Cell Therapy

Cell therapy refers 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 cells

- **Stem cells** E.g., hematopoietic stem cells, umbilical cord blood cells, and induced pluripotent stem cells
- **Blood cells** E.g., modification of clinical relevant leukocyte and immune system disease
- **Immune cells** E.g., cells that target cancer or autoimmune disease
- **Other mature cells** E.g., cells that target specific tissues

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 (T-ICL) are immune cells.

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.

Advanced 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 diseases. 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. 3

Cell Therapies

- **CAR T cell therapy**
  - CAR T 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

- **Allogeneic CAR T cell therapy**
  - Allogeneic CAR T cell therapy involves using a patient’s own cells to treat their disease

- **Autologous CAR T cell therapy**
  - Autologous CAR T cell therapy involves using a patient’s own cells to treat their disease

- **Engineered T cell receptor (eTCR) cell therapy**
  - Similar to CAR T cell therapy, but using natural antigenic machinery that allows the engineered T cell to target antigens expressed both inside and on the surface of cancer cells therefore allowing more patients to benefit from cell therapy

- **Advanced gene editing**
  - Advanced gene editing and cell therapy target selection

- **Optimization of manufacturing processes**

- **Takings 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 scientists have access to one of the largest CAR T product, translational, and clinical datasets in the industry. 11

1. CAR T cell therapy


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 new cellular and gene therapy products.

5. Technologies that make possible by informed drug discovery and sophisticated manufacturing technologies.

6. Immune-oncology as well as its broad approach to R&D as it advances a robust pipeline of cell therapy projects.

7. E/f_f.ligaorts include:

   - Optimization of manufacturing processes
   - Alternative methods of delivering genetic material into T cells (non-viral gene delivery)
   - Advanced gene editing, cell engineering and cell therapy target selection

8. Experience to Build Upon

9. Bristol Myers Squibb scientists have access ongoing and future clinical trials to access

10. eTCR therapy can be either autologous or allogeneic, as defined above for CAR T cell therapies.

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   - eTCR therapy can include either autologous or allogeneic, as defined above for CAR T cell therapies.