bio-techne®

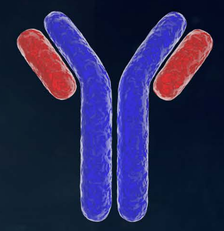
IMMUNE CELL THERAPY WORKFLOW

1 LEUKAPHERESIS

The first step in the manufacture of an immune cell therapy is the collection of white blood cells by leukapheresis. For autologous therapies, leukocytes collected from a patient are the starting material for the production and infusion of a cell therapeutic back into the same patient. For allogeneic therapies, a donor provides leukocytes for a cell therapy that is used to treat a broader population of patients.

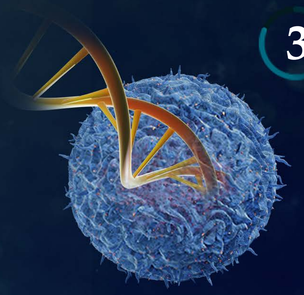
2 CELL SELECTION

Specific immune cell subsets (e.g. T cells, NK cells) are often separated from the apheresis material to obtain an enriched cell population for downstream genetic engineering and expansion. Multiple techniques are used for cell separation, including flow cytometry sorting, magnetic separation, and bead-based separation. Antibodies are a critical component of affinity cell separation in current manufacturing processes. The use of GMP-grade antibodies that can be fluorophore-conjugated for flow sorting is a necessity for advancing cell therapy manufacturing. Learn more at bio-techne.com/cgt



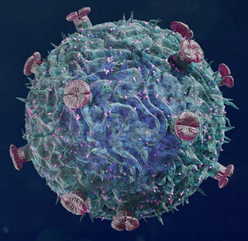
3 GENE ENGINEERING

Gene engineering techniques are increasingly being used to improve the targeting and efficacy of cell therapies. For example, enriched populations of immune cells can be engineered to express a chimeric antigen receptor (CAR), which recognizes a unique cellular marker on the target cell and directs the killing action of the immune cell. There are several methods of gene engineering, including viral and non-viral technologies. Non-viral technologies are quickly becoming the preferred method for gene engineering. Their ability to deliver larger genetic cargo, achieve efficient transfection rates, and minimize cell therapy immunogenicity helps reduce the risk and the overall cost of manufacturing process. Learn about Bio-Techne's non-viral technologies at Gene Engineering Services (bio-techne.com/services/gene-engineering-services)



4 EXPRESSION VERIFICATION AND TARGETING VALIDATION

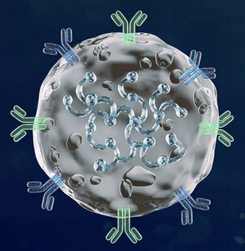
Before scaling up production of engineered immune cells, it is important to verify successful expression of the CAR construct and function of the edited cells. A variety of methods are currently employed to verify expression and functionality, including RNAseq, flow cytometry, immunocytochemistry, and genetic knockout. Sensitive, flexible, and efficient methods for single cell or population verification of gene editing improves the efficiency and quality of cell therapy manufacturing. Bio-Techne's innovative RNAscope™ and BaseScope™ assays are designed to visualize edited transcripts, define the allelic status of an edit, detect the guide RNA and Cas9 enzyme, and confirm downstream effects of gene editing, with spatial and cell type specificity. Learn more at bio-techne.com/reagents/rnascope-ish-technology



5 CELL EXPANSION

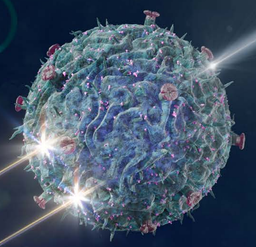
Cell culture expansion is a crucial step in immune cell therapy manufacturing. Specific combinations of GMP-grade cytokines, activating reagents, and culture media will promote robust cell expansion to meet therapeutic dosing requirements. Cloudz™ Cell Activation and Expansion reagents allow for flexible and gentle immune cell expansion. Post-expansion cell selection steps may be needed to isolate the final cell product. Learn more at rndsystems.com/cloudz

An important component of the cell culture expansion is the ability to add media, cytokines, and other factors aseptically. Bio-Techne offers GMP media suitable for closed systems for cell manufacturing as well as the novel GMP ProDots™ Proteins, single dose GMP cytokines designed to eliminate aliquoting and minimize handling time. Learn more at rndsystems.com/gmpprodots



6 CELL PHENOTYPE VERIFICATION

Once cell cultures have been expanded, verification of cell phenotype and purity is required for product release. Flow cytometry, immunoassay profiling, cell viability assays, and single-cell analytic technologies are often employed for product characterization. Standardizing and automating common verification methods will simplify and expedite product quality control (QC) testing. Bio-Techne offers expert analytic solutions, such as flow-validated antibodies for cell phenotyping and gene expression verification and a full range of immunoassays, including the Ella platform for automated multianalyte analysis. Learn more at bio-techne.com/cgt



7 FORMULATING THE FINAL CELL THERAPY PRODUCT

Formulating the QC-released final cell product for delivery to the patient is important to maintain product viability during storage and transport. Product formulation and vessel choice is dependent on specific manufacturing process and patient treatment requirements. For immune cell therapies, the product is often transferred to sterile IV bags that are either delivered fresh and unfrozen to the clinic or are cryopreserved for future use.

8 TRANSFUSION & PATIENT MONITORING

Finally, the cell therapy product is ready for delivery to the patient! This exciting step comes with a whole new set of challenges as the patient must be monitored post-infusion to determine if their condition improves or if the cell therapy induces an adverse effect. The time required for patient monitoring may be several years for some therapies.

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