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Implementation of a course-based undergraduate research experience into an undergraduate immunology course

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Course-Based Undergraduate Research Experiences (CUREs) are a widely used pedagogical tool that effectively engage students in the process of doing science, leading to increased retention and student success in STEM. I have designed a CURE in which students in my upper-level immunology course investigate the immunomodulatory properties of herbal supplements. Students work collaboratively in a group to develop a hypothesis based on data from primary literature, design an experiment to test their hypothesis, collect and analyze data, and present their findings to their peers. By participating in this CURE, students gain valuable research experience and develop several "Key Competencies" that align with the Immunology Learning Framework.

KEYWORDS

immunology, course-based undergraduate research experience (CURE), inflammation, macrophages, undergraduate education

1 Introduction

Course-based undergraduate research experiences (CUREs) provide broad access for STEM undergraduate students to participate in genuine scientific research (Corwin Auchincloss et al., 2017; Bangera and Brownell, 2017). By integrating research into undergraduate courses, the number of students who can benefit from the experience of independent research is substantially increased. Students in STEM courses who participate in CUREs are more likely to self-identify as scientists as compared to students in STEM courses without CUREs (Esparza et al., 2020). Bradshaw et al. (2023) demonstrated that students participating in a CURE had increases in their sense of belonging and retention in STEM as compared to their peers who did not participate in a CURE.

Immunology is an inherently interdisciplinary field with ever-increasing public relevance (Bruns et al., 2019; Bruns et al., 2021; Porter et al., 2021). Despite its broad implications and applications, immunology is generally only included in undergraduate biology education as part of a microbiology course or anatomy & physiology courses (Cheesman et al., 2007; Pandey et al., 2024). Stand-alone immunology courses are uncommon at the undergraduate level, and even less common are undergraduate immunology courses that include a laboratory component (Bruns et al., 2021). I have the unique opportunity to regularly offer an undergraduate immunology course with a laboratory component, and I was motivated by the numerous educational benefits of CUREs to develop a new CURE for my immunology course.

In recent years several activities and resources for undergraduate immunology lab courses have been published. Garrison and Gubbels Bupp (2019) provided an excellent set of resources and guidelines for setting up an undergraduate immunology laboratory course, including examples of several "inquiry-driven lab modules." In one of these inquiry-driven lab modules students expose THP-1 macrophage cells to a substance that they hypothesize will influence the phagocytic ability of the THP-1 cells and then quantify the phagocytosis of FITC-coated beads through flow cytometry (Garrison and Gubbels Bupp, 2019). In response to the online learning made necessary during the COVID-19 pandemic, Baid et al. (2022) developed a CURE for an undergraduate online immunology laboratory course focused on vaccine design methodology. Students in this online CURE completed Labster simulations of various techniques and worked with mock data sets as well as data sets from COVID-19 vaccine clinical trials. Students then used their knowledge gained from these experiences to design a new vaccine for a pathogen of their choice and propose a research plan for testing the effectiveness of their novel vaccine. Mesmer and Gaudier-Diaz (2022) developed a CURE for an interdisciplinary psychoneuroimmunology course in which students designed and tested hypotheses related to psychosocial variables and markers of inflammation in blood samples.

In 2016 and 2018 I taught an undergraduate immunology course with a laboratory component in which I ran an initial version of the CURE described in this paper in which students worked with splenocytes from mice to test the immunomodulatory properties of commercially available herbal supplements. One student group from my 2018 immunology class continued their project with me in my research lab the following semester and published their results in which they characterized the influence of *Echinacea purpurea* root extract on cytokine production by ConA-activated mouse splenocytes (Cadiz et al., 2019). Due to a change in my research direction, I no longer had access to primary cells from mice so switched over to using an immortalized cell line for the CURE. I chose to work with RAW 264.7 cells, a cell line widely used by researchers as a model for macrophages (Raschke et al., 1978). Due to a sabbatical and taking on an interim administrative role, I was not able to offer my immunology course again until 2023. For the 2023 and 2024 offerings of my immunology course I modified the CURE to more closely align with "essential dimensions" of a CURE as outlined by Corwin Auchincloss et al. (2017), described further in the Pedagogical Framework section below.

2 Pedagogical framework

This CURE was developed with the goal of providing students enrolled in an immunology course a genuine research experience during their undergraduate career. The alignment of this CURE with the "Key Competencies" from the Immunology Learning Framework (Pandey et al., 2024) will be described later in this paper. This CURE aligns with the five essential dimensions of a CURE as outlined by Corwin Auchincloss et al. (2017) as demonstrated below:

1) "Use of science practices" – For this CURE students develop a focused research question about the immunomodulatory properties of their assigned herbal supplement with guidance from the instructor. Students then locate primary literature articles related to their research question and develop a hypothesis. Students design their experiments to test their hypothesis with guidance from the instructor on which methods will be available and appropriate. Students gather, analyze, and interpret their data. They develop an interpretation of their data and present to their peers in the class.
2) "Discovery" – For this CURE students are investigating a scientific question that has not been asked before and the outcome is unknown to the instructor.
3) "Broader relevance or importance" – Students gain the ability to apply their knowledge about the immune system and think critically about the claimed health benefits of commercially available herbal supplements and related products.
4) "Collaboration" – Groupwork is an essential part of this CURE. Later in this paper I describe the structure for establishing positive group interactions between peers in the course.
5) "Iteration" – Students generate "messy data" as part of this CURE. They design their experiments with numerous replicates in order to appreciate the "messiness" of generating data. Time and resource constraints unfortunately prevent students from completing their experiments multiple times during this CURE, but students do present their "next steps" at the end of the semester with revisions to their research plan based on conclusions that they have drawn from their data. Additionally, student work for this CURE is evaluated through "standards-based grading," a practice that emphasizes the iterative process of scientific endeavors (Feldman, 2019; Knight and Cooper, 2019).

3 Learning environment and learning objectives

The CURE that will be described in this paper is taught in an upper-level immunology course that is an elective in the biology major the University of Minnesota Morris, a four-year public liberal arts college, and Native American Serving Non-Tribal Institution. The immunology course meets each week for two sixty-five-minute lectures and one three-hour lab section. The last two offerings of this course in which the CURE was implemented had, on average, sixteen students enrolled. The pre-requisite for this course is an upper-level molecular biology course with lab. The pre-requisites for that molecular biology course are cell biology and organic chemistry, both with lab. Students have also completed course work in introductory statistics and a "Biological Communications" course. In the communications course, students learn to use online databases (ex/ PubMed and Science Direct) to find primary literature articles related to a research topic and practice writing summaries about primary literature articles to demonstrate their understanding of the article.

The following learning objectives for the laboratory portion of the immunology course are achieved by student completion of the CURE:

1 Interpret data obtained by immunology research techniques
2 Perform immunology research techniques
3 Communicate understanding of immunology concepts and research techniques
4 Work effectively in a group

4 Results, processes and tools

At the start of the immunology course, each lab group of three to five students is assigned a commercially available herbal supplement that is advertised to have immunomodulating properties. During the semester students characterize the immunomodulatory properties of their assigned herbal supplement by exposing a mouse macrophage cell line (RAW 264.7 cells) to varying doses of the herbal supplement. Students work in their lab groups to write a literature review on the research that has been done about the immunomodulatory functions of their herbal supplement. Students then use the information in their literature review to design a research proposal. Students choose two to three cytokines that they would like to measure from the macrophage cells after exposure to varying doses of the herbal supplements. They must provide a rationale in their research proposal to explain their cytokine choices based on data from primary literature. Students then set up their experiments and perform ELISAs to quantify their chosen cytokines. After collecting and analyzing their data, students finish the semester with an oral presentation to their classmates. A week-by-week outline of the CURE is included in Table 1.

4.1 Instructor preparation and required equipment, supplies, and reagents

The implementation of this CURE requires that an instructor has access to the equipment required for culturing mammalian cells (including a biosafety cabinet and CO_2 incubator). I have chosen RAW 264.7 murine cells to work with due to their ease to work with and widespread use as a model for macrophages (Raschke et al., 1978). RAW 264.7 cells are categorized as BSL-2, so it is important to check with on-campus safety officers to ensure proper training and safety protocols are followed by both the instructor and students. Access to a microplate reader is also needed for data collection. A complete list of the equipment, supplies, and reagents that I use are included in the Supplementary materials. I use commercially available herbal supplements and choose plants that are advertised as having immunomodulatory properties. The total estimated cost for supplies and reagents to run this CURE for one semester is $1,500. This estimate is based on pricing available through the University of Minnesota and does not include shipping and handling or any of the necessary equipment. The first semester of running the CURE will be the most expensive, as some consumable supplies that do not expire will likely be left over and can be used in subsequent semesters. I am able to purchase the supplies and reagents that I need each semester using departmental budget allocations.

TABLE 1 Outline of weekly activities and assignments.

Week	Activities and assignments
Week 1	Assign herbal supplements
	Review pipetting skills
	Complete group norms activity
	Start literature review assignment
Week 2	Complete endotoxin detection assay Work on literature review revisions
Week 3	Write research proposals
	Cell counting activity
Before week 4	Instructor sets up co-cultures
Week 4	Harvest co-culture supernatants
	Perform MTT assays
Week 5	Perform ELISAs
Week 6	Analyze data
	Prepare presentations
Week 7	Group presentations

4.2 Forming lab groups and assigning herbal supplements

During the first week of the semester, I introduce the CURE to my students and have them choose their lab groups. Samudra et al. (2024) studied the benefits and drawbacks of assigning student lab groups versus letting students choose their own lab groups. Given that I am on a small campus, my students know each other quite well by the time they take this upper-level class, so I allow my students to form their own lab groups. I have my students complete an exercise together once they form their lab groups to set group norms and establish communication plans and expectations (see Establishing Group Norms document in the Supplementary materials, based on resources provided by the University of Minnesota Center for Educational Innovation). I also have students complete a peer-assessment of their lab group mates at the mid-point of the project that I use to identify any group work issues that have arisen (see Peer Assessment of Lab Group Participation document in the Supplementary materials). As briefly stated earlier, I use a standards-based grading model for the assignments related to the CURE. The assignments that are described below are completed together by the members of each lab group and the lab group members all receive the same grade for their group assignments (unless irreconcilable issues arise in a group). Since the revision process is essential to the standards-based grading model that I use, I discuss with the students at the start of the semester that my expectation is that each lab group will achieve "proficiency" on each aspect of the CURE project.

Students work together in their lab groups during the first week of the CURE to refresh their knowledge from previous lab courses about how to properly use a micropipettor by completing a pipetting task. I use the "Pipette Olympics" protocol outlined in Richter et al. (2022). I then assign each lab group their herbal supplement and introduce the literature review and research proposal assignments. Their first task for their research project is to perform an LAL Assay to quantify endotoxin contamination of their herbal supplement. There is usually some level of endotoxin contamination from store-bought herbal supplements, so I discuss with the class about how we will take that into account when interpreting their data later in the semester. Generally, the herbal supplements that we are working with have anti-inflammatory properties, so low levels of endotoxin contamination will not negatively impact the students' research projects.

4.3 Literature review and research proposal

Students work with their lab group to write a literature review on the plant that their herbal supplement is prepared from. The students are asked to provide general background information about the plant, what part of the plant is used to prepare the herbal supplement, any important active compounds that have been identified in the plant, medicinal uses of the plant, and any cultural significance of the plant. Students then search online databases to find primary literature articles about prior research on the immunomodulatory properties of their assigned herbal supplement. I encourage students to look for research in which macrophages were used to characterize the immunomodulatory properties. Students are tasked to find three primary literature sources and write a summary on each source that includes three parts: (1) background information and the hypothesis being tested in the paper, (2) experimental design and methods used to test the hypothesis, and (3) an interpretation of the data presented in the paper. Students are encouraged to consult with me as they are searching the literature, reading the papers that they find, and drafting their literature review. I grade their literature reviews on a proficient/not yet proficient basis, with feedback about how to reach proficiency and I provide opportunities for revision (see Literature Review Assignment and Evaluation Rubric in Supplementary materials).

Students are then instructed to write a research proposal with their lab group that has four sections: hypothesis, approach, rationale, and expected results (see Research Proposal Assignment in Supplementary materials). Students write their research proposals during a lab session so that I can check in with them while they are working and ensure that their proposal will be feasible. Students use the data from the papers that they read for their literature review to develop a hypothesis about the immunomodulatory properties of their herbal supplement. Then they develop an approach to test their hypothesis. Students determine a range of doses of the herbal supplement to test on the macrophages based on the methods from the papers that they read for their literature review. Each lab group picks out two to three cytokines that we can test by ELISA to test their hypothesis. Most often the herbal supplements have anti-inflammatory properties, so we use LPS as a control to induce production of pro-inflammatory cytokines, and then look for a decrease in pro-inflammatory cytokine production induced by the herbal supplement. Students describe their rationale for their hypothesis and approach, based on what they learned from previous research outlined in their literature review. Finally, students outline their expected ELISA results based on their hypothesis.

Once students have completed their research proposals, I order the required ELISA kits. Most students' research proposals call for a 48-h co-culture of the macrophages with the herbal supplements and LPS. I will generally set up the co-cultures myself such that the 48-h co-culture period is complete on our lab day. I do not have the students set up their own co-cultures for several reasons. Since our lab meets just one time per week, setting up the co-cultures must occur outside of our assigned lab time. Most students have not learned aseptic technique and I do not have adequate biosafety cabinet space for multiple students to work in the hood at a time, so teaching aseptic technique to a lab section of sixteen students would take more time than I have available for the lab. I instead walk students through to process of setting up the co-cultures. I also include a lab activity in which students learn how to count cells using Trypan blue staining and hemocytometers so that they can better grasp the concept of setting up co-cultures with precise cell numbers.

4.4 Data collection, analysis, and final presentation

Students harvest supernatants from the co-culture plates at the appropriate time points (48-h for most students), and we freeze the supernatants for ELISA analysis in subsequent weeks. On the day that the co-culture is complete we perform an MTT assay to determine whether or not their plant extract had a cytotoxic effect on the macrophage cells. Then in the following weeks we use the co-culture supernatants to quantify cytokine levels by ELISA. I split my lab section in half for the MTT assay and ELISAs so that I can more easily guide students through the techniques. So, half of the lab groups do the MTT assay one week and the other half of the lab groups do the MTT assay the next week. When students are in their "off week" and not in the lab, they work through a case study assignment. I do the same for the ELISAs, half of the groups complete their ELISAs one week and the other students complete a case study assignment during their "off week." An experienced laboratory teaching assistant might prevent the need for splitting the lab sections. Additional assays could be incorporated to the CURE if desired such as flow cytometry, fluorescence microscopy, or qRT-PCR.

After the MTT data and ELISA data have been collected, we spend a week in lab performing data analysis and preparing figures for their oral presentations. I instruct students to prepare their presentation with an intended audience of immunology professionals. In their presentations they provide background information on the plant extract that they worked with, using information that they gathered for their literature review. They present their hypothesis and rationale, then go on to present their data and conclusions (see Presentation Assignment and Evaluation Rubric in Supplementary materials). It would be possible to design additional final projects for this CURE, such as a written lab report in the style of a primary literature article or a presentation for a more general audience. I often have students opt in to present their CURE project at an on-campus "Undergraduate Research Symposium" during the following semester, either as an oral presentation or poster. When students chose to do so they work on revising their presentation so that it will be understandable to a more general audience.

5 Discussion

This CURE is an excellent way to provide students the opportunity to develop in several of the "ImmunoSkills Core Competencies" from Pandey et al. (2024). In Table 2 I have charted the alignment between the CURE activities and the "ImmunoSkills Core Competencies" that are addressed. While not all the Core Competencies and Illustrative Skills are addressed in this CURE, there is additional time during the semester to incorporate lab activities and modules to address those skills. In particular, the CURE as described here does not incorporate Core Competency #2: "Ability to understand the relationship between science and society." Since students are using commercially available herbal supplements that are advertised to have anti-inflammatory properties, it would

TABLE 2 Alignment of CURE activities with ImmunoSkills core competencies.

Core competency	Illustrative skill	CURE activity
1. Ability to apply the process of science	1.1. Locate and evaluate peer-reviewed articles pertaining to immunology	Literature review assignment
	1.2. Critically analyze key findings and experimental design within primary immunology literature	Literature review assignment
	1.3. Design an experiment to address an immunology-based research problem	Research proposal assignment
3. Ability to communicate and collaborate with others	3.1. Present an immunological topic at a level appropriate to the intended audience	Group presentation assignment
	3.2. Contribute with a team to move a task forward	Group norms activity
	3.3. Contribute within a team to promote a positive environment	Group norms activity
4. Ability to use quantitative reasoning	4.2. Interpret different types of graphical representation of immunological data	Literature review assignment
	4.3. Draw meaningful conclusions from an immunology-related data set	Group presentation assignment
5. Ability to perform basic lab procedures	5.1. Use standardized safety practices in an immunological laboratory	Adherence to lab protocols and safety requirements
	5.2. Use best technical practices in an immunological laboratory	Adherence to lab protocols and safety requirements
	5.3. Use best record-keeping practices in an immunological laboratory	Adherence to lab protocols and safety requirements
6. Ability to explain and/or perform laboratory methodology to address an immunology-based research question	6.2 Measure effector functions of immune components	Research proposal assignment and completing an ELISA and MTT assay
	6.3 Detect the presence of an antigen or an antibody	Research proposal assignment and completing an ELISA
	6.4 Measure the immune response upon manipulation of an experimental system	Research proposal assignment and completing an ELISA

ImmunoSkills core competencies and illustrative skills are from Pandey et al. (2024).

be possible to incorporate a discussion about how immunology terms such as “inflammation” are used by the general public when referring to health and disease. Core Competency #4: “Ability to use quantitative reasoning” is part of this CURE when students are analyzing their MTT and ELISA data, but since they only complete each of their tests one time, we are not able to run statistical analyses on their data. This CURE is particularly robust in Core Competency #1: “Ability to apply the process of science” since students go through the process of starting with a literature review that they use to shape their hypothesis and research proposal, followed by data collection and communication out to peers. I also have built in intentional scaffolding for the group dynamics with the “Establishing Group Norms” activity and “Peer Assessment of Lab Group Participation” activity, helping students achieve the Core Competency #3 “Ability to communicate and collaborate with others.”

An obvious limitation to the ability to implement this CURE is the cost associated per semester and the required equipment and facilities. To save on costs, the LAL endotoxin contamination assay and/or the MTT assay could be removed since these assays are not core immunological assays. Another limitation is the level of prior knowledge and experience required by students to succeed in this CURE, making this CURE most appropriate for undergraduate students at the senior or possibly junior level. The design of this CURE and cost considerations for purchasing reagents does limit students in terms of their choice of methodology. I also only maintain the one cell culture line, so students are limited to researching the immunomodulatory properties of their herbal supplement on macrophages.

Despite these limitations, I have found that this CURE is a very effective way to address most of the ImmunoSkills Core Competencies in my undergraduate immunology course. Through student evaluation comments and informal conversations with my students, I have received feedback that students enjoy this project and “feel like a real scientist.”

Data availability statement

The original contributions presented in the study are included in the article/Supplementary material, further inquiries can be directed to the corresponding author.

Author contributions

RJ: Writing – original draft, Writing – review & editing.

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Conflict of interest

The author declares that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Generative AI statement

The authors declare that no Gen AI was used in the creation of this manuscript.

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Supplementary material

The Supplementary material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/feduc.2025.1603665/full#supplementary-material

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