Bristol Myers Squibb™

Cell Therapy

What is Cell Therapy?

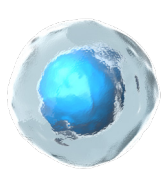
Cell therapies refer to therapies comprised of cells that are injected, implanted or engrafted to treat diseases.

The type of cell used is dependent on the condition being treated. Cells may come from the patient themselves (autologous) or a healthy donor (allogeneic).[1]

Types of Cell Therapies

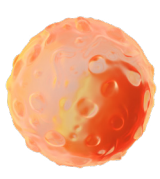
Cell therapies may be classified in various ways. They vary based on the types of cells used, the technologies used to manipulate and administer them and the therapeutic indications they treat or are being investigated in.[1,2]

Types of cells

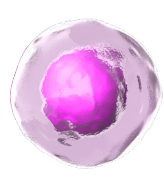


Stem cells
E.g., hematopoietic stem cells, used for blood cancers, blood disorders and immune deficiencies

Blood cells
E.g., transfusions of blood or blood components. ***This is the most common type of cell therapy***



Immune cells
E.g., T cells, natural killer cells (NK cells), used for cancer immunotherapy



Other mature cells
E.g., cells of a specific tissue type to serve a specific purpose

Technologies

The technology used to manipulate and administer cell therapies varies based on the cell type and the goal of the therapy. In some cell therapies, the cells are simply harvested, then purified, propagated and/or differentiated and administered to the patient without any further manipulation.
E.g., Tumor infiltrating lymphocytes (a type of immune cell)

Other cell therapies involve modifications such as gene editing or engineering of the cells. This can be done both in vivo (in the body) and ex vivo (outside the body).
E.g., Chimeric antigen receptor (CAR) T cell therapy; gene modification of cells using a viral vector; CRISPR gene editing

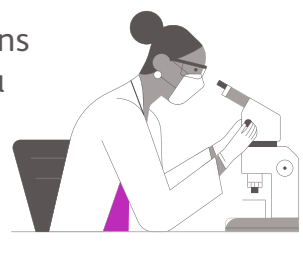
Additional technologies are also being investigated in the field of regenerative medicine and tissue engineering using various cells and cell engineering techniques.[2]

Indications

Cell therapy is already being used in diseases where the need for innovative, effective treatments is high, such as cancer and autoimmune disease.[3] However, it has the potential to treat a wide range of diseases (e.g., liver disease, eye diseases), with the number of anticipated cell therapies in regulatory review and approval expected to grow drastically over the coming years.[4]

Approach to Cell Therapy Research

While transformative outcomes have been observed for some patients with cell therapy, it remains an emergent field with innovation sourced from multiple technologies. Therefore, BMS is taking a diverse approach to continue its leadership in this growing and dynamic space.



By investigating many different areas in cell therapy, we're poised to move quickly on the approaches that the science shows will provide the greatest benefit to patients. **Efforts include:**

- CAR T cell therapy
  - CAR T cell therapy reprograms a patient's T cells (a specific type of immune cell) to attack cancer
  - T cells are engineered to express a protein that recognizes and binds tumor antigens that are expressed on the outside (surface) of cancer cells. Binding then leads to activation and expansion of the CAR T cells, resulting in the killing of cancer cells

Autologous CAR T cell therapy

- Autologous CAR T cell therapy involves using a patient's own cells to start a highly sophisticated and personalized manufacturing process.
- The complexity of delivering autologous CAR T cell therapies is unlike any other traditional biologic or medicine. Efforts are underway to make autologous CAR T cell therapies more efficient, scalable and accessible through new manufacturing platforms.

Allogeneic CAR T cell therapy

- Allogeneic or "off-the-shelf" CAR T cells made from T cells of healthy donors—rather than the patient's own reprogrammed T cells—can be delivered to patients without the wait time required of autologous CAR T therapies.
- Healthy donor T cells may have better functionality than cancer patient's own T cells–however the patient's body could reject the cells.
- BMS is engineering these allogeneic T cells to minimize their rejection by patients' immune systems.

- Engineered T cell receptor (eTCR) cell therapy
  - Similar to CAR T cell therapy, but using natural cellular machinery that allows the modified T cell to target antigens expressed both inside and on the surface of cancer cells therefore allowing more patients to benefit from cell therapy.
  - eTCR therapy can also be either autologous or allogeneic, as defined above for CAR T cell therapy.
- Cell therapies using other types of immune cells, such as NK cells
- Advanced gene editing, cell engineering and cell therapy target selection
- Alternative methods of delivering genetic material into T cells (non-viral gene delivery)
- Optimization of manufacturing processes
- Taking learnings from translational data of current products and using them to inform design and engineering of next generation products that are more likely to work in patients who are not responding or become resistant to current therapies

Experience to Build Upon

Bristol Myers Squibb draws upon its transformative work and unparalleled experience in hematology and immuno-oncology as well as its broad approach to R&D as it advances a robust pipeline of cell therapy projects made possible by informed drug discovery efforts and sophisticated manufacturing technologies.

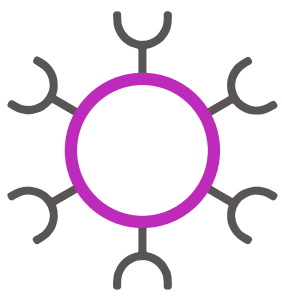
With

~1,800
clinical trial patients...

...treated across

6
indications

11
manufacturing process variations



Bristol Myers Squibb scientists have access to one of the largest CAR T **product**, **translational** and **clinical datasets** in the industry.

Bristol Myers Squibb is committed to maintaining leadership in cell therapy and continuing to deliver these innovative treatments to patients in need and where potential impact is greatest. Cell therapies comprise a significant part of our long-term research, development and commercialization efforts. As such, we are focused on advancing cell therapy research across a wide spectrum of blood cancers and solid tumors, as well as exploring potential uses in other disease areas like autoimmune conditions.

1. Gene & cell therapy FAQs. American Society of Gene & Cell Therapy. Accessed July 22, 2021. https://asgct.org/education/more-resources/gene-and-cell-therapy-faqs
2. Mount NM, Ward SJ, Kefalas P, Hyllner J. Cell-based therapy technology classifications and translational challenges. *Philos Trans R Soc B Biol Sci.* 2015;370(1680):20150017. doi:10.1098/rstb.2015.0017
3. Approved cellular and gene therapy products. US Food and Drug Administration (FDA). Published June 15, 2021. Accessed July 23, 2021. https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/approved-cellular-and-gene-therapy-products
4. Statement from FDA Commissioner Scott Gottlieb, M.D. and Peter Marks, M.D., Ph.D., Director of the Center for Biologics Evaluation and Research on new policies to advance development of safe and effective cell and gene therapies. US Food and Drug Administration (FDA). Published March 24, 2020. Accessed July 23, 2021. https://www.fda.gov/news-events/press-announcements/statement-fda-commissioner-scott-gottlieb-md-and-peter-marks-md-phd-director-center-biologics