



STAYIN' ALIVE

STRONG, BASIC CELL CULTURE TECHNIQUES KEEP THIS LAB'S CELL LINES SAFE AND HEALTHY
BY SARA GOUDARZI

▲ Placement of essential equipment to accommodate the workflows of multiple groups within Chromocell's discovery process.

Unexpected cell loss is the fear and challenge of those who work in cell culture labs. Cells are living organisms that can't be left on a shelf and forgotten about until needed. Instead, they require constant care and contingency plans at all times. Laboratory staff need to ensure that cells are maintained under precise and optimized conditions to get the most reliable and reproducible results possible. This makes the jobs of those who manage cell culture laboratories especially challenging.

"You can purchase more materials and hire more team members, but you can never buy back lost time," says Jennifer Miller, the Cell Culture Core (C3) laboratory manager at Chromocell Corporation, located in North Brunswick, New Jersey.

Researchers at Chromocell are engaged in discovering and developing flavor compounds for consumers and therapeutic

compounds for patients through science and technology. With an emphasis on biological research, the corporation has invested heavily in large-scale cell culture. To fulfill these requirements, Chromocell formed the C3 lab.

"The C3 lab is responsible for providing consistent, affordable cells as needed to all cell-based projects," Miller says.

The cells are identified using Chromocell's proprietary Chromovert® technology, which allows researchers to make rare cells that transcribe multiple RNAs of interest.

"We develop methods and/or conditions for optimal cellular growth [and] produce high-quality cells in support of projects and all discovery," Miller says. "Our work includes maintaining established cell lines as well as creating and optimizing cell culture conditions for new cell lines and ensuring a long-term, consistent cell supply."



▲ Jennifer Miller, manager of Chromocell's Cell Culture Core laboratory.

The result is healthy, robust cells—the foundational material for assays and screening. According to Miller, healthy cells will produce excellent predictive data.

For that reason, it becomes especially important to ensure that cells, which the staff works tirelessly to maintain



▲ One of Chromocell's part-time team members contributes toward program goals.

and culture, are available when needed. This task is possible only through a combination of effective management, teamwork, communication, appropriate instrumentation, and proper scheduling.

Lab structure

The Cell Culture Core lab is one of seven labs within the business. Miller manages the approximately 1,900-square-foot C3 laboratory and its team. Her team consists of four full-time lab staff and 20 part-time interns.

The C3 team, whose members possess strong biology backgrounds with concentrations in biotechnology, biomedical engineering, and animal

sciences, among others, provides cells to other labs within the corporation—such as the assay development lab for compound discovery—and to core technology, the lab group responsible for employing Chromocell's Chromovert technology to isolate cells of interest.

Together, Miller's rather small team processes an impressive number of cells.

"We typically process dozens of cell samples daily in a variety of formats and scales for their intended purposes," Miller says. "For maintenance only, this translates to roughly 25,000 cell preps per year. In addition, we prepare 156,000 screening plates per year, or approximately 6 million different cell wells."

Multiple groups within Chromocell use not only the services of the C3 lab but also the lab itself.

"In total, we have dozens of full- and part-time team members circulating through the cell culture lab every day in shifts that keep the lab functioning 24/7," Miller says. "This includes the robotics, nighttime crew, flow cytometry, core technology, and assay development teams."

Instrumentation

Due to the nature of a cell culture lab, the equipment is organized and arranged to optimize workflow while minding potential physical bottlenecks. The cell culture lab contains 14 incubators, six

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PERSPECTIVE ON: A CELL CULTURE LAB

two-person biosafety cabinets, three microscopes, two cell counters, two centrifuges, four water baths, two label printers, one automation platform, four refrigerators, five freezers, two cryostorage units, and numerous pipettors and pipette aids.

“We use microscopes and cell counters most frequently, as they are involved in processing each cell sample,” says Miller of the instrumentation.

Most of C3’s instrumentation does not use the newest technology, and Miller and her team don’t often trade in their lab devices for newer models. Instead, the group focuses on using strong, basic cell culture techniques.



▲ Cell plate organization is essential to allow the 24/7 staff to operate seamlessly.

“We have not had a need to upgrade to new instruments for some time,” Miller says. “We continue to improve our workflows and make the best use of what we have, bringing on additional equipment as needed to increase capacity or throughput.”

As for incorporating robotics, Miller says that the initial need for robotics in the cell culture lab grew so quickly it spurred the development of an entire automation group dedicated to using robots in both cellular and compound applications.

Maintenance and inventory

Equipment maintenance is especially imperative in a cell culture lab because a failure could mean cell damage or even loss. For this reason, the bulk of the C3 equipment is on a routine maintenance

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regime. Service technicians perform preventive maintenance once to twice yearly on equipment such as the centrifuges and cell counters.

“Due to the nature of cell culture, we keep on top of decontamination cycles to ensure that our cultures stay contamination-free,” Miller says. “For example, we decontaminate water baths and cell counters weekly, biosafety cabinets monthly, and incubators quarterly. In the event there is contamination, we take extra steps to decontaminate equipment.”

A laboratory operations manager, a recently revived role at Chromocell, coordinates the maintenance of equipment, such as freezers, incubators, and centrifuges, shared between different labs.

“The cell culture-specific items are handled within the cell culture group, with one of us taking the lead to ensure concise communication between the team and vendor,” Miller explains. “Due to our round-the-clock operations, communication of performance issues or breakdowns is crucial. Emails are shared within the entire team. The responsible party is identified early on in order to keep the process on track. We implement equipment ID tags across all labs to facilitate the reporting and documentation of issues.”

The lab also has in-house quality control checks, such as equipment temperature and performance monitoring.

Similar to equipment maintenance, keeping inventory of consumables is another important aspect of ensuring that procedures are not interrupted.

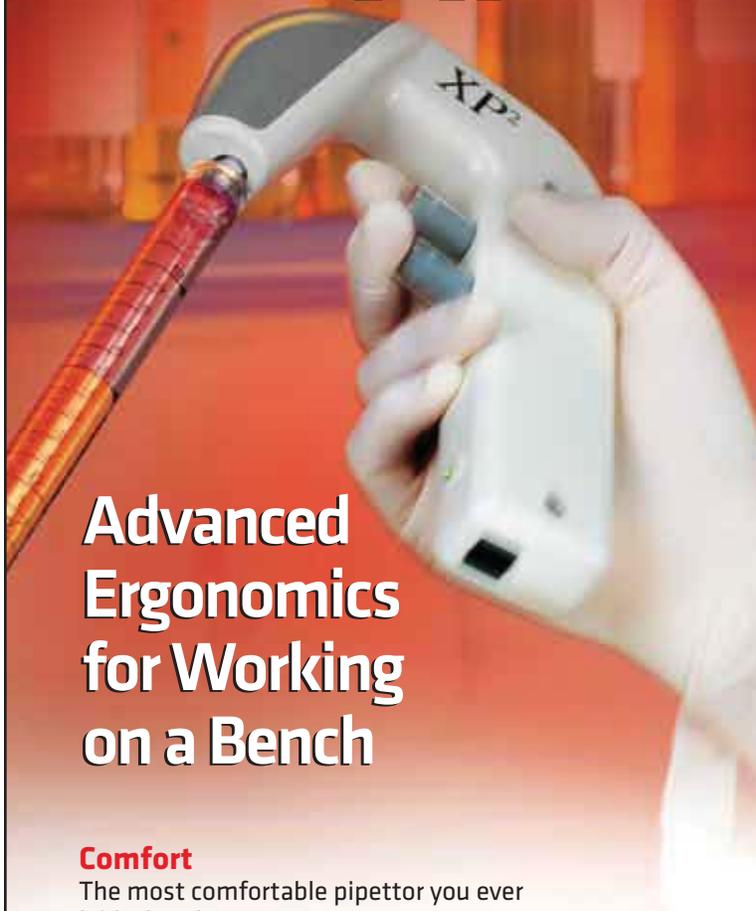
“Select team members serve as point people for different facets of inventory,” Miller explains. “For example, there is one person on my team who inventories all consumables within the cell culture lab itself. Another team member takes inventory of our common area and orders shared consumables as well as materials that are strictly for cell culture.”

The right team

As team lead, Miller is responsible for ensuring that there is a properly sized, fully trained staff to handle the workload for her lab.

“For lab skills, we have training refreshers every six months to confirm proper technique and accurate job knowledge,” Miller explains. “Formal

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▲ *Chromovert-enabled stable cell lines are immediately available for rapid screening and consistent results.*

reviews are conducted company-wide every six months, reviewing past performance and setting goals for the next six months.”

The majority of teams within Chromocell have a substantial number of part-time members. Within each team, there’s an established hierarchy based on performance and leadership.

“Our lab assistants are entry-level team members who, based on performance and ability, are available for promotion to senior lab assistant,” Miller says. “Our senior lab assistants are responsible for providing leadership to junior team members on a daily basis—this includes training on technical skills and workflow as well as providing mentorship.”

The full-time team interacts closely with part-time team members to ensure that company projects and individual careers move forward in a positive direction.

“Each person is treated as a team member and not an employee,” Miller says. “Individuals are not replaceable parts but rather highly valued team members whose input is taken seriously.”

“At the end of the day, while my team provides work for the company, I work for my team to make sure they have all the tools necessary to succeed.”

To further ensure this success, Miller and other managers work hard to keep up the spirit of their teams by providing incentives beyond just performance-based pay raises. Free lunches, tuition support, parties, school

credit, and a fun yet challenging environment are encouragements that Chromocell provides its teams. However, quality time spent with each employee is perhaps the most impactful incentive in terms of team morale and progress.

“The most valuable time is spent in one-on-one meetings where team members are encouraged to speak freely about their experiences,” Miller says. “These discussions enable me to identify positive trends as well as problem areas. It also serves to foster positive relationships and provide clarity for team members.”

With such importance placed on each team member, hiring the right team member is also of great importance. At Chromocell, team leads such as Miller also take on the role of hiring managers with responsibility for interviewing and training.

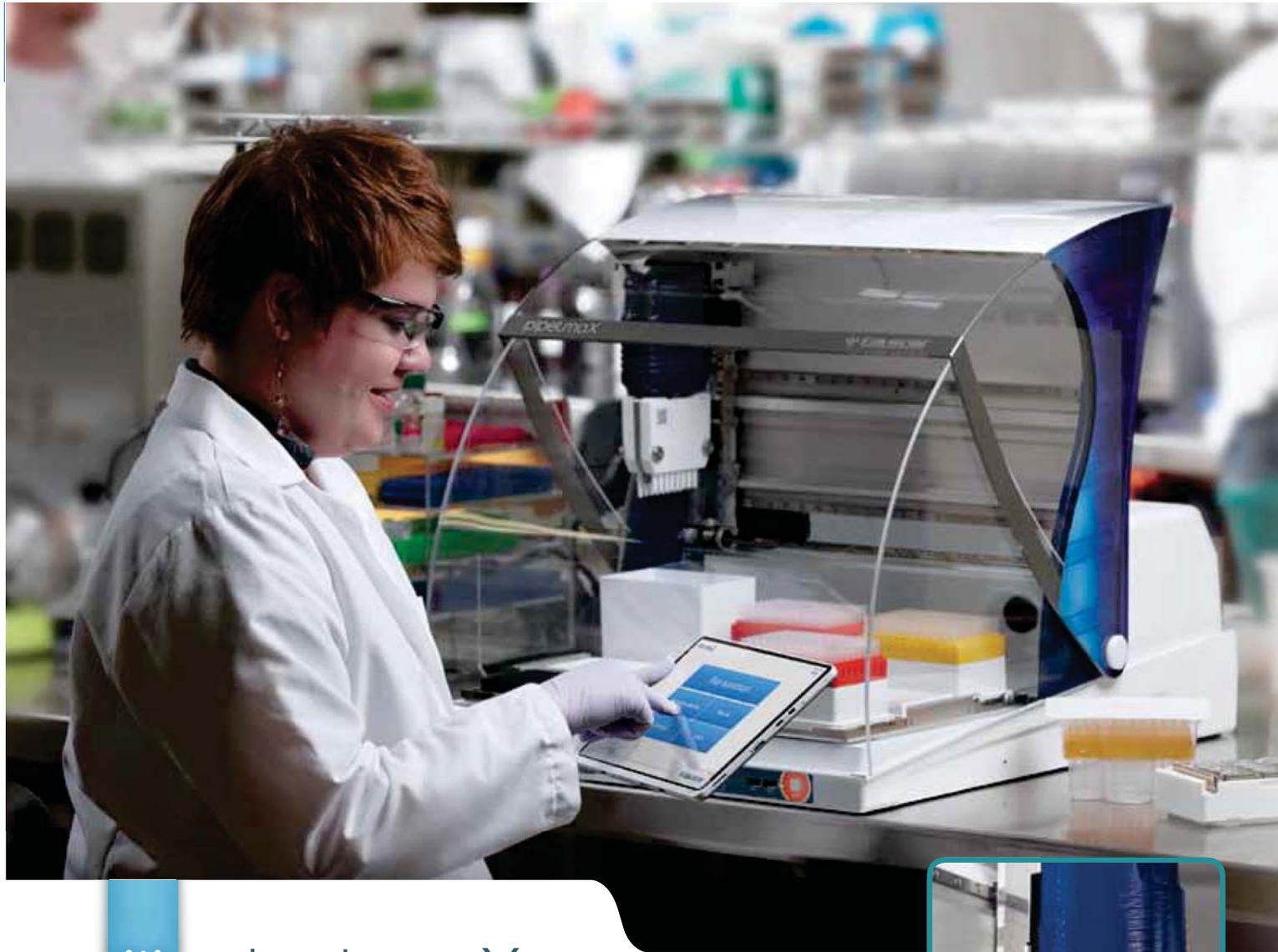
“Due to the fact we work with interns, we typically need to replace a portion of our part-time team each year as they graduate,” Miller says. “We hire our interns proactively, taking into consideration the fact that it typically takes around nine months to become technically proficient in all required areas.”

When a position opens up for a full-time employee, Miller doesn’t have to look far.

“All the C3 full-time hires within the past two years have been made directly from the C3 part-time team after graduation,” she says. “They are exceptional team members who have made and continue to make significant contributions to department and project goals.”

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Day-to-day routine

In the cell culture lab, there is a significant amount of coordination every day. Each morning, the team collectively reviews the work list for the day and assigns tasks to team members based on schedule and technical ability.

“As the cell culture assignments and routine maintenance are completed over the course of the day, we keep a weather

eye on the lab to ensure that everything goes smoothly,” Miller says. “When we encounter an issue, whether it arises from cell line development or from an error, we troubleshoot it in a collaborative effort to gain different perspectives and provide team members with experience.”

Between team and project meetings, Miller and other lab managers plan out the work for the following days. This requires coordination with project leads and other departments to ensure the successful completion of HTS campaigns, DRC runs, assay development, and other goals.

“In addition, we perform basic analysis of cell data frequently to verify cell health and performance,” she adds. “While working toward our performance goals, we also monitor the efficiency of our cell usage both from an environmental and a monetary standpoint, adjusting plans as needed to get the most out of lab work.”

But that’s not all: When working with new cell lines, there is another layer of complexity due to the quarantine procedure and additional optimization steps required. Once optimized, all teams—C3, robotics, nighttime crew—are trained as needed to handle the new cells.

“We also train on a continual basis to advance team members and to make sure techniques do not deviate over time,” Miller says. Managers are always working toward team development.

Despite the tremendous amount of work involved for managers such as Miller, the predominant aspiration of Miller’s work makes it a worthwhile and rewarding effort.

“My motivation to come to work stems from the potential to help others, on both an individual basis and a global scale,” Miller says. “We work with the common goal of increasing the quality of life and health for the general population. For instance, we have an anti-pain compound that is rapidly moving to an investigational new drug (IND).”

In addition, the company’s interns are college students, for many of whom this is a first job in the industry.

“We need to teach them all the best practices to work in the lab and on a team from the get-go to set them up for long-term success,” Miller says.

On all fronts, Miller says, “It is a privilege to help move those projects forward.”

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