.1053/j.seminhematol.2019.11.003>.
13. Hunter, T.L.; Bao, Y.; Zhang, Y.; et al. *In Vivo* CAR T Cell Generation to Treat Cancer and Autoimmune Disease. *Science* **2025**, *388*, 1311–1317. <https://doi.org/10.1126/science.ads8473>.
14. Stroncek, D.F.; Ren, J.; Lee, D.W.; et al. Myeloid Cells in Peripheral Blood Mononuclear Cell Concentrates Inhibit the Expansion of Chimeric Antigen Receptor T Cells. *Cytotherapy* **2016**, *18*, 893–901. <https://doi.org/10.1016/j.jcyt.2016.04.003>.
15. Dreyzin, A.; Shao, L.; Cai, Y.; et al. Immunophenotype of CAR T Cells and Apheresis Products Predicts Response in CD22 CAR T Cell Trial for B Cell Acute Lymphoblastic Leukemia. *Mol. Ther.* **2025**, *33*, 3360–3374. <https://doi.org/10.1016/j.ymthe.2025.03.019>.

16. Ahmed, N.; Sun, F.; Teigland, C.; et al. Chimeric Antigen Receptor T-Cell Access in Patients with Relapsed/Refractory Large B-Cell Lymphoma: Association of Access with Social Determinants of Health and Travel Time to Treatment Centers. *Transplant. Cell. Ther.* **2024**, *30*, 714–725. <https://doi.org/10.1016/j.jtct.2024.04.017>.
17. Ahmed, N.; Shahzad, M.; Shippey, E.; et al. Socioeconomic and Racial Disparity in Chimeric Antigen Receptor T Cell Therapy Access. *Transplant. Cell. Ther.* **2022**, *28*, 358–364. <https://doi.org/10.1016/j.jtct.2022.04.008>.
18. Rioufol, C.; Wichmann, C. Receiving, Handling, Storage, Thawing, Distribution, and Administration of CAR-T Cells Shipped from the Manufacturing Facility. In *The EBMT/EHA CAR-T Cell Handbook*; Springer International Publishing: Cham, Switzerland, 2022; pp. 37–43. https://doi.org/10.1007/978-3-030-94353-0_7.
19. Talarmin, C.; Kerob, S.; Cartier, F.; et al. Quality Risk Management of the Chimeric Antigen Receptor T Cell Pharmaceutical Circuit in One of the First Qualified European Centers. *Cytotherapy* **2020**, *22*, 792–801. <https://doi.org/10.1016/j.jcyt.2020.06.009>.
20. Xu, J.; Chen, Z.; Su, L.; et al. *In Vivo* CAR Cell Therapy: From Bench to Bedside. *J. Hematol. Oncol.* **2025**, *18*, 105. <https://doi.org/10.1186/s13045-025-01759-2>.
21. An, N.; Wang, D.; Zhang, P.; et al. *In Vivo* Generation of Anti-BCMA CAR-T Cells in Relapsed or Refractory Multiple Myeloma: A Phase 1 Study. *Nat. Med.* **2026**, *32*, 1257–1266. <https://doi.org/10.1038/s41591-026-04244-6>.
22. Greco, B.; Doglio, M.; Casucci, M. Engineering *in Vivo* CAR-T Cells. *Nat. Med.* **2026**, *32*, 1194–1195. <https://doi.org/10.1038/s41591-026-04296-8>.
23. Wang, R.; Yu, J.; Caligiuri, M.A.; et al. Optimizing *in Vivo* CAR T-Cell Engineering for Cancer Immunotherapy. *Cancer Res.* **2026**, *86*, 1823–1835. <https://doi.org/10.1158/0008-5472.can-25-3748>.