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What Do You Need To Know About Tech Transfers For Autologous Cell Therapy Products?

By Trisha Gladd, Editor, Life Science Connect

While interest in the cell therapy market has increased dramatically over the last couple of years, a major source of innovation in this area still remains in academic labs. As companies acquire cell therapy product licenses from academia, they will, of course, need to transfer the technology to their own labs or to a contract manufacturing organization. And while tech transfers have always been a challenging area for the industry, the sensitivity of cell therapy products can make this process even more onerous for companies pursuing these types of products. That is why Ali Siapush, president of Pharmefex Consulting, plans to tackle this topic at this year's Cell Therapy Bioprocessing & Commercialization conference in a presentation titled *Practical Challenges in the Manufacturing and Technology Transfer of Autologous Cell Therapy Products*.

Set Your Expectations Accordingly

Working with both pharmaceutical and biotechnology companies, the Pharmefex team specializes in assisting its clients with accelerating the development and approval of recombinant proteins and cellular and immunotherapy products. Of the clients they serve, Dr. Siahpush says about 50 percent are pursuing a product in the cell therapy market and many acquire these from an academic setting. "For these transactions to be successful, it's important to understand the characteristics of an academic-to-industry transfer, the characteristics of autologous cell therapy products, and the relationship between them," he explains. "The objectives and the priorities of the two organizations involved—the academic organization and the industrial organization—must be aligned. Often though, they are not."

Because some companies go into this with a finite amount of time and resources, this misalignment can make it difficult to demonstrate promising results within the expected timeline, which is necessary when trying to raise the additional capital needed to continue development of the program. "If they were to underestimate the complexity and/or the

duration of the project by a significant amount, then they can have a serious problem on their hands," says Dr. Siahpush. "They may not have enough funds to continue and they still don't know whether or not the product works."

What you need for a successful technology transfer is an in-depth understanding of the process, its limits, and how to control and measure. "This is not what academia does," says Dr. Siahpush. "They want to be in the business of discovering things, so innovation is at the top of their list. As a result, what you get from them is promising results but for a product and process that are poorly characterized." He adds they also do not often have the ability to assess how long it is going to take and how much it will cost to transition this new technology to a place where it can be reliably produced for the purpose of clinical and commercial use. This will eventually become a major source of problems.

Make A Plan For Variability

The production process for making autologous cell therapy products has a lot of inherent variability built in. The reason for this is because the starting material is cells from an individual donor, or patient, with each individual being slightly different. These processes also tend to be very manual, which can introduce additional variability. How you deal with variability tends to create a level of complexity that Dr. Siahpush says some companies tend to underestimate. "If you remember that the product is from an academic setting and therefore probably not very well characterized, then you know there's a high likelihood that you're going to have to do various studies to better understand how to control the process," he explains. "In running those studies, you are essentially trying to understand how many studies you need to do and how long it will take you to complete them. To do each experiment, you will need to know how many replicas you need to run, in order to be able to know whether or not you've measured a real effect."

Because of the limited amount of material from each donor, the number of experiments that can be run with a single donor's cells is small. If you try to run experiments across donors, then donor-to-donor variability becomes built into your experiment, which increases the number of replicates needed to be able to measure a meaningful effect. This can become very complicated, expensive, and ultimately stretched over a longer period of time. "If you try to go the other way and stick within the same donor to run the experiment, you can exclude the donor-to-donor variability," says Dr. Siahpush. "However, then you are starting with a finite amount of material and your ability to run multiple experiments really requires that you have an adequate scale-down model. This is another part that is often underestimated by companies—how soon do I need my scale-down models?"

According to Dr. Siahpush, you'll need them early on. He continues, "If you can't run these experiments at a much smaller scale from single donors, in order to be able to eliminate the donor-to-donor variability, your designs now span a longer period of time

by virtue of the fact that you need material from many different donors. As the number of replicates needed to measure any effect becomes larger, your ability to successfully run that experiment becomes limited by your ability to successfully execute very complex designs." As the studies become more complex, your staff will find it increasingly more difficult to manage all the splits as well as the timing of samples being taken and analyzed.

It is at this point when Dr. Siahpush says clients turn to him and his team for help. And while he recognizes this isn't a bad thing for consulting companies, he knows it is for the companies that find themselves in this predicament. "Now they need to either get more money or account for more time in the development of their products," he explains. With traditional products, such as protein-based therapeutics or even small molecules, many companies have a template for these transfers and know what to expect. However, until the cell therapy market matures, it will require more awareness of its specific challenges and issues, in order to successfully bring them to market. And, even more importantly, to do so in an efficient and affordable way.

Dr. Siahpush will discuss this topic as well as some specific best practices he recommends adhering to when carrying out a tech transfer for an autologous cell therapy product. His presentation is scheduled for October 1st at 2:30 PM.