Gene-to-Protein Project: 3D-printing in Biology Curriculum for the 6th International Symposium on Academic Makerspaces

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Introduction

Many human genetic diseases are caused by mutations in sequences of DNA that encode for proteins. Proteins are large structurally complex molecules that fold into unique three-dimensional shapes crucial for their biological function. To help students understand protein structure and function, I have developed a gene-to-protein project where students research a genetic disease of their choice and ultimately 3D-print the protein responsible. The ability for students to physically hold and manipulate a protein gives them a deeper understanding of how proteins function as tiny molecular machines. This project only requires access to the internet and some experience in 3D-printing.

Materials and Methods

Students were tasked to research a genetic human disease of their choice. The only requirement was that the disease had a defective protein product with a known structure as the root cause. Students wrote a research paper describing the molecular basis for their disease explaining how mutations in the DNA sequence are responsible for the subsequent structural protein changes. Students then used the Protein Data Bank (PDB), the worldwide archive of structural data of biological molecules, to find their disease protein (https://www.rcsb.org/). Once proteins were identified, the PDB format was downloaded from this website. To visualize the protein structure students utilized a free open-source download called PyMol, a molecular visualization software (https://pymol.org/2/). Within PyMol students can identify and color specific mutations, functional protein domains, and any structural complexities. For 3D-printing, the proteins were converted to a surface view within PyMol and then exported directly as a standard tessellation language file (.stl) which can be utilized on any standard 3D-printer. Students then used paint pens to highlight relevant structural elements and presented how their protein functions normally and how a defective protein can cause the symptoms expressed in the human disease that they researched.

3D-printed Protein Example: The Cystic Fibrosis Transmembrane Conductance Regulator Protein

Cystic fibrosis is a genetic disease that results from mutations in the *CFTR* gene that encodes for the cystic fibrosis transmembrane conductance regulator (CFTR) protein. Defects in this protein lead to a dysfunctional chloride channel resulting in formation and build-up of thick and sticky mucus [1]. The CFTR protein is 1480 amino acids long and the structure has been determined through electron micrographic methods [2]. The CFTR protein is listed in the Protein Data Bank as 5UAK and visualized as a surface view with PyMol software (Fig. 1). The 3D-printed version of the CFTR protein is shown in Fig. 2 and allows for coloration and manipulation by students.

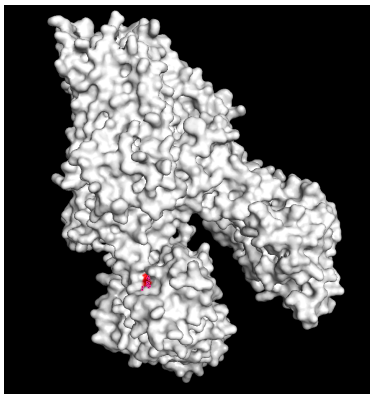

Fig2. PyMol visualization of the CFTR protein with the most common mutation highlighted in red.

Fig 2. 3D-printed ion conductance channel that is mutated in patients with cystic fibrosis. Green lines represent where the CFTR protein is located within the cell membrane and the location of the most common mutation is indicated in red.

Conclusions

This gene-to-protein project involves a student research paper and an accompanying 3D-print of a disease protein. The 3D-printed protein allows students to gain a deep understanding of how protein structure directly dictates protein function and

how a small change in the DNA sequence can have detrimental effects on human health.

References

[1] Dickinson K.M. and Collaco J.M. “Cystic Fibrosis.” *Pediatr Rev*, 42(2):55-67. 2021

[2] Liu F., Zhang Z., Csanády L., Gadsby D.C., Chen J. “Molecular Structure of the Human CFTR Ion Channel.” *Cell*, 169(1):85-95.e8. 2017.