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CRISPR In A Box™ and the Journey Toward Inspiring New Scientists

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It all started with a call from ChristianaCare's Gene Editing Institute to Delaware Technical Community College looking for a potential student that could help do beta testing on a CRISPR kit. That plan expanded to a National Science Foundation (NSF) grant and an educational kit called CRISPR In A Box™ (see Figure 1). The goal was to test a kit that was very complex and had many moving parts to demonstrate gene editing, but before we got to the fancy experiments, we had to prove that the basic principles of gene editing could be done successfully in a simple microorganism. It was this proof-of-principle experiment that drove the two institutions to submit an NSF grant, which was awarded, called Technical Training in Gene Editing (TTiGE) (NSF ATE DUE awards #1700660 and #2000696).

Figure 1. CRISPR in a Box™

The grant is designed to teach community college instructors how to incorporate the topic of gene editing into their curricula and give their students a hands-on demonstration. In 2017, CRISPR/Cas gene editing was still a new tool, and most academic institutions were not yet including CRISPR technology discussions into their classes; however, the science is advancing so rapidly that STEM students are going to start seeing CRISPR/Cas technology in their careers

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whether or not it is taught to them. In 2020, the Nobel Prize in Chemistry was awarded to Jennifer Doudna and Emmanuel Charpentier for developing the CRISPR/Cas method for genome editing – the first women to be awarded the prize without a male counterpart.

The TTiGE grant allows me to work as the Science Educator where I am housed at the Gene Editing Institute (GEI) to watch, listen, and learn everything I can about CRISPR. I get to determine if any possible experiments or scientific discoveries can be adapted into laboratory exercises that students and teachers could study in their classrooms. It was during this time that GEI was creating a gene editing platform to study and understand the mechanisms of CRISPR/Cas reactions. The *in vitro* gene editing system is a simple reaction using common biological techniques and a cell-free extract that allows the users to conduct the experiment on the benchtop without expensive equipment. The cell-free system allows for students to do the reaction "in a tube" rather than the typical technical setting of a living cell. It is this experimental reaction that led to a renewal of the NSF grant as well as the production of an educational kit – CRISPR In A Box™.

CRISPR In A Box™ is a fully inclusive gene editing laboratory exercise educational kit that can be implemented into a variety of educational settings including high schools, community colleges, and four-year universities (Figure 2). The primary experiment is based off the *in vitro* gene editing reaction where students will be able to see their results with a blue-to-white color change on a bacterial plate. While the GEI uses the *in vitro* reaction to study the mechanisms of CRISPR, students can use that same reaction to experience an innovative gene editing reaction in their classroom.

Figure 2. St. Georges Technical School was the first school to teach the CRISPR in a Box™ gene editing experiment in March 2021.

One important feature of CRISPR In A Box™ is that the students will be gene editing a plasmid, a small circular piece of DNA that can be expressed in bacteria, without actually modifying the bacteria. There are many moments within this kit's experimental process that can help facilitate the learnings of a biological system, but the most relevant aspect is the kit's ability to have a diverse readout at the end of the reaction. In gene editing, the final result of an experiment is not

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often a yes or no answer. Some parts of CRISPR may work perfectly, but overall, perfection is not regularly achieved in the field yet. This kit is able to show an array of outcomes that are representative of the CRISPR field as a whole when gene editing is being conducted. Gene editing isn't perfect, and the students will see that within the reactions they perform, leading to the strongest "teachable moment" of them all.

At the GEI, we are using CRISPR In A Box™ to reach a variety of students that may not have previous exposure to gene editing, or even genomics/molecular biology as a subject of interest they could pursue. Our goal is to be a vehicle in bringing cutting edge science to students and communities that may not have had easy access to the fundamentals in the past. Science depends on the future scientists who will think differently and creatively to solve problems that have continuously impacted society. CRISRP/Cas is an important technology, but now we need scientists to figure out how to use that technology to make impactful changes. We hope that CRISPR In a Box™ can be used to spark the next generation of scientists' interests in gene editing.

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