HemaCare Leukapheresis Material Powers CAR T Cell Discovery Platform

Introduction

Cell and gene therapy is a new field of medicine with the potential to change how we think about treating disease. Research into conditions once considered to be incurable is now being rewarded with positive outcomes based on a deeper understanding of the intricate interactions between living cells and tissues. One of the largest pharmaceutical companies in the world is currently in the midst of a collaborative effort to build a new research platform that will support the discovery and development of novel cell and gene-based technologies. The hope is that the new UK-based facilities will expand the company’s capabilities and expertise in the field.

One of the most important aspirations of this innovative research platform will be the development of CAR (chimeric antigen-receptor) T cell therapeutics. The company already has several T cell-based pharmaceuticals in clinical development. Their headlining clinical program, which is being carried out in collaboration with a partner company, is based on engineered T cells that target a peptide present on multiple cancer cell types. These targeted T cells have already been used with promising results in several different phase 1 and phase 2 clinical trials. A more recent collaboration with another biotechnology company is intended to help overcome cell therapy scale-up issues, by incorporating new automated technologies that will allow both companies to expand to a wider patient population.

HemaCare spoke with the lead T cell processing scientist who has been part of the cell therapy program at one of the world’s largest pharmaceutical companies for the last three years. As a T cell process development scientist, part of his job is to ensure that isolation, handling, and storage protocols optimize cell viability and function. The T cell processing scientist’s first concern is the quality of the precursor material from which various T cell therapies will be derived. The pharmaceutical company’s T cell therapy program obtains most of their precursor material from HemaCare, whose large donor database makes it easier to match donor profiles to specific project requirements.

“The quality of precursor material is absolutely essential since it will determine the quality of the downstream product. You need to have high-quality material going in because it will affect a lot of other parameters downstream.” - Head of T Cell Processing, Global Pharmaceutical Company

Along with assuring high-quality precursor material, scientists based in the United Kingdom face a more basic hurdle; that of obtaining human donor material in the first place. Like other European-based researchers, the T cell processing scientist notes that it is very difficult to get locally sourced healthy donors, since European ethics guidelines, unlike those in the U.S., prohibit donors from being compensated for human biological samples. This is one of the reasons he chose to source the research center’s starting material from HemaCare.

Quality Control During Shipping and Handling

While it’s a practical necessity for the UK-headquartered pharmaceutical company to do so, shipping internationally can present challenges. Human blood products that are held up in customs risk lower cell viability rates. Arrival times can vary, and products that don’t make the company’s 4 pm receiving deadline will be sent back to the distribution center. The T cell processing scientist stresses that there needs to be close and consistent coordination between all agencies involved in the shipping process, in order to ensure that leukapheresis products arrive punctually and can be processed in a timely manner.
Once leukapheresis materials arrive in house, one of several things can happen. More often than not, the material will be reformulated and then frozen for later processing. This procedure takes about a day. More rarely, leukopaks will be processed completely upon arrival, after which the freshly isolated cell types are cryopreserved. If mobilized leukapheresis products have been ordered for the manufacture of a stem cell therapy, the leukopak will be processed and the cells used on site as a freshly isolated product.

An important part of the preparation process for cell-based material consists of carrying out the appropriate quality control assays. Cell viability counts are done shortly after leukapheresis products arrive in-house. When cryopreservation is necessary, viability counts are repeated post-thaw. This is the most basic measurement of product quality, and in general, the pharmaceutical company expects to see viability rates ranging from 90-95%.

“**Apheresis is key. For example, if post-thaw viability is good, say greater than 90 percent, you know things are going to work out well. If post-thaw viability falls to, say, 80 percent, the cells just aren’t going to perform as well**” - Head of T Cell Processing, Global Pharmaceutical Company

Functionality criteria, on the other hand, vary from project to project. Basic assessments of cell function are carried out as soon as possible, while parameters such as cell expansion and proliferation are assessed further down the line. The T cell processing lab performs a number of different assays, including extensive cell characterization assays, phenotyping, metabolic monitoring, and blood gas monitoring.

All pharmacodynamics (PD) assays are carried out in-house, since they’re specific to the project or therapeutic being tested on any given day. Since PD assays are so important in assessing therapeutic safety and efficacy, the company will soon be expanding cell therapy potency testing to a greater number of specific targets.

Protecting therapeutic efficacy by definition involves optimizing cell handling methods, especially when a product may need to be shipped to different points across the globe. The scientist interviewed by HemaCare regularly orders cryopreserved leukopaks to help with ease of scheduling, for example, when material from several donors is being processed simultaneously. While some researchers still express skepticism that cryopreserved products measure up to those that are freshly isolated, the T cell scientist questions this prejudice. “**What is fresh?**” he asks. A fresh leukopak that has to be shipped off-site, or is held up in customs or needs to be stored until it can be processed, can end up having a lower viability rate and compromised quality, compared to a cryopreserved product. He believes that cryopreservation not only fills an important practical role in the cell therapy industry, but, when done right, is a valuable way to protect efficacy. The UK-headquartered pharmaceutical company is currently optimizing isolation and cryopreservation methods as part of their process development, so that they can guarantee a consistent product from one clinical site to the next. If a cellular product is actively part of the clinical process, the company must be able to show definitively that any changes in methodology don’t affect the quality of their material.

CAR T cell quality can make a life or death difference to a patient. If a CAR T cell product fails the manufacturing process, precious time will be lost while another batch is prepared. Starting material quality is the single most important factor affecting a CAR T product. Thus, it is crucial to establish optimal methodology and quality criteria that will minimize overall variability and risk to the patient.

**References:**