

Cell Therapy: Expert Perspective



Anvay Ukidve, Ph.D.

Scientist, Formulation and Process Development, Sanofi, Framingham, MA 01701

Q.1. Could you briefly describe what cell therapy is and delineate the major types of cell therapy?

Cell therapy is the use of cells as active entities to remove and/ or replace the damaged or diseased cells in a patient's body, wherein, the therapeutic cells can directly or indirectly interact with the native tissues or their designated targets to either modulate the pathological condition or completely replace their diseased counterparts. There are multiple ways of delineating different types of cell therapy. Based on origin of the cells, they can be classified as autologous-derived from the host patient or allogenic- derived from alternate source in the same species. Based on the type/ techniques for cells employed, cell therapies are classified into stem-cell, adoptive-cell transfer, cell-based vaccines and so on. Another important way of delineating cell-therapies is the application for which they are intended for- oncology, auto-immune disorders, cardiovascular diseases and so on.

Q.2. What are the key factors or opportunities that provided an impetus to the research and market growth of cell therapy?

Cells represent a unique class of therapeutic modalities. For starters, they are living and functional entities. This means that they have the potential to modulate their microenvironment and foster cultivation of entire tissue-systems. This attribute has been utilized by stem cell-based therapies for regenerative applications. Differentiated cells have highly specialized functionality. Use of such cells is an obvious choice for tissue repair and replacement applications. From a delivery perspective, specific biology of the cells- including their unique target engagement as well as natural tropism towards certain tissues makes them an attractive candidate to consider, especially given the transport related biological barriers that drug delivery strategies encounter. All these considerations and many others provided a huge impetus to research on cell therapies and its consequent market growth.

Q.3. How are cell therapies administered, and could you also comment on the use of medical devices for the safe and efficacious delivery of cell-based therapeutics?

Almost all the cell therapies that have been approved by health authorities are being currently administered by intravenous infusions. Therefore, at the moment , the use of medical devices has been is limited to intravenous administration using infusion lines driven via

infusion pumps. However, novel cell therapies being explored in the clinic are exploring alternate routes of administration such as subcutaneous, intradermal, intracranial, etc. For stem- cell therapies, accessing the bone marrow directly as opposed to intravenous is also being considered. These different routes of administration would certainly bring more medical devices into play to ensure safe and efficacious delivery of cells.

Q.4. In light of recent FDA-approved cell therapy products, what are some of the most promising clinical applications of cell therapy?

While the initial set of cell therapies were targeted against blood-based malignancies or specifically aimed at restoration after myeloablative events, their clinical success has opened avenues for other indications. In oncology itself, the ability of cells to penetrate deep within the tissues makes them an effective strategy against solid tumors. Autoimmune indications, cardiovascular disorders and trauma are important indications where there could be additional impact of cell therapy. Use of genetic engineering coupled with cell therapy has the potential to add non-druggable targets and/or manage the safety profile of existing therapies across a wide variety of indications. Another emerging set of application is the use of microbes for treating infections, metabolic disorders, and inflammation besides the already proven utility for nutraceutical purposes

Q.5. What are the challenges or restraints that hinder the growth of the cell therapy market?

As with any other therapy, a few challenges are encountered by cell therapy. Firstly, cells themselves are very potent modalities and managing the safety of such potent therapies has been a very significant challenge. Cytokine storm is a very common side effect associated with T-cell based immunotherapies for oncology indications. Safety concerns greatly impact the applicability of cell therapies as patients are generally in an immunocompromised state. Hence, the delivery route as well as the delivery mechanism for such therapies is under investigation. Secondly, maintenance of the functional and effector functions of the cell is central to a successful cell therapy intervention. Often, manufacturing processes themselves present a significant challenge to the viability of the cells and in turn their potencies as cells are used to a certain microenvironment in the body and typical manufacturing processing may not be ideal, especially for certain cell-therapies that rely on receptor-based pharmacological effects. Thirdly, manufacturing cell therapies is a significant challenge considering that many of them heavily rely on expanding cells isolated from patients. Further, management of drug product filling and shipping to the clinical sites in a way that is not compromising to the quality of cells and their potency remains a work-in-progress. Lastly, lack of universal standards of regulatory framework for cell therapies adds a logistical hurdle to fast development and deployment of these strategies.

Q.6. What are the current regulatory frameworks and regulatory challenges for the manufacture and scale-out of cell-based therapies?

Ans: There isn't one-size fits all regulatory framework for dealing with cell therapies. FDA's Center for Biologics Evaluation and Research (CBER) and EMA's committee for advanced therapies (CAT) advise and regulate the entry of new cell therapies in the clinic.

At the moment, there is a high degree of uncertainty over manufacturing considerations – reporting of critical quality attributes and around product purity. Unlike, protein-based products where manufacturing process and the underlying must haves are clearly defined by the regulatory agencies, diverse cell therapies and their unique manufacturing processes as well as parameters to be considered for their functional effectiveness make it very difficult to have a universal standard set for advancement of such products. Sometimes economics of a rigorous regulatory requirement versus a very small market also skews companies against pursuing novel therapies. Nevertheless, it is an ongoing effort between industries and regulatory agencies to streamline this workflow and facilitate entry of novel therapies

Q.7. Could you comment on the global market size, market trends, and key market players in the cell therapy industry?

As of 2022, cell therapy was value at ~ \$10.7 billion and is projected to grow with a compound annual growth rate (CAGR) of 19-20% by 2030-2032. This growth is driven by investment of big pharma into niche small or mid-scale companies who have a heavy cell-therapy driven focus. A few key market players as far as the cell therapy is concerned are- Kolon Tissue Gene, Inc., Osiris Therapeutics, Inc., JCR Pharmaceuticals Co. Ltd., NuVasive, Inc., Stemedica Cell Technologies, Inc., Cells for cells, Holostem Therapie Avanzate S.r.l., Mesoblast Ltd., and Medipost Co., Fibrocell Science Inc., PHARMICELL Co. Ltd., MEDIPOST, Vericel Corporation, Anterogen Co. Ltd., Inc. , Celgene Corporation and AlloCure

Q.8. How is the cell therapy industry likely to evolve over the next decade?

Cell therapy has the potential to evolve both from a research and development perspective. From a research perspective, the applicability, and the multitude of cells in clinical trials are indicative of how the field continues to evolve in terms of more cell types and indications being explored. Apart from that, there is an active interest for using cell therapies in combination with other therapeutic modalities, in some cases, even using cells as delivery vehicles to improve the effectiveness of molecules which were previously hindered due to off-site deliveries. From a development perspective, a huge effort will be invested in setting up scale-out strategies for making manufacturing processes robust and easily implementable for a variety of cell types. As with protein-based therapies, understanding process parameters and their impact on product quality will be extremely crucial in making sure that quality of manufactured product is maintained. Manufacturing of allogenic therapies and innovative techniques of cell-expansion are likely to evolve over the next decade. Storage and transportation of currently existing therapies is likely to see more advancements as cryogenic storage and transport could add to logistical and product quality issues, if not well characterized. Lastly, definition of product purity will likely be consolidated and solidified with active engagement between industry leaders and regulatory agencies. All in all, scientific, process development and regulatory advancements are expected in the field of cell therapies.

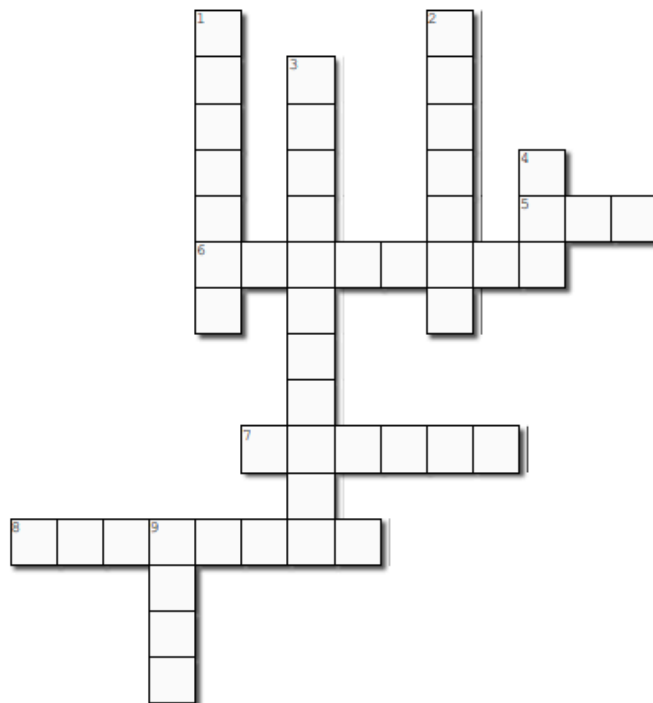
Disclosure:

The view and opinions expressed within this content are solely the author's and do not reflect the opinions and beliefs of Sanofi or its affiliates.

References:

1. Wang, L.L.W., Janes, M.E., Kumbhojkar, N., Kapate, N., Clegg, J.R., Prakash, S., Heavey, M.K., Zhao, Z., Anselmo, A.C. and Mitragotri, S., 2021. Cell therapies in the clinic. *Bioengineering & translational medicine*, 6(2), p.e10214.
2. <https://asgct.org/education/more-resources/gene-and-cell-therapy-faqs>
3. <https://www.astrazeneca.com/r-d/next-generation-therapeutics/cell-therapies.html>
4. Iglesias-Lopez, C., Agustí, A., Obach, M. and Vallano, A., 2019. Regulatory framework for advanced therapy medicinal products in Europe and United States. *Frontiers in pharmacology*, p.921.
5. <https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products>
6. <https://www.ema.europa.eu/en/committees/committee-advanced-therapies-cat>
7. <https://www.precedenceresearch.com/cell-therapy-market>
8. <https://www.thebusinessresearchcompany.com/report/cells-therapy-global-market-report>
9. <https://www.alliedmarketresearch.com/cell-therapy-market>

Fun & frolic – Crossword



Created using the Crossword Maker on TheTeachersCorner.net

Across

5. Immortalized cell line
6. Cell-based therapy to treat Type 2 diabetes
7. Dermal fibroblasts for wound repair from Arita Medical
8. CAR-T therapies for the treatment of relapsed or refractory large B-cell lymphoma,

Down

1. CAR-T therapy for the treatment of acute lymphoblastic leukemia
2. Approved in vivo gene therapy
3. World's first 'personalized' cancer therapy marketed by Dendreo
4. Abbreviated Michigan Cancer Foundation Breast Cancer Cell Lines
9. Chimeric antigen receptor T-cell therapy

Solution on page 52