Establishing a Reputation by Producing Translational Results: Interview with Bruce Levine, PhD, Director of the Clinical Cell and Vaccine Production Facility

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FACT is interviewing personnel at facilities FACT-accredited for more than minimal manipulation processing activities to share their knowledge and experience to members of ISCT. Bruce Levine, PhD, presented a philosophy of teamwork while describing the activities of the Clinical Cell and Vaccine Production Facility at the University of Pennsylvania. He accounts how focusing on results drives his facility’s solid reputation in the cellular therapy field and with the public.

Establishing Relationships with Investigators Produces Results

Dr. Levine is the director of the Clinical Cell and Vaccine Production Facility (CVPF), which is a core facility serving the University of Pennsylvania Perelman School of Medicine and the Abramson Cancer Center. It consists of two GMP-compliant facilities on opposite ends of the university’s hospital; one is two thousand square feet and the other is three thousand square feet. The CVPF has additional laboratory space for process development and quality control. Although not contiguous, facility personnel keep in touch via pagers and intercoms.

CVPF’s repertoire of clinical trials and Investigational New Drug (IND) applications are primarily driven by investigator-initiated trials from the University of Pennsylvania and the Children’s Hospital of Philadelphia (CHOP). Its mission is to “help translate insights into novel cellular therapies.” Investigators utilizing the CVPF receive assistance with writing and editing the Chemical, Manufacturing, and Controls (CMC) section of IND applications and background information and letters of support for grant submissions.

Almost all products processed by the CVPF are autologous. “We have performed a trial with allogeneic mesenchymal stromal cells (MSCs) and we’ve performed a few allogeneic directed T-cell trials, but the vast majority of what we are doing is autologous.”

The facility receives some funding as an Abramson Cancer Center Shared Resource as part of its comprehensive cancer center NCI core grant. Industry funding comes mostly from the Penn collaboration with Novartis. Additional funding is obtained through fees charged to investigators for their services. “Whether it’s industry or not, there is a Penn investigator or a CHOP investigator,” says Dr. Levine. “We’re different from some of the other core facilities at the university where samples are sent, service is performed, and data is provided. Anyone we work with has to have clinical and translational expertise. Because of that, we become aware of them and they become aware of us.”
This awareness has led to a large number of projects. Dr. Levine’s facility is currently working on about 12 clinical trials and is in the process of opening up another 8 to 10 trials over the next several months. “As some trials are completed, we replace them with new trials.” This is a typical volume, says Dr. Levine. “Since the facility opened, it has supported over 20 INDs.” Marketing includes a web page and information is disseminated to investigators via the cancer center shared resources program; however, most activity is driven simply by the facility’s relationships with current investigators and with a considerable amount of attention from the media. “Over the past few years we’ve gotten a lot of press, so investigators are aware of our services.”

**Impactful Manuscripts Increase Public and Institutional Support**

When asked about exciting projects currently underway, Dr. Levine’s first response was, “Everything is exciting.” Indeed, the facility has contributed a role in several intriguing studies. “Just speaking in my role as a Core Director, we have published significant papers and have supported significant products.” He then described a few projects that came to mind, careful to point out that the facility is just one player among several who drive ideas and provide support.

For example, a trial using dendritic cells for high-risk ductal carcinoma in situ (DCIS) of the breast, for which the first trial resulted in a significant publication in 2007 (Czerniecki et al, “Targeting HER-2/neu in Early Breast Cancer Development Using Dendritic Cells with Staged Interleukin-12 Burst Secretion,” 2007), is supported by the philanthropy of Pennies in Action.

Earlier this year, there was press regarding the use of dendritic cells for ovarian cancer, a trial presented at the American Association for Cancer Research (AACR) Annual Meeting in April 2013. This trial preserves the patient’s tumor to develop a vaccine.

The CVPF collaborates with Novartis on a trial using T cells for cancer. Chimeric Antigen Receptor-Modified T Cells (CART) with specificity for CD19 are being used to eradicate leukemia. This particular trial has received a lot of attention in the popular press with articles describing the impact Dr. Levine and his colleagues are having on patients’ lives.

How is all of this media attention managed? All media interest is generated by the Penn Medicine Department of Communications when it feels a published manuscript is worthy or when a journal publishes its own press releases. This attention has increased patient referrals to the University of Pennsylvania and CHOP; CVPF in turn receives increasing support from the institution.

**Teamwork and Flexibility Allow the Facility to be Responsive**

Given the large number of trials the CVPF participates in, facility personnel must be both focused and flexible. Senior staff members work closely with collection centers to schedule apheresis at a time the lab can accept the cells. “Patients’ schedules change due to their disease course, so there needs to be flexibility. Someone at our facility has to work closely with either someone at the collection facility or with the investigator’s nurse manager. In the end, it is not a ‘click and submit’ scheduling process.”
Processing procedures also vary. The main difference in processing is between T cells and dendritic cells. Staff working on the various products are trained and focused on specific products. “We have SOPs that cover everything.”

FACT Accreditation Enhances Future Success

Dr. Levine pointed out that the effort dedicated to achieving FACT accreditation is worth it in the end. “Having gone through the initial accreditation and now the renewal, it gets us to a better place because it forces us to be more efficient.” He added, “It may be painful to prepare, but it in the end it reduces long-term difficulties. There are always challenges with a large facility in multiple locations with diverse products. The main challenge of FACT accreditation with our facility was accounting for the wide scope of products and creating SOPs and labels for a diverse repertoire."

Dr. Levine also pointed out that all academic facilities face challenges obtaining funding for quality programs. “That is not something easy to write a grant for. A lot of facilities have a challenge with this.” However, one of the benefits of FACT accreditation is increased competitiveness in funding applications. “I know it has made a difference for our facility because I’ve seen the comments come back from the reviewers.”

Personnel devote a lot of work and time to prepare for accreditation and Dr. Levine perceptively mentioned the importance of maintaining process awareness among staff members. “We had some staff turnover between our initial and renewal accreditation, so maintaining academic memory and translating it to the submission was difficult.”

Just as FACT encourages teamwork and communication within accredited facilities, Dr. Levine’s ability to establish productive relationships and work towards a common goal improves the quality of cellular therapy and produces results. We appreciate his support and will continue to enjoy reading the many accolades his facility is so deserving of in future publications.

About Bruce Levine, PhD, Director

Dr. Levine received his Ph.D in Immunology and Infectious Diseases from the John Hopkins University in 1992. His post-doctoral fellowship was with Dr. Carl June at the Naval Medical Research Institute (NMRI). During his time as an investigator at the NMRI, he developed a system for large scale efficient culture of lymphocytes, the foundation for several current Phase I clinical trials of adoptive immunotherapy.

(http://www.afcri.upenn.edu/ourfaculty/levine_bio.html)

About the Clinical Cell and Vaccine Production Facility (CVPF) at the University of Pennsylvania

The CVPF performs cell processing on a large number of different cell types, including expansion ex vivo with or without genetic modification. The facility provides scientific, technical,
and regulatory support for investigator-initiated trials. For more information about the facility and contact information, visit

http://www.med.upenn.edu/cores/clinical_cell_and_vaccine_production.shtml.

About FACT

FACT is committed to high quality patient care and laboratory practice in cellular therapies and regenerative medicine. The non-profit organization promotes improvement and progress by establishing minimum standards, providing education, and inspecting and accrediting programs worldwide. Expert inspectors and the comprehensive accreditation program verify programs provide high quality cellular products and help to achieve desirable outcomes for patients. Since 2007, FACT accreditation has been used in determining the U.S. News & World Report rankings of cancer centers for the “America’s Best Hospitals” and “America’s Best Children’s Hospitals” lists.