Development of a Course-Based Undergraduate Research Experience to Introduce Drug-Receptor Concepts

Hollie I. Swanson  
*University of Kentucky, hswan@uky.edu*

Ok-Kyong Park-Sarge  
*University of Kentucky, ok-kyong.park-sarge@uky.edu*

Thushani Rodrigo-Peiris  
*University of Kentucky, thushrodpeiris@uky.edu*

Lin Xiang  
*University of Kentucky, lin.xiang@uky.edu*

Vincent M. Cassone  
*University of Kentucky, vincent.cassone@uky.edu*

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Development of a Course-Based Undergraduate Research Experience to Introduce Drug-Receptor Concepts

Hollie I. Swanson¹, Ok-Kyong Park Sarge², Thushani Rodrigo-Peries³, Lin Xiang³ and Vincent M. Cassone³

¹Department of Pharmacology and Nutritional Sciences, University of Kentucky, Lexington, KY, USA. ²Department of Physiology, University of Kentucky, Lexington, KY, USA. ³Department of Biology, University of Kentucky, Lexington, KY, USA.

ABSTRACT: Course-based research experiences (CUREs) are currently of high interest due to their potential for engaging undergraduate students in authentic research and maintaining their interest in science, technology, engineering, and mathematics (STEM) majors. As part of a campus-wide initiative called STEMcats, which is a living learning program offered to freshman STEM majors at the University of Kentucky funded by a grant from Howard Hughes Medical Institute, we have developed a CURE for freshmen interested in pursuing health care careers. Our course, entitled “Drug-Drug Interactions in Breast Cancer,” utilized a semester-long, in-class authentic research project and instructor-led discussions to engage students in a full spectrum of research activities, ranging from developing hypotheses and experimental design to generating original data, collaboratively interpreting results and presenting a poster at a campus-wide symposium. Student’s feedback indicated a positive impact on scientific understanding and skills, enhanced teamwork and communication skills, as well as high student engagement, motivation, and STEM belonging. STEM belonging is defined as the extent to which a student may view the STEM fields as places where they belong. The results obtained from this pilot study, while preliminary, will be useful for guiding design revisions and generating appropriate objective evaluations of future pharmacological-based CUREs.

KEYWORDS: course-based research experience, inquiry-based learning, pharmacology

Introduction

Course-based research experiences (CUREs) are currently receiving considerable attention given their potential for providing authentic research experiences and also allowing students to enhance their scientific understanding and develop core competencies required for successful STEM endeavors and careers in the 21st century.¹ These courses are designed to ensure that students engage in the same type of work typically performed by working scientists. In the majority of the CUREs implemented within undergraduate institutions, a number of common features are utilized, which include (1) reading and evaluating the literature, (2) selecting or designing methods, (3) collecting novel data, (4) analyzing results, (5) working collaboratively, and (6) presenting results outside the classroom setting. A CURE is distinguished from an independent laboratory experience by the fact that it involves many students who are mentored by a single or a few instructors, is typically open enrollment, and restricts students’ time to specific class periods.²

The overall goals and thereby the strategies of a CURE seek to generate a set of interconnected short-term, medium-term, and long-term student outcomes.¹,² For example, short-term outcomes such as increased content knowledge, analytical, and technical skills would lead to the medium-term outcomes of increased self-efficacy and comfort level of STEM. Short-term outcomes such as enhanced communication and collaboration skills that result from collaborative work with peers and faculty, sharing of results and giving presentations, together with a supportive environment and increased project ownership, would lead to an increased sense of belonging to a larger STEM community. These collective outcomes in-turn would lead to medium-term outcomes such as increased motivation in science and increased tolerance for obstacles. Finally, these medium-term outcomes will lead to the long-term outcomes such as enhanced science identity, career clarification/decisions, and persistence in science. Thus, by participating in a CURE during their initial, freshman year, students may gain notable progress primarily toward these short-term and medium-term outcomes, which in the longer term could influence their interest in the STEM field and their pursuit of STEM-associated careers.¹,²
The success of a CURE often hinges on the extent to which the research question addresses issues that are of relevance to the student. Drug–receptor concepts, which form the foundation of pharmacology, provide an excellent source for developing authentic research with immediate application to real-life situations. For example, by using a specific patient scenario involving a typical drug–disease paradigm, an instructor may be able to better engage students who have friends or family members sharing these patient attributes. Thus, by addressing a pharmacological based question, an appropriately designed CURE can be of high personal relevance that is useful for eliciting engagement and enthusiasm by the students. This should ultimately result in the retention of students within STEM majors and promote their interest in pursuing science careers. In addition, the research projects should have a reasonable scope, be feasible, involve the process of discovery, and generate data that the students can interpret. Areas of pharmacological research that best align with the desired attributes of CUREs include those that query how different drugs bind and activate a variety of receptors, how genetic polymorphisms may contribute to patient-to-patient variations in drug response, and how the administration of a combination of drugs can contribute to drug–drug interactions.

Educators often encounter a range of problems when attempting to incorporate a CURE into the undergraduate curriculum, such as ensuring high student involvement, maintaining a relatively low laboratory cost, implementing the laboratory activities within a reasonable (ie, 3–4 hours/week) period of time, and designing learning tasks that align with the skill level achievable by minimally experienced undergraduate students. Some reports indicate that the costs associated with course-based research are cost neutral in some institutions and typically less than that of independent research experiments. In considering these costs, however, it is essential that the costs associated with the course should be reconciled with not only the cost recovery to be gained via increased student retention but also the overall benefits to the students, and to society as a whole through contributions to health care research. The most common barrier reported by faculty is the lack of time available for developing new research experiences. In addition, faculty at research-intensive universities also cite class size and number of sections as important barriers to the implementation of a CURE. Interestingly, instructor resistance, lack of administrator support, lack of facilities, and issues pertaining to student evaluations, content, or assessment are not considered to be significant barriers. Other faculty perspectives include positive benefits associated with teaching a CURE versus a traditional laboratory course such as an improved alignment of their teaching and research responsibilities and a more enjoyable teaching experience.

Among the best-known CUREs currently implemented by over 70 institutions is the SEA-Phage (Science Education Alliance-Phage Hunters Advancing Genomics and Evolutionary Science) course where students isolate and identify novel bacteriophages. Similar CUREs exploit the many attributes of model organisms such as *Drosophila*, zebrafish, and yeast, given the relatively low costs associated with their maintenance and their amenability to genetic and pharmacological manipulations. Carefully selected pharmacological and drug–receptor-related research using yeast as the model organism not only incurs low costs but can also be easily manipulated by undergraduate students who are research novices. Additionally, yeast enables the research project to progress relatively quickly during the course of a semester due to its relatively short generation time and the ease by which it can be handled by all students with a wide range of skill levels and thereby facilitating high engagement of all students. Thus, drug–receptor-based pharmacological research using yeast cultures provides an ideal platform for developing a successful CURE.

This manuscript reports on the design and outcomes of a CURE that incorporates inquiry-based learning and pharmacological principles, such as receptor–ligand interactions and dose–response relationships using yeast as a model system. The student population of particular focus for this course was freshmen who selected this research section among other biomedical and nonbiomedical STEM research projects to meet their freshman research requirement as part of a recently initiated program at the University of Kentucky called STEMcats. This cohort of students formed the first intake of the program in the 2014–2015 academic year. Supported by a 5-year grant from the Howard Hughes Medical Institute, STEMcats is a program aimed at improving STEM freshman persistence, academic success, career diversification, and student diversity. The postcompletion short-term and medium-term outcomes measured here pertain primarily to the student perceptions on the extent to which the research experience contributed to the student’s scientific and experimental knowledge and expertise, communication, and teamwork skills, as well as motivation for STEM and sense of belonging to the STEM fields.

**Methods**

**Class characteristics and participant composition.** The class, BIO 199, is a 1-credit hour research experience with approximately 3 hours of class-related work per week (ie, time commitment equivalent to a 1-credit hour laboratory course). In the 2015 Spring semester, BIO 199 offered 16 sections (ie, 16 life sciences-related authentic research projects led by faculty members from the Department of Biology, College of Medicine [COM], and College of Agriculture) to the freshman cohort in the STEMcats program. In the second semester of their freshman year (ie, Spring semester), each participant of the STEMcats program is required to enroll in one authentic research project guided by one or a few faculty members. Students in the program who are majoring in an array of STEM majors, such as Biology, Chemistry, Earth
and Environmental Sciences, and Physics, selected to enroll in a BIO 199 research section or in an alternative engineering, chemistry, or earth and environmental sciences research section of a similar format.

The present study involved students enrolled in five biomedical sciences research projects (ie, five sections of BIO 199) offered in the COM. Each section contained 7–11 students. The pharmacology-related research project was one of these five sections and was entitled “Drug–Drug Interactions in Breast Cancer” or “Drug–Drug Interactions” section. Ten students, nine female and one male, were enrolled in the Drug–Drug Interactions section with six biology majors, two chemistry majors, one premedical laboratory major, and one biotechnology major. The class was guided by two faculty instructors and one senior undergraduate instructional assistant. The class meetings occurred twice a week (Tuesday 2:00–3:50 pm and Thursday 2:00–2:50 pm) in the research laboratory of one of the faculty instructors. The materials for this project cost approximately $1,000 in total for the semester for all 10 student participants, while all the laboratory equipment needed for the experiments were already available in the faculty instructor’s research laboratory.

Course design. The course was designed to provide inquiry-based learning and allow the students to collaboratively participate in original research. Class meetings typically involved a 2-hour laboratory-based activity and a 1-hour follow-up discussion session. As shown in Table 1, during the first part of the semester, the students engaged in instructor-led discussions on biomedical research, breast cancer, hypothesis testing, laboratory safety, and ethics. During the next module, they participated in laboratory exercises that were designed to help them develop teamwork and basic laboratory skills required for molecular biology approaches. Working in pairs, the students recorded the weights of a variety of substances including candy-coated chocolate and albumin. To enhance pipetting skills, they recorded the weights of a range of increasing volumes of water. In addition, they performed serial dilutions of albumin (dissolved in water), recorded the absorbance of each sample, generated a standard curve, and identified the concentration of an unknown sample prepared by the instructor. Finally, they prepared solutions such as Luria Broth and became familiar with autoclaving and how to use sterile technique.

After a brief discussion on the basic concepts of molecular cloning and relevant laboratory protocols, the students isolated plasmid DNA from a bacterial culture (using the Zippy™ Plasmid Miniprep kit; Zymo Research), performed restriction digests and visualized the digests using an agarose gel stained with ethidium bromide. The class then compared different plasmid maps to identify the map that correctly corresponded to the results obtained from their restriction digests.

Inquiry-based learning was then incorporated into the second module of the course (ie, during week 8 and onward). The general principles of pharmacology that were covered in this module included receptor theory, agonists, antagonists, and dose–response relationships. The instructors first described the role of estrogens in breast cancer, how estrogens activate the estrogen receptor (agonists) and increase the growth of breast tumor cells and how estrogen receptor antagonists, like tamoxifen, inhibit their growth. They explained that these key observations provided the rationale for our current use of estrogen receptor antagonists to treat breast cancer. The students were asked to share an experience of a friend or relative who had been diagnosed with breast cancer. Next, they were asked to identify scenarios wherein a breast cancer patient undergoing tamoxifen treatment may develop disease conditions that would also require treatment. The students identified disease conditions such as depression, heart disease, diabetes, and epilepsy. The students were then asked to investigate what types of drugs may be used to treat these other disease conditions and consider whether patients may also decide to take dietary supplements. The instructors

<table>
<thead>
<tr>
<th>WEEK</th>
<th>MODULE</th>
<th>ACTIVITY</th>
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<tbody>
<tr>
<td>1</td>
<td>Biomedical research and breast cancer</td>
<td>Discussion</td>
</tr>
<tr>
<td>2</td>
<td>Hypothesis testing</td>
<td>Discussion</td>
</tr>
<tr>
<td>3</td>
<td>Laboratory safety and ethics</td>
<td>Discussion</td>
</tr>
<tr>
<td>4</td>
<td>Laboratory skills</td>
<td>Wet laboratory and calculations</td>
</tr>
<tr>
<td>5</td>
<td>Principles of molecular biology</td>
<td>Discussion</td>
</tr>
<tr>
<td>6, 7</td>
<td>Plasmid preparation and analyses</td>
<td>Wet laboratory</td>
</tr>
<tr>
<td>8</td>
<td>Yeast as a model organism</td>
<td>Discussion</td>
</tr>
<tr>
<td>9</td>
<td>Steroid receptors, agonists and antagonists</td>
<td>Discussion</td>
</tr>
<tr>
<td>10</td>
<td>Study design and task assignment</td>
<td>Discussion</td>
</tr>
<tr>
<td>11–14</td>
<td>Characterizing estrogen ligands in yeast</td>
<td>Authentic research and calculations</td>
</tr>
<tr>
<td>14–16</td>
<td>Data analysis and poster preparation</td>
<td>Group work</td>
</tr>
<tr>
<td>16</td>
<td>Poster presentation</td>
<td>Group presentation</td>
</tr>
</tbody>
</table>
introduced the class to recent studies reporting on drugs such as dobutamine and phenytoin that are used to treat heart failure and epilepsy respectively, which may interfere with a patient’s response to drugs such as tamoxifen.\textsuperscript{10,11} Similar events may also occur when patients are coadministered tamoxifen and nutritional supplements containing phytoestrogens such as liquiritigenin.\textsuperscript{12} The instructors explained that this type of competition of drugs for binding to the estrogen receptor may lead to drug–drug interactions. After some discussion, the students were asked to describe experiments that they could perform to test the hypothesis that the coadministration of dobutamine, phenytoin, or liquiritigenin may interfere with the ability of tamoxifen to block the estrogen receptor and thereby inhibit the growth of breast tumors. The students suggested that studies could be performed in human patients, laboratory animals, cultured cells, and model organisms such as yeast. The instructors encouraged the students to consider the limitations and challenges associated with each experimental paradigm. The instructors pointed out that using yeast that expressed estrogen receptor $\alpha$ to test their hypothesis had many advantages for the class project including its low cost and ease of manipulation. In addition, use of a yeast-based approach would provide the students with an ability to quickly obtain quantitative data.

After some discussion, the class then agreed to test the hypothesis using yeast that expressed estrogen receptor $\alpha$ and the estrogen receptor response element (ERE)-driven $\beta$-galactosidase reporter gene.\textsuperscript{13} The students examined the figures shown in the Miller et al\textsuperscript{11} and were asked to predict their results if they cultured the yeast with increasing concentrations of 17$\beta$-estradiol, tamoxifen, 17$\beta$-estradiol+ tamoxifen, or 17$\beta$-estradiol+ tamoxifen and the addition of dobutamine, phenytoin, or liquiritigenin. They were also asked to identify negative and positive controls for their experiments. The instructors then organized the class into teams of two. When they reached the laboratory, each team treated the cultured yeast suspension with a specific drug combination (assigned by the instructor), which included increasing doses of an estrogen receptor $\alpha$ agonist (17$\beta$-estradiol), increasing doses of an estrogen receptor $\alpha$ antagonist (tamoxifen), and varying combinations of dobutamine, phenytoin, or liquiritigenin. Each team also prepared samples containing the vehicle control for comparative purposes.

After determining the $\beta$-galactosidase reporter activity in each laboratory session, the students entered the data on a spreadsheet in a shared Google drive. Class discussions then focused on how to graph the data and how to calculate the standard errors for each data point. The instructors asked the students to evaluate their standard errors, consider reproducibility, and assess the extent to which the data mirrored their expected dose responses. The students agreed that since the standard errors were quite large for the majority of the data points and that they would consider the sources of variability and perform a final set of experiments. To encourage students to actively participate in data analyses and the development of the poster, the class was divided into two teams headed by a team leader and each team independently developed a poster. Each team was asked to graph the collective results obtained from the class, analyze the results, and state the conclusions. The class then compared both posters and selected the best components from each to generate their final poster. The printed class poster was presented by all of the students at a university-wide symposium on undergraduate research.

All BIO 199 sections were led by not only faculty instructors but also an undergraduate instructional assistant. The undergraduate instructional assistant, a student who was several classes ahead of the freshman students (ie, senior level), served as a near peer tutor. As a near peer tutor, the undergraduate instructional assistant was able to empathize with the learners and assist them in overcoming challenges associated with grasping key concepts.\textsuperscript{14} In the Drug–Drug Interactions BIO 199 section, the senior undergraduate instructional assistant provided aid in a number of areas. She assisted the faculty members in preparing for each laboratory session. In addition, she often facilitated communication between the faculty members and the students by providing the students with insights into her own first-time experiences with research. Finally, she served as a liaison between the Drug–Drug Interactions section and the other sections of BIO 199.

**Laboratory materials and methods.** The ability of 17 $\beta$-estradiol, dobutamine, liquiritigenin, phenytoin, or tamoxifen to either activate or inhibit estrogen receptor $\alpha$ signaling was analyzed using a yeast bioassay.\textsuperscript{13} The YCM3 yeast cells bearing a receptor-reporter (pRR) plasmid were maintained in glucose-containing medium (0.67% yeast nitrogen base without amino acids, 2% glucose, supplemented with 0.01% uracil, adenine, leucine, and histidine). The plasmid contains five copies of the EREs and is designed to express estrogen receptor $\alpha$ (under control of the galactose promoter) and the LacZ reporter gene. Immediately prior to class, the yeast cells were diluted into galactose medium (similar to the media described previously except using 2% galactose instead of glucose) to a final $A_{600}$ nm of 0.04. The diluted yeast cells were then aliquoted into 96-well plates (200 $\mu$L/well) and were treated with either the dimethyl sulfoxide vehicle control (<1%) or the chemicals of interest. The cells were placed on a laboratory rotator and incubated at 30°C. After 18–24 hours, the cell densities were read on a plate spectrophotometer ($A_{600}$ nm). Aliquots of 70 $\mu$L were placed in a separate 96-well plate and 70 $\mu$L of working solution (Yeast $\beta$-Galactosidase Assay Kit; ThermoScientific) was added. The mixtures were vortexed and incubated at 37°C for 30 minutes or until the solutions containing the positive control turned yellow. The $\beta$-Galactosidase Assay Stop Solution (56 $\mu$L) was added to each well, the plates were vortexed, and the absorbance at
420 nm was determined. The β-galactosidase activity was calculated using the formula:

\[
\beta\text{-galactosidase activity} = \frac{1,000 \times A_{420}}{t \times V \times OD_{660}}.
\]

**Assessment and Results**

**Student characteristics.** To understand the characteristics of the students who opted to undertake a biomedical sciences research project, the students from the five COM sections were assessed for their academic strengths and interests via a survey calibrated on a Likert scale at the beginning of the semester. Of the students enrolled in the five sections, 37 students responded to the survey as described in Figures 1 and 2. All survey procedures were considered by the institutional review board at the University of Kentucky (IRB protocol #15-0160-X1B), and found to be exempt from the requirement to undergo full review. This research was performed in compliance with the principles of the Declaration of Helsinki.

As shown in Figure 1A, self-reports from the students indicated strong backgrounds in Biology. Here, 33 of the 37 (89%) student respondents in the five COM courses and 7 of the 10 student respondents in the Drug–Drug Interactions section reported strong or very strong biology backgrounds. In contrast, only 8.1% (3 of the 37 respondents) and 10% (1 of the 10 respondents) of the COM and Drug–Drug Interactions sections reported strong or very strong biology backgrounds.

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**Figure 1.** Characteristics of class participants. A survey was performed to assess the scientific background and academic/professional interests of the students who enrolled in five biomedical sciences research projects/sections in the COM. The results of the survey represent students enrolled in the COM sections (number of respondents = 37) or those enrolled in the “Drug–Drug Interactions” section (number of respondents = 10). (A) Student background. (B) Student interest.
Figure 2. Student reported biomedical science knowledge level and comfort levels in communicating science. A survey was performed to assess the biomedical science knowledge level, comfort level with respect to engaging in discussions about biomedical sciences, and understanding scientific manuscripts of the students who were enrolled in five biomedical sciences research projects/sections in the COM. The results of the survey represent students enrolled in the College of Medicine (COM) sections (number of respondents = 37) or those enrolled in the “Drug–Drug Interactions” section (number of respondents = 10).
Interactions section, respectively, indicated strong or very strong backgrounds in physics. With respect to backgrounds in mathematics and chemistry, the students responded moderately, ranging from very weak to very strong. For example, 5.4% (2/37) of the respondents from all five COM sections indicated that their Mathematics backgrounds were weak while 59.5% (22/27) and 70% (7/10) of the respondents from all five COM sections and the Drug–Drug Interactions section, respectively, indicated that their mathematics backgrounds were either strong or very strong. Further, 20/37 (54%) of the respondents from all five COM sections and 5/10 (50%) of the Drug–Drug Interactions section indicated that their backgrounds in Chemistry were either strong or very strong. Thus, these results suggest that students who selected biomedical projects felt confident about their biology background, only moderately confident about their mathematics and chemistry backgrounds and the least confident about their physics background. However, it should be noted that at the University of Kentucky, most Biology majors (who constituted about 80% of the students in this research cohort of the STEMCats program) would not take physics introductory courses until their sophomore or junior years, although they take mathematics, chemistry, and biology courses during their first semester as a freshman. Therefore, their lower confidence levels in terms of their physics backgrounds may be due to the fact that their physics backgrounds were restricted to what they had acquired during their high-school preparation.

With respect to student interest (Fig. 1B), 100% of the student respondents in the five COM sections surveyed expressed interest in learning more about biomedical sciences. In addition, the majority of students (78.4% of the five COM sections and 90% of the Drug–Drug Interactions section) were interested or very interested in undertaking independent research in biomedical sciences. Finally, the majority (89% of the five COM sections and 90% of the Drug–Drug Interactions section) were interested or very interested in pursuing either careers in biomedical sciences or the health care professions. These results corroborate with the high demand which we experienced during student enrollment for the biomedical sciences research sections. The Drug–Drug Interactions section was among the top 4 research sections (out of a total 20 sections/research projects from diverse STEM disciplines available for STEMCats freshmen) with respect to the fastest enrollment rates and the highest student enrollment numbers. Thus, to the STEMCats freshman cohort that consisted of approximately 80% biology majors and approximately 12% chemistry majors, the Drug–Drug Interactions section appealed well, and attracted a group of students who are highly interested in pursuing careers in the fast-expanding health care field that is projected to have a severe shortage of an educated workforce in the near future.15

The students were also questioned on their biomedical science knowledge and comfort level in communicating biomedical science (Fig. 2). The majority of students of all COM sections (ie, 29/37) and 5/10 of the Drug–Drug Interactions section reported that they were either somewhat knowledgeable or knowledgeable about biomedical sciences. With respect to engaging in discussions about biomedical sciences and reading and understanding scientific manuscripts, 29/37 (78.4%) of student respondents in all COM sections and 3/10 (30%) in the Drug–Drug Interactions section were either somewhat comfortable or very comfortable. Finally, only approximately half (21/37 of the COM sections and 5/5 of the Drug–Drug Interactions) admitted to being either somewhat comfortable or very comfortable with respect to reading and understanding scientific manuscripts.

The student self-reported, assessment outcomes from the Drug–Drug Interaction section are shown in Figure 3. These outcomes were anonymous and submitted by the students upon their completion of the course. All of the student respondents (7/7) responded favorably (either somewhat agree, agree, or strongly agree) to all of the survey statements. With respect to short-term outcomes (Fig. 3A), all of the student respondents (7/7) either agreed or strongly agreed that the course improved their scientific thinking, enhanced their critical thinking skills, and provided a supportive environment. In addition, a majority of students (6/7) responded to either agreed or strongly agreed that the course improved their experimentation skills, enhanced their knowledge in scientific communication, improved their comfort level with faculty, enhanced their sense of belonging to the field of STEM, and improved their understanding of scientific concepts. Finally, five out of seven students either agreed or strongly agreed that the course enhanced their skills in teamwork and troubleshooting. With respect to medium-term outcomes (Fig. 3B), the majority of students either agreed or strongly agreed that their participation in the course enhanced their motivation/enthusiasm for STEM (6/7), enhanced their motivation for discovery (7/7), and improved their comfort level with STEM (6/7).

A few of the student comments are shown in Table 2 to elaborate their ranking. According to these postcompletion student self-report results, the Drug–Drug Interaction section was notably successful in achieving the tested key short-term and medium-term student outcomes that have been previously described for CUREs.1,2 Accordingly, with the progression of time in the undergraduate degree, it could be expected that this freshman research experience may contribute to desirable long-term student outcomes such as enhanced science identity, career decisions, and persistence in science of the students who participated and favorably contribute to the future STEM and health care workforce.

**Discussion**

In this pilot study, we present the design and student-reported outcomes of a CURE that allows freshman students to experience research related to pharmacology. Better incorporation of certain aspects of pharmacology into the undergraduate STEM curriculum can be used within a CURE to improve
the quality of research questions addressed via enhancing personal relevance and/or importance to society.\(^7\) Many aspects pertaining to the discipline of pharmacology coincide with the necessary attributes that define a successful CURE, such as relevance to society to elicit student enthusiasm and the ability to design projects that are engaging and of high educational value, yet within the scope of what’s achievable with the limited time of a CURE and the minimal experience level of undergraduate freshmen. Despite this, pharmacology is currently underrepresented in the typical STEM undergraduate curriculum. Several contributing factors likely include lack of faculty expertise, lack of institutional support, and a lack of models to be used for incorporating pharmacological principles that can be used for designing an effective CURE.\(^{16}\) Some of these barriers can be overcome with the development of collaborative faculty consortiums, modifications of campus infrastructure, faculty incentives, and evidence that student participation in a CURE significantly improves learning.

The study reported herein provides insights for a possible blueprint for designing an effective CURE based on pharmacological principles using yeast as the model system and also provides suggestive evidence of improved student learning and other desirable outcomes elicited through this

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**Table 2. Sample student comments.**

<table>
<thead>
<tr>
<th>FROM EVALUATIONS AT THE END OF THE DRUG–DRUG INTERACTIONS LABORATORY CLASS</th>
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<tbody>
<tr>
<td>- I liked the experience it gave me in a lab. I also liked how it introduced me to a lab and important techniques that I will need if I continue research.</td>
</tr>
<tr>
<td>- I liked that I got to experience things that I had never done before.</td>
</tr>
<tr>
<td>- I liked that I got to work with my classmates on this project.</td>
</tr>
<tr>
<td>- I liked that there was guidance, but at the same time, we were able to formulate our question and work to solve it.</td>
</tr>
</tbody>
</table>

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**Figure 3.** Assessment of the Drug–Drug Interactions in Breast Cancer section. An anonymous survey was administered to the students enrolled in the Drug–Drug Interactions in Breast Cancer section upon completion of the course. Results of the respondents \((n = 7)\) are summarized. (A) Short-term outcomes. (B) Medium-term outcomes.
freshman experience. While pharmacology is traditionally introduced with considerable breadth and depth in undergraduate medical education and doctoral programs, the trend of the former toward an abbreviated 3-year premedical curriculum (as opposed to a 4-year premedical curriculum) as well as an increasing emphasis on clinical skills may lead to an underappreciation of pharmacological principles by practicing physicians. Thus, a student’s participation of a pharmacology-based CURE while completing their undergraduate degree may address this potential gap in knowledge and serve as a foundation with which to build a successful career in the health care professions.

During the Drug–Drug Interaction Course, the students learned how to design an experiment that would be performed by a typical pharmacologist, which would include use of positive and negative controls, identifying issues pertaining to receptor specificity, use of increasing doses of drugs, constructing and comparing dose–response relationships, as well as basic concepts related to drug–drug interactions. However, near the completion of the course, as students began to submit written work to be incorporated into their poster presentation, it became clear that the students’ ability to grasp concepts related to steroid receptor pharmacology was incomplete. Further, our study design of the course detailed in Table 1 was not sufficient for allowing necessary replicative studies and substantial data analyses by the students. Thus, in future offerings, the course design will be modified to delete the 3-week period involving introduction to general molecular biology (ie, weeks 5, 6, and 7 depicted in Table 1) and expanded to focus primarily on the yeast-based assays with more time allotted for replicative studies, extensive data analysis, and understanding related concepts including steroid receptor pharmacology. The practice modules of basic molecular biology techniques that were intended to provide the students with a pretraining of the necessary skills using mock material was helpful to minimize errors and increase efficiency during subsequent experimental research. However, we felt that, particularly in the interest of time, this training could be provided in combination with using the real experimental platform, instead of mock material used in the current offering. Additional future modifications will include enhancing the active role of the student such that the students, rather than the instructors, lead the majority of the discussions to not only enhance their engagement in the course but also facilitate and formatively assess in-depth understanding of pharmacological concepts. With the incorporation of these modifications, minimizing the breadth of the experimental methodology and enhancing the active role of the student, the staffing needs of this CURE could easily be reduced.

As previously described,1,2 the overall design of this course closely resembled the CURE logic model. Landmark references on the assessment of CUREs recommend that the short-term outcomes of a CURE should include evaluation of scientific knowledge and skills, ownership of research, interaction with the faculty, collaboration with peers, communication skills, and a sense of belonging to a larger community. Short-term outcomes can be evaluated at any point during a CURE or upon completion of a CURE.1 Medium-term outcomes that are typically assessed upon completion of a CURE include measures of motivation, self-efficacy, and tolerance for obstacles. In the drug–drug interaction project reported here, some of these key short-term and medium-term student outcomes were evaluated using their self-reported ratings (Fig. 3). Long-term outcomes that would ultimately provide measures relevant to retention in the STEM major and persistence in science would measure increased socioemotional support, enhanced science identity and career clarification, and increased ability to navigate uncertainty. A longitudinal research study of the students who participated in our study with respect to these outcomes could reveal insights on long-term impacts of this freshman research experience on their future academic and professional decisions.

In considering the data presented in Figure 3, it should be noted that they represent self-reports from a limited number of students and that these outcomes were evaluated primarily using single questions rather than using a validated assessment. While the assessment of student learning used in institutions of higher education typically rely on student self-reports, their use is plagued by a number of biases and errors that pertain to the psychological processes involved in a student’s response.17 This includes varying comprehension of the language or phrases used in the survey questions, difficulties in the retrieval of memories that allow them to estimate their previous skills as well as judge the completeness and relevance of these memories and finally, biases that can alter how a student selects a response option. Future work will be focused on addressing these problems by using a validated instrument for student self-reports (eg, the Undergraduate Research Student Self-Assessment18 and Survey of Undergraduate Research Experiences19) coupled with the Biological Experimental Design Concept Inventory20 to assess student thinking in experimental design. In addition, knowledge assessment administered as a pre-test and post-test’ could be utilized to query for knowledge of the basic pharmacological concepts covered in this course (receptor theory, agonists, antagonists, and dose–response relationships). Other assessment tools that will also be considered include those proven to be effective in evaluating other CUREs and involve oral interviews and problem-sorting tasks.21

A recent meta-analysis of the published literature pertaining to inquiry-based learning and teaching experiences in undergraduate biology has revealed that overall, these experiences result in learning gains that are higher than those achieved in more traditional courses.18 However, the majority of studies examined did not use published, validated instruments. Further, the reported inquiry-based learning and teaching experiments focused primarily on upper level courses in biochemistry, cell biology, developmental biology, genetics,
and molecular biology with few reporting on outcomes from introductory courses. Thus, the ability to appropriate assess a student’s understanding of key fundamental concepts of each scientific discipline requires that concept inventories specific for these disciplines be carefully constructed using established best practices in concept and inventory design at a level appropriate for each learning stage. Similar to that of biology and physiology, the discipline of pharmacology would benefit from the development of concept inventories which could then be used to guide the assessment of conceptual understanding of key pharmacological principles in CURE and other types of classwork.

Conclusion
In conclusion, the results reported herein represent an important first step toward incorporating pharmacology into a freshman research experience and provide insights on designing a CURE based on drug–drug–receptor interaction pharmacology. The lessons learned indicate that this new inquiry-based curriculum is accomplishing its major goals, but additional steps toward improving the course design and assessment methods should be taken to improve student outcomes and appropriately determine its ultimate impact on student learning.

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Author Contributions
Conceived and designed the experiments: HIS and OKPS. Designed the outcomes assessment surveys: HIS, OKPS, TRP, and LX. Analyzed the data: HIS. Wrote the first draft of the manuscript: HIS. Contributed to the writing of the manuscript: HIS, OKPS, TRP, LX, and VMC. Agree with the manuscript results and conclusions: HIS, OKPS, TRP, LX, and VMC. Jointly developed the structure and arguments for the paper: HIS, OKPS, TRP, LX, and VMC. Made critical revisions and approved final version: HIS, OKPS, TRP, LX, and VMC. All authors reviewed and approved of the final manuscript.

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