Applications of Flow Cytometry to Support CAR T Cell Therapy: More or Less!!

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Regenerative medicine (RM) involves the process of re-engineering or modifying human cells, tissues or organs to establish or restore normal biological/immunological function. The development of chimeric antigen receptor T (CAR T) cell therapy is a branch of RM that has demonstrated tremendous success in treating hematological malignancies in patients previously relapsed or refractory to standard of care or other exploratory treatments. CAR T cell therapy has the potential to revolutionize the treatment of oncologic and immune disorders and, following the FDA-approval of the first two autologous CAR T products in 2017. This personalized medicine approach is poised to become the next major class of pharmaceutical therapeutics. This has led to significant investment in this field by both the established pharmaceutical and biotechnology industries as well as private investors funding new research ventures, all with a common goal of delivering high-quality, safe, efficacious and cost-effective treatments to patients.

Compared to biologics, the manufacture of cell therapy products is highly specialized, and control of the manufacturing process is critical for generating a safe and efficacious product. Since the final product is cellular material, analytical methodologies such as flow cytometry and immunofluorescence are essential for determining the identity, purity and dose of the CAR T cell therapy. Multi-parametric, high-dimensional cytometric analysis provides the ability, in a research and development laboratory, to characterize starting material, cellular intermediates and drug product for CAR T. However, standardized and validated high-throughput flow cytometry methods, performed in a quality control laboratory under good manufacturing practice (GMP) regulations, are required to monitor critical stages of the process and for release of the final product for administration to patients in clinical studies or commercial manufacture.

Therefore, we have this dichotomy of how flow cytometry is applied to support CAR T based upon the end use of the data, balancing the need for scientific complexity and flexibility with the requirement to meet strict regulatory guidelines. Furthermore, as we move to the next generations of CAR T, the need to reduce cost through scalability and automation is essential so that these therapies are cost effective and available across global markets. These applications of flow cytometry used during clinical development of CAR T will be discussed with respect to characterization testing and the translation of analytics to a GMP-compliant testing environment. We will also review the relevant, phase-appropriate assay qualification and validation, and the supporting systems that are necessary as we move through clinical development towards approval and commercial manufacture.