INTRODUCTION

The 2020 pandemic of COVID-19 has had a devastating impact on human health, economies, cultural practices, and higher education, but it has also provided a unique opportunity to teach about microbes in a highly relevant context (1–3). Modern technology has allowed a robust and rapid research response to this virus that has not been seen in viral outbreaks in the past. Data have been made publicly available at a record rate, allowing open access to the latest results and helping to direct public health decisions (4, 5). The genome for SARS-CoV2 (causative agent for COVID-19) was sequenced and made publicly available before most of the general public even knew it existed (6–8). Professors and instructors teaching microbiology and other biology courses can capture the enthusiasm and true curiosity surrounding COVID-19 by providing engagement with scientific literature and helping students find answers for themselves (9). Free online databases make it possible for students to access cutting-edge genomic data for the virus causing COVID-19, SARS-CoV-2. With a basic introduction to genomics and bioinformatics, students can generate alignments, search for related ancestors, and discover unique mutations and sequences that make COVID-19 different from other coronaviruses. This article presents a COVID-19 case study that was generated and used during the COVID-19 pandemic and will allow students to compare genomic sequences of different coronaviruses to better understand the origin of SARS-CoV-2.

PROCEDURE

SARS-CoV-2 genome analysis case study

Case studies have been used in active learning classrooms for decades to help the learner connect course objectives with real world applications (10–12). Some courses are designed exclusively around case studies and have shown impressive learning and beneficial retention of course concepts (13). The emergence of COVID-19 surprised most of the public population and there was a lot of confusion regarding where the virus came from. This case study was developed with the following objective: to introduce bioinformatics and genomics to the students so they can compare genomic sequences of different coronaviruses to better understand the origin of SARS-CoV-2.

Students enrolled in a 300-level Microbiology course with little or no prior bioinformatics knowledge were given this case study as an online learning activity during unit 3 (viruses and infectious disease). They were given a week to work on it and were instructed to complete it individually or with a partner. The case study directed students to the National Center for Biotechnology Information (NCBI) website and the Basic Local Alignment Search Tool (BLAST) for finding genomes for four different coronaviruses: SARS-CoV-2 (COVID-19 GenBank #MN908947.3), a bat coronavirus (RatG13; GenBank #MN996532.1), the SARS coronavirus (GenBank #NC_004718.3), and the coronavirus that causes the common cold (J0304/229E; GenBank #JX503061.1). Students perform paired alignments to look at genetic similarities and differences as the genomes align. As students complete the case study handout (see supplemental material), they identify that the SARS-CoV-2 (COVID-19) genome is most similar to the bat coronavirus genome.

Students then have to scroll through the alignment in order to identify the largest difference between the bat coronavirus and the novel SARS-CoV-2 and determine which gene is affected. Upon discovery that the surface glycoprotein is the most mutated between the two genomes, several questions and learning opportunities are presented for students to think critically regarding why mutating a surface glycoprotein will affect viral transmission. Depending on the
The case study can provide great discussion points for molecular biology, immunology, virology, serology, etc. In the molecular biology course where this case study was implemented, the focus was on the viral genome, and further analysis discussed why an RNA genome would have different implications than a virus with a DNA genome.

Case studies have been implemented in this course (300-level Microbiology) for a few years. Each of the three units has a corresponding case study for the students to work through. In 2020, the usual Unit 3 case study was replaced with a case study of COVID-19 and genome alignment. Interestingly, students were very curious and much more engaged with the COVID-19 case study. Compared with the prior two case studies, the COVID-19 genome alignment learning activity had significantly more questions and student inquiries (Fig. 1A). Most of the questions were conceptual, with students inquiring deeper about the viral genome and asking what certain results mean. Additionally, students spent nearly double the amount of time on the assignment than they did on the other case studies (Fig. 1B). Although the data do not reveal whether the extra time was due to a more technical case study or due to interest and curiosity, feedback from the students indicated the extra time was not because it was harder but because they were genuinely interested and continued their search for knowledge as they worked through the questions. Student comments stated that they appreciated the COVID-19 course material and case study because it helped them understand the virus outbreak and the scientific reasoning for the pandemic and global response (Table 1).

**CONCLUSION**

This COVID-19 genome analysis case study provides relevant and very applicable hands-on opportunities for students to test out bioinformatics, genome alignments, and BLAST tools to discover real world answers for where the COVID-19 virus originated. This is a first exposure to genomics for many students, and yet, with the detailed case study handout (see supplementary material), the students were able to walk through step-by-step to find the answers. This curriculum activity can be implemented through online learning formats or in-person classrooms to teach critical molecular and genomic aspects of virology, microbiology, immunology, or any course that is relevant to COVID-19. The case study can be modified and extended to include elements of transmission, prevention, treatment, etc. Responses from students indicate that the COVID-19-specific course material was greatly appreciated.

**TABLE 1.**

| Student comments. |
|-------------------|
| “I think that it was very relevant and informative to learn about the COVID-19 outbreak in the class and outside of class. Trying to educate people with their limited knowledge of COVID-19 and being aware of its capabilities was really helpful.” |
| “I like how it offered perspective for the entry mechanism of the virus into the cell. Combined with Biochem and Genetics from last semester I feel like I knew what was happening and was very educated on attempts and efforts to help and reasons why masks, social distancing, and research are effective.” |
| “I enjoy direct applications. The COVID-19 material helped bring a sense of purpose to the material.” |

**FIG 1.** Analysis of student involvement in COVID-19 Case Study. (A) The total number of e-mail inquiries sent to the professor regarding the assigned case study ($P<0.05$). (B) The average amount of time (minutes) spent on each case study. Data determined through email analysis, blackboard analytics, and student feedback ($P<0.005$). Spring 2020 enrollment was 49 students.
and helped them understand the course objectives by providing a real world context.

As educators and scientists prepare for future semesters, it is important to consider the COVID-19 world that we are living in and understand the risks but also the great opportunities that this provides for teaching and educating students and the general public about microbiology and the power of genomic data. The world is seeking answers for COVID-19 and it is important that relevant, data-backed, and science-driven information be provided to understand SARS-CoV-2 and the resulting COVID-19.

SUPPLEMENTAL MATERIAL

Appendix 1: Genome analysis SARS-CoV-2 case study
Appendix 2: Genome analysis SARS-CoV-2 case study (answer key)

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