



# Bringing Cellular Therapies Closer to

# PATIENTS

Cellular therapy researchers are making enormous strides in the laboratory to develop treatments for diseases such as cancer and autoimmune disorders. But benchside discoveries are just the first step in a process that ideally ends with new therapies for patients, perhaps even at a lower cost. To bring cell therapies closer to the people who need them, investigators are becoming more versed in the manufacturing process and are teaming with organizations such as the National Heart, Lung and Blood Institute, or NHLBI, which provides assistance with translational research — research that bridges the gap between laboratory discovery and bedside treatments.



By Lamont Williams  
AABB STAFF WRITER

## The PACT Program

Translational research comprises activities that optimize the manufacturing of clinical-grade cell products and includes the scale-up process (to make large quantities of products) as well as the development of standard operating procedures, or SOPs. NHLBI, which is committed to the advancement of effective cell therapies, became involved with translational research after leaders within the institute recognized that there was not much assistance for investigators to transform their laboratory findings into therapies produced under regulatory safety and efficacy standards for use in clinical studies.

To address this deficiency, NHLBI created the Production Assistance for Cellular Therapies, or PACT, program, which supports the development of novel cell therapies through assistance to investigators. Through contracts, PACT funds a coordinating center — the EMMES Corporation — and five facilities that assist researchers with production and testing services for cell therapy products: the Baylor College of Medi-

cine, Center for Cell and Gene Therapy in Houston; Center for Human Cell Therapy Boston; City of Hope – Center for Applied Technology Development in Duarte, Calif.; University of Minnesota, Molecular and Cellular Therapeutics facility; and the University of Wisconsin, Madison – Waisman Biomanufacturing. These institutions produce and scale up cell therapy products under current Good Manufacturing Practice and current Good Tissue Practice regulations. The investigators can then use the products in their research.

“PACT provides services in the space between laboratory discovery and clinical trials,” said Traci Heath Mondoro, PhD, a project officer at NHLBI, adding that the program, which is available to all researchers in the United States, also may offer production assistance in clinical research (e.g., helping investigators study the appropriate dosages for patients) if the scope of that research is within NHLBI’s mission. She emphasized, however, that investigators focused on therapies outside of NHLBI’s mission still can apply for PACT services.

“The manufacturing of cell products has become a science unto itself,” Mondoro said. “NHLBI’s expertise is in the preparation and optimization of cell products, regardless of what they are indicated for.” Once researchers investigating topics outside of NHLBI’s mission have completed the translational phase, they can seek funding from other organizations to perform clinical trials.

Jamie Winestone, a project director at EMMES, noted that PACT provides translational research services for an investigational new drug, or IND, application to be accepted by the U.S. Food and Drug Administration. (INDs are necessary to begin human clinical trials.) Once this occurs, the product can be used in clinical trials. “We call our activities IND-enabling,” Winestone said. “The information the FDA requires in the manufacturing section of an IND is the work we contribute.”

Derek Hei, PhD, a project director at Waisman Biomanufacturing, added that PACT helps researchers develop SOPs to cover all aspects of cell growth and differentiation.

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“These SOPs can help the scientists from the translational stage through clinical trials to commercial launch.” He noted that some researchers who previously used PACT services have returned to seek assistance in driving down production costs or fine-tuning the potency of a therapy following a clinical trial.

Mondoro explained that NHLBI also works with investigators to address intellectual property issues. “The scientists are encouraged to understand what their intellectual property is and how it is protected,” she said, adding that NHLBI does not

“own” the scientists’ research. The institute, however, has the right to publish information from the product development activities it supports, such as cell performance data.

In addition, PACT provides educational programs to the greater cell therapy community, explained Lisbeth Welniak, PhD, who works alongside Mondoro as a project officer at NHLBI. Last September, PACT conducted a workshop on developing cell therapies for pediatric indications, specifically rare diseases. Welniak noted that an important aspect of PACT’s educational programs is that they offer

continuing medical education credits. (AABB has been running this CME programming for PACT since 2006.)

“The CME credits are an extra benefit to attending our educational sessions,” she said.

## Regulators and Industry

Collaborating with government regulators and industry manufacturers is an important part of ensuring the therapies eventually reach the patient’s bedside. Michael Matthay, MD, professor of medicine and anesthesia at the University of California, San Francisco, is working toward an IND for FDA

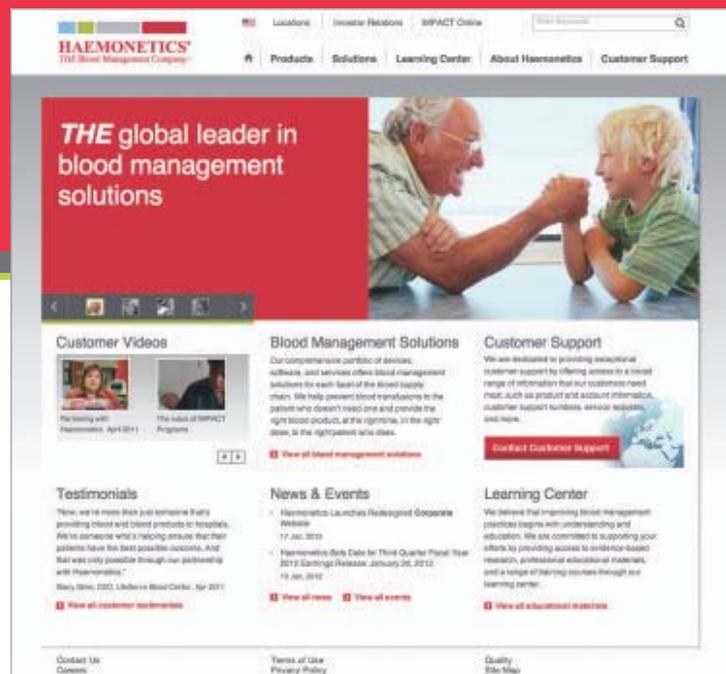
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**“There are products and there are protocols ... In some cases, researchers use cells we already have and techniques we already know in novel ways.”**

review with assistance from PACT. Matthay, who is studying the use of bone-marrow derived human allogeneic mesenchymal stem cells to treat acute lung injury, submitted pre-IND information in the summer of 2010 and is in close communication with FDA, particularly the agency’s Center for Biologics Evaluation and Research, to submit a full IND by this spring. FDA acceptance would clear the way for Matthay to conduct phase I and II clinical trials using the clinical-grade cell products supplied to him by PACT.

In some cases, after an investigator’s IND is accepted by FDA, he or she may work with a device manufacturer that produces equipment, for example, to store the cell product. Herb Cullis, president of American Fluoroseal Corporation, explained that researchers submit letters to manufacturers seeking permission to use their biologic with the manufacturer’s device. Once they receive approval from the company, the investigators submit a letter to FDA to determine if the biologic and device may be used together.

Cullis, a pioneer in the development of apheresis equipment and who developed the first closed apheresis system, explained that he began

developing storage bags for biologics more than 30 years ago when a researcher at the National Institutes of Health noted that the plastic in some early apheresis equipment interacted with the cells, causing them to differentiate.

He investigated the problem and discovered a plastic that did not interact with the cells — a plastic that now has been used since the 1980s. He noted that manufacturers always need to be vigilant regarding these types of problems and work with scientists to augment devices as necessary.

### **Products and Protocols**

Harold Atkins, MD, FRCP(C), medical director of regenerative medicine at the Ottawa Hospital Research Institute, explained that not all cell therapy research leads to products that can be placed on shelves. For example, Atkins, who works with stem cell transplantation to treat auto-



immune diseases, is applying well-known techniques to develop a new protocol (or procedure) that involves a powerful immune system-destroying chemotherapy regimen followed by hematopoietic stem cell transplantation. The stem cell therapy is used to reconstitute the patients' immune systems following destruction by the chemotherapy.

Through this work, Atkins is "resetting" his patients' immune systems. He emphasized that his research is not leading to a new product but rather applying techniques already in use. Preliminary results are favorable and if his treatment proves to be safe and

effective, he envisions other physicians referring to his published protocol to produce similar results among their patients. "There are products and there are protocols," Atkins said. "In some cases, researchers use cells we already have and techniques we already know in novel ways."

### Accelerating Research Advances

"Translational research is a critical step in creating new treatment options for patients," said EMMES' Winestone. "The further along investigators progress through translational activities, the more defined their products

become and the better positioned they become to work with government and industry. With PACT, the infrastructure to conduct cell therapy-based translational research does not have to be recreated each time there is a new idea to test, which helps accelerate the process of bringing novel cell therapies to the bedside." *BB*

To learn more about PACT, visit the program's website at [www.pactgroup.net](http://www.pactgroup.net).

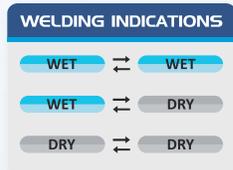
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