Perspective
DOI: https://doi.org/10.1128/jmbe.v22i1.2619
JMBE Journal of Microbiology & Biology Education

Transitioning Cell Culture CURE Labs from Campus to Online: Novel Strategies for a Novel Time†

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Course-based undergraduate research experiences (CUREs) provide a way for students to gain research experience in a classroom setting. Few examples of cell culture CUREs or online CUREs exist in the literature. The Cell Biology Education Consortium (CBEC) provides a network and resources for instructors working to incorporate cell-culture based research into the classroom. In this article, we provide examples from six instructors from the CBEC network on how they structure their cell-culture CUREs and how they transitioned the labs to online in the spring semester of 2020. We intend for these examples to provide instructors with ideas for strategies to set up cell culture CUREs, how to change that design midterm, and for creating online CUREs in the future.

PERSPECTIVE

Course-based undergraduate research experience (CURE) labs feature scientific practices, discovery, broadly relevant or important work, collaboration, and iteration (1). CUREs have emerged as a way to provide research experience for students in a classroom setting. They have been shown to better support students than traditional labs in a wide variety of ways, including self-efficacy, self-determination, problem-solving, student's conceptions, and scientific thinking (2, 3). CUREs are also one solution to increase diversity and inclusion in STEM fields by providing an opportunity for more students to gain research experience than the limited few who can secure independent opportunities in faculty laboratories (4). Students from historically underrepresented backgrounds face many barriers to research, and CUREs provide a way to provide all students with research experiences (5).

The Cell Biology Education Consortium (CBEC) is an NSF-funded Research Collaborative Network for Undergraduate Biology Education (RCN-UBE) that involves a network of faculty and students who are incorporating cell-culture-based research into the classroom (cellbioed.com). The CBEC provides funding to develop Cell Blocks which are modules consisting of written and video protocols, classroom implementation strategies, and assessments. Faculty and students involved in the CBEC can use these Cell Blocks as instructional materials within their own classes and add their own protocols to the library for others to use. The Cell Blocks are so named because they can be used interchangeably as "building blocks" to support instructors' particular learning goals. The CBEC supports faculty who are in the early stages of incorporating cell culture into their classrooms through those who are experts with using cell culture and want to provide additional resources and experiences for their students. Faculty projects supported by CBEC range from cell-culture modules within a course to entire cell culture–based courses.

While many labs include cell culture techniques and projects, few examples of cell culture CUREs or online CUREs exist in the literature (6–8). The hands-on component of a cell

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Received: 16 January 2021, Accepted: 15 February 2021, Published: 31 March 2021

culture–based CURE supports students to develop necessary technical and critical reasoning skills and engage in scientific practices. Therefore, the online pivot due to the COVID19 pandemic was challenging for instructors of cell culture–based CUREs. Nonetheless, the instructors came up with unique solutions to accomplish the student learning outcomes, and their perspectives and experiences are noted here. We provide examples from six instructors involved in the CBEC from various institutional types on how they initially structured their cell culture CURE and how they transitioned their course to online in the spring semester of 2020. If they taught the course again in the fall semester of 2020, we also provide information on their modifications due to the continued online/virtual environment. We provide examples of ways to set up cell culture CUREs and change lab design mid-term. Through faculty interviews and discussion groups, we provide a framework for creating online CUREs in the future. While we have focused our attention on the transition to the virtual learning environment, information and design of the original on-the-ground courses can be found in Appendix 1. Additionally, a summary of each course with pre- and post-transition tasks can be found in Table 1.

STRATEGIES FROM A COMMUNITY COLLEGE

Two faculty members at NorthWest Arkansas Community College serving over seven thousand have started a small research lab with NSF funding. They conduct student-led research investigating the effects of plant-derived chemicals on glioblastoma using mammalian cell culture with cell biology students and plant tissue culture in a largely non-majors plant biology course.

Within Gary Bates's Plant Biology course, his students had finished the plant tissue culture techniques and skills portion of the lab prior to going virtual. However, the research portion of the project was just beginning. Students were able to collect one replication of data for analysis in a final lab report. Students had also started making CBEC cell block videos of their plant tissue culture methods before classes went virtual. Students were able to edit and finalize their video protocols virtually. Interestingly, since students only had one repetition in the plant tissue culture lab, Gary Bates noted, his student did not see the importance of routine cell maintenance procedures. Antidotally, this supports the idea that multiple iterations are key to student learning as traditionally, the need for good aseptic technique is learned through trial and error in the lab. However, Gary Bates indicated he was able to meet the learning objectives at a base minimum.

In LaShall Bates's Cell Biology course, the switch to online shortened their cancer cell culture and molecular analysis (DNA isolation and PCR) experiments. Students were able to begin their experiments but were unable to collect final data points. Her students were not able to complete the cancer cell culture experience virtually. As a result, LaShall Bates completed lab learning objectives using online experiments with a focus on molecular techniques such as gel electrophoresis and DNA isolation from Learn. Genetics (Genetics Science Learning Center, University of Utah, https://learn.genetics.utah.edu/) and LabXchange (Harvard University, https://www.labxchange.org/explore). Both resources were developed for educational use and are freely available. In this case LaShall Bates chose online labs that mirrored techniques that would have been utilized with glioblastoma cell lysates had the in-person lab continued.

Despite going virtual, both instructors noted similar positive impacts of their respective CUREs on student learning. The opportunity for students to develop their own experiments, no matter how limited, increased student engagement and subsequently increased assessment scores when compared to the classes they taught that did not have a CURE lab component. For example, the opportunity to experience plant tissue culture techniques has greatly increased student understanding of totipotency in plant cells and the importance of sterile technique. Additionally, more of these students have indicated an interest in continuing scientific research in the laboratory and the sciences in general.

For fall 2020, the Plant Biology course was remote synchronous with limited lab materials sent to the students. Unfortunately, this means that these students were unable to physically perform plant tissue culture experiments due to a lack of equipment. Students watched CBEC cell block videos and images produced by the spring 2020 class. To offset the lack of wet lab experiments, the plant tissue culture CURE for the fall 2020 semester involved a bioinformatics component focusing on an oxidase gene found in multiple organisms. These adaptions appeared to capture student interest, as students seem to spend the same amount of time outside of class working on their online CURE projects. The biggest adaption was the need to scale back the student's research goals and expectations. Dr. Bates indicated that the take-home CURE and bioinformatics project worked so well they will be utilized in future labs as well.

Dr. LaShall Bates offered Genetics in the fall of 2020 as a remote synchronous course with lab materials sent to the students. As with plant biology, the students observed videos and images of experimental procedures produced by past students. This online course included a CURE focusing on the relationship between genetics and cancer. Students were extremely invested in the two projects compared to her traditional weekly prescribed labs. While successful, Dr. Bates again noted that students struggled with understanding the need for proper experimental design and how to deal with large data sets.

STRATEGIES FROM FOUR-YEAR LIBERAL ARTS UNIVERSITIES

Two primarily undergraduate liberal arts institutions (PUI) participating in CBEC projects used cancer cell

TABLE 1.

Instructor	Course	On the Ground Summary	Switch to Online Summary	Fall 2020
Dr. Gary Bates, NorthWest Arkansas Community College	**Plant Biology** (24 students, both majors and non-majors, primarily freshmen)	Heirloom plants grown in tissue culture and on-campus gardens. Traditional and molecular cloning technologies, exptl design, proposal writing	Used cell counts from preliminary data collection to write lab reports, made methods videos	Repeated with changes: Seedling stress expt and bioinformatics project focused on an oxidase gene, students observed videos and images of the process produced by past students
Dr. LaShall Bates, NorthWest Arkansas Community College	**Cell Biology** (24 students, freshmen and sophomores)	Effects of human glioblastoma cells treated with phytochemicals. Preliminary molecular work with collection of initial results	Completed online experiments on gel electrophoresis and DNA isolation	**Genetics** (24 students, freshmen and sophomores), Remote synchronous course with lab materials sent to students, focused on the relationship of genetics and cancer.
Dr. Jacob Adler, Brescia University	**Introductory Cellular and Molecular Biology Laboratory** (30 students, primarily freshmen)	Students add their chosen long-chain fatty acid to HeLa cells to induced lipid droplet formation examining quantitative data in fluorescence images. Students learn fluorescence microscopy, exptl design, proposal writing, website publication, and peer review.	Adler finished the projects and sent results via Instagram videos and photos, put video tutorials online to help students analyze data. Groups met remotely with instructor, analyzed data, and created websites to showcase their results, peer reviewed websites, created methods videos to showcase their understanding of the process.	Will be repeated Spring 2021 with students using previous cohorts' fluorescence images and analyzing them for their new hypothesizes. Students will have the same learning outcomes as previously noted and utilize the method videos created last Spring 2020 to help them navigate the process.
Dr. Sarah J. Swerdlow, Thiel College	**Cell Biology** (13 students, freshman/sophomore biology majors and junior/senior conservation biology majors)	Use of HL60 human leukemia cells to explore autophagy and apoptosis. Basic tissue culture techniques, exptl design, Partial data collection, data interpretation, poster design	Students made posters of their process and gave final presentations through Zoom or voice recording, met with instructor remotely, completed a lab practical which required them to walk through the project on paper	Not repeated
Dr. Sumali Pandey, Minnesota State University Moorhead	**Cell Culture** (10 students, primarily sophomores and juniors)	Effect of and anti-fibrotic drugs on airway remodeling. Cell culture techniques and assays, exptl design, exposure to primary literature, data collection and presentation.	Students virtually presented a poster at the on-campus academic conference, that included their cell viability data, the instructor provided mock ELISA data for analysis, students completed online content and quizzes focused on techniques, lab math, and cell culture basics, and students developed and	Not repeated

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TABLE1. (Continued)

Instructor	Course	On the Ground Summary	Switch to Online Summary	Fall 2020
			peer-reviewed grant proposals for their projects	
Dr. Amanda Simons, Framingham State	**Research Experience in Biology,** Senior Capstone Research Course (3-5 students per section, all seniors)	Students designed individual research questions that used qRT-PCR to measure changes in gene expression in mammalian cells. Students grew cells and most then froze RNA for use later. One student was able to collect gene expression data.	Students worked together to create a team annotated bibliography, and wrote individual research proposals on their project	Repeated with changes: CBioPortal project, students explored data available and developed research questions based on wet-lab experiments by previous students, collected data through CBioPortal queries, evaluated data, wrote a final paper to report their finals and reported results through a department-wide online research symposium

culture to teach students about basic cell processes and visualization of processes. These projects impact students from introductory-level cellular and molecular biology courses to senior-level research courses. In the spring of 2020, students participating in these CUREs had designed experiments and used basic tissue culture techniques to carry out their experimental protocols when classes moved online. Data collection was not complete in either case, but the instructors were able to create effective online methods to continue the authentic research experiences and allow for project completion and assessment.

At Brescia University, Jacob Adler completed his students' projects and sent them their fluorescence images before left campus. He recorded the live results using Instagram videos (@CellBioEd) and photos. For data analysis, he posted video tutorials on the class website to help students gain a better understanding of how to utilize ImageJ to process their images and Excel to analyze data. Students worked remotely with-in their groups and met virtually with their instructor during regular lab times. Student research groups submitted their data analysis for review and published their results as an internal website. Individually, students then completed formal peer reviews of each website.

Additionally, students created CBEC cell block method videos on specific techniques that were to be used in the project. These method videos were challenging as students were not familiar with the equipment needed to accomplish these techniques. Additionally, students did not have access to lab equipment and had to use some creativity to demonstrate their assigned techniques. This was a unique way for students to learn techniques without physically using them in the lab. Surprisingly, student published products were on par with previous cohorts and, in many cases, were better. Adler indicated that he felt this project was successfully implemented and accomplished all the desired learning outcomes, even in a partial virtual format.

After the transition to online at Thiel College, Sarah Swerdlow's students were able to make posters of their research techniques and record a final presentation through Zoom or voice recording using Screencast-o-Matic. Swerdlow met with students during virtual office hours. Assessment was accomplished by using a written lab practical requiring students to outline and explain their experimental design and research plan. Swerdlow identified the need for more structured content at the beginning of her class to introduce the students to apoptosis, autophagy, and ways of measuring if cells are undergoing these processes. Swerdlow indicated she was still able to meet all of her learning objectives for the semester even after the shift to online.

STRATEGIES FROM REGIONAL STATE UNIVERSITIES

Two primarily teaching-focused regional state universities participating in CBEC projects used mammalian cell culture prior to molecular analysis. These CUREs impact students from the sophomore level through the senior level.

At Minnesota State University Moorhead, Sumali Pandey's students were able to complete the first round of their cell viability (MTT) assay before the switch to an online platform. Post-switch, students performed MTT data analysis and virtually presented a poster on their research project (recorded using Kaltura/Zoom) at an academic conference on campus. The learning management systems were used to share mock ELISA data for TGF-β, a pulmonary fibrosis relevant protein.

The online content and quizzes focused on the relevance of different techniques (ELISA, Western blot, and quantitative real-time PCR), lab math, and cell culture basics. Students also developed and peer-reviewed a grant proposal.

What worked well was the fact that students were able to perform some basic cell-culture related techniques and assays before the pivot. Despite the online pivot, the focus of this CURE was sustained, and students were immersed in cell-culture related techniques and literature throughout the semester. Regardless, some techniques had to be taught through demos rather than with hands-on experience. Similar to what others have observed, multiple experimental iterations in the hands-on portion of the class remain indispensable. However, the virtual components created due to the online switch (video links, quizzes, and mock data) will become an integral part of the pre-lab setup move forward as a way of standardizing techniques and promoting successful experimental outcomes. Further, these types of demonstrations have been shown to improve students' mastery of laboratory techniques (9). Integration of virtual components may also allow for modular lab projects instead of semester-long labs.

At Framingham State, Amanda Simons's students were in the process of a four to 5-week cancer cell culture that would have been followed by transcription analysis experiments when course moved online. I s-semester student was further ahead in the process and was able to collect gene expression data and completed a project similar to what was planned, albeit curtailed. The others froze the RNA to use in future projects. Though students were unable to finish their experiments or conduct data analysis before the online pivot, the lab moved to a research "grant" proposal format on their project, including specific aims, rationale, experimental approach, and innovation.

While all students completed the course in Spring 2020 with a respectable proposal, some wrote more sophisticated proposals than others. Some students also felt overwhelmed by the abrupt pivot from in-person lab work and unprepared to focus on experimental design without the hands-on application to help it all make sense. In the future, Simons thinks students would benefit from more structure provided by CBEC Cell Block videos. While Cell Block videos do not replace the physical lab experience, they are at least a way for students to visual techniques even if they cannot be in the lab. Dr. Simons indicated she had to slightly modify some of her original learning objectives for the course after the transition. Instead of applying the scientific method to solve a novel research question, students applied the method to design a novel research question. Further, students were still able to work in teams to design experiments but could not collect and interpret data. However, students completed two critical learning objectives: use information from the scientific literature to formulate a research question, and culture mammalian cells while maintaining sterility.

Dr. Simons also taught a section of the course in Fall 2020. Rather than repeat the grant-proposal format she used the previous spring, she instead used virtual cancer genomic (cBioPortal) database mining CURE created by the CBEC [see Barnes et al., 2021 (10) for example of using the cBioPortal in the classroom]. Her students began with a critical review of gene expression analysis collected by students in the previous semester. Students used the first few weeks of the semester to review the existing literature about those genes, specifically their role in cancer biology. They then developed a series of research questions based on previous students' wet-lab experiments. Students queried cBioPortal to collect and evaluate data, reviewed the results of their queries, and spent the last few weeks of the semester discussing the implications of their findings and drafting a summary paper. Students presented their work at a department-wide online symposium and may also present at a state-wide undergraduate research conference in the spring. Simons said both students were dedicated and enthusiastic about their findings.

ACROSS INSTITUTIONS: WHAT WORKED AND WHAT DID NOT

The scenario presented here pertains to a mid-semester pivot of cell culture–based CUREs to an online platform. An overarching theme emerging from these perspectives is that while an online platform is not a perfect solution for all face-to-face lab courses, it was still possible to engage students. Faculty identified and then modified critical components of their respective CUREs (data analysis, experimental design, presentations) and developed them for the virtual learning environment (e.g., mock data, images, grant proposals, zoom meetings/presentations). Interestingly, many virtual components will be built into future classes to enhance the learning experience, standardize techniques, and better understand the concepts. While each instructor took different approaches, the overall results were the same. Classes kept moving forward, and student learning continued. Pandey summed it best, "Learning happened, despite the online pivot, although the approach to accomplish the learning outcomes differed."

All instructors kept students working in groups and working on novel hypotheses. Pandey mentioned that "getting stuck" happened more often in the virtual environment and having peer support in the form of teams was helpful to keep students motivated. To address data analysis learning objectives, instructors shared the previous semester's data, collected current data for their students, or had students reanalyze published data sets. Students appeared to engage in data analysis even after the transition. While it is not sustainable for instructors to collect and report data to students, Adler plans to adopt the idea of using previous cohorts' images and data as a foundation for novel hypotheses. This modification is a way to maintain continuity across semesters and makes the class more prepared for future

unexpected disruption while still allowing students to maintain project ownership and creativity.

Most instructors maintained research presentation requirements at the end of the semester. However, some indicated that student presentations' success and quality were correlated to the lack of experimental replication. Students struggled with interpreting and presenting partial or incomplete data sets. All instructors indicated how impressed they were by the quality of presentations, particularly given the sudden transition to the virtual lab. However, faculty expressed concern about the much-added stress the virtual environment added for the students at the end of the semester. Simons suggested providing more scaffolding (such as with Cell Block videos) and managing expectations differently. Repeated communication with students on changing expectations is essential but was difficult during the sudden transition. Swerdlow also suggested breaking the project down into smaller pieces to help the students feel less overwhelmed.

SUGGESTIONS FOR IMPLEMENTING ONLINE CELL CULTURE CURES

Keys to successful CUREs must be maintained in the virtual environment. Students need to take part in experimental design to feel ownership of their projects. Many also need the "aha" moment where concepts they have read in textbooks come to life in the lab. We can use Adler's CURE as an example. In analyzing past cohorts, the "aha" moment was where students, having worked all semester, finally observe their results live using the fluorescence microscope. Adler noted that his students have previously stated this "aha" moment was key to their STEM retention. Thus, he was curious if the digital version with Instagram videos and virtual sessions would still provide students with the connecting moment.

Interestingly, 73% (13/18) of the 2020 respondents to an end of semester survey indicated that this moment was the most exciting part of the project. Swerdlow mentioned other "aha" moments in her class, such as understanding what cell culture was, realizing the time it takes to complete a project and the types of questions that cell culture can help answer. Instructors agreed that maintaining the student's sense of project ownership, no matter how limited, was crucial for keeping them engaged and motivated after the transition. Despite their best efforts, Gary Bates pointed out the "The transition was difficult, and some students stopped participating or completely disappeared. The ones that remained were very excited about the implications of their work."

With the shift to virtual learning, authentic research experiences focus from data generation to data analysis. For projects that must be designed as partially or completely online, Cell Block protocols, data-analysis tools like cBioPortal (10), and publicly-available image databases (see reference 11 for an example) can provide a meaningful way for students to engage in research in the virtual lab environment. Faculty will continue using these resources as a meaningful and low-cost way to approach research in future semesters regardless of social distancing guidelines.

We caution against attempting to make the online version of the cell culture CURE exactly like an on-the-ground version. Some aspects of the traditional on-the-ground lab do not translate well to an online environment. The CBEC's philosophy is that students should be taught to think like a scientist in addition to learning lab technques and skills. While the online or virtual environment develops different types of skills than the traditional on-the-ground lab, these skills are equally important to student maturation into a scientist. Online labs do require different considerations in student engagement. Dr. Gary Bates pointed out that "getting the students to share data in a group is difficult remotely," and recommends "getting the students comfortable with speaking up and participating in an online system has to be the first priority." Dr. Pandey also recommends being very purposeful in scaffolding the projects. "Meaningful data analysis projects can be accomplished in an online environment; they just need to be planned that way."

CONCLUSION

We have provided examples from six instructors engaging their students in cell culture CUREs during a unique time for educators. Semester-long plant or mammalian cell culture research projects designed to be completed in the lab were forced online by the global pandemic. Faculty were able to adapt their plans to maintain project ownership and complete learning outcomes despite this unexpected pivot. Through faculty interviews and discussions, we have provided evidence that cell culture-based labs can be successful in the virtual environment and involve first-year students through seniors in research. We intend for these examples to provide a framework for instructors interested in starting cell-culture CUREs with ideas for implementation in both on-the-ground and online environments. With this intent, the CBEC faculty network will continue to expand the pool of virtual components and resources. The perspectives shared provide suggestions and ideas that could be adopted by any face-to-face lab course.

SUPPLEMENTAL MATERIALS

Appendix 1: Course descriptions

ACKNOWLEDGMENTS

Source of Support: Cell Biology Education Consortium, NSF-RCN-UBE Award #1827066 and Department of Education Title III Strengthen Institutions Program Grant. The authors have no conflicts of interest to declare.

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