Biol 322 Fall 2012

Inspired Choices & The Power of Forward Genetic Analysis

Part 1: Due on Friday Nov 16 at noon
Part 2: Have your paper preapproved ASAP and no later than Friday Nov 16 at noon.
Part 3: Due on Monday Nov 26
Part 4: Student presentations during the last week of the quarter (Tues Dec 4 & Thurs Dec 6).

PART 1: (15 pts.) Identification of SLEEPLESS, a Sleep-Promoting Factor

Science 321: 372. 2008 See link under Required Reading.

Browse through *entire* article and carefully read **pg 372- 374 and examine figure 1 closely**.

Please word-process your answers to these questions. Unless otherwise indicated each answer should be *one-two complete sentences*.

1. What is the advantage (stated twice in the introduction of this article) of a forward genetic screen?
2. How many mutant candidates were screened and what general type of mutation did they carry?
3. Examine Figure 1a. What is the sleep phenotype of *sss* mutants? Be sure to state your answer in ***quantitative*** terms.
4. What is the difference between *sleepless (sss)* and SLEEPLESS (SSS)? In other words, what do the upper and lower case versions refer to?
5. How did the researchers establish that sleepless and quiver were alleles of the same gene? Site two different lines of evidence.
6. Is the sleepless gene likely to play a significant role in vertebrate sleep processes? Defend your answer in one sentence.

PART 2 Inspired Choices. Find an original research paper that uses a forward genetic screen strategy to identify genes that play roles in a specific biological process.

1. Your paper may be recently published or NOT.
2. As soon as you find a candidate paper for this part of the assignment, send CT a pdf file or a link to the paper or abstract. ***One student per a given paper.*** First come, first served. ***Your choice of paper must be preapproved! Do this no later than 10/13.***
3. You have free online access to Science, Nature, Cell, Genetics, Nature Genetics, PNAS, PLoS One, PLoS Genetics and many other journals via the Western Libraries. You can find your paper in a number of different ways:
    a. Go to PubMed and do a general search: http://www.ncbi.nlm.nih.gov/pubmed/

b. Go to a specific journal (such as Genetics) that you have online access to and search that journal
c. Google it!
d. If you search with the term *forward genetics* you won't find any older articles (pre 1990s?) since this jargon came into use only with the advent of reverse genetic technologies.
e. Be sure to pick a topic and research organism of interest especially to YOU.

PART 3 Written Work-up of your selected paper to CT

Submit the following by Mon Nov 26

a. Title of paper, author list (first and last only if there are more than 2 authors), name of journal, volume, page and year of publication
b. A short summary (several sentences) of the paper including the biological process under examination, the model organism used, how the researchers screened or selected for phenotype of interest, the scale of the screen (how hard did they look for mutants?), the mutagen or other technique used to generate mutations, the number of mutants discovered and ***especially any interesting biology that the researchers uncovered***.

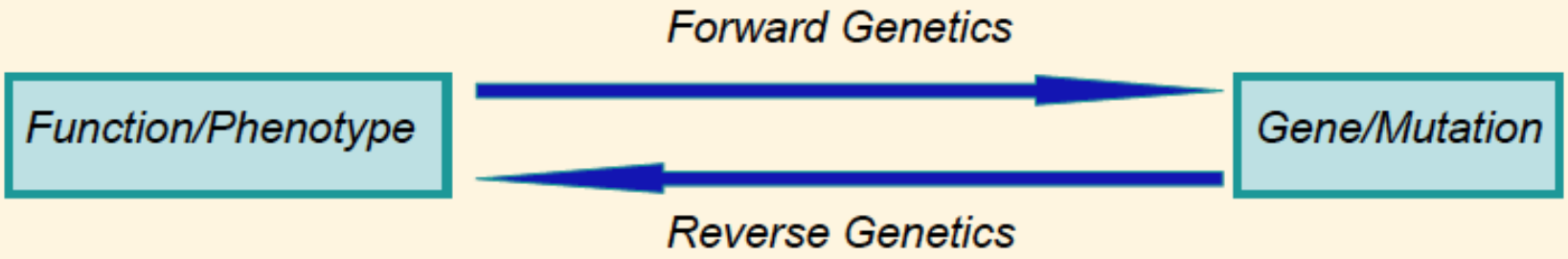
PART 4: (15 pts.) 10-12 minute in-class presentation of your paper (Dec 4 & 6)

- Structure your talk around the guidelines for the homework assignment -- in other words, be sure to convey the biological process under investigation, the model organism chosen (and why), the phenotype screened (or selected for), what the researchers learned that was interesting, the scale of the screen, etc.
- *Work up a couple of slides WELL IN ADVANCE OF YOUR TALK and practice your talk on a friend or classmate to make sure it is coherent & of the appropriate length*
- *On Tues and Thurs Nov 27 & 29, the labs will be on the short side giving you extra time to work on your presentation*

What is the genetic basis of a particular phenotype?
(How does one determine the function of a gene, or the identity of genes responsible for a trait?)

Forward Genetics:
Starts with a phenotype and moves towards the gene

Reverse Genetics:
Starts with a particular gene and assays the effect of its disruption



Reverse genetics*

Julie Ahringer, ed. §
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1. Introduction to reverse genetics in *C. elegans*

Through genetic analyses, the function of genes is investigated by studying organisms where gene function is altered. In classical forward genetic screening, individuals are treated with mutagens to induce DNA lesions and mutants with a phenotype of interest are sought. After a mutant is found, the gene mutated is identified through standard molecular techniques. Detailed studies of the mutant phenotype coupled with molecular analyses of the gene allows elucidation of the gene's function. Forward genetics has been responsible for our understanding of many biological processes and is an excellent method for identifying genes that function in a particular process.

In reverse genetics, the functional study of a gene starts with the gene sequence rather than a mutant phenotype. Using various techniques, a gene's function is altered and the effect on the development or behaviour of the organism is analysed. Reverse genetics is an important complement to forward genetics. For example, using reverse genetics, one can investigate the function of all genes in a gene family, something not easily done with forward genetics. Further, one can study the function of a gene found to be involved in a process of interest in another organism, but for which no forward genetic mutants have yet been identified. Finally, the vast majority of genes have not yet been mutated in most organisms and reverse genetics allows their study. The availability of complete genome sequences combined with reverse genetics can allow every gene to be studied.