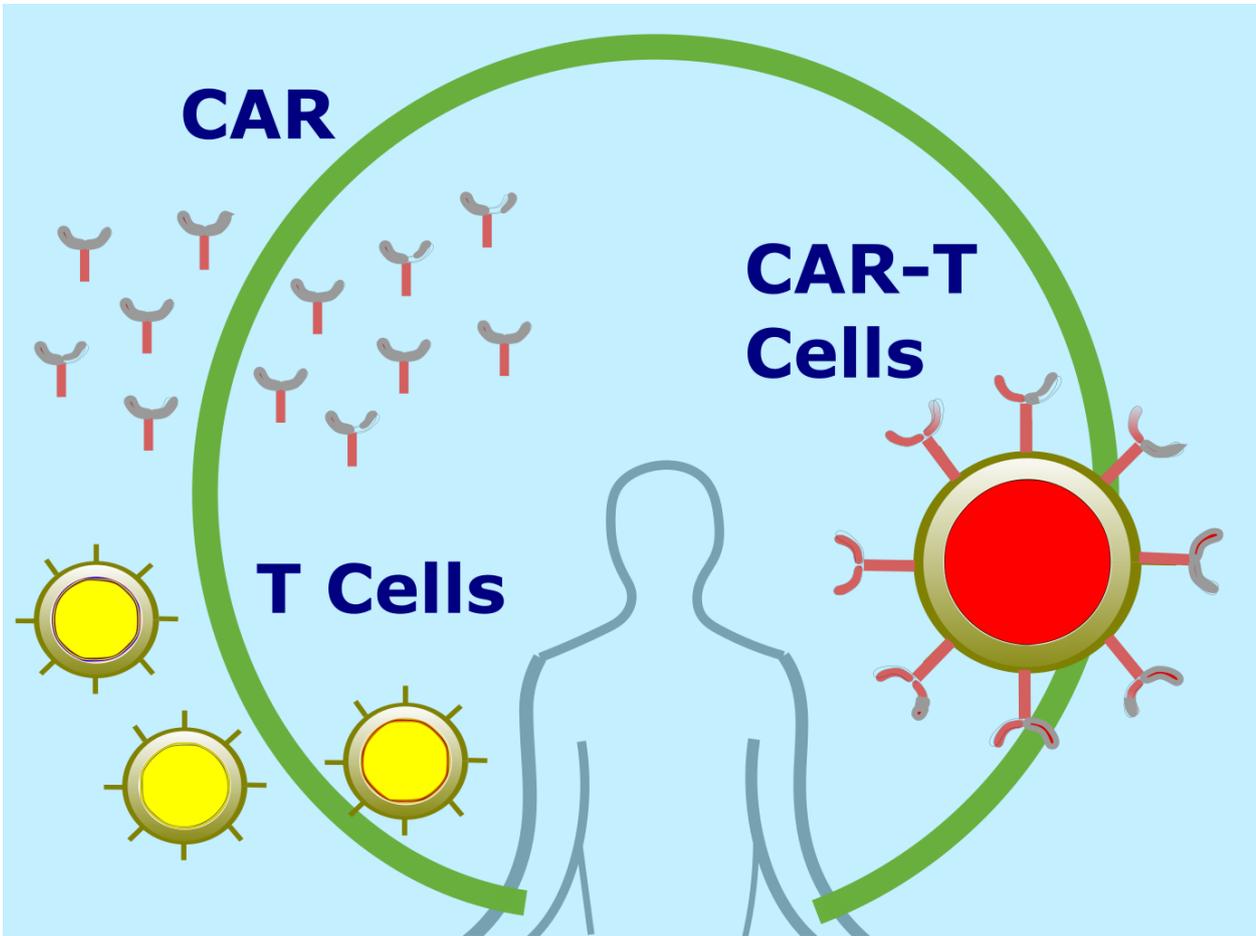


The Promise Of Cell Technologies In Immunotherapy

Feb. 9, 2020 by Irina Bilous

The number of immunotherapies in clinical trial rolls over 5000 now, and immunology has become a common approach in some cancers. Cell technologies, as a growing sub-field in the immunotherapy landscape, have progressed considerably and now represent a \$26 billion financial opportunity by 2030, according to a report by Roots Analysis.



Evolutionarily, the immune system has adapted to distinguish between foreign or tumor antigens and the body's own cells. To prevent autoimmune reaction, T-lymphocytes carry on special PD-1 (programmed cell death-1) receptor, that verify foes before attacking them. Insidious cancer cells often express a ligand to this receptor - PD-L1, triggering intracellular mechanisms that block T-cells response. Inhibitors for this

PD-1/PD-L1 and other checkpoint pathways (Opdivo, Keytruda, Yervoy) are being routinely used.

Thanks to the success of checkpoint therapies, immunotherapy ramped up its popularity, shifting toward the development of cell therapies. The Car T-cells have shown success in treating blood cancers in patients who have not responded to almost any of available treatments. Car T-cells are engineered to express Chimeric Antigen Receptors with a high affinity to tumors antigens. Despite groundbreaking results, the technology has its own limitations and required significant improvements.

Common Car T-cells have an autologous origin, implying that cells must be retrieved from the patient's blood, modified and infused back to the bloodstream, that takes about three weeks and enormous costs. Making allogeneic, also called of-the-shelf, therapies is a new challenge for biotech companies. Century Therapeutics raised \$215 million from Bayer for this purpose in July 2019, focusing on producing Car T-cells from induced pluripotent stem cells (iPSC). On the other hand, Cellectis and Allogene Therapeutics employ gene editing technologies to modify T-cells derived from healthy donors. This will enable companies to transform complex and costly personalized treatments into more unified treatment schemes, and 'off-the-shelf' cell therapies.

Both approved therapies (Novartis' Kymriah and Gilead's Yescarta) are targeting CD19 antigens on the surface of B lymphocytes. However, several patients have died during clinical trials of such drugs due to the cytokine release syndrome and brain bleeding. New generation of CAR T-cells should make the cure more controllable. As an example, Bellicum Pharmaceuticals employs a safety switch ensuring T cells are activated only in the presence of the additional drug, rimiducid.

Furthermore, Car T-cells are weak when coping with solid tumors, and cancers might become resistant and relapse. To overcome the barriers, Autolux created a cell line that simultaneously targets CD19 and CD22 antigens. Cellyad combines properties of NK cells and T-lymphocytes, constructing NKR T-cells that are able to recognize eight receptors expressed in tumors and surrounding tissues. BioNTech boost Car T-cells with RNA encoded claudin 6, a protein which expressed specifically on the surface of certain cancers, forcing them to penetrate solid tumors.

Companies strive to make T-cell therapy safer and expand it for more cancers and even apply against autoimmune diseases. Advances in gene technologies, such as CRISPR, and the emergence of IP stem cells work well for immuno-oncology, allowing us to create precise cell therapies.

Below we have summarized several biotech companies focusing on discovery and development of cell therapies. If you want to add your company to this list, or update information in the existing company

profile, please, use our Editor Tool.

- Autolus
- Bluebird Bio
- BrainStorm Cell Therapeutics
- Century Therapeutics