GENA project: Understanding Basic Genetic Principles through Sickle Cell Anemia

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Target: Sickle Cell Anemia and Basic Genetic Principles

The purpose of this unit was to make sure students have a basic concept of transcription, the genetic code, translation, and protein folding, since these processes underlie the understanding of genetics. The goal was not to teach these topics in depth, but to give sufficient background so that students can apply their knowledge to real world situations and to synthesize the broader contexts and consequences of these basic genetic principles. The unit utilizes the sequence and structure of the \( \beta \) globin gene to reinforce the genetic principles and introduces the students to Sickle Cell Anemia (SCA), a genetic disease par excellence, to broaden their appreciation.

Throughout the year, SCA was used to connect classroom concepts with real world situations, particularly areas related to: mutations, autosomal recessive inheritance, prenatal diagnosis, recombinant technology and its application to disease diagnosis (i.e. PCR, restriction endonucleases, gel electrophoresis), protein folding and misfolding, phenotypes associated with genotypes in human diseases, genetic engineering for therapeutic reasons, heterozygote advantage, population genetics, evolutionary considerations of maintaining mutant alleles, the interaction of environment and genetic makeup, and the social and cultural implications of genetic disease.

Course: Genetics

Chapter/Topic: Transcription & Translation

Objectives:

SWBAT:
- Examine the process of transcription of mRNA from DNA.
- Examine the genetic code and relate it to the process of translation
- Examine the structure and physical properties of different amino acids
- Describe the process of translation in ribosomes and the assembly of polypeptides.
- Construct 3 dimensional proteins, RNA, and DNA accurately.
- Define mutations and investigate the role of mutations in altering protein structure and function.
- Relate mutations to the evolutionary process.
- Analyze the relationship between protein structure and cellular function.

Timeline: 5-7 blocks (80 min/block).

Prior Knowledge:
Students have taken Biology I during their sophomore year. It is not known if all the students have studied transcription and/or translation. It is expected that all students have studied the structure of DNA. All students have taken Chemistry during their junior year.

5E Learning Cycle Model:

**Engagement:** Students were given a pre-quiz to measure prior knowledge (see Appendix 1). They were not formally graded on the quiz, but they were informed that they would receive the quiz again at the end for a formal grade (see Appendix 2).

Dr. Gabriel, Rutgers University Department of Molecular Biology and Biochemistry, visited the school and gave a PowerPoint presentation on the disease model of sickle cell anemia (See Appendix 3). Students were expected to take notes, but they were not told formally the relationship between sickle cell as a disease and what they would be subsequently learning.

**Exploration:** Mrs. Chazan tailored lessons around transcription and translation depending on the answers given during pre-test. While teaching transcription and translation, part of the β globin gene was used as the primary example. Teaching was done through guided questioning and answering and web-based animations.

Students took notes based on lecture, Q&A, and animations. Students reinforced learning by transcribing part of the β globin gene, then creating parts of β globin protein

Teacher used this information to discuss protein folding. β globin and hemoglobin were used as models to reinforce concepts of hydrophilicity and hydrophobicity, three dimensional structure and function, protein-protein interactions, changes in protein conformation based on ligand interactions (O2 or CO or CO2), effects of mutations (e.g. sickle cell mutation, on protein folding and interaction)

**Explanation:** Students reinforced protein folding using the Amino Acid Starter Kit (3D Molecular Designs). Groups constructed one of the units and the class combined all the units to create a complete β globin structure. Using their knowledge of transcription, translation, proteins, protein folding, and cellular function, students constructed the steps when the sickle cell mutation is introduced

Students were asked about the implications of hemoglobin structure to its function in the red blood cell: Using the model-relate the structure of the hemoglobin to the red blood cell. Why is the red blood cell round with a concave center? What are the functions of red blood cells and how does the structure of hemoglobin make this possible. How does the sickle cell mutation alter the structure and function of hemoglobin and red blood cells, and what are the implications to the organism? Based on the earlier lecture on sickle cell disease, concepts were reinforced concerning polymerization of the hemoglobin protein leading to sickling of the red blood cells which causes reduced oxygen exchange in affected organs.
**Evaluation:** The teacher repeated the same quiz used as the pre-quiz at the end of the unit to evaluate the extent to which the unit succeeded. (see Appendix 3)

**Extension:**
Dr. Carolyn Rouse, Princeton University Department of Anthropology, came to the classroom to discuss disease models on a public policy level and to discuss the many medical and social implications of the sickle cell gene. How does the government constitute a disease? How could hospitals treat a disease like sickle cell anemia? How can societal views affect treatment or management of a disease? What could we predict about the quality of life for those afflicted with Sickle cell disease? Finally, how can understanding the basis of the disease aid in designing treatments or cures?

**Evaluation/Extension:** Students read the book *Survival of the Sickest* by Dr. Sharon Moalem. This book discusses the potential advantages of having a disease gene and the strength of the heterozygosity advantage. Examples include:

- Diabetes
- Sickle cell Anemia
- Tuberculosis

Students have been reading *Genome* by Matt Ridley to reinforce central ideas of genetics through a weekly seminar class. Included are the following:

- Genes do not exist to cause disease
- One gene does not equal one function/disease
- Diseases can be advantageous in extreme environments.
- Genetics is based on probability and therefore, cannot be viewed in terms of “black and white.”

Students will write a paper reviewing the book and summarizing central ideas in the book. They will utilize correct vocabulary from class discussions and their genetics book. This assignment serves as their exam for the third marking period. It also springboards discussions from molecular genetics to population genetics. This is currently ongoing.

**Insights of the Intervention after teaching:**

Chazan: This unit was taught starting at the end of October and continued until mid January. This time is very volatile due to holidays, field trips, assemblies and after school club participations. DNA structure, replication, transcription and translation was completed before the winter break. Mutations and gene expression was completed after the winter break. These latter two components were lacking depth of participation and ultimate learning performance that the former three contained. In particular, the protein folding exercise was started, but abandoned due to difficulty of grasping the kit’s purpose. For the
curriculum of Genetics, it was important for me to move on to bacterial genetics instead of slowing the pace in order to focus on it.

If I could repeat the unit identically next year, I would choose to move the unit in time such that the entire unit could be safely completed before winter break. Alternatively, I would start the unit at the new year. This change would require purchasing the laboratory equipment that we borrow from Princeton University.

Gabriel: It was very useful to review the pre-test before giving my lecture on basic aspects of sickle cell disease. I realized the limitations in their basic knowledge and structured the talk to reinforce basic principles of genetics and trying to keep the topic at the student level. I was impressed with the students during my talk, in terms of their willingness to suggest answers, to ask good questions, and maintain interest in the lecture which ran > 1 hour. It was also useful that the teachers invited students at the school who have relatives with sickle cell disease to take part in the class for that day. Their personal comments reinforced the lecture points and really brought home the "real life" connections.

Subsequent to giving the talk on sickle cell disease, I realized that this would be a great topic for University students to use a springboard to appreciating the intersection of genetics, medicine, evolution, history, race, government policy. As a result, I am in the process of designing an honors seminar course for Fall 2008 that I will offer for Rutgers Honors Students.

Reviewing the results of the post-unit test, it was clear that the students had improved their understanding of basic genetic principles, but that there were some principles that they did not really know. They might have been able to answer these questions if they had foreknowledge that they were going to have an exam, but this was more or less sprung on them to see what they really knew. The idea of the genetic code, missense and nonsense mutations are still a mystery to most of them, but they have a better idea about what a gene is, and the path from dna to protein.

In addition to my basic talk on sickle cell disease, I invited a colleague, Dr. Carolyn Rouse, from the Princeton University Department of Anthropology, who has just completed a book on sickle cell disease to come and speak to the Genetics class. The students were given several papers to look over before the lecture (two included in Appendix 4a and 4b). Dr. Rouse gave more of a chalk talk with a great deal of student participation, that centered on government policies toward disease, reimbursement, perceptions related to race. The class was very enthusiastic to this approach and the discussion was lively, with students relating their personal experiences and opinions, mirroring broader social and cultural biases. I think it was eye opening for the students to appreciate how issues of health and disease, genetics and the environment, and governmental and societal decisions impact on their lives. A picture of the class with the teachers, Kristi Chazan and Renee Borgen, and Carolyn Rouse and Abram Gabriel is in Appendix 5).

I plan to give an additional class at Pemberton in April to cover recombinant DNA technologies, using sickle cell anemia as the model to illustrate restriction digestion, RFLPs, Southern blotting, PCR, and sequencing.