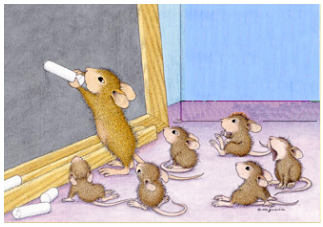

PSYC1193 Laboratory in Genes and Behavior
OR What's Wrong With My Mouse ?

SYLLABUS FOR SPRING 2013
(updated January 26, 2013)

Instructors: Rebecca D. Burwell, Ph.D.
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Office Hours: By appointment

Course Instruction Time: Fri, 9 am to 10:50 am
Metcalf 105
(required for all students)

Laboratory Sections: Monday, 9 am to 10:50 am
Wednesday, 9 am to 10:50 am
Bio-Med 178 (except as on syllabus)

Lecture Classroom: Fridays Metcalf 105 (MC105)

Teaching Lab: Monday and Wednesday
Bio-Med 178 (BM178)
(unless otherwise noted)

Teaching Assistants: Brendon Kent (brendon_kent@brown.edu)
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Overview of the Course: Students in this course will work together in a laboratory setting to study a mouse model of a human pathological condition. Like older children and adults, neonates and infants can be susceptible to epilepsy, yet little is known about the effects of antiepileptic drugs on development. In this class, we will expose mice to an antiepileptic drug, Topirimate, and then examine behavioral sequelae during development.

Attendance: Attendance is mandatory for all Friday classes and for one or lab section per week. Some weeks more or less time will be needed in the lab, so there may be some times when the Friday time is used in the lab. The instructor will make sure that Friday labs are distributed across lab sections.

Objectives: The purpose is to gain experience with a variety of behavioral assays used in assessing the effects of genetic background and genetic alterations on behavior. Emphasis will be placed on the planning and execution of experiments, analysis and interpretation of data, and science writing. The final

written product will be a manuscript reporting the results of the semester's experiments in publication format. Throughout the semester attention will be paid to development of science writing skills.

Background: The rat has traditionally provided the primary model for studying behavioral processes within a psychological framework. There is also a long tradition of using mice in behavioral research. Prior to the development of technology for manipulating the genome, behavioral geneticists relied primarily on comparisons of inbred strains of mice. In the past decade or so, neuroscience has increasingly employed targeted manipulation of genes expressed in the brain as a way of understanding the neural substrates of behavior. Most of this work is done in mice. **Transgenic** mice have an extra gene. This can either be a mutated gene, a new gene not normally expressed in the mouse, for example an aberrant human gene, or an added extra copy of a gene for the purpose of studying over-expression of the gene product. **Knockout** mice have a gene deleted. A null mutant homozygous knockout is missing both alleles of the gene. The genotype is (-/-). The heterozygote is missing one of the two alleles (+/-). The wildtype normal control has both copies (+/+). The new developments in molecular genetics have resulted in very powerful approaches to the study of the brain, but very few neuroscientists are trained in behavioral analysis using mouse models. Finally, life experiences can cause **epigenetic** alternations in mice and other animals. The term epigenetic is currently defined as changes in gene expression resulting in a different phenotype brought about, not by changes in DNA sequence, but by changes in a number of molecular mechanisms, including DNA methylation, histone modification, and nucleosome remodeling. These mechanisms appear to underlie long-lasting and persistent changes in behavior. For example, DNA methylation can be altered by environmental risk factors during development, such as drug exposure and environmental stress. In this class, we will assess the effects of epigenetic alterations induced by early life drug exposure on the subsequent behavioral phenotype in a mouse model.

Animal Model: We will expose very young mice to an antiepileptic drug, Topirimate, and then examine behavioral sequelae during development. Following birth, on postnatal day 4 mice will be randomly assigned to a control or drug group and will receive daily subcutaneous injections (until P11) with either vehicle (saline) or drug (Topirimate 200 mg/kg dissolved in saline). Starting at P6-8 (while still with their mothers) pups will begin basic neurodevelopmental testing (Early Battery, EB). This will include assessment of righting reflex, locomotor activity, and and other tests. Litters will remain with mothers until P20 and then will be sex segregated and group housed. Following weaning, mice will undergo additional behavioral testing on a second battery of tests (Late Battery, LB).

Goals: The overarching goal of this course is to teach basic principles involved in designing, conducting, and reporting behavioral analysis of mouse models of human disease. Over the course of the semester students will to establish a behavioral phenotype for a mouse model. That is, students will determine how the behavior of their mouse model differs from that of normal, wild type control mice. Students will also learn science writing skills and will produce a research manuscript suitable for publication in a scientific journal in the format accepted for the American Psychological Association (APA) journal, Behavioral Neuroscience.

DISCLAIMER: Although we have a vigorous breeding to provide mouse pups for the research you will conduct in this class, we cannot guarantee the availability of pups at the right age for testing. Though we have a schedule for the class, be prepared for changes to that schedule. We may need to test multiple cohorts of mice in order to generate experimental groups of sufficient size to provide the necessary power for our analyses.

Workload:

Attendance at all scheduled Friday sessions and all Monday or Wednesday labs (depending on your section).
Background readings including assigned chapters, research papers, and protocols.
Four written assignments as described below.

Course Grade:

100%: Four written experiments, each counts 25% of the grade. Professor Burwell will grade all writing assignments and will give feedback using the MS Word, Track Changes tool. Students who submit assignments on time are allowed to revise and resubmit the first three assignments within one week of receiving the graded assignment.

There is no explicit grading on participation in labs, but it is understood that all students will participate fully in order to receive credit for the course.

Written Assignments:

All written assignments should follow the Instructions to Authors for the journal, Behavioral Neuroscience. It is expected that the background papers will be cited, but most likely it will also be necessary to consult other research articles. The best search machine is PubMed. The url is http://www.ncbi.nlm.nih.gov/sites/entrez. Pubmed can also be accessed directly through EndNote.

When you submit your assignment, also attach the pdf files for any references that are not in your background readings.

Note that as we go through the semester, each assignment will build on the earlier ones, such that at the end of the class you have a full scientific manuscript with all the proper components and headings. You will be expected to add citations as you go.

Grading Scheme (25% will be translated into 25 points per assignment)

22-25 A
18-21 B
17-20 C

Anything below a C will be returned with comments for a mandatory revision.

First Assignment: Title Page and Introduction (25 %)

Length (3-4 pages, double spaced)

The first writing assignment is to provide an introduction to your particular study. The content will depend on which experiment your group is conducting. A general outline for the introduction to a research paper includes the following:

1) A description of the problem to be addressed. For example, if you have a mouse model of Down's Syndrome (DS), you should include a description of the impact of DS on human life

2) Rationale for the work. For example, perhaps this is the first good mouse model of DS and the behavioral phenotype of the model needs to be established.

3) A statement of the exact question to be addressed and a brief explanation of how you will address it. For example, you want to characterize the learning deficits in the mouse model of DS so that the model can be used to develop ways to improve cognitive function in DS. You are going to do that by…….

4) A statement of the impact of the findings. How more knowledge about DS could improve human life. Refer to the Sample Manuscript for an idea of how an introduction to a research paper should be organized. See also the following handouts:

Instructions to Authors
Checklist for Manuscripts.
The Elements of Style
Science of Science Writing

Length: As needed (but be very precise).

2nd, and 3rd Assignments: Experiments 1 and 2 (25 % each)

During the semester several behavioral tests will be conducted. The tests will be organized into two batteries, the Early Battery and the Late Battery. The Early Battery will largely be tests of motor function. The Late Battery will test cognitive and affective function. We will call each battery an Experiment. In some cases, several tasks may be grouped together to form an Experiment. Two Experiments will be conducted over the semester. Your manuscript will generally be due one week after the last day of data collection. Manuscripts will be doublespaced and should include the following:

1) A very short explanation of the behavioral test(s) and why those particular tests were employed in the overall study (about one paragraph).
2) A methods section.
3) A results section.
4) A very brief discussion section, mainly summarizing the results (perhaps one paragraph).
5) Figures showing the results with caption. It is not necessary to show negative results but you may if there is a good reason.
6) Citations. Throughout the course, you will be adding to your paper including the reference section.

To the extent possible, these reports should follow the Behavioral Neuroscience Instructions to Authors. Experiment 1 in the Sample Manuscript provides an example of what is expected for each experiment.

Final Research Manuscript (25%)

At the end of the semester, you will add an Abstract, General Discussion, and Conclusions. In this assignment you will briefly summarize your results, discuss your findings across all three experiments, and draw conclusions about what the complete study contributes. It will be expected that you have revised the manuscript as needed using instructor feedback and made sure that the manuscript is written according to the Behavioral Neuroscience Instructions to Authors.

Recommendations for Software: SPSS, Excel, EndNote.

Topics and Assignments

Readings will consist of a main text book as well as research papers and handouts available on Canvas. The text book chapters (Crawley, J. N. (2007). What's Wrong With My Mouse, 2nd Edition. New York: Wiley-Liss.) will be available on the course website. All other readings will be posted on Canvas. In addition, students will be expected to complete all readings before coming to class.

CLPS1193 Schedule

Week of January 21

Wednesday: No Class

Friday (MC105): Introduction to the Course (Rebecca Burwell, CLPS)
Introduction to Stress and Behavior (Kevin Bath, Neuroscience)
Readings:
Ohmori, H., K. Yamashita, et al. (1997). "Effects of low-dose phenytoin administered to newborn mice on developing cerebellum." Neurotoxicology and teratology **19**(3): 205-211.
Bath, K. G. and H. E. Scharfman (2013). "Impact of early life exposure to antiepileptic drugs on neurobehavioral outcomes based on laboratory animal and clinical research." Epilepsy & behavior : E&B.

Week of January 28

Mon (MC107): Ethovision Introduction
Ethovision XT Quick Start Guide

Wed (MC107): Ethovision Introduction
Ethovision XT Quick Start Guide

Friday (MC105): Care and Use of Animals In Research (Rebecca Burwell, CLPS)
Animal Care Facility Orientation (Ann Beauregard-Young, ACF)

Week of February 4 **Readings:**
What's Wrong With My Mouse, Chapter 4, Motor Functions
Brooks, S. P., T. Pask, et al. (2004). "Behavioural profiles of inbred mouse strains used as transgenic backgrounds. I: motor tests." Genes Brain Behav 3(4): 206-215.

Mon and Wed (lab): EB: Righting Reflex

Friday (MC105): Statistics and Writing Workshop
Behavioral Neuroscience, Instructions to Authors
The Science of Science Writing
The Elements of Style
SPSS Instructions

Week of February 11 **Beginning of Early Battery (Experiment 1)**

Mon and Wed (lab): EB: Small Open Field

Fri (lab): To be scheduled, if needed

Mon Feb 15, 12am: Manuscript with Title page, Introduction, and References due

Week of February 18

Mon:	University long weekend, no class
Wed (lab):	EB: Wire Hang
Fri (lab):	Monday Group, EB: Wire Hang

Week of February 25

Mon and Wed (lab):	EB: Large Open Field
Fri:	To be scheduled, if needed

Week of March 4

Mon and Wed (lab):	EB: Pole Climb
Fri:	To be scheduled, if needed

Monday, March 12, 5 pm: Manuscript with addition of Experiment 1 due

Week of March 11	**End of Early Battery (Experiment 1)** **Beginning of Late Battery (Experiment 2)**
Mon and Wed (lab):	EB: Rotarod
Fri (lab):	Wednesday Group, LB: Novel Object Location
Week of March 18	**Beginning of Late Battery (Experiment 2)** **See Canvas for Readings**
Mon (lab):	LB: Novel Object Location
Wed (lab):	LB: Novel Object Identity
Fri (lab):	Monday Group, LB: Novel Object Identity

Mar 23-March 31: Spring Recess, no class

Week of April 1

Mon and Wed (lab):	LB: Fear Conditioning
Fri:	To be scheduled, if needed

Friday, April 5, 5 pm: Manuscript with addition of Experiment 1 due

Week of April 8

Mon (lab): LB: Grip Strength

Wed (lab): LB: Grip Strength

Fri (lab): Wednesday Group, LB: Forced Swim

Week of April 15

Mon (lab): LB: Forced Swim

Wed (lab): LB: Von Frey Tactile Sensitivity

Fri (lab): Monday Group, LB: Von Frey Tactile Sensitivity

Week of April 22

Mon and Wed (lab): LB: Hot Plate

Fri: To be scheduled, if needed

Wednesday, May 1, 5 pm: Manuscript with addition of Experiment 2 due

April 29-May 6 Reading Period, no class

Monday, May 13, 5 pm: Complete Manuscript due including General Discussion