Exploring Protein Structures of SARS-CoV-2 Variants of Concern within an Undergraduate Research Course

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Abstract

Lane College is a Historically Black College with a legacy of educating underserved minority students. As a primarily undergraduate teaching college, faculty and students have limited opportunities to engage in undergraduate research. To address this concern, the biology department created the undergraduate research course sequence (Undergraduate Research I and II) to provide course-based undergraduate research experiences for students. During the Spring 2021 semester, to limit the spread of COVID-19, the College began the first few weeks with complete online instruction before switching to hybrid or face-to-face modality. For the biology undergraduate research students, the projects were redesigned based on input from the students to explore the viral protein structural changes in newly emerging SARS-CoV-2 variants of concern (VOC). First, students explored the virology of SARS-CoV-2 and structures of key viral proteins using curriculum available from Rutgers University on the Protein Data Bank during the online instruction period. Then the students selected a variant of concern, B.1.1.7 (Alpha), B.1.351 (Beta), or P.1 (Gamma), and a specific viral protein containing at least one mutation for further study. During the hybrid instruction period, using open-source bioinformatics tools, including NCBI SARS-CoV-2 genome sequences, PANGO Lineage VOC data, UCSC Genome Browser and SNAP Gene, the students mapped the location of the VOC mutation on their chosen protein's known structure. They then modeled the effect of the mutation on the protein structure using Chimera or iCN3D, since Chimera is not compatible with Chromebooks. Students determined that the mutations found in nsp3 in Alpha variant and ORF8 in Gamma variant did not have a large impact on the overall structure of the proteins and predicted that there would not be significant effects on protein function. In contrast, several mutations found in Beta variant spike protein likely impact receptor binding domain interactions with angiotensin converting enzyme 2 receptor. The methods developed here will be useful for further investigations of protein structures from emerging variants of concern. This experience demonstrates the utility of bioinformatics research projects in online and hybrid courses and the importance of consideration of compatibility of various open-source tools with student devices.