Curriculum

JMBE Journal of Microbiology & Biology Education

A CURE for the COVID-19 Era: A Vaccine-Focused Online Immunology Laboratory

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During the COVID-19 pandemic, universities across the globe quickly shifted to online education. Laboratory courses faced unique challenges and were forced to reevaluate learning objectives and identify creative projects to engage students online. This study describes a newly developed online immunology laboratory curriculum focused on vaccine development. The course incorporated learning objectives to teach the scientific process, key experimental design components, and immunology techniques to evaluate vaccine efficacy. The curriculum, a course-based undergraduate research experience (CURE), asked students to engage in the research literature, propose a vaccine design and assessment, and interpret mock results. Instructor evaluation of student work as well as student self-evaluations demonstrated that students met the curriculum's learning objectives. Additionally, results from the laboratory course assessment survey (LCAS) indicate that this curriculum incorporated the CURE elements of collaboration, discovery and relevance, and iteration.

KEYWORDS immunology, laboratory, immunology laboratory, inquiry-based learning, vaccine, COVID-19, course-based undergraduate research experience, online

INTRODUCTION

The COVID-19 pandemic has led to widespread, rapid online course transformations across higher education. The need for these transformations has provided instructors both the challenge and the opportunity to think creatively about our learning objectives, pedagogical approaches, and assessment techniques within the context of online education. Due to the COVID-19 pandemic, we developed an engaging and inclusive online course in immunology with an emphasis on process of science as a replacement for an immunology laboratory course that requires extensive in-person activities. The course was designed within the context of broader undergraduate biology (1) and immunology-focused calls (2–4) for improved education recommending authentic research practices, particularly in laboratory courses. Using revised learning objectives as our guide, we developed a course-based undergraduate research experience (CURE), as undergraduate research is a particularly effective pedagogical approach for creating an inclusive environment (5, 6) and immerses students in the process of science (Fig. 1).

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The authors declare no conflict of interest.
Received: 11 November 2021, Accepted: 17 April 2022,
Published: 16 May 2022

The course was designed to incorporate the current public health challenges of COVID-19 and contemporaneous peer-reviewed scientific research accomplishments associated with vaccine development. The course also emphasizes correlates of immunity and their relevance to vaccine development as well as techniques for assessing immune responses. These lessons were then applied to student-developed research plans to design and propose evaluation of immune-response components for a vaccine against an infectious agent of their choice.

INTENDED AUDIENCE

The intended student audience for this course is junior- or senior-level biology-related majors and those on pre-health professions tracks. At our university, microbiology majors are required to take this course. Other biology-related majors, such as human biology and biology majors, at our institution also take this course to fulfill lab-course graduation requirements. Pre-health professions students (e.g., pre-medicine and pre-physician assistant) may also be interested in the course due to its relevance to human health. This course curriculum is scalable and would be appropriate for a small or large course size with proper faculty and/or graduate teaching assistant support (see discussion for further suggestions on scalability).

Learning time

This curriculum is intended to be implemented over the course of a full semester. Our course met weekly for 14 weeks.

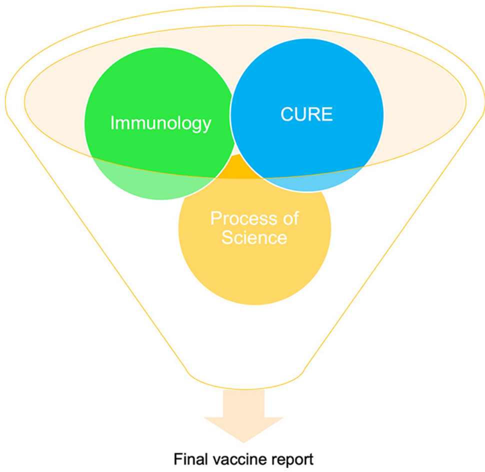

FIG 1. Components of the course. This course integrated the elements of course-based undergraduate research experience, scientific process, and immunology as students prepared to write their final vaccine reports.

Class periods were 2 h each and took place online via Zoom. Students were also required to spend 2 to 4 h per week outside the classroom completing reading assignments or writing activities.

Prerequisite student knowledge

Students taking this course need to have completed or be concurrently enrolled in an Immunology lecture course. At our institution, in order to take Immunology lecture and lab, students will have completed an Introductory Microbiology lecture course. Students will need to be familiar with or in the process of learning about the major cellular and molecular components of the immune system.

Learning objectives

Upon completion of this course, students will be able to do the following:

- Define correlates of immunity and their importance to vaccine development strategy.
- Select an appropriate vaccine format and antigen for a pathogen of interest.
- Describe methods used to assess immune effector functions.
- Describe essential components of experimental design.
- Interpret methods, results, and conclusions of immunology-focused research literature.

PROCEDURE

Materials

This course was taught online, and students had the option to complete the class during scheduled class time (synchronously) or by viewing recordings of the class period (asynchronously) on Blackboard, the university's learning management system. Thus, each student was expected to have a computer with Internet access and Zoom software. In-class polls via Zoom were utilized to assess student comprehension and obtain in-class feedback. For most class assignments, students needed access to the PubMed database, Labster (https://www.labster.com/; access provided by the university), and Microsoft Office (Word and Excel).

Student instructions

The course was designed to introduce concepts through preclass reading, online exercises, in-class discussion, and postclass activities. As concepts were being introduced and explained throughout the semester, students applied these concepts in a scaffolded approach as they developed their independent vaccine research projects. Students were initially introduced to the final project via the syllabus (Appendix 1). At the start of each class period, we reviewed this portion of the syllabus to explain how that week's learning fit into the final project and overall course goals (Table 1). The week-by-week student instructions for course activities and goals, which include pre-, in-, and postclass activities, are described below. Preclass assignments encouraged student readiness for the class period, in-class assignments gauged student understanding during class, and postclass assignments asked students to apply their new knowledge. All the postclass assignments were designed to contribute to the final report (see Appendix 2 for weekly assignment prompts and Appendix 3 for final report guidelines and grading notes). As seen in Table 1, topics discussed included experimental design, immunological assays, and vaccine development as follows.

Week 1. Prior to class, students were expected to review the syllabus and complete a preclass syllabus quiz within the course learning management system. During class, students were introduced to the course syllabus, which included course learning objectives, format, and final report. The first class began with a discussion of the components of good experimental design and why it matters. Students completed the Labster experimental design module as a postclass assignment.

Week 2. This week's class again aligned with our course learning objective related to experimental design. Using iBiology videos (https://www.ibiology.org/) and the previously completed Labster module, instructors provided more detail about aspects of experimental design with a focus on understanding hypotheses, controls, and replicates. Student understanding was evaluated using Zoom polls in class (see Appendix 2 for questions). Students were also introduced to PubMed, journal impact factor, and how to use PubMed to identify relevant peer-reviewed scientific articles. This week's postclass assignment asked students to start laying the groundwork for their final vaccine project by selecting a target of interest based on articles they identified via PubMed (see assignment prompt in Appendix 2).

Week 3. This week's activities were focused on experimental design as well as students' abilities to interpret peer-reviewed literature. This week's discussion of experimental design focused on *t* tests, *P* values, and power analysis to determine sample size. Next, students were assigned to Zoom breakout rooms

TABLE 1
Course outline

Week no.	Educational goal(s) for the week
1	Course orientation; selecting credible scientific information—PubMed and journal impact
2	Key aspects of experimental design; scientific foundation—hypothesis, controls, replicates, data analysis
3	Experimental design: statistical analyses; final project: independent research of project vaccine target
4	Experimental design: scientific bias; final project: independent research of vaccine formats
5	Experimental design: data management and transparency; discussion of COVID-19 vaccine research publication; final project: evaluation of experimental design and techniques in paper
6	Correlates of immunity: humoral and cell-mediated; final project: independent research of correlates of immunity
7	Methods of measuring immune responses; final project: studying correlates of immunity (continued)
8	Methods for evaluating neutralizing antibodies; final project: measuring immunity and analyzing data
9	Methods for cell-mediated immunity: helper T-cells; final project: Labster exercise for technique
10	Methods for cell-mediated immunity: cytotoxic T-cells; final project: experimental design to assess cell-mediated response to antigen/vaccine
11	Introduction to vaccine report guidelines; final project: outline first draft
12	Initial vaccine project evaluation and peer review; final project: second draft with feedback incorporated in the reports
13	Open review for vaccine project (FAQs and questions from students); final project: final draft of vaccine report
14	Final vaccine report submitted

to discuss the homework assignment describing their vaccine target. Students were asked to report particularly compelling components of their peers' rationales for picking a target back to the larger group. Instructors then shared the introduction sections of peer-reviewed literature and discussed what made each introduction compelling. Students were introduced to their postclass assignment: to write a first draft of the introduction section of the final vaccine project (see Appendix 2 for prompt).

Week 4. This lab period started with a discussion of how to avoid bias in experimental design, including an iBiology video and Zoom poll questions (Appendix 2), to assess student understanding of bias. We then pivoted toward our immunology-focused learning objectives. The instructors introduced a framework of crucial components of vaccine development: antigen selection, format, and correlates of immunity. The remainder of the class was focused on reviewing vaccine formats. Examples of various COVID-19 vaccines under development were used. Students took part in Zoom breakout sessions to discuss the formats that might be appropriate for their vaccine target. For the postclass assignment, the students were asked to propose 3 different vaccine formats and potential benefits for each of the formats with respect to their target (see prompt in Appendix 2).

Week 5. This class period built toward our experimental design learning objective by discussing transparency and documentation. Instructors shared videos from iBiology on these topics, discussed with students, and used Zoom polls to gauge student understanding (Appendix 2). Following that, students were given a refresher on vaccine formats, were introduced to the SARS-CoV-2 spike protein as an antigen, and were briefed on a research publication regarding the Novavax candidate vaccine for COVID-19 (7). The postclass assignment revolved around reading this article and answering questions that required students to apply their knowledge of experimental design and immunological techniques (see prompt in Appendix 2).

Week 6. This week, instruction focused on the correlates of immunity learning objective. The class period began with poll questions regarding the article from last week (7), asking students to apply their knowledge of experimental design and immunological assays to ensure students understood the assignment (see Appendix 2 for questions). Then, instructors discussed correlates of immunity, dividing the discussion into antibody effector functions and cell-mediated effector functions. Similar to past class periods, examples referred to COVID-19 vaccine development. The postclass assignment asked students to search the research literature and write about what is known about the correlates of immunity for the target of their final vaccine project (see Appendix 2 for assignment prompt). Similar to other assignments, this postclass assignment was a first draft for one section of the final vaccine project.

Week 7. This class period focused on two learning objectives: correlates of immunity and methods to assess immune effector function. Students began with a structured peer discussion in Zoom breakout rooms of the week 6 assignment. Importantly, instructors provided direction on how to provide feedback constructively and guiding questions on which to focus the peer review. Students were asked to type out notes from their peer-review session and upload these into Blackboard (LMS) as their in-class assignment (Appendix 2). Following this discussion time, students were introduced to Endnote and appropriate in-text citation methods, as the instructors noticed that students were not proficient in this area. Students were encouraged to incorporate the feedback into their reports and resubmit. The students were also introduced to different techniques to measure correlates of immunity. This week, instructors introduced enzyme-linked immunosorbent assay (ELISA) and flow cytometry (FACS). The students were also asked to complete the ELISA module of Labster as their postclass assignment.

Week 8. This week, we continued to focus on the methods to assess immune effector function learning objective. Instructors focused most heavily on methods assessing antibody effector functions, including ELISA and viral neutralization assays. The students learned the steps of ELISA and received an Excel spread sheet with mock data to analyze with their peers (Appendix 2). In breakout rooms, students were asked to calculate average optical density (OD) reading, subtract out background noise, log transform data, determine a regression line and equation, calculate each patient's antibody concentration, and calculate *P* values using a *t*-test. Finally, students were asked to evaluate the data and draw conclusions (Appendix 2). Students turned in this work as their in-class assignment. Instructors then introduced viral neutralization assays as they were completed for SARS-CoV-2. For their postclass assignment, the students were expected to design an experimental method and generate and interpret hypothetical results for a viral neutralization assay (see Appendix 2 for prompt).

Week 9. This week continued to address the learning objective focused on methods to assess immune effector function. However, the topic shifted from antibody-mediated effector functions to cell-mediated effector functions, with $CD4^+$ helper T-cells as the primary focus. Instructors started with a review of the T-cell response, including antigen presentation, types of T-cells, and cytokines secreted upon activation. This review led to an introduction to identification of $CD4^+$ T-cells using methods like flow cytometry and cytokine staining. Examples were drawn from COVID-19 vaccine development. At the end of the class, the postclass assignment was to complete the Labster cell culture module.

Week 10. This week's class period continued the focus on methods to assess immune effector function with $CD8^+$ cytotoxic T-cells as the primary focus. Instructors began with a review of the T-cell response leading to effector function of cytotoxic T-cells. The students were also taught techniques for isolation and quantification of $CD8^+$ T-cells via techniques like flow cytometry and enzyme-linked immunosorbent spot assay (ELISpot). Examples showed data from clinical trials of COVID-19 vaccine candidates. Poll questions during class assessed student understanding of techniques and concepts. The postclass assignment (see Appendix 2) asked students to design an experiment to assess T-cell response ($CD4^+$ or $CD8^+$) for their vaccine target and to include example data with analysis.

Week 11. During this class period, we introduced the detailed guidelines for the final vaccine project (see Appendix 3). Instructors explained how each assignment over the semester contributed to the final vaccine project. Students were provided with most of the class period to review the guidelines and ask instructors questions. The postclass assignment was for students to create an outline of their final project that identified what information they already knew as well as what was still unknown to them or needed to be written (see Appendix 2 for prompt).

Week 12. This week, students were sorted into groups of three in Zoom breakout rooms and asked to peer review the outlines completed as homework. Using the final report guidelines as a rubric, peer reviewers provided at least five suggestions to their partners. Each student then submitted an in-class assignment that listed the suggestions they received from their peers. The postclass assignment was for students to write their first draft of their final vaccine project incorporating the peer review (see Appendix 2).

Week 13. This class period was spent addressing student questions regarding their final vaccine project. Some of these questions required review of experimental design, methods, or immunology concepts. Other questions were focused more on the guidelines for the report itself. Following this class period, the students were expected to submit the second draft of the vaccine project, making sure to address feedback received from the first draft (Appendix 2).

Week 14. During finals week, students submitted their final vaccine project incorporating all previous feedback from peers and instructors.

Faculty instructions

In order to successfully teach this curriculum, the instructors should be familiar with undergraduate-level immunology concepts and methods used to assess immune effector function. Due to the online nature of this curriculum, instructors will need to be able to use basic Zoom functions such as breakout rooms, polling, and screen sharing. Labster access was provided to students to complete three online modules. These modules could be replaced with other activities online or with in-person lab training when available.

Suggestions for determining student learning

This curriculum utilizes a variety of assessment formats to assess student learning, including preclass quizzes, in-class polls, in-class assignments, postclass assignments, Labster modules, and draft and final versions of the vaccine final project. Assessments for each week are included in Appendix 2.

Sample data

Two student vaccine final projects are included in Appendix 4 with consent of the students.

Safety data

There were no safety concerns, as this class was conducted online. A protocol to assess this curriculum was submitted as Study00146798 to the KU Human Research Protection Program

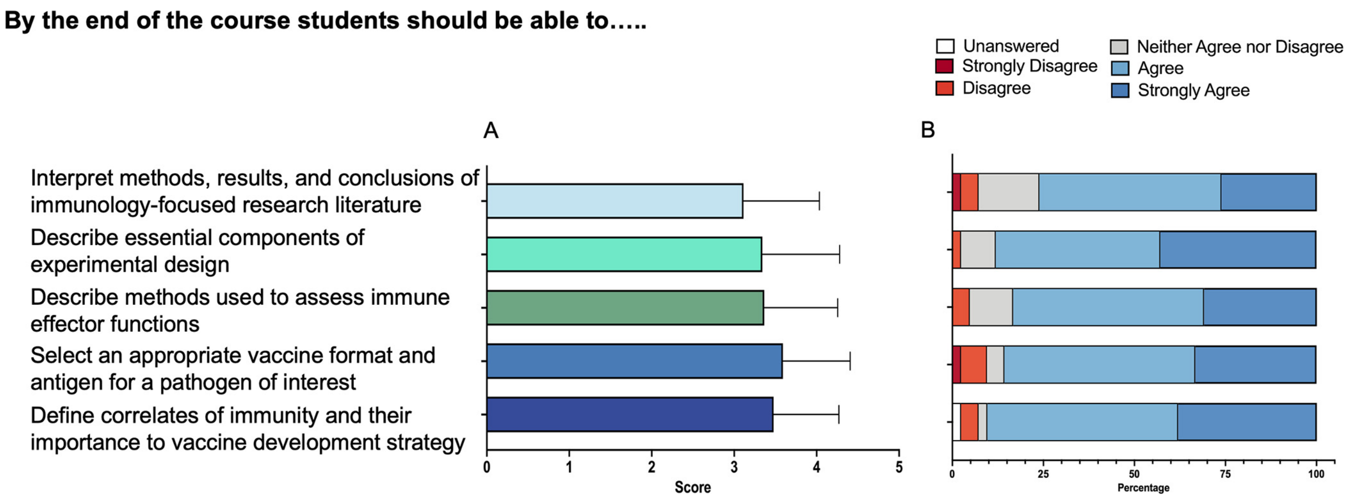

FIG 2. Instructor and student assessment of student learning. Graphs of student learning as assessed by instructor (A) or students (B). (A) Student learning was evaluated via rubric-based scores on their final project. Class mean score for each learning objective is graphed, and error bars represent the standard deviation ($n = 44$). (B) Students were asked to self-assess their learning. An end-of-course survey asked students to select whether they strongly agreed (dark blue), agreed (light blue), neither disagreed nor agreed (gray), disagreed (light red), or strongly disagreed (dark red) with the statement "After taking this course, I am able to…" regarding each learning objective ($n = 42$).

after the class was completed and assigned a determination of "Not Human Research."

DISCUSSION

Field testing

We field tested this curriculum in a fully online Immunology Laboratory course at the University of Kansas during the Fall 2020 semester. This course normally meets in person during fall semesters but was shifted online during Fall 2020 due to social distancing constraints and out of consideration for student and instructor health concerns. Forty-six students were enrolled in the course, including 36 students completing the course synchronously online and 10 students completing the course asynchronously online. The instructional team included two faculty members and one graduate teaching assistant.

Feedback from students and instructors about this curriculum was positive overall. When asked "Which aspects of the course did you find most beneficial to your learning?" on end-of-semester student evaluations of teaching, most student responses highlighted the scaffolded nature of the final project that incorporated feedback from instructors and peers. No strong themes emerged from responses regarding areas for improvement or change in the course. Instructors found that, overall, incorporating this new online curriculum went smoothly. However, instructors did find that students did not necessarily have the foundational knowledge or skills that they expected in some areas. For example, students were less familiar with PubMed and with reading peer-reviewed research literature than expected and struggled with components of experimental design such as power analysis. Providing students the opportunity for feedback on sections of the final research paper proved to be critical, as instructors were able to identify and clarify misunderstandings.

Evidence of student learning

Student learning was evaluated via in-class polls, postclass written reports, and a final project. Students also evaluated their perceived learning via an end-of-course survey, the results of which are consistent with the instructors' measurements of student learning.

The student's final project serves as the best overall measure of student learning, as it was scaffolded with smaller assignments earlier in the semester. Students received feedback about these smaller assignments targeting particular components of the project as well as a rough draft of the final project. Instructors used a rubric based on the previously outlined student learning objectives to evaluate student learning on a 4-point scale (Fig. 2A). Based on performance on their final reports, students were able to define correlates of immunity and their importance to vaccine development strategy at a mean rating of 3.5. Students were able to select an appropriate vaccine format and antigen for a pathogen of interest with a mean score of 3.6. Students were able to describe methods used to assess immune effector functions with a mean score of 3.4. Students were able to describe essential components of experimental design with a mean score of 3.3. Finally, students were able to interpret methods, results, and conclusions of immunology-focused research literature with a mean score of 3.1. Overall, students met the course learning objectives according to instructor evaluation of student final reports, with all mean scores landing above 3 on a

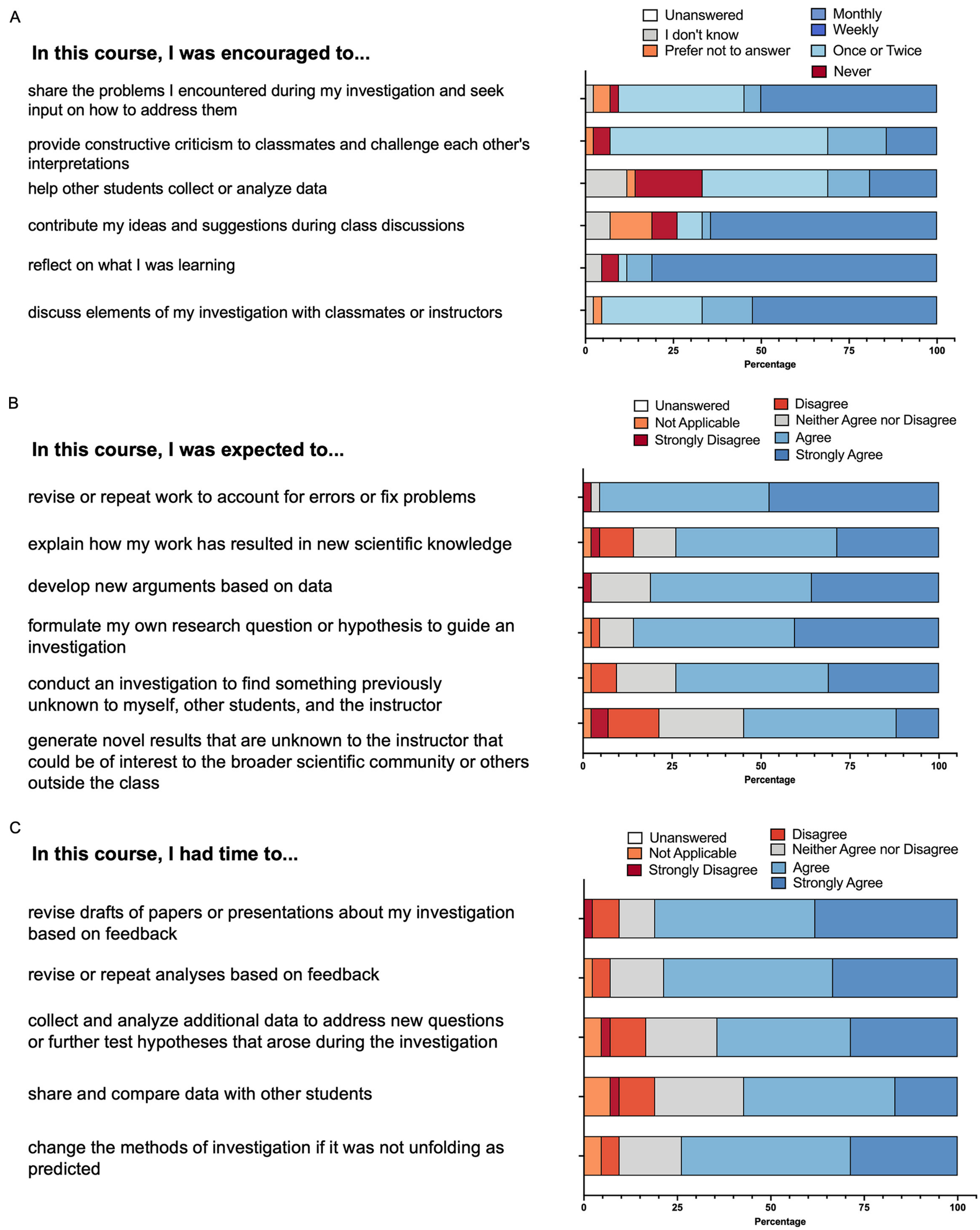

FIG 3. Results of Laboratory Course Assessment Survey (LCAS). Students completed the LCAS at the end of the semester ($n = 42$). Students were asked to evaluate statements related to collaboration (A), discovery and relevance (B), and iteration (C). Each graph shows

(Continued on next page)

4-point scale (Fig. 2A). This high level of achievement on the final project likely reflects the opportunities students had to revise their work over time, reflecting the process of science.

As mentioned above, instructors also asked students to self-assess their achievement of course learning objectives. Student responses were collected via an anonymous survey administered for 10 points of extra credit within the course learning management system during finals week. For each course learning objective, students were asked to select whether they strongly agreed, agreed, neither agreed nor disagreed, disagreed, or strongly disagreed that they had met that objective. For each learning objective, the majority of students responded that they either agreed or strongly agreed (Fig. 2B) that they had met the learning objective, consistent with instructor evaluation of their final projects. It is worth noting that students reported the strongest competencies in learning objectives tied to immunology content but were more likely to "neither agree nor disagree" that they had met learning objectives related to experimental design or research literature (Fig. 2B), consistent with instructor evaluation of their work. As part of their end-of-semester survey, students also completed the Laboratory Course Assessment Survey (LCAS) (8), a validated survey designed to evaluate student perceptions of the nature of laboratory courses. Using this survey, students evaluated the course based on what they were encouraged to do, expected to do, and had time to do (Fig. 3). This survey provides us with information about whether this laboratory course incorporates three key features of course-based undergraduate research experiences (CUREs): collaboration, discovery and relevance, and iteration. Based on the LCAS results (Fig. 3), we can conclude that the majority of responding students perceived this curriculum to be incorporating the CURE elements of collaboration, discovery and relevance, and iteration. Of these categories, the "discovery and relevance" aspect of this CURE seemed least clear to students, so the instructors plan to place greater emphasis on communicating the "discovery and relevance" aspects of this CURE to students going forward.

Possible modifications

The authors see four main areas of focus for future modifications of this curriculum: class size, modality, lecture, and timeline.

Class size. This curriculum was tested with a cohort of 46 students. However, as mentioned above, this curriculum could be scaled for much larger or smaller class sizes with proper faculty and/or graduate teaching assistant (GTA) support. We suggest that, if instructors plan to scale up this activity, they select a more restricted set of vaccine targets but allow students the ability to pick their own vaccine target from this smaller set. It was at times challenging for the instructional team to keep up with the variety of targets our class of 46 students had selected. By limiting the set of targets, faculty and/or GTAs will be better able to evaluate student work and will limit their time spent on outside reading about each vaccine target.

Modality. This curriculum was field tested in an online modality. Some students were participating synchronously via Zoom while others were in an asynchronous section relying on recordings. This curriculum could be modified for in-person instruction or a hybrid or flipped format or could remain fully online. If modifying to in-person instruction, students would have the advantage of being able to physically do many of the techniques we discussed (ELISA, flow cytometry, etc.) and could apply the elements of experimental design we discussed to data that they generate themselves. A hybrid or flipped format would also work for this curriculum. Students could complete techniques in lab but watch prerecorded modules prior to lab. Peer review of proposals could also be done in person. Finally, a fully online version could be continued. This approach could be advantageous for fully online programs as well as programs that do not have funds available to fully equip an immunology laboratory.

Lecture. Although we developed this course to satisfy revised learning outcomes for an online immunology laboratory, this curriculum could also be further modified to meet the needs of an immunology lecture course. For example, the final project for this course could take the place of exams or of a final cumulative exam. The curriculum could be implemented into the latter portion of the lecture course. Instructors could add to our curriculum by also asking students to explain how the immune system typically responds to their vaccine target. Instructors of lecture courses may want to remove or add content as discussed below in order to incorporate a portion of the curriculum in their courses.

Timeline. We tested this curriculum over the course of a full semester and were pleased with having this time to scaffold each aspect of the final report. However, instructors may be interested in incorporating this curriculum into a smaller time period of their lab or lecture course. Instructors have a variety of options available to shorten the length of this curriculum. For example, if earlier lab courses in the department's curriculum teach experimental design, instructors could eliminate

FIG 3 Legend (Continued)
the percentage of students responding to the statement with a given answer. (A) Students responded to statements regarding collaboration during the course with responses reflecting the frequency at which they were asked to complete particular activities. Student response options plotted include unanswered (white), never (dark red), prefer not to answer (orange), I don't know (gray), once or twice (lightest blue), monthly (medium blue), and weekly (dark blue). (B) Students responded to statements regarding discovery and relevance during the course with responses reflecting their perception of what they were expected to do. Student response options included unanswered (white), not applicable (orange), strongly disagree (dark red), disagree (red), neither agree nor disagree (gray), agree (light blue), and strongly agree (dark blue). (C) Students responded to statements regarding iteration during the course with responses reflecting whether time was provided for particular activities. Student response options included unanswered (white), not applicable (orange), strongly disagree (dark red), disagree (light red), neither agree nor disagree (gray), agree (light blue), and strongly agree (dark blue).

these sections of the curriculum. Additionally, rather than having students utilize the primary literature to identify background information about their vaccine target, instructors could do this work and present this information to the students. The students could then focus on selecting vaccine format and antigen, designing experiments, and evaluating data. Alternatively, the students could complete a literature review on a vaccine target and select an appropriate format and antigen, similar to the project described by Sparks-Thissen (9).

SUPPLEMENTAL MATERIAL

Supplemental material is available online only.
SUPPLEMENTAL FILE 1, PDF file, 1.9 MB.

ACKNOWLEDGMENTS

We thank Eileen Hotze and Nicole Perry for helpful discussions.

We declare no conflict of interest.

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