AMERICAN SOCIETY FOR MICROBIOLOGY | JMBE Journal of Microbiology & Biology Education

Curriculum

# Engaging students in a genetics course-based undergraduate research experience utilizing *Caenorhabditis elegans* in hybrid learning to explore human disease gene variants

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**ABSTRACT** Genetic analysis in model systems using bioinformatic approaches provides a rich context for a concrete and conceptual understanding of gene structure and function. With the intent to engage students in research and explore disease biology utilizing the nematode *Caenorhabditis elegans* model, we developed a semester-long course-based undergraduate research experience (CURE) in a hybrid (online/in-person) learning environment—the gene-editing and evolutionary nematode exploration CURE (GENE-CURE). Using a combination of bioinformatic and molecular genetic tools, students performed structure-function analysis of disease-associated variants of uncertain significance (VUS) in human orthologs. With the aid of a series of workshop-style research sessions, students worked in teams of two to six members to identify a conserved VUS locus across species and design and test a polymerase chain reaction-based assay for targeted editing of a gene in the nematode and downstream genotyping. Research session discussions, responsible conduct of research training, electronic laboratory notebook, project reports, quizzes, and group poster presentations at a research symposium were assessed for mastery of learning objectives and research progress. Self-reflections were collected from students to assess engagement, science identity, and science efficacy. Qualitative analysis of these reflections indicated several gains suggesting that all students found many aspects of the GENE-CURE rewarding (learning process of research, self-confidence in research and science identity, and personal interest) and challenging (iterative research and failure, time management, COVID-19 pandemic, and life issues).

**KEYWORDS** GENE-CURE, genetics, CURE, *C. elegans*, hybrid learning, bioinformatics, nematode, personal interest, COVID-19 pandemic

With the intent to engage students in research and explore disease utilizing the *Caenorhabditis elegans* model, we developed semester-long genetics course-based undergraduate research experience (CURE) in a hybrid (online/in-person) learning environment: the gene-editing and evolutionary nematode exploration CURE (GENE-CURE).

Bioinformatics is an important area of science that uses computer technology to collect, store, and analyze biological data. Bioinformatic tools have been designed to allow researchers to compare genetic and genomic data and better understand the evolutionary aspects of molecular biology. There are several CUREs that have been developed to engage students through bioinformatics-based research and computer-based learning (1–7). The GENE-CURE is specifically designed to explore disease biology utilizing the nematode *C. elegans* model, leveraging a hybrid learning environment. The distinctive aspect lies in its integration of genetic analysis in model systems with

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The authors declare no conflict of interest.

**Received** 24 May 2023
**Accepted** 13 October 2023
**Published** 16 November 2023

bioinformatic approaches, providing students with a multifaceted understanding of gene structure and function.

*C. elegans* is an ideal model system for genetics and molecular biology studies *in vivo* for numerous reasons: simple to manipulate and propagate, small and observable under a dissecting microscope, short generation cycle and lifespan, and ease of long-term frozen storage (8). There are numerous recent studies showing the value and utility of nematodes in engaging undergraduate students in inquiry and research through a course, including CUREs (9–15). In the GENE-CURE, students engage in comprehensive research, focusing on the structure-function analysis of disease-associated variants of uncertain significance (VUS) within human orthologs. This approach allows them to bridge the gap between genetic concepts and practical application in scientific research.

The global COVID-19 pandemic has presented instructors and students with unique obstacles in the learning environment with largely how we interface (16–18). In-person courses, labs, and experiences transitioned to various virtual and online formats. There were already several factors present that deterred faculty from developing and implementing CUREs, including time, scale, resistance, and assessment (19). An evolving, global pandemic added new barriers for CURE instructors that have required creativity, empathy, persistence, and resilience to overcome. Importantly, CUREs are being designed and adapted to provide flexibility to meet the evolving demands and needs of students and instructors (20–25). Specifically, the GENE-CURE places a significant emphasis on collaborative learning, where students work in teams to identify conserved VUS loci across species. They then proceed to design and test polymerase chain reaction (PCR)-based assays for targeted editing of genes in the nematode, facilitating a hands-on exploration of molecular genetic tools. This aspect of the GENE-CURE is particularly notable, as it took place amidst the challenges posed by the COVID-19 pandemic. Despite the unprecedented obstacles students faced during this period, the collaborative nature of the GENE-CURE not only enhanced their understanding of molecular genetics but also acted as a unifying force, strengthening the sense of community within the learning environment. Students persevered and thrived, showcasing resilience and determination, which played a pivotal role in the success of the GENE-CURE and the overall academic and research experience.

Here, we describe the format of the GENE-CURE and share numerous tools, which can be used to model similar courses that include bioinformatics, genetics, the *C. elegans* system, and CRISPR-Cas9 technology.

## Intended audience

Students in the Undergraduate Biology Program at Jacksonville State University (Jax State) complete a diverse biological sciences training plan. This plan is guided by a concentration that students self-select based on their training and career interests. Biology majors and minors are required to complete a basic core curriculum, including ecology, genetics, cell biology, and senior seminar. The GENE-CURE is offered as a 300-level genetics course taken after a year of introductory biology courses and labs, typically during the second or third year of undergraduate study.

The GENE-CURE was designed and offered to students to introduce them to authentic research practices and genetic techniques. We suggest that it can be offered in any year during undergraduate or graduate training with necessary modifications. This workflow can also be utilized to train technical skills in bioinformatics and genetics.

## Learning time

The course was 4 credit hours and met three times a week, including two class sessions (1.5 hours each) and one lab session (2 hours). Due to the COVID-19 pandemic and transitions in learning modalities, the course was taught in different formats over four semesters (Table 1).

During Fall 2020, the course was offered hybrid synchronous. Students met virtually through Microsoft Teams. Time was split between large group discussions and break-out

**TABLE 1** Summary of the GENE-CURE offerings from Fall 2020 to Spring 2022

| | Fall 2020 | Spring 2021 | Fall 2021 | Spring 2022 |
|---|---|---|---|---|
| Number of students | 44 | 41 | 52 | 20 |
| Number of sections | 2 | 3 | 3 | 2 |
| Teaching modality | Hybrid synchronous | Hybrid synchronous | In-person | In-person |
| Instruction team | Instructor, GTA | Instructor, GTA, GOLA | Instructor, peer instructor | Instructor, peer instructors (4) |

sessions for small group collaborative time. In-person "wet lab" sessions were offered to students inside and outside of normal class and lab time. For Spring 2021, the course was offered hybrid synchronous utilizing the same organization with a rotation schedule for in-person and virtual participation for all research sessions. During Fall 2021 and Spring 2022, the course was offered in person and consisted of the same organization.

The time spent by students and instructors on research tasks is summarized in Table 2. There are tasks specific for the instructors to ensure the progression of experiments across research sessions. Students and instructors also spent time outside of the scheduled research sessions to troubleshoot and repeat experiments to achieve specific research goals. This outside time was coordinated through reserved sessions and varied between individual students. At the start, students complete a set of online training modules focused on responsible conduct of research (RCR), basic lab safety, and other related areas (Table 2; Appendix 1).

## Instructional team

The GENE-CURE has been primarily led by an instructor and supported by graduate and undergraduate students. Due to the COVID-19 pandemic and transitions in learning modalities, the instruction team varied across the semesters depending on the type of support available (Table 1). The instructional team ranged from the instructor to a graduate teaching assistant (GTA) to a graduate online learning assistant (GOLA) to

**TABLE 2** Summary of the GENE-CURE research tasks along with estimated time expenditures

| Task | Instructor preparation[a] | Research sessions (class and lab time)[a] |
|---|---|---|
| Lab safety and RCR training | – | 2 hours |
| Create a Benchling account and join course space | 15 minutes | 15 minutes |
| Benchling walkthrough | – | 2–4 hours |
| Disease selection | – | 1 hour |
| Disease gene and nematode ortholog | – | 1 hour |
| Literature search and review | – | 6–8 hours |
| Hypothesis construction | – | 1 hour |
| Clinical variant identification | – | 2 hours |
| Evolutionary conservation analysis (multiple sequence alignments) | – | Varied (4–8 hours) |
| Nematode VUS target primer design and order | 2 hours | Variable (0–1 hour) |
| Preparing reagents | 2 hours | – |
| Preparing bacterial and nematode plates | 2 hours | – |
| Nematode maintenance | 4 hours (across semester) | – |
| Nematode observation and manipulation | 1 hour (across semester) | 2 hours |
| Nematode DNA extraction | 15 minutes | 2 hours |
| PCR | 30 minutes | 2 hours |
| Gel electrophoresis and imaging (polyacrylamide gels) | 15 minutes | 2 hours |
| PCR analysis | – | 1 hour |
| Outside time (reserved sessions) | Varied (10 hours) | Varied (0–6 hours) |
| Group poster preparation | 2 hours | 4–6 hours |
| Research symposium | 2 hours | 2–4 hours |
| Additional time for research | – | 15–20 hours |
| Total (estimation) | ~26.25 hours | ~49.25–73.25 hours |

[a]Time is not projected for tasks with "-" in the column.

undergraduate peer instructors. The GTAs were assigned and fulfilled their teaching assistance for their assistantship. The GOLA enrolled in a 2-hour graduate biology elective and assisted in the hybrid learning environment. The peer instructors are undergraduates who have successfully completed the GENE-CURE and want to serve as mentors. The instructor has genetics and molecular biology expertise along with experience with *C. elegans* husbandry and the CRISPR-Cas9 technology. GTAs were trained by the instructor on molecular genetic techniques and nematode manipulation. Undergraduate peer instructors were trained initially in the GEE-CURE.

### Prerequisite student knowledge

Students were required to have at least 1 year of introductory biology knowledge and experience. This includes two introductory biology courses and subsequent labs. The first course is an introduction to the concepts of biology, including cellular structure and function, bioenergetics, patterns and mechanisms of inheritance, the processes of evolution, and ecology. The second course is an introduction to the concepts of biodiversity, from bacteria to plants and animals, with an emphasis on their structure, function, and ecological interactions. Students also enroll in two introductory labs that engage in basic biology topics.

### Learning objectives

The GENE-CURE was designed to engage students in authentic research for the development of basic research skills and to address a scientific question of interest to the students, instructor, and the scientific community. For numerous students, this was their first exposure to scientific research. Student learning objectives (SLOs) focused on three major scientific practices, including experimentation, writing, and presentation (Table 3). SLOs were evaluated with formative and/or summative assessments.

## PROCEDURE

The course encompasses a series of workshop-style research sessions and modules integrating bioinformatic and "wet lab" tools (Fig. 1). The introductory modules engage students with the foundational pillars of scientific research, the fundamental concepts of genetics, and a working knowledge of bioinformatic tools. The experimentation modules include both bioinformatic and "wet lab" genetic experiments culminating in a group-constructed poster and presentation at a research symposium. We briefly describe these modules and tasks next.

**TABLE 3** SLOs and course assessments for the GENE-CURE

| Learning objective | Assessment (implementation) |
|---|---|
| Students will employ principles of modern genetic analysis. | • ELN (grading rubric)<br>• Quizzes (multiple choice) |
| Students will evaluate RCR and assess RCR issues in science. | • RCR training (interactive module and activity) |
| Students will apply the scientific method to test a hypothesis-driven question. | • ELN (grading rubric)<br>• Project reports (grading rubric) |
| Students will revise science writing in project reports. | • Project reports (grading rubric) |
| Students will report on individual and group findings during a poster presentation. | • Group poster preparation and presentation (grading rubric) |

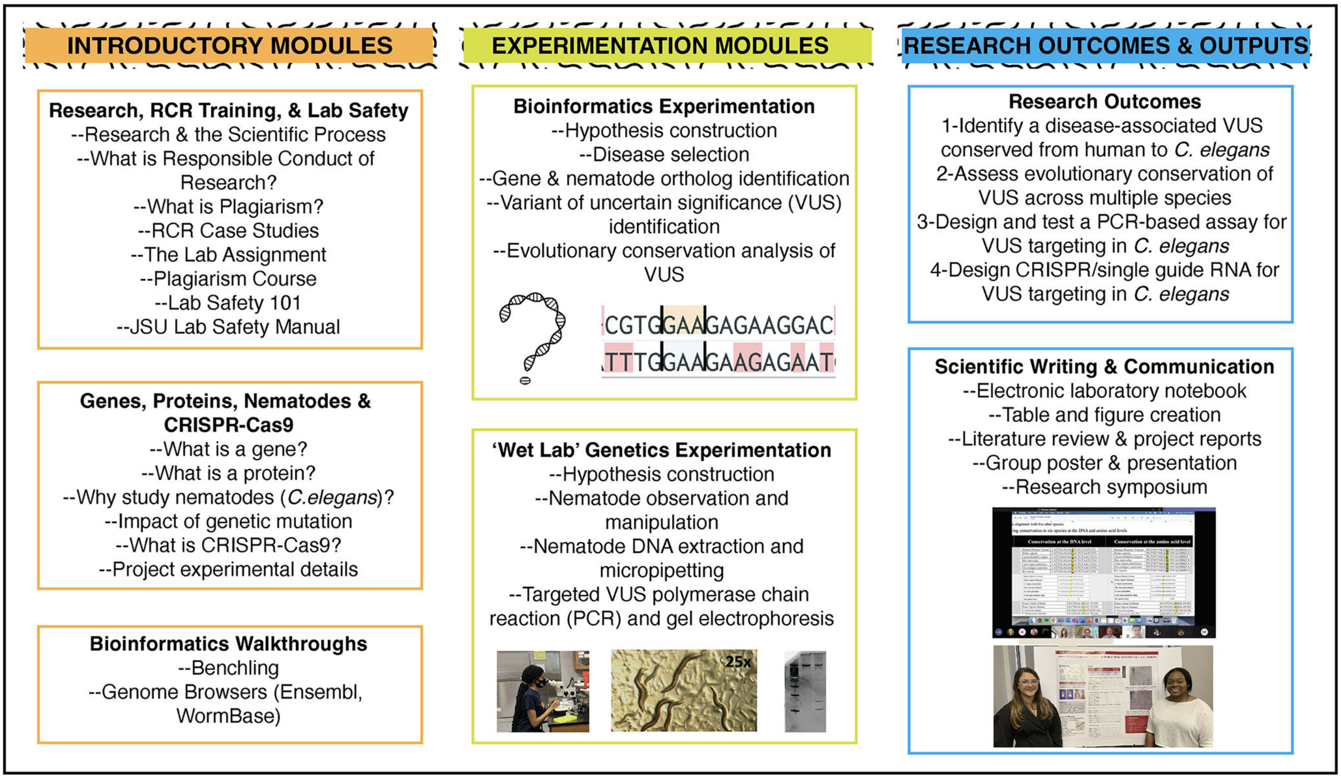


**FIG 1** The layout of the GENE-CURE with modules and research outcomes and outputs. The orange boxes show the introductory modules. The lime green boxes show the experimentation modules. The blue boxes show the research outcomes and outputs.

## Execution and modules

Students work and collaborate in research groups (two to six members per group) in a series of workshop-style research sessions, modules, and "wet lab" sessions. Students have ample time to conduct background literature research, construct scientific hypotheses, and design and execute experiments. An array of formative and/or summative assignments are assessed for mastery of learning objectives and research progress (Fig. 1; Appendix 4). Brainstorming and peer and instructor feedback are incorporated across all assessments.

### *Research, RCR training, and lab safety*

Students engage in introductory modules through Canvas and interactive activities. Initial topics include research and the scientific process, RCR, and laboratory safety (Fig. 1). A flipped design introduces students to each topic through Canvas modules (content, videos, and activity) (Appendices 1 and 2). Students enter the following session with front-loaded knowledge to discuss, ask questions, and apply the content. For example, students interact with the "what is RCR?" Canvas module introducing RCR (26). During the following session, students are presented with case studies spanning the RCR areas. Within groups, students read through each case study, apply RCR principles, and justify their RCR decision-making skills (Appendices 1 and 2). Before entering the lab space, each student is required to read, acknowledge, and accept the Jax State Student Laboratory Safety Manual. Additionally, each student is required to read, acknowledge, and accept the GENE-CURE authorship guidelines. This introductory module comprises 5% of the overall course evaluation (Appendix 4).

### *Genes, proteins, nematodes, and CRISPR-Cas9*

The next introductory module's topics include genes, proteins, nematodes, and CRISPR-Cas9 (Fig. 1). Flip design is also employed. Students review gene, protein, and genetic mutation and explore nematodes and CRISPR-Cas9 through Canvas modules (content, videos, and activity) (Appendices 1 and 2). Additional project and experimental details are provided through Canvas and discussed during the research sessions to prepare students for future experimentation modules. Students collaborate in research groups to brainstorm and discuss individual interests and the proposed research outcomes of the upcoming research project (Fig. 1).

### *Bioinformatics walkthroughs*

The final introductory module's topics include Benchling and genome browsers (Fig. 1). Flip design is also employed. The main program utilized for experimentation is Benchling (Appendices 2 and 5). Benchling is a cloud-based platform for life sciences research and development. The instructor creates an organization for the course that allows instructors and students to collaborate and share data and analyses within Benchling. Students create a free account and join the course organization. To become familiar with using Benchling, students complete a series of experimental tasks that guide them on importing a gene file, locating a disease variant locus within a gene file, constructing a multiple sequence alignment of orthologous genes across multiple species, and analyzing the evolutionary conservation of a variant locus. Students are introduced to the organization of the *C. elegans* genome and how to search for specific genes using ENSEMBL and WormBase genome browsers (Appendix 2).

### *Bioinformatics experimentation*

The first experimentation module allows students to apply the knowledge and experience acquired from the previous bioinformatic walkthrough module. Initially, students construct a hypothesis, select a disease of interest, and identify genes associated with their selected disease and the corresponding nematode orthologs. Next, they analyze the evolutionary conservation of missense VUS locus associated with the disease (Appendix 2). Multiple sequence alignments are carried out using Benchling. The experimental aim is to identify a missense VUS associated with the disease that is in a conserved locus from human or animal to *C. elegans* that can be assessed further *in vivo*.

### *"Wet lab" genetic experimentation*

The second experimentation module allows students to take identified conserved VUS regions into "wet lab" sessions to design and test a PCR-based assay to serve as a downstream genotyping assay (Appendix 2). Materials, recipes, and experimental procedures are provided for "wet lab" nematode and genetic experiments, including bacterial and nematode reagents and culture (Appendix 5).

Students revise their previously constructed hypothesis based on working knowledge and design oligonucleotides for amplifying VUS region in the nematode gene. Students then observe nematodes in culture and extract DNA from collected nematodes. Extracted DNA is used for the initial rounds of PCR for each student's VUS targeting. PCR results are analyzed through poly gel electrophoresis and gel imaging (Appendix 5).

### *Scientific writing and communication*

There are several opportunities for students to engage in scientific writing and communication (Fig. 1).

1. Electronic laboratory notebook (ELN). The ELN is an iterative assignment evaluated three times using a grading rubric and comprises 25% of the overall course

evaluation (Appendices 3 and 4). Each student maintains an ELN with details of experimental background, objectives, materials and methods, results, and discussion (Appendix 6). The student ELNs are executed using Microsoft OneNote through Microsoft Teams. Students collaborate in research groups through a private channel within Microsoft Teams. During ELN evaluations, students are provided the grading rubric along with constructive feedback for improvement.

2. Literature review and project reports. A literature review and two project reports are evaluated using grading rubrics and comprise 25% of the overall course evaluation (Appendices 3 and 4). Each student conducts a literature search for their research project and constructs a literature review. Following experimentation, students compose two project reports summarizing their current project progress and research findings. The report is iterative and evaluated with a grading rubric and contains the following components: title page, background, stated hypothesis, materials and methods, results, and conclusion. Additional writing resources are available through Canvas (Appendix 2). Assignments are submitted and evaluated through Canvas.

3. Group poster and presentation and research symposium. A group poster and presentation are evaluated using a grading rubric and comprise 15% of the overall course evaluation (Appendices 3 and 4). Students are provided basic instructions and guidelines for constructing a poster, including a poster template. Additional poster creation resources are available through Canvas (Appendix 2). Students construct a poster sharing their research findings across the group (Appendix 6). The group posters are executed using Microsoft PowerPoint through Microsoft Teams and the private channel. The final poster file and a recorded group poster presentation file are submitted by a single group member through Canvas. Feedback is provided to students. Ultimately, they present the group posters to a larger audience at the GENE-CURE research symposium held each semester. Each student evaluates their own level of contribution and group members' contributions. Students submit the self and peer evaluations individually through Canvas (Appendix 3). Each student's contribution evaluation scores are averaged across the research group and derived from each student's individual contribution points for the group poster and presentation rubric.

## Safety issues

Students are required to complete a set of online training modules, including basic lab safety. Students are required to read, acknowledge, and accept the Jax State Student Laboratory Safety Manual. Both requirements align with the American Society for Microbiology Guidelines for Biosafety in Teaching Laboratories, specifically for working with BSL-1 microorganisms (27). Students used OP50-1 *Escherichia coli* to feed and propagate *C. elegans* that need to be handled using safe practices and do not pose a biohazard risk. The appropriate personal protective equipment was worn by students while performing their experiments, including lab coats, gloves, closed-toed shoes, and protective eyewear. This was to avoid exposure to cholesterol, streptomycin, acrylamide, and TEMED. Acrylamide was obtained and dissolved in water to reduce the risk of acrylamide inhalation. GelRed was used to stain PCR reactions as a safer alternative to ethidium bromide. Ultraviolet exposure was avoided by imaging gels using a gel documentation system. Bacteria and chemical reagents were properly contained and disposed of in the appropriate biohazard waste containers within the laboratory. Bacterial cultures were disposed of following bleaching (10% bleach solution). Bacterial and nematode plates were disposed of following autoclaving. Students were instructed to tie back long hair and loose clothing to avoid safety risk from alcohol burner flame. Students disinfected their bench space before and after each experiment and cleansed their hands before and after each experiment with soap and water or an alcohol-based hand sanitizer. Due to institutional guidelines for the COVID-19 pandemic, students were required to wear a mask or face covering (covering mouth and nose) when inside campus buildings regardless of distancing. For the last 5 weeks of the Spring 2022 semester, students could choose to mask based on personal preference.

## DISCUSSION

The GENE-CURE was developed to include several high-impact practices, including course projects, collaborative assignments, writing-intensive course, undergraduate research, and diversity/global learning. It was also initially designed during the global COVID-19 pandemic and transitioned in response to the changing circumstances of the university policies. It has been offered as a hybrid synchronous or in-person course for two semesters, a total of four semesters. Therefore, the course design is adaptable to different learning modalities and has been taught in different formats. The size of the course ranged from 20 to 52 students depending on the enrollment for a given semester. To examine and analyze the impact of the GENE-CURE, institutional review board approval was obtained (protocol # TURNER_11162020).

### Student experience

We surveyed students following the research symposium to obtain their views on the value of the experimental tasks and activities that were performed during the course and their overall learning experience. We used two questions to obtain a general idea of each student's experience, specifically the most challenging and rewarding parts of the course that were adapted from a previous instrument (28). Student surveys were analyzed to identify the main themes that emerged, and responses were assigned to each theme. When examining the students' perceived rewards and challenges of the course, we report the top four themes that were reported by the students across the four semesters (Table 4). Students highlighted an array of rewards and challenges of the course.

All students (100%) who completed the questionnaire shared reward(s) from their experience in the GENE-CURE (Table 4). Many students (82.8%) highlighted that they found learning the process of research to be the most rewarding part of the course. Some students shared that this was their first exposure to scientific research and that they were fortunate to gain this research experience as undergraduate students. Students described learning the process of research and their experience in the GENE-CURE prepared them for future science courses and endeavors in research. Another top student-perceived reward was seeing hard work payoff and their research project progress across the course (70.3%). Students described being intrinsically satisfied with observing their self-generated results and project progress. In line with previous research, the GENE-CURE also observed notable advancements in students' scientific identity and emotional connection to research when engaging in data analysis within a CURE (29). Additionally, increasing self-confidence in research and gaining an identity as a scientist were mentioned by several students as the most rewarding (28.9%). Notably, numerous students (35.9%) shared that having a personal interest and/or connection to their selected research topic made their own scientific research the most rewarding part of the course. This indicates a potential connection between personal interest and students' ownership of their research projects. We suspect that students who select their research topic based on a personal connection to the disease may feel more emotional or cognitive ownership toward the overall research project. These hypotheses need to be further explored in future research. Supporting previous findings, this underscores the positive influence of engaging students in meaningful discoveries on their sense of project ownership and academic engagement (30).

The top student-perceived challenge related directly to one of the features of a CURE, the opportunity for students to make discoveries and engage in iterative research (Table 4). Students (41.4%) described being frustrated and overwhelmed with dealing with failure during their research project. Numerous students shared that they were

**TABLE 4** Student-perceived rewards and challenges of the GENE-CURE

| Theme | % (*n*)[a] | Example student quote | Example student quote |
|---|---|---|---|
| Rewards of CURE | | | |
| Learning process of research | 82.8 (106) | "The most rewarding part of this class for me is the knowledge and experience I have gained in doing this undergrad research. I feel like I know more about genetics and I am more prepared to work in a lab and come up with my own research that I can report about throughout each phase." Student from Fall 2020 | "The most rewarding part of this course would have been learning how to go about research. For my major, it will be necessary to know the proper ways to conduct research and write a scientific paper, and with this course I am able to do so." Student from Spring 2022 |
| Seeing hard work payoff and project progress | 70.3 (90) | "The most rewarding thing about this semester is when the hard work pays off and you can actually see progress and results in my project. It is also rewarding to make it to the point where I can test my experiments in the lab." Student from Fall 2020 | "Although this was a challenging class, it was very rewarding to see my progress. After entering the lab and setting up PCR, it felt amazing to see all of my research align and I had a mental breakthrough that although research can be challenging and have roadblocks, they can usually be overcome by reaching out." Student from Spring 2021 |
| Personal interest | 35.9 (46) | "The most rewarding part of this CURE was completing my own scientific research about a disease that affects people that I know and care about." Student from Spring 2021 | "The most rewarding part of this GENE-CURE was being able to tell my aunt that I had spent this entire semester working on and studying her baby's disease. She was so excited to hear what I had worked on and even shared it with her doctors and many people on Facebook! This class was easily one of the best courses I've taken at Jax State. I can't wait to use what I learned in this course and apply it to other aspects in research!" Student from Fall 2021 |
| Self-confidence in research and science identity | 28.9 (37) | "GOING TO LAB!!!! I have never been more excited to be in lab. I have loved every moment. I loved being able to look at the worms and manipulate them. I felt like a true scientist. I would also say that making small breakthroughs in my research has been rewarding. I'm used to knowing the answer on a test, but I have learned that this course doesn't provide answers. I have to find them on my own terms." Student from Fall 2020 | "The most rewarding part of this CURE was the result of what I mentioned in the previous question. I have become so confident in my research abilities because of this CURE. At first, I was terrified at the fact everything was on a blank canvas; however at this point, I realize it is not as strenuous as I first believed. Now, I feel so much more confident in my abilities to conduct my own research instead of putting all my hope in it being provided and me just making sense of it." Student from Spring 2021 |
| Challenges of CURE | | | |
| Iterative research and failure | 41.4 (53) | "The most challenging part about this course is simply dealing with the frustrations of failure. There were many times that I thought things would pan out in my project that led to failure. However, persistence pays off!" Student from Fall 2020 | "The most challenging part of this course has been making sure my project progresses. It's easy to become stuck at a certain part and become overwhelmed because you feel like you aren't as far along as you think you should be. I've come across some roadblocks while working on my project but having [our professor's] support has helped a lot." Student from Spring 2021 |
| Time management | 34.4 (44) | "The most challenging was my time management and self-discipline. I really liked that it was more move at your own pace based because that gave me time to completely focus on my experiment or not feel bad when I have to focus my attention on another class. I knew what needed to be done and if it was not | "The most challenging part of this course has been the ability to work at my own pace. I struggled with this at first because I was used to having due dates and I started getting behind. I am now caught up and I think this |

(*Continued on next page*)

**TABLE 4** Student-perceived rewards and challenges of the GENE-CURE (*Continued*)

| Theme | % (*n*)[a] | Example student quote | Example student quote |
|---|---|---|---|
| | | completed then it's nobody's fault but my own and I really liked that." Student from Spring 2021 | has benefitted me and improved my time management skills." Student from Spring 2021 |
| Learning new tools and research | 21.1 (27) | "I think for me, it has been learning how to work Benchling and fully understand what I am doing. I get very confused when having to do research on my own because sometimes I do not actually know what I am even looking for, so that has been pretty difficult for me, but honestly I think I have gotten so much better this semester and I am so thankful for that because it will help me in other classes." Student from Spring 2021 | "The most challenging part of BY322 for me was making sure I understood and was comprehending the research I was doing. I did not want to just be going through the motions of just doing the experiments, so I tried understanding what the underlying meaning was to the research. To reiterate, just the process of making sure I understood the basics of what we were doing." Student from Fall 2021 |
| COVID-19 pandemic and life issues | 13.2 (17) | "The most challenging part of this year has been to stay focused even when life has thrown everything at you at once. I have been able to stay afloat not only in this class but in all my classes this semester and I am beyond proud of myself for staying strong and pushing through." Student from Spring 2021 | "Learning how to navigate Benchling was particularly challenging for me. I was quarantined very early on in the semester so I missed lab/class during this part of instruction. Meetings with [the professor] on TEAMS helped so much!" Student from Fall 2021 |

[a]Note: "%" is the percentage of students who shared a response representing a theme calculated as a percentage of total students who completed the questionnaire (128 of 157 enrolled students completed the questionnaire). *n* is the number of students who shared a response representing a theme.

able to troubleshoot and work through a negative result or roadblock with persistence and support from their research group members and instruction team. Examples such as these illustrate that students were able to work through their challenges and failures. The next two student-perceived challenges relate to student struggle with time management (34.4%) and learning new tools and research (21.1%). While these features were reported to be challenging, there were numerous students who added that this experience improved their time management skills and ability to learn new tools and conduct research. Particularly, some students (13.2%) shared struggles with life situations, including issues related to the COVID-19 pandemic. These ranged from students having issues staying focused and on-task in the course to hurdles associated specifically with COVID-19 quarantine and infection. Importantly, numerous students described the resources and support they utilized to overcome these challenges to succeed. In congruence with previous findings, these observations align with the understanding that students can derive valuable benefits from participating in a CURE, even if they do not meet predetermined research objectives (31).

## Evidence of student learning

The assessments were designed to critically evaluate the mastery of SLOs and student research progress, ensuring a comprehensive evaluation of students' understanding and skills. Multiple formative and summative assessments were designed to measure student learning across SLOs and examine the effectiveness of the GENE-CURE (Table 3). The ELN assignment helps guide and support students in experiment documentation and data collection and analysis and is evaluated three times across the course (initial, middle, and final). The project report assignment introduces students to scientific writing through scaffolding and revision and is evaluated twice across the course (initial and final).

Most students showed learning gains across assessments by applying the scientific method to test a hypothesis-driven question and revising science writing. For SLO-1, the assessment data reveal that students effectively applied principles of modern genetic analysis during research projects while recording generated data and maintaining ELNs (Fig. 2A; Appendix 6). Both the ELN and the project report assessment score means were significantly higher from the initial to the final student evaluations (Fig. 2). The mean of differences between the ELN assessment scores was 4.248 (Fig. 2A). A total of 112

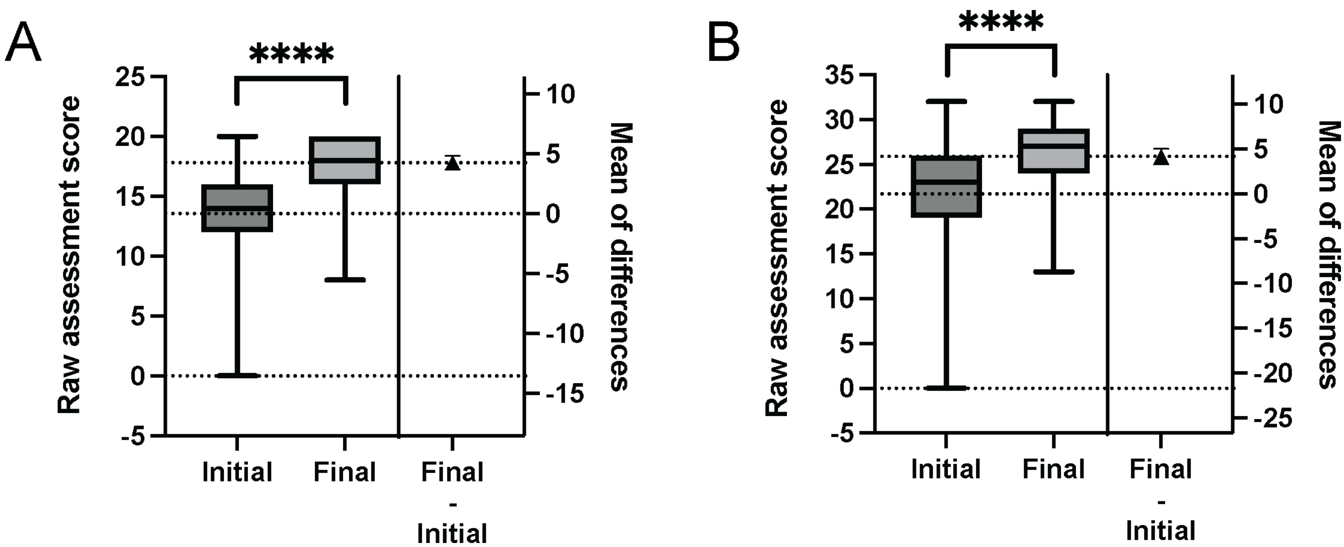


**FIG 2** Assessment of student learning from ELN and project reports across four semesters of the GENE-CURE. Each assessment was evaluated with a grading rubric and assessment score, the ELNs out of 20 points (A) and the project reports out of 32 points (B). There are 125 student scores for the initial and final ELN assessments and 121 student scores for the initial and final project report assessments. For the left side of each graph, the data are shown by box and whisker plots with minimum and maximum scores, median, and first/third quartiles and analyzed with a paired *t*-test (*****P*-value < 0.0001). The *t*-test for paired ELN assessments is the following: $t(124) = 14.65$, $P < 0.0001$. The *t*-test for paired project report assessments is the following: $t(120) = 9.515$, $P < 0.0001$. For the right side, the data are shown by the mean (triangle) and SEM (bars) of differences.

out of 125 students (90%) improved their performance from the initial to the final ELN evaluation.

For SLO-3, the assessment data affirm the students' competence in utilizing the scientific method effectively, as evidenced by their ELNs and project reports, wherein they tested hypothesis-driven questions (Fig. 2A and B; Appendix 6). Additionally, for SLO-4, the assessment data provide clear evidence of students' ability to revise and enhance their science writing skills within their project reports (Fig. 2B). The mean of differences between the project report assessment scores was 4.170 (Fig. 2B). A total of 100 out of 121 students (83%) improved their performance from the initial to the final project report evaluation. For SLO-5, students reported on individual and group findings through effective preparation and presentation of group posters, and their poster presentations and active involvement in this process demonstrate their achievement (Appendix 6).

RCR education is key to helping trainees create a solid scientific foundation and to improving research integrity (32). Due to the nature of CUREs, it is crucial for students to be introduced to scientific research and RCR, including authorship (33–35). In numerous instances, a CURE is a student's first exposure to and experience with scientific research (36). Module content and activities were specifically designed to introduce students to these topics during their training and research in the GENE-CURE. For SLO-2, students engaged in training focused on RCR and their active participation and successful completion of the training demonstrate their understanding and assessment of RCR issues in the context of science and scientific research.

## Potential applications and modifications

The diverse nature of teaching ecosystems should be considered when planning to implement a CURE, including the GENE-CURE curriculum. This highlights the need to consider various educational contexts and the potential variations that may affect the applicability of the study's framework in different educational settings. Specific factors encompass variations in educational institutions, curriculum structures, student demographics, and available resources. We emphasize the importance of recognizing and understanding these factors when considering the implementation of the framework. To facilitate effective implementation, we provide insights into potential adaptations or modifications needed to tailor the framework to different educational settings. These adaptations may involve adjusting the curriculum to align with specific SLOs for a course, customizing teaching strategies based on student demographics, and considering available resources and technological support.

Numerous modifications are possible depending on the SLOs, research outcomes, and course sequencing. As such, alternative experimental methods can be employed to introduce different scientific skills. For example, the bioinformatic experimentation module can be expanded to include protein modeling experiments to examine the potential structural impacts of VUS on human and/or nematode proteins. A modified version of this GENE-CURE was executed for an undergraduate bioinformatic course (8 students) and a graduate genetics course (15 students), with a focus on assessing the potential structural impact of identified VUS through protein modeling.

Depending on student progress and course sequencing, there are a few experimental tasks that can be modified for student enrichment or with instructor support. For example, students can design their oligonucleotides to move into the "wet lab" sessions. However, if students are slower to progress to a conserved VUS locus, the instructor can design oligonucleotides for students to advance into these experiments quickly. Also, students who advance their projects beyond the genotyping assay can be given the opportunity to design an RNA guide for CRISPR-Cas9 targeting of the VUS region in *C. elegans*.

Just as with scientific research, the GENE-CURE will evolve with students' discoveries as conclusions are drawn and new questions emerge. In the coming year, it will transition to allow future students to generate CRISPR-Cas9-engineered *C. elegans* VUS models based on previous students' findings. This will allow for further investigation of VUS models with *in vivo* functional assays to decipher significance. The GENE-CURE has also spurred independent research projects and fostered mentored research allowing students to continue exploring their research question and gain a broader exposure to scientific research.

## ACKNOWLEDGMENTS

This work represents the GENE-CURE offered in the Department of Biology at Jax State. We are thankful for funding from Jax State Graduate Studies for a Graduate Teaching Assistantship (NRF) and College of Science and Mathematics for an Innovative Teaching Grant (ANT). A special thanks to all the amazing undergraduate students who conducted research in the GENE-CURE.

Financial support was provided by the Department of Biology and College of Science and Mathematics. Sources of support were provided by the Graduate Teaching Assistantship, Jacksonville State University Graduate Studies (NRF), Innovative Teaching Grant, College of Science and Mathematics, Jacksonville State University (ANT), and Department of Biology, Jacksonville State University.

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## ADDITIONAL FILES

The following material is available online.

### Supplemental Material

**Supplemental material (jmbe00078-23-s0001.pdf).** Full supplemental text, figures, tables, and legends.

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