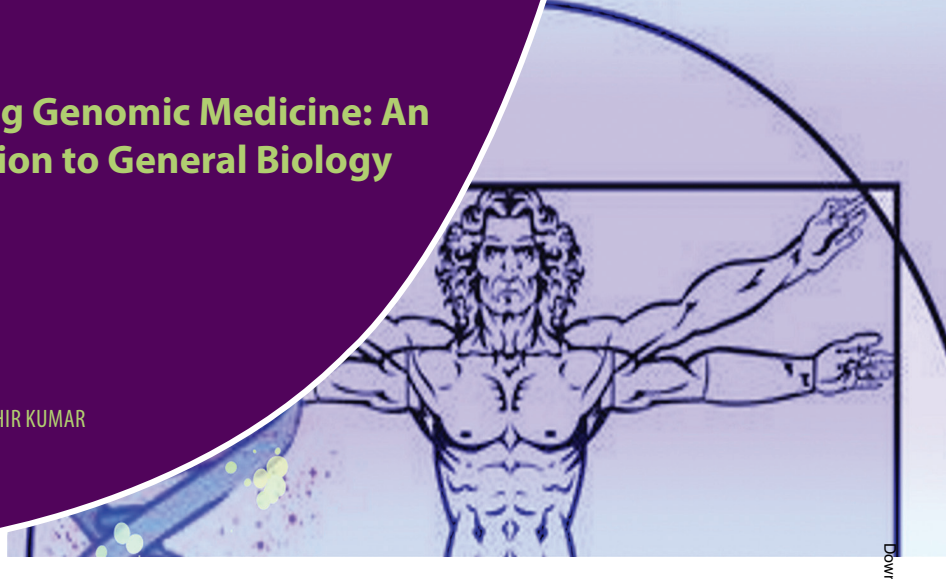
FEATURE ARTICLE

Visualizing Genomic Medicine: An Introduction to General Biology



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Abstract

The emerging field of genomic medicine offers an opportunity for biology and anatomy teachers to bring the topics of DNA, genetics, molecular processes, and evolution together into one experience. Through the genomic medicine paradigm, students see the unbroken connection between small biological topics such as mutations and their potential connection to disease phenotypes. In this paper, we present as a main example cystic fibrosis, which is an often-studied genetic disease in general biology class, for examination through the genomic medicine lens. Concepts such as genes, the plasma membrane, variation, mutations, the nucleus, and chromosomes can be used in a narrative and visual approach to genetics through the genomic medicine standpoint to engage and connect students with next-generation genomics and with the fundamental unit of life—the cell. It is through the genomic medicine lens that the cell's context and relationship to the evolving world takes place.

Key Words: *Genomic medicine; visualizing; biology; conceptual; disease; mutation.*

○ Introduction

Today's students are faced with a widely scaled range of biological concepts. On one hand, they are expected to appreciate the global view of ecosystems, interconnecting webs, and deep evolutionary time, but on the other hand, they are expected to absorb and digest intricate, often intangible molecular concepts such as genes and mutations. These highly variable scaled perspectives are also meant to form some sort of conceptual framework for what life processes or biology might look like. Biology students are also now exposed to bioinformatics, computational software, and coding, adding to the layered complexities that become normalized in biological curriculum and which students are supposed to absorb and understand (Etobro, 2017). These scaled concepts are often represented by acronyms and codes (gene names) and are not easily grasped. Understandably our senses limit us to experiences and landscapes that are projected from a human organism's view. Students often accept the symbolic representations and visualized conceptual images (codes/abbreviations/timescales) as reality for the sake of memorization and often do not realize that they are theoretical models and representations that change with emerging data. A mutation can seem like a strange, otherworldly sequence alteration that spontaneously arises in the dark abyss of loops and winding DNA regions, while natural selection, acting on microorganisms, cells, and populations, is a vague force playing itself out through the ether of space. We all internalize this information differently. When biology students encounter the chromosome level of the genome, the chromosome comes across as an elusive entity in interphase and a tangible structure in metaphase, and yet the label of chromosome is associated typically with the distinct form. How will a student connect these disparate ideas to the concept of a genome? It is the standard imagery of a chromosome looking like two connected poles that becomes committed to a student's memory and yet this is a temporary form that relates to only part of the cell's cycle even though it is contiguous throughout the cell's life. As a student once said to me, "The chromosome is just a bunch of scribbles, how can it do anything?" Students do not associate wiggly lines with biological realities and rarely consider how densely packed chromatin is and that it is biologically active. Another missing piece is how quickly activities happen within the cell and that the chromosome moves, changes, and evolves in that subcellular space. The simplified representative loops or scribbles have a biological, organism-genomic purpose. On the other hand, the vast expanse of geological time and the planet as elusive epochs of change appear unrelated to changes within the nucleus of a cell. How mutations are related to this change is an important question. To achieve an amalgamation

The exploration of the nucleus, chromosomes, and the plasma membrane through genomic medicine expands a student's view of cellular complexity, which acts as a foundation for microevolution.

The American Biology Teacher, Vol. 86, No. 5, pp. 265–273, ISSN 0002-7685, electronic ISSN 1938-4211. DOI: https://doi.org/10.1525/abt.2024.86.5.265.

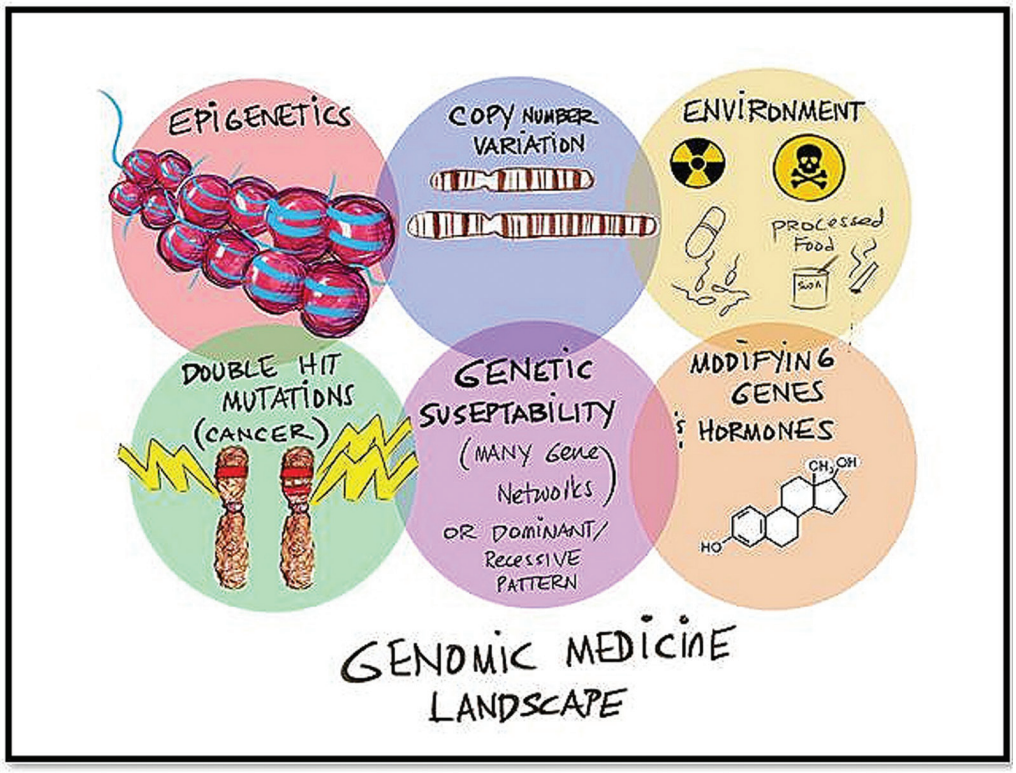

Figure 1. A visual overview of how genomic medicine integrates concepts and paints a bigger picture of the genotype to phenotype problem.

of knowledge, biological information is represented without too much consideration to the fast-moving structural details or the fluctuating and variable vistas of interdependency. The dynamic nature of biology creates problems in representation and therefore in conceptualizing. It is at this point of knowledge where a student's internal visualization of the biology "facts" fails to connect and instead breaks down. Somewhere between the geological time scales and the chromosome with its genes are unifying ideas that would showcase variable phenotypes and their emergence, and which could connect students from genomes to phenotypes and to evolution. Understandably it is difficult to keep track of expanding data, the increasing terminology, and the scales of life, and even more difficult to visualize them together. A more functional approach that focuses on the intricacy of the smaller realm of biology might shed some light on larger scaled systems from the organism to the evolution of populations. The cell and its chromosomes are actually a beautiful and fascinating world-within-world vista that continually evolves. It is this little genomic world that might help students see a pattern. It is the compacted territories of chromosomes where genes perform their essential functions. So, how can students become engaged and fascinated with a genomic world that projects into the phenotypes of nature's biology without simply seeing at a bunch of disconnected parts? How can their computational experiences have biological meaning rather than just being conditioned technology-based lab activities or meaningless Google searches? And how can this biological picture become relatable to their own body? This can be achieved firstly by creating a human genetics section on genomic medicine that can connect the busy compact world of the genome to the larger scaled phenotype, evolution, and disease. Diseases fascinate students (Bly, 2006) and it is easy to relate these conditions to oneself. Combining the visualization of diseases through step-by-step dissection of the genomic and molecular concepts can help. Genomic medicine with its analysis of patterns along with visualization (the arts) of abstract concepts can assist students in seeing into biological dynamics. Adding case studies can also be a very effective strategy for reflecting genomics back to ourselves and seeing how parts connect to the larger whole.

The developing field of genomic medicine can bridge these contrasting and indistinct processes together highlighting and connecting mutations to variability in gene expression, through protein synthesis pathways and ultimately to a gamut of phenotypes. It is the phenotypes functioning in populations that stipple the ecosystems of the world generating diversity and encouraging natural selection and selective sweeps. Diverse phenotypes are also seen in diseases of the same name. In genomic medicine there are many facets and perspectives, including epigenetics, modifying genes, genomic instability, and environmental factors accounting for variability (see Figure 1). These many overlapping subdisciplines paint a more vivid landscape of the genotype to phenotype problem. It is the details of these molecular worlds that are absorbing and captivating. This perspective also accentuates and emphasizes why variation exists at every level of biological function and why a personalized approach to disease is also very important. From an evolutionary perspective, we see the significance of variability through natural selection, which is taking place continually and at all levels of the multiplex of physiological function. In this article/activity, we will address and illuminate these points through a commonly taught monogenic disease: cystic fibrosis. Utilizing an authentic STEAM paradigm, we will present the variations and complexities of cystic fibrosis within the construct of the cell and the plasma membrane through drawing and coloring exercises, which showcase the phenotypic change that produces the disease phenotype.

○ What is Genomic Medicine?

The human genome consists of over 3 billion base pairs that reside in every nucleated cell of the body (https://www.genome.gov/). The genome, which has remained well conserved throughout evolution, is at least 99.9% identical between any two humans on the planet (https://www.genome.gov/). High school students may not have had exposure to this information unless they have a strong interest in medicine or are hoping for a career in it in the very near future. Genomic medicine focuses on the genome, chromosomes, the small differences in that great similarity, and the relationship between genes as a direct cause of disease and agents of variable influence in diseases such as diabetes, obesity, and heart disease. Oftentimes genomic medicine includes an evolutionary perspective. The exploration of the nucleus, chromosomes, and the plasma membrane through genomic medicine expands a student's view of cellular complexity, which acts as a foundation for microevolution. Showcasing chromosomes is a step in bringing the abstract world inside the nucleus to life. For students in genomic medicine, a chromosome is not just a structure identifiable in metaphase but a dynamic organizing system of both the exome and non-coding DNA, so-called junk DNA that contains regulatory features. The chromosome is also subject to mutations, to large structural changes and to evolution. The chromosomes are the genome along with a small amount of mitochondrial DNA. Genomic medicine also focuses on the physiological underpinnings of disease phenotypes and which genes do what. In the big picture, it shows how complex nature is. This is always an important take-home message for students. Mutations and variations in genes including single nucleotide polymorphisms along with small and large changes in genes and chromosomes are considered. The ideas that each organism is unique and each genome is unique and that technology enables us to evaluate an individual's genomic profile and treat a patient accordingly, are highlighted through the personalization of medicine and show the application of genomic medicine in everyday life. Along with the technology that refines a patient diagnosis with each SNP (single nucleotide polymorphism) is the personal and unique story of each person's illness. For students not interested in medicine, GM can still offer insight into the relationships between genomes and phenotypes. A branch of genomic medicine involving evolution (phylomedicine) can also facilitate an understanding of phylogenetic trees, evolution, microorganisms, and disease (Kumar 2011).

> Established in 1990, the Human Genome Project was one of the most expensive and collaborative ventures ever undertaken in science. Ten years since its completion, it has continued to provide a wealth of novel information, the implications of which are not yet fully understood (Karki, 2015).

The field of human genetic variation is a major focus of genomic medicine and while biology classes should not focus primarily on human biology, comparing genomes from closely related species provides insight into evolutionary process. One salient feature that applies to life, in general, is the diverse ways variation can arise in DNA. "*The genetic variations span a spectrum of sizes from single nucleotides to megabases* (Ku, 2010)." Everything from chromosomal rearrangements to single nucleotide variations can occur, and entire genomes can rearrange themselves. Asking students why they think chimps have 48 chromosomes and humans 46 is a great way to connect the genome to evolution and to a common ancestor. This helps create a picture of a diverse and dynamic genome that is a far cry from the stationary, inert, and simplified nucleus most students get from textbooks or computer-generated imagery. Some genetic variations have not been clearly defined and boundaries may shift and overlap. Terms such as Indels (insertions and deletions) and CNVs (copy number variation) might be easily confused in the world of mutational events, but for most students the general idea of small variations is what is important in exploring the evolutionary perspective and the disease perspective.

When we think of biodiversity we forget that it is only possible because of what is happening at the genomic-environment interface, peering into human variation and disease as a variation in a genome or gene is an excellent example of nature's diversity at all levels of life activity.

○ Student Engagement Through a STEAM-Based Approach to Genomic Medicine

At Temple University over the last two years, high school students got an opportunity to explore the field of genomic medicine through a pre-college program. Much of the feedback from this program is presented in this paper. From our Student Feedback Forms, most students were fascinated with the subject. They offered statements in their survey that were summed up into two important teaching points and paraphrased as follows: "I learned about many different types of diseases and the inner workings of the cell, and drawing out the ideas during lecture really helped." Most students were appreciative and excited about the visualization of genomic processes in the cell and expressed this throughout the course.

○ Looking More Closely at Variation in Mendelian Disease

Some medical schools have used art to teach about disease and disease identification. The Hapsburg jaw is both a visual and genetic story of inbreeding in humans and recessive genes that is chronicled through classical portraiture of Spanish royalty, but art can also enhance our understanding of the genome. Mendelian diseases viewed through the genomic medicine lens in combination with, artistic processes can take big data such as those of genome wide association studies (GWAS) and transform global views of disease so students can begin to see patterns. The combined effect of that big data and art can offer students a glimpse into the complex and unique nature of even a one gene, one enzyme disease such as cystic fibrosis, placing it in evolutionary context. Once students have mastered the dominant/recessive concept, they can learn that there is more to Mendelian disease than meets the eye. In cystic fibrosis and Huntington's as examples, we see variations in types of mutations, a wide range of potential defective protein outcomes, and clinical phenotypes that also include inducers and modifier genes that can alter phenotypic outcomes. Suddenly genetics and our simplistic view of nature isn't so tidy and minimal anymore, and this should be an important overarching theme in teaching biology, a continual reminder of how complex it really is. Mendelian diseases through the GM microscope help both teachers and students begin to appreciate the astonishing range of possibilities often hidden behind labels of dominant and recessive. We might think that unveiling complexity beneath the Mendelian

surface would confuse students further, but the opposite may be true. With a glimpse into these variability-making systems at the genomic level, phenotypes students observe on the surface might start to make sense. This also helps students appreciate why disease in general is so difficult to treat. A genomic medicine perspective sheds light on the reasons why even identical twins present with very different outcomes with the same disease. GM also helps explain why almost every trait from the nose tip to the thyroid gland has such a wide range of variable shapes. What underlying genomic pathways make this possible and why does that variation exist? GM also examines physiology and ties that physiology to the gene, which brings students back to the cell and to the nucleus. It soon becomes apparent that there is a viable, hypothetical possibility of metabolic fates and networks that go with those genes and their microenvironment. Top this genomic layer cake of complexity off with an epigenome and the possibilities of changeable, wavering outcomes and you have another level of complexity and possibilities. Interesting questions emerge about the treatment of disease: How can we approach every patient as a unique being? Why does one person get a more serious disease and their twin does not? The GM paradigm also ties biology together, including epigenetics (nature/nurture) with levels of compounding futures, social and humanities-based issues, and diseases. These events are riddled with chance and alterations through mutations and environmental influences over time.

○ Adding Dimension to Genetics Through GM & Art

In a standard unit on genetics students also encounter the monogenic diseases of sickle cell anemia, Tay Sachs, Huntington's, and cystic fibrosis. Table 1 compares the genomic medicine vs. standard genetic lesson plans for Mendelian diseases. These autosomal Mendelian diseases are showcased through the traditional Punnett square in monohybrid crosses. The Punnett square is a great way to show probabilities, but it's not very good at transmitting what the landscape of probability looks like in a complex living cell with its

Table 1. Outline of some differences between a genetic unit's focus and a genomic medicine focus. Note, GM integrates several biological disciplines as they relate to the genome. Educators can use this system to expand their genetics' unit with a GM perspective.

Standard Diseases in Genetics	Genetic Perspective Students Experience	Genomic Medicine Perspective	GM Perspective with Evolutionary Perspective	GM Cell Biology/ Physiology Perspective
Cystic Fibrosis	Autosomal recessive Mendelian disease	Chloride ion channel defect/ variable effects/autosomal recessive/heterozygote advantage/epigenetic influence	Origins of Delta F508 mutation/micro satellite markers track evolutionary change/time of divergence	Individual/general phenotype variations at molecular, cellular, and physiological levels
Huntington's	Autosomal dominant Mendelian disease	Late onset/early onset progressive neurological disease/autosomal dominant/modifier genes/ epigenetic influence	HD allele may have a reproductive advantage	Individual/general phenotype variations at molecular, cellular, and physiological levels
Sickle Cell	Autosomal recessive Mendelian disease	RBC disease/variation/ heterozygote advantage/ epigenetic influence	Selection for malaria resistance/co-evolution of pathogens	Individual/general phenotype variations at molecular, cellular, and physiological levels
Lactose Intolerance	Negligible discussion in genetics	Malabsorption disease/variation/ adaptation/ Some autosomal dominant pattern/microbiome/ epigenetic influence	Lactase persistence variant LCT-13910 C/T/times of divergence	Individual/general phenotype variations at molecular, cellular, and physiological levels
Altitude Adaptation	Negligible discussion in genetics	Adaptation/variation/Dominant haplotype/Epigenetic influence	Evolution of Hypoxia Inducible Factor (HIP)/ pathway/Denisovans/EPAS 1 gene/convergent evolution	Individual/general phenotype variations at molecular, cellular, and physiological levels

dynamic variables. With the use of multiple visual points of view students can get a better mental picture of what a genomic landscape is. Using multiple artistic depictions can shape visual perspectives. Just search images of the cystic fibrosis transmembrane conductance regulator (CFTR) channel and you will see hundreds of different depictions. The more students see how data is interpreted and represented the more they can start to form their own mental framework of the genome.

A unit on genetics with GM perspectives could just highlight one disease or many with case studies comparing outcomes and highlighting uniqueness traced back to the genome, lineage, and life events. For example, educators can look at three CF patients and how they represent multiple phenotypes of the sample disease and students can apply role-playing, create art by drawing the actual mutated protein and phenotype, and watch videos that show real patients with the disease. The videos can be about the personal struggles a young patient might have with CF, including their future, having a family, and how the disease affects their goals and aspirations. This can be contrasted with an animation of the translation of a defective protein. Students can see patients as young as eighteen dying from CF and see other patients in their forties still active. Contrasting personal CF stories lets students observe the variation and the personal sagas of patients with the same disease. When that same disease is examined at the DNA level, it becomes clear that many events can happen along the way from DNA to a protein, ultimately affecting the phenotype. The disease is labeled the same but at the level of the genome, transcriptome, and proteome, outcomes of each process can be subtly different. A few video examples are provided under "Resources." Biology teachers may discuss CF as a chloride ion channel defect and focus only on the plasma membrane. From sequence changes to translation of a protein to personal stories, the GM perspective paints a fuller picture of biology and disease. Just exploring the manifestations in phenotype of the different mutations in the ion channel protein showcases biology's complexity (see Table 2). This allows genetics to move out of flatland and into multi-dimensionality with highly interactive quasi-living components, many levels of networking, and, of course, evolution. In many ways, this drives the valuable points of biology's dynamic, interdependent nature home for many students.

Table 2. A range of CFTR mutations, proteins, phenotypes, and treatments.

Mutation Type	Protein Effect	Phenotype of Channel Protein	Potential Therapeutic Approaches
Type I	PROTEIN SYNTHESIS DEFECT: Class I mutations (such as G542X) lead to the premature termination of CFTR protein translation (approximately 10%) of CF cases)	Truncated protein inserted in PM with nonsense mutations, splice mutations, and deletions	Read through agents and stabilizers (Ivacaftor)
Type II	MATURATION DEFECT: Type II mutations include the common F508del (or ΔF508), which lead to the misfolding of CFTR protein and subsequent polyubiquitination and destruction by the cell proteasome. (Most common) Results in trafficking defects	Protein is fully translated but missing Phe results in misfolding and degradation and doesn't make it to the surface.	Correctors and potential/ion stabilizers
Type III	CHANNEL GATING DEFECT: Defective regulation	Protein is made and appears functional but when it moves to the surface the channel gate does not open.	Potentiator/ion stabilizers
Type IV	CONDUCTANCE DEFECT	Protein is created but the function of the channel is faulty, conduction impaired.	Stabilizers and amplifiers
Type V	REDUCED QUANTITY OF PROTEIN	Protein is created but there isn't enough of it.	Stabilizers and amplifiers
Type VI	REDUCED STABILITY: No mRNA	No mRNA, no translation	Variable treatments; most severe cases of CF

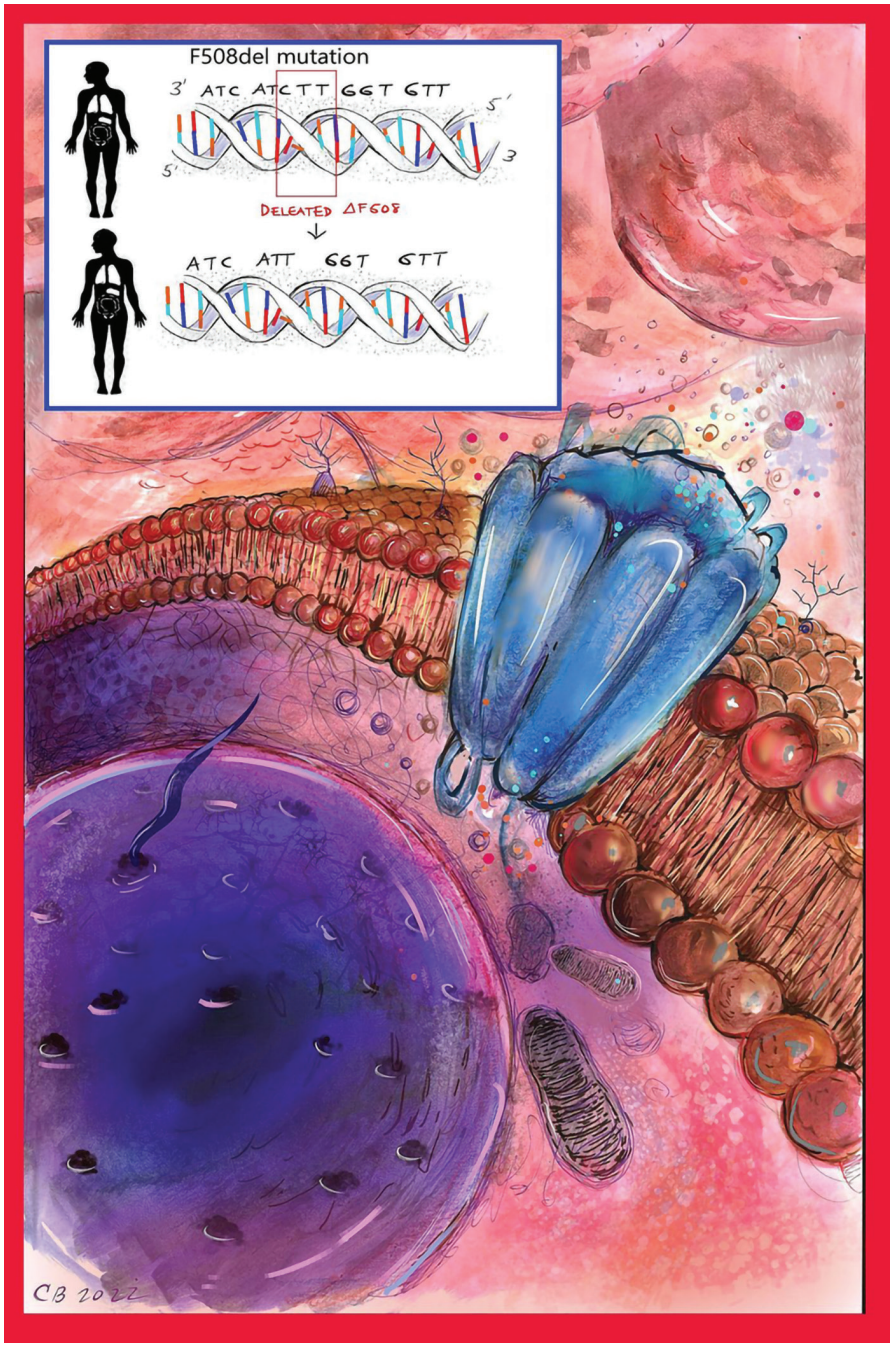

Figure 2. A visualization of the cystic fibrosis landscape of the cell and plasma membrane and its relationship to the most common mutation, delta F08. Students would receive a coloring book page to label or see this visualized on the board.

○ A Cystic Fibrosis Interactive Lecture

For an interactive lecture as an example, teachers can go back in time thousands of years for CF and can present anthropologic background for cystic fibrosis (CF), as a lethal genetic disease, which affects Northern European populations substantially more than other ethnic groups. Or teachers can start off a lecture by simply drawing a large chromosome 7 on the board as an anchor for a discussion on the location of the CFTR gene. The large chromosome acts as a central organizing visual. Supply students with basic information about CF on 3 x 5 cards and ask each student to use the giant chromosome as a graphic for adding their information on their 3 x 5 card. One card can have the current statistics and say, "1 in 20 European persons is a carrier of the CF gene." Another card might say "cystic fibrosis usually is fatal by the age of 50 with the oldest living person succumbing to the illness in their late 50s." After watching a video with varied age groups affected with CF, and doing the chromosome activity, teachers can hand out the coloring page (Figure 2, which is available on the website) and talk a little about basic physiology of mucus-secreting tissue by drawing a large mucus-producing cell. Physiological symptoms can be added to this visual that can provide students with clues how the disease presents within the entire body. Mentioning the "salty skin" symptom used as a diagnostic decades ago helps create a timeline of diagnostics. Students can also draw in the CFTR transmembrane regulator in Figure 3 as part of the activity.

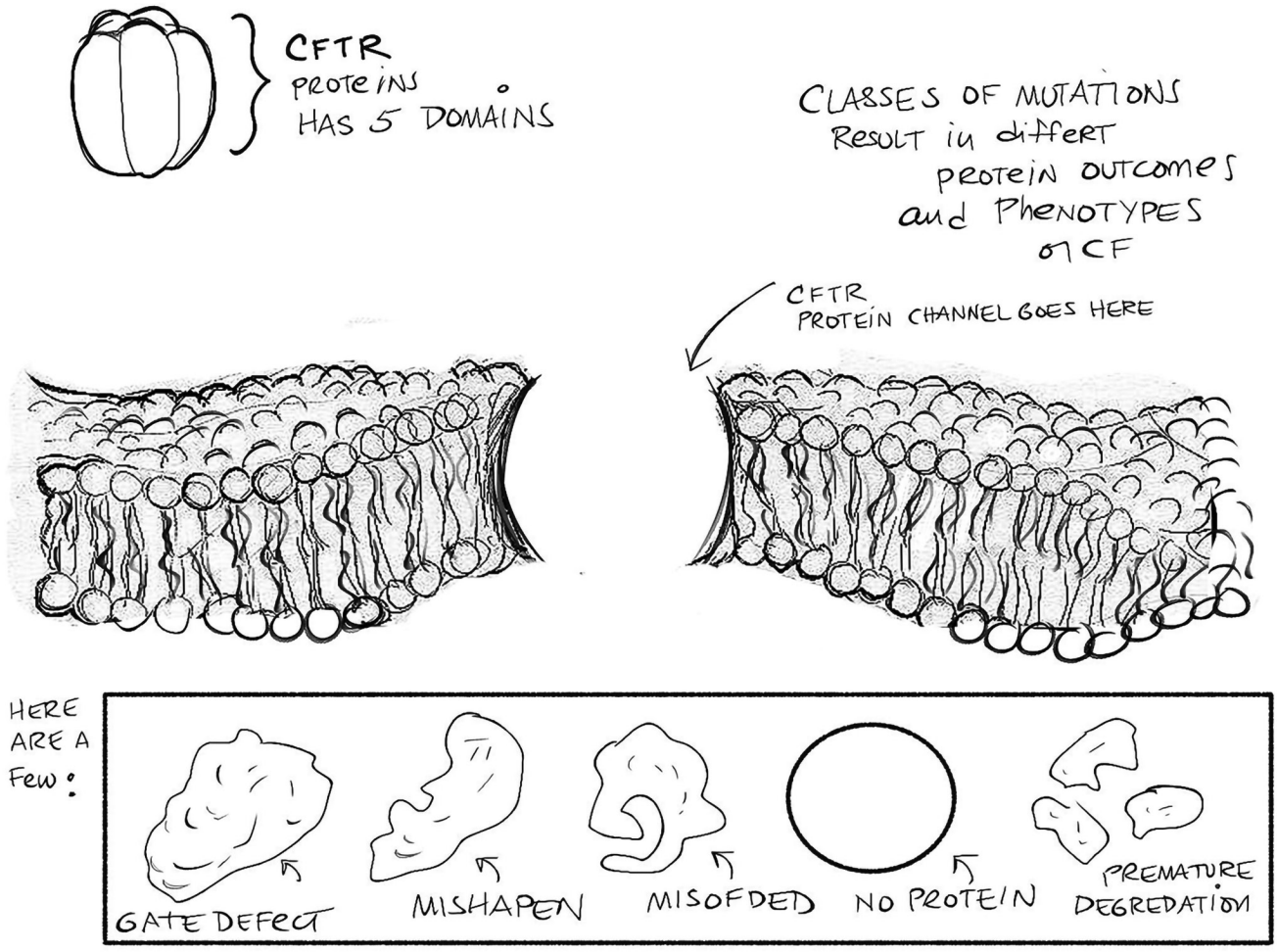

Figure 3. Students can use this plasma membrane to draw in one of the many types of defects associated with CF. A few examples have been shown below, others are described in Table 2. Students might also want to google other types.

Teachers can also approach the topic with a traditional Punnett square to show the ratios of potential progeny for CF. By adding the genomic medicine perspective, the CF example will allow teachers to dig a little deeper into the variable nature of disease, and note that CF is characterized by substantial clinical heterogeneity (Lucidi, 1995). Heterogenicity is a good topic to discuss because it overlaps with other areas of genomic medicine such as cancer. Studies have begun to identify chromosomal locations that identify specific genes as contributing to this variation. Transcriptomic and proteomic data, sampling hundreds and thousands of genes and their products, point to pathways that are altered in the cells and tissues of CF patients (Drumm, 2012) for more advanced classes. Students can now envision that each person's disease is different as a result of disease-modifying processes, everything from the type of mutation, the tissue and its expression patterning, the epigenetic patterns, and the transcript that writes the physicality of the protein's shape teach us about the complexity of CF's underlying biology. This provides students and teachers with new insights into variation and the myriad of biochemical subtleties that need to occur for phenotypes to be realized. Some of these include variations in fundamental biological processes such as altered apoptotic responses, the amount of oxidative stress dysregulation occurring in the local cellular environment, the energy capacity and health of the mitochondria, the lung–gut microbiome landscapes, which encompass diet, stress, and much more. The discovery of cystic fibrosis in 1938 was marked by the recognition that it was an inherited disorder, but we now know that the genome is far more interactive and complex.

After the chromosome activity students can role-play as medical interviewers or genetic counselors and patients as mentioned previously, only this time they can present as patients with different mutations in the CFTR gene and, therefore, different clinical outcomes. They can briefly talk about their personal form of the disease in front of the class. They can also role-play with other Mendelian diseases or as a parent of a child with CF. The coloring page should assist students in familiarizing them with the CFTR protein, and you can ask them to reference that coloring page and use it for notetaking. Figure 3 will allow them to try out different misfolded proteins or defects within the plasma membrane by drawing the defective protein or channel. Table 2 includes the current six types of CFTR protein outcomes and some of their variable effects. Advanced students (honors/genetics) can speculate about how the protein might change the function and the disease. Students can also obtain the type of CF defect and mutation by chance and draw in the disease protein. In these simple genomic medicine STEAM exercises students may gain a deeper appreciation of the genomic/cellular processes. There are multiple ways to arrange the interactive class—storytelling is another.

○ Genetic Variation, Epigenetic Expression, & Phenotypical Uniqueness

Epigenetic inheritance adds another dimension to the Mendelian genetics concept and fulfills the idea of nurture or environment affecting the genome through epigenetic tags that can be passed down to future generations. DNA methylation and histone modification are involved in regulating patterns of gene expression. These processes are crucial to normal development and differentiation of distinct cell lineages in the adult organism. CF is not different from any other disease and is shaped by epigenetics. As an example of epigenetics in CF, lung macrophages, part of the innate immune response, have difficulty carrying out their anti-inflammatory effects because of excessive, viscous production of mucus. Those macrophages can be epigenetically affected to be more responsive or less responsive because of DNA methylation (Magalhães, 2017). This can change the phenotype of the patient and the outcome of the disease. The point of including some epigenetic concepts is that now a student's view of the one-dimensional autosomal recessive disease becomes more than a memorized term of cross but of an interactive, multifaceted progression of possibilities.

○ Anatomical Models as Springboards into Genomic Medicine

One of the best ways to deploy and anchor a discussion of the minute and the abstract is through a physical object. Most biology classrooms have anatomical models of human anatomy, frog anatomy, plant anatomy, cell models, and mitosis models. Some of these models just decorate the classroom acting as a backdrop for discussions but are never put to any use. For genomic medicine, they can do more than adorn and fade into the surroundings; they can, in fact, stabilize a student's focus on the anatomical geography, the phenotype of disease, and the genomics. For the disease cystic fibrosis and we have provided a coloring page of both a full anatomy model and a cell anatomy model. This can be used along with a whiteboard or chalkboard discussion, of which we will be providing a video on our website (https://igem.temple.edu/genomicmed/). With the anatomy model and the drawing (see Figure 3), students have the tangible, multi-layered perspective of CF's translation from a sequence of nucleotides to protein (channel ion) to its defective function in the organ of interest (lungs). In a storyboarded sequential representation, students can also come to appreciate the variations that might occur to the CFTR gene and ultimately its manifestation to varying levels and variations of the disease. In general, the anatomical model supplies the tangible and relatable scale to a student, and that is why it is important for teaching genomic medicine.

○ Focus on Patient and Evolutionary Storytelling

An evolutionary component is often included in the genomic medicine perspective and can allow for a narrative-style classroom experience. An easy-to-read article by Smithsonian, entitled "Tracking Down the Origins of Cystic Fibrosis in Ancient Europe" (Farrell, 2018) can be used as a storytelling introduction that can then lead to case studies into the present. Some of the images from the article can be placed in a short PowerPoint to depict skeletons, maps, and timelines, which raise questions about the CFTR mutations origins. Following this article, students can be given a fictitious patient in the present, which leads to another kind of personal history and maintains the storytelling theme. Depending on the time frame or the grade level, teachers can incorporate the cell, genetics, physiology, and molecular mechanisms of DNA, including mutations, SNPs, GWAS studies, and environmental influences with a clinical and patient perspective. Both the evolutionary history and the patient history give large studies, graphs, and abstract concepts a name, a face, and an individual human touch. Educators can tailor the time frame to suit their classes and embark on a genetics unit having flavored it with a genomic medicine perspective. CF has a few hypotheses of how it may have evolved in European populations in relation to respiratory infections in those populations that can be explored separately and used as a homework assignment. For students, the general terms of mutations, selection, positive selection, and negative selection can be introduced, not so much for students to ponder the complexities but just for them to see the connection between the diminutive deleterious gene and effects through time on phenotypes in populations as they continue to evolve. Another way to approach the storytelling of genomes is through the creation of graphic novels. We have currently generated graphic novels that incorporate the evolutionary and cellular components on protein misfolding, the microbiome, and epigenetics. Once created they can be used for a single hour-long lesson plan where the instructor reads the story and asks questions or the students get a copy and participate in a role-playing storytelling experience.

Some student learning outcomes:

- Students will describe the fundamental concept of a genome, using the appropriate terminology associated with chromosomes, genes, phenotypes, and genotypes.
- Students will explore the multifaceted nature of a Mendelian disease from a genomic medicine perspective.
- Students will explore the diversity of mutations in the CFTR gene and explore variable phenotypes.
- Students will consider CF from the genomic perspective with coloring book pages, drawing, and role-playing.

Resources:

- Cystic Fibrosis Foundation, (May 27, 2008) "Dying Young," https://www.youtube.com/watch? v=Twjg7v-pTO4
- "Living with Cystic Fibrosis (Being Me: OJ)," https://www.youtube.com/watch?v=4kHsqBkVuMI
- Cystic fibrosis animation: https://www.youtube.com/watch?v=9hKIMMdiu28
- Bozman Science. Epigenetics explained simply: https://www.youtube.com/watch?v=i9a-ru2ES6Y

○ Conclusion

Genomic medicine is an emerging field in life science and can have an impact on student understanding of genetics as well as the genetic underpinnings of physiology. It also casts a wide lens on evolution through the perspective of disease in distinct populations

and through examination of GWAS studies of diseases such as cystic fibrosis and sickle cell anemia. Repurposing the biology classroom for genomic medicine is easy and it allows students to see one application of biology and a translational direction research may be taking. Genomic medicine also provides a microscopic view into the changing genomic landscape of an individual through the examination of mutations, linking evolution to genetics and to phenotypes. There are many ways to platform a genomic medicine unit and creative teaching methods that can be the vehicle for students tying together complex biological topics.

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