Biol 322  Fall 2009   Forward and Reverse Genetic Analysis

This assignment is due on Tuesday Dec. 8 at 3:30pm and is worth 10 homework points and 5 final quiz points.  Total points: 15

Reading Assignments (links on 322 web page under Required Reading)

**Forward genetics**

Browse through entire article and carefully read the following carefully: pg372 and figure 1. Answer questions on next page.

**Reverse genetics via targeted gene knockout:**

*Biologists claim Nobel prize with a knock-out.* NatureNews 10/9/07
*Sleep in Kcna2 knockout mice.* BMC Biology 5:42. 2007
Read all of the Nobel article and pages 1&2 and Figures 2&3 of the Kcna2 knockout paper.  Answer questions on next page.

Targeted Gene knockout in mice uses **homologous recombination** to introduce null mutations into a specific gene.

See very nice illustration of this process at this web site:
http://www.bio.davidson.edu/Courses/genomics/method/homolrecomb.html

![Diagram](image-url)
Please word-process your answers to these questions. Unless otherwise indicated each answer should be *one-two complete sentences*. Questions 1-6 cover the sleepless article and 7- the *Kcna2* knockout article.

**sleepless**

1. How many mutant candidates were screened and what general type of mutation did they carry?
2. Examine Figure 1a. What is the sleep phenotype of *sss* mutants? Be sure to state your answer in quantitative terms.
3. Examine Figure 1. Is the *sss* mutation dominant or recessive? Defend your answer by citing data from an appropriate panel.
4. Is the expression pattern of the *sss* mRNA consistent with a role in the sleep process? Yes or No and specific data to back up your answer.
5. What is the difference between *sleepless (sss)* and SLEEPLESS (SSS)? In other words, what do the upper and lower case versions refer to?
6. What is the advantage (stated twice in the introduction of this article) of a forward genetic screen? Contrast this advantage to targeted knockout of genes that are candidates for involvement in the sleep process. *Three sentences OK here.*

**Kcna2** knockout

7. How does this article illustrate the principle of reverse genetics?
8. What complicates the study of mouse homologs of the fly Shaker gene? Very briefly describe the author’s logic for picking the *Kcna2* gene for this study. *Three sentences OK here.*
9. Is this gene involved in the sleep process? Which data set in Figures 1 & 2 is the most compelling?
10. What is the most striking phenotype observed in the knockout homozygote?