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CRISPR CUREs: Running with Molecular Scissors in the Classroom

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Introduction

As undergraduates, science students receive the educational foundation required for their future STEM careers. They build their knowledge base of basic science concepts, as well as learn hands-on skills that will help them in their future fields [1,2]. Often, this education is transmitted through lectures and teaching labs, where students play a passive role. However, undergraduate research experiences can serve as a more enriching alternative to such methods by combining biological concepts with laboratory skills in the context of novel scientific discovery [1,3]. Due to this, many undergraduate courses are incorporating discovery-based research into their curricula.

Such classroom undergraduate research experiences, or Course-Based Undergraduate Research Experience (CUREs), expose groups of students to research in the classroom. This approach to an undergraduate research experience benefits more people than selective internships, allowing the research community to become more inclusive and diverse [1,2]. In addition, implementing CUREs in introductory courses exposes students to research earlier than summer internships, which typically take place later in their college careers [1]. As a result, CUREs can heavily influence students' academic interests, and a good CURE experience can result in increased retention rates in STEM majors and careers [1,3,4].

During a CURE, students use basic science practices to complete novel, relevant, collaborative research, which the student is required to present in some form at the end of the course [1]. This creates a learning experience that does not only impart knowledge, but also teaches students important scientific skills like asking impactful questions, forming hypotheses, gathering and analyzing data, and drawing conclusions from their work [1,3]. In addition, students also gain an aptitude for problem solving and independent work, equipping them well for future endeavors whether they choose a scientific career, or not [3]. Though CUREs are rigid in the components they should contain, they are flexible when it comes to the research included within their framework [1]. This allows instructors to customize CUREs to reflect their own research, 3 maximize impact on both the students as well as the scientific community, and include the use of cutting-edge technologies, such as CRISPR/Cas9 gene-editing.

As CRISPR methods have developed over the past few years, it becomes apparent that CRISPR has the potential to revolutionize science education [5]. The simplicity of the CRISPR system lends itself particularly well to undergraduate research experiences, allowing students possessing only basic laboratory skills to participate in CUREs [4,6]. Additionally, CRISPR can be used on a variety of model systems [4,6-10] which allows institutions to develop CRISPR-based labs around the model systems and resources already present, rather invest in specific systems tailored to less inclusive technologies. Likewise, CRISPR has a wide range of research applications, permitting its use to fold seamlessly into whatever research is already occurring at an institution, as well as allowing students to customize their projects to fit their interests [4,8].

In recent years, the many benefits of CRISPR have led to its integration in undergraduate classrooms. Specifically, classes in microbiology and genetics seem to benefit the most from the use of this technology, as it imparts a skill set conducive to both fields [6-10]. Current CRISPRbased CUREs tend to follow one of two general approaches, either exploring the in vivo implications of CRISPR as an adaptive immune system in bacteria, or examining the downstream applications of CRISPR as a genome-editing technique [6-10]. The former approach is demonstrated in multiple published CUREs implemented by the State University of New York at Geneseo as well as the Université Laval in Quèbec, Canada. Both programs focus on the presence of CRISPR in the context of microbiology, aiming to teach students about bacterial immunity and microbiology lab techniques [6,9,10]. In the Geneseo program, students were tasked with identifying CRISPR loci in previously uncharacterized field strains of *E. coli* [10]. Similarly, the CURE presented by the Université Laval involves the selection of *S. thermophilus* strains 4 with CRISPR-immunity based on their survival of a challenge with a lytic phage [6,9]. Both courses teach culturing techniques, DNA isolation and purification, PCR, and bioinformatics, as well as general scientific techniques like writing lab reports and communicating science [6,9,10]. Similar techniques are also present in genetics-focused CRISPR CUREs. Programs implemented by the University of Alabama at Birmingham and the University of New Mexico allowed students to create specific mutations in zebra fish and Drosophila model systems. These programs required students to execute a CRISPR protocol from the selection of the desired mutation, to the assembly of required CRISPR reagents, to the screening of injected organisms for desired phenotypes [7,8]. The Alabama program is particularly notable for its promotion of faculty-student collaboration, as the genes edited by students were all of interest to active research at their institution [8].

Another benefit of utilizing CRISPR in undergraduate research is the bevy of ethical implications unearthed by its use in scientific experimentation. Because CRISPR allows scientists to manipulate the genome of various organisms, including human embryos, many concerns have been raised about how CRISPR should be regulated and where gene editing crosses the line between groundbreaking and pernicious [4]. Undergraduate researchers can learn a great deal from this debate, both about the implications of the CRISPR system, as well as how to deal with the implications of their own work in the future.

CRISPR is an excellent technique to include in CURES teaching microbiology, evolutionary biology, molecular biology, and genetics. Students who participate in these CRISPR-based CURES report a great satisfaction with the immersive style of teaching as well as the ability to use cutting-edge technology in their work [8,10]. Particularly, students surveyed mentioned the potential impact of their work as a powerful motivating factor for their interest in 5 the class, as well as the research they were conducting [8]. The use of CRISPR in the classroom can nurture scientific interest among students, as the possible research implications of genome editing are vast and untapped. The development of CRISPR methods has, and will continue to enhance undergraduate science education by integrating a revolutionary scientific technique into the early stages of students' careers [9].

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