Gen 564 Semester-Long Project Spring 2017

The goal of this project is an in-depth, genomic and bioinformatic analysis of a human disease gene or trait. This disease gene must be homologous to one or more genes in one or more model organisms (the bacterium *E. coli*, the single-celled yeast, *S. cerevisiae*, the budding yeast, *S. pombe*, the roundworm *C. elegans*, the arthropod *D. melanogaster*, the mouse *M. musculus*, the plant, *Arabidopsis thaliana*).

Keep in mind that your project should include both a "global" analysis of your selected disease gene and the implied "local" analysis of a single, isolated gene. A global analysis reflects the central themes of the course: structural, functional (both transcriptomics and proteomics), and comparative genomics. A local analysis reflects the gene's structure and function and its primary role in the disease etiology. Both analysis types should reflect the intricate relationships among sequence, structure, function, genome organization and expression, and evolution. The lab activities throughout the semester will assist you in conducting these analyses.

Some specifics in your research should reflect the ways in which you have been studying genomics and bioinformatics. For example, how was the gene discovered and mapped? How was the gene sequenced? What is its sequence? What are the molecular features and properties of this gene (i.e., describe and analyze its gene "anatomy")? What is the sequence of the protein produced by this gene? What are the important and relevant structural domains and motifs in the protein, and how are they related to the disease pathology/etiology? Has the gene's expression been characterized by microarray or RNA-seq analysis? *Are the protein domains and motifs related to similar domains and motifs in the other model organisms?* Is the disease gene a member of a conserved gene family? Is the protein's domain a member of a super-family of protein domains? These questions cover a full range of analysis, from cytogenetics, to gene and protein molecular characterizations, to functional and evolutionary comparisons with other genomes in other organisms.

You will, of course, be making extensive use of bioinformatics programs and databases found on the Internet (NCBI, etc.). My evaluation of your project will be based in part on the depth of your analyses, and on how well you use these available bioinformatics tools. But a tool is only a tool, and its use generates data that must be interpreted, analyzed, compared, and critiqued from a variety of perspectives. Finally, conclusions must be drawn along with recommendations for future experiments or analyses.

The format of your project should be that of a Web Page, so you will want to use **Weebly.com** (or any other web-based program you are familiar with) to construct the final version with all text and images. The length depends on the amount of information associated with a particular disease gene, and you should strive for brevity and clarity but not at the expense of completeness.

- Find a disease or trait and an associated gene/protein for which they have found a mutation.
- You will be working on this gene/protein for the entire semester.
- You will present your findings at the end of the semester in a **15-minute presentation** to the class.
- You will have built a website with all of the research and bioinformatic information you have obtained in class, outside class and in lab. ***This website will be your published work which can be used in your resume as published research.***
- Your final talk and website will be peer reviewed by the class as well as by the instructor.

Semester-Long Project Details

Gene & Disease/Trait choice:
Select a human genetic disorder or trait, by which we mean a disease or heritable predisposition to a certain condition. It can be a single gene disease/trait, or a polygenic one. In the case of a polygenic disorder, you need only do the genomic analysis for *one* of the involved genes. The role of the selected gene in disease should be featured in your project, and you should review the underlying genetic evidence for the role of the gene in the disease. Some disorders are not polygenic traits, but you will find that more than one gene can cause or predispose different individuals to the disease (BRCA1 and BRCA2 for heritable predisposition to breast cancer, for example). In a case like this, you would introduce both genes as causing the predisposition, and then select one to focus on in detail for the rest of the website project.

Specific Aims:
*Over the course of this semester you will be writing a **Specific Aims** for your project to help you craft a **hypothesis** and **experimental approach** for your project. You must use genomic and proteomic techniques you learned in class that would address the specific aims you are proposing and discuss why these techniques are appropriate for your project. You should have 3 aims in your Specific Aims. You will present your project and defend your ideas you have outlined in your Specific Aims in a 15 min presentation at the end of the semester. Your peers and Ahna will be evaluating you with rubrics over the course of the semester, just as you would experience as a scientist in real life.

What is required for the website (your publication of your work):

- *Homepage*: About your gene and disease + world hit map of website viewers
- *Multiple Pages*: corresponding to each lab/topic & data you obtained (i.e. homology, protein domains)
- *Specific Aims*: pasted on this page and upload a PDF version here
- *Conclusions/Future Directions*: basically the written version of your final talk with figures
- *Final Presentation:* uploaded in PDF format on your Conclusions/Future Directions page
- *References:* every page!
- *About me*: Optional but good
- *Contact Info*: Good if you want readers to contact you
- *Lots of creativity! Lots of necessary and informative visuals!*

Each data analysis page should have this format:

- Intro
- Results
- Figures
- Analysis
- References: Write out references and link out to Pubmed papers and other online literature. Link out references to figures you use using hyperlinks or paste links in Reference section
  *Note: except for the specific aims and conclusions pages

Things to keep in mind over the course of the semester…

Website & Specific Aims Feedback: You must schedule time to meet with Ahna to go over your website or specific aims with you and get feedback. Don't wait until the last minute!

Specific Aims: Along with the research question, well-defined specific aims or objectives are key to the successful completion of a research project. The specific aims should answer the question "What are you going to do?" You will need to spend more time planning than writing. You really need to think, read and do research about your project before you proceed until you can ASK a Question! Then: 1) Decide on a hypothesis, 2) Define the aims to test your hypothesis and 3) Choose genomic and/or proteomic approaches that you learned from your readings that you think are the best way to address your hypotheses and questions. Mapping out a strategy will pay off in the end. **HINT**: Each week your readings are chosen to be models for genomic and proteomic approaches for your own project. So pay attention and get inspired by your readings and your research. By writing specific aims, you will be prepared for your final presentation and in writing up your conclusions and future research sections of your project.

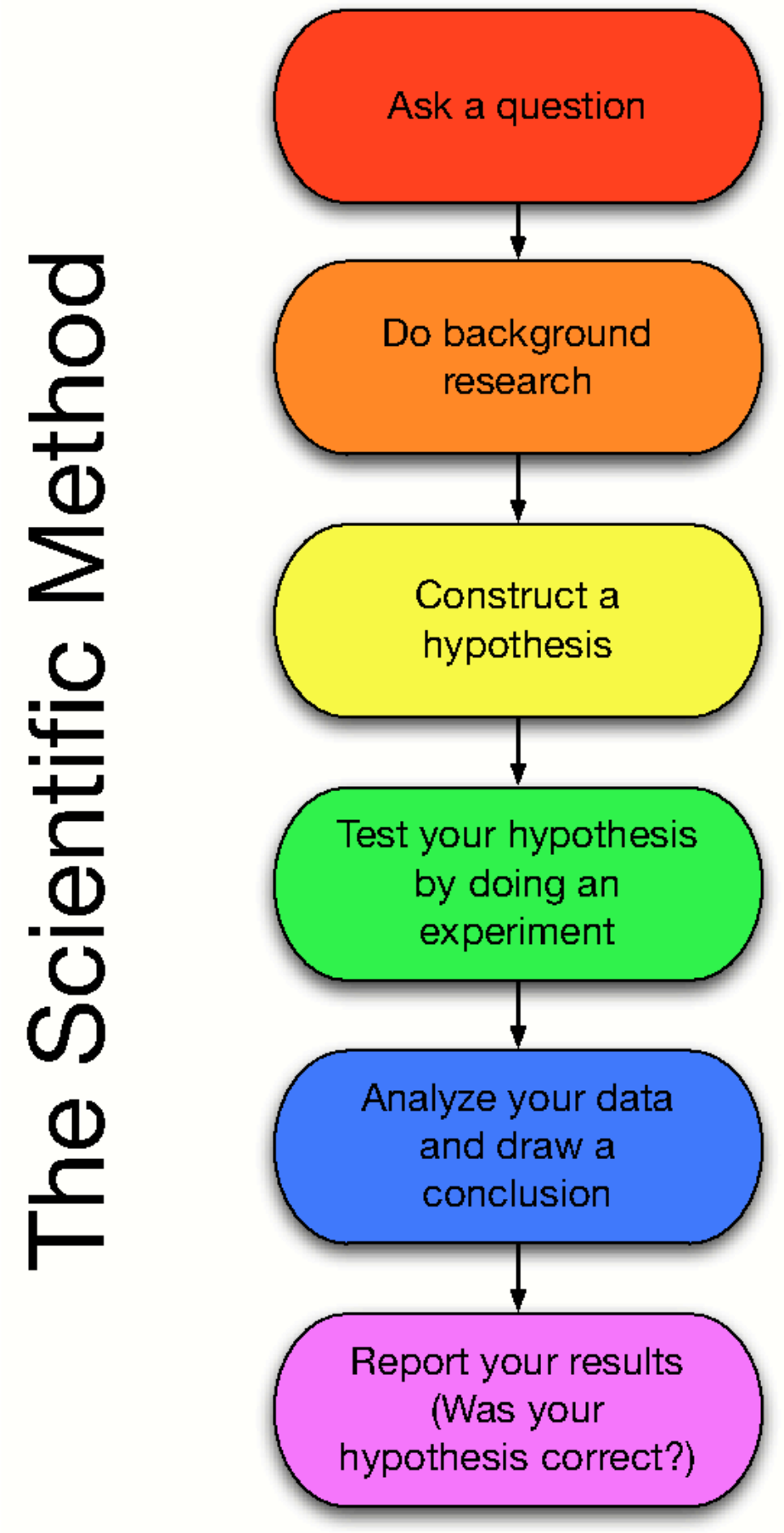
Hypothesis: Your hypothesis triggers everything you do. Conceptually, think of it as your destination, determining the course of your semester-long research. Choose a hypothesis that is well focused and testable, and that your experimental results will be able to prove or disprove. Your classmates and Ahna must believe that your hypothesis is sound and important enough to be tested.

Final Presentations: You are going to present what you learned and found out about your gene/protein in the last few weeks of class. This presentation is 15 minutes long. It's about a 12-minute talk with 3 minutes of questions. Briefly go over what your main findings over the course of semester were for your gene/protein and how these findings helped you craft your **hypothesis** (which you will state) and the subsequent experiments you are going to perform to test these hypotheses. *You are required to have a slide with your protein domains and a slide with your orthologs.* Conclude with a brief discussion of what you think is the most important thing to find out next about this disorder/trait and the gene(s) that cause it, and discuss why. You should assume that lab money and manpower are not your limitations.

Presentation rough draft: Successful final presentations result from well-planned and thought-out presentation drafts. You will turn in 2 pre-final presentations. This should be sent to Ahna as a Powerpoint (.ppt) or Keynote (.key) file. Ahna will provide you feedback and a time to meet with her one-on-one.

Final Website:
Your final web project includes all of the assignments plus data that you obtained about your gene/protein over the course of the semester. Using bioinformatic approaches, you are to use what you learned from our in-class discussions and in-lab hands-on experiences about a particular technique and online database to figure out everything there is to know about your gene/protein. By the end of the semester you should have discovered a lot. And by all means you are welcome to venture off to any online database that is available to you to try to understand and possibly come up with some ideas on how to "cure" your disease that you are studying. The website is not due until after finals and can will be considered published work by you! You can use this on your resume as published research.

References: Put the references to journal articles, images and websites (including bioinformatic websites you use) that you used over the course of the semester on your project *on each page that you create.* Figures should be referenced as you use them on each page in a figure legend. *Every page that you create should have references* (overall grade by **-10% pts** if this is not the case). If you use a bioinformatic website, like PFAM, link out to that website you used for each analysis. **References should be on every slide where you have shown data or images that are not your own.*


The Scientific Method
Ask a question
Do background research
Construct a hypothesis
Test your hypothesis by doing an experiment
Analyze your data and draw a conclusion
Report your results (Was your hypothesis correct?)