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Combining 3D-Printed Models and Open Source Molecular Modeling of p53 To Engage Students with Concepts in Cell Biology†

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INTRODUCTION

Students learn best when engaged, for example with student-centered learning strategies that allow them to experience concepts through multiple modes, including kinesthetically (1–4). In STEM fields, easy access to tools such as 3D printers and open-source molecular structure viewers has provided affordable and practical alternatives to engage students by allowing them to model biologically relevant entities—including molecules and electron orbitals—and their functions (5–15).

In this report, we describe the combined use of 3D-printed macromolecular models and Jmol (an open-source Java 3D molecular structure viewer) to facilitate students' engagement with molecular concepts in cancer biology. While the literature has demonstrated the individual utility of 3D-printed models and Jmol exercises in the undergraduate classroom, we chose to combine these complementary activities to deepen students' understanding of the relationship between structure and function of macromolecules through multimodal learning (16–18). This report's modules focus on the biology, structure, and function of the human p53 protein, a tumor suppressor molecule famous for coordinating DNA repair, senescence, and apoptosis and for its frequent mutation in many different types of human cancers (19). The role of p53 as a transcription factor that binds DNA and activates target gene expression exemplifies the close relationship between macromolecular structure and cellular function. Student engagement is also encouraged by the relevance and relatability of the content, including the importance of p53 to human disease states that have touched many of their lives at a personal level.

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We share two modules: one that was implemented at the undergraduate level and the other at the graduate level. To complete these modules, students used a 3D-printed model of p53 bound to DNA, its corresponding Jmol files, and database and literature searches to answer a series of questions. In the process of doing this work, students had the opportunity to review and integrate previously learned content that helped them hit the ground running with course material.

PROCEDURE

Materials

Students require access to an instructional handout (Appendix 1 or 2; answer keys for instructors are available from the authors upon request), a white 3D-printed model of p53 bound to DNA (see Appendix 3 for detailed instructions and tips), and different color paints and a brush to paint the model as indicated. Students receive their own 3D-printed p53 bound to DNA model kit (Fig. 1). Students also need a computer for access to relevant Jmol sites.

Below we describe not only the two contexts in which we have implemented these modules but additional alternatives for course implementation.

Upper-Level Undergraduate Course: Cell Biology

Our module (Appendix 1) was used as a beginning-of-the-semester take-home assignment so that students could review concepts they had learned previously through foundational biology courses, setting the stage for subsequent discussions of new cell biology course content. The worksheet was introduced and assigned during the very first class period and covered macromolecules, protein and DNA structure, and basic cellular functions. During the 2-week period provided to complete it, students reached out to the instructor for assistance as needed, kicking off the semester with open communication and conversations between instructor and students. Students ultimately turned in their assignments through the online course management

system and orally presented their findings to the class (see Appendix 1 for presentation details and options). At the end of the activity, students were encouraged to keep their 3D model to use it as a study aid for future discussions and content. We referred back to p53 several times during the course to help segue between topics or units, for example, to transition from basic macromolecular structure to how different macromolecules (e.g., proteins, DNA) can interact with one another to generate new functionalities in cellular processes, such as transcription. Other content segue examples that benefitted from this exercise included transitions from transcription to control of gene expression, from intracellular compartments to systems like nuclear protein transport, and from cell cycle and cell death to cancer. Students' engagement in the exercise provided them with a wealth of information to refer to as they strived to make connections between new content and fundamental principles of macromolecular structure and function. Some of these details are reflected in the student comments provided in Appendix 4.

Graduate Biology Course: Molecular Mechanisms of Cancer

This is a graduate-level course modeled after a published Course-Based Undergraduate Research Experience (CURE) (20). In brief, students worked in pairs to analyze different p53 missense mutations identified in one or more human tumors but not yet fully characterized. This activity (Appendix 2) was implemented in the third week of the course, after students were introduced to the molecular mechanism of p53 function. The introduction period focused on p53 regulatory elements required for transactivation and provided training in qualitative and quantitative assays (growth fitness, beta-galactosidase filter assays) to assess the ability of each p53 mutant to transactivate expression of reporter genes. The mutants worked on by the students presented different transactivation defects, enabling the students to develop hypotheses for why their mutant was defective. During the activity, students conducted DNA sequence alignments on their mutant versus normal p53 and determined the amino acid identity of their missense mutation. They then used online molecular modeling software (Jmol) to view the published structure of p53 binding to DNA. As part of this exercise, each student received their own 3D-printed p53 bound to DNA model kit (Fig. 1) and located their mutation on the painted models.

Interestingly, mutations that mapped directly to the p53/DNA interface were easily interpreted by the students as clear DNA binding defects, using either visualization software or 3D-printed models. On the other hand, mutations merely in close proximity to the DNA interface proved difficult to interpret using visualization software alone, and students only recognized the potential of these mutations to indirectly influence DNA binding upon visualizing them on their 3D-printed models. Additionally, students used their models throughout the semester to discuss their results during mock lab meetings as well as during their final poster presentations. Students found their models particularly useful during poster presentations, because they provided an easier platform for discussing their findings (Appendix 4).

FIGURE 1. 3D-printed p53 bound to DNA model kit. Each undergraduate and graduate student received the kit to work with as part of the activity described. They were encouraged to keep their model throughout the semester to use as a learning tool as needed.

Alternative Applications

This activity could benefit students enrolled in introductory courses. It could be implemented as an in-class lab.

Safety Issues

None

CONCLUSION

Coupling macromolecule 3D-printed models and online molecular viewing provides students with two learning tools that immediately engage them in questions of structure and function in a visual, memorable, and kinesthetic way while also providing downstream benefits following the activity. We found that the two components complemented one another well, providing opportunities for students to recall prior knowledge and apply it to novel situations.

SUPPLEMENTAL MATERIALS

Appendix 1: Instructional handout for undergraduate students
Appendix 2: Instructional handout for graduate students
Appendix 3: Step-by-step guide
Appendix 4: Table S1, student feedback from two pilot institutions

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