GRADUATE PHARMACOLOGY PCL1002Y

Our core required course for all Pharmacology graduate students in M.Sc. and Ph.D. programs

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A few defining features of our Graduate Program…

- **strong undergraduate B.Sc. Specialist Programs in Pharmacology and Toxicology as valuable "feeders"**
- **popular programs leading to M.Sc. (44 students) and Ph.D. degrees (38 students)…82 current registrants**
- **institutional training grants are relatively rare**
- **less emphasis on formal course work**
- **each student has a Supervisor, financial support and starts thesis research project from Day 1 in program**

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The 2004-05 course contents at a glance…

Course Coordinators: Dr. Allan B. Okey & Dr. David S. Riddick
Fridays 10 am - 12 pm, Medical Sciences Bldg Room 4227
2004-05 student registrants: 24 [19 M.Sc. and 5 Ph.D.]

17 Sep to 8 Oct	**Drug Metabolism**	**Okey/Riddick**	 
15 Oct to 5 Nov	**Molecular Biology**	**McPherson**	
12 Nov to 3 Dec	**Pharmacogenomics**	**Grant**	
14 Jan to 4 Feb	**Signal Transduction**	**Mitchell**	
11 Feb to 4 Mar	**Clinical Pharmacology**	**Lanctôt**	
11 Mar to 8 Apr	**Behavioral Pharmacology**	**Burnham/Grupp**	 

EACH FOUR-WEEK MODULE CONSISTS OF:

- **2 X 2-hr lectures by faculty members**
- **2 X 2-hr sessions of student presentations of research paper critiques**

OBJECTIVES OF THE COURSE

- **introduce students to topics in pharmacology at a research level**
- **develop students' abilities to critically analyze research literature**
- **give students experience at organizing and presenting scientific talks**
- **give students experience at writing and reviewing a research proposal**

[social: meeting place for geographically dispersed students]

HOW ARE STUDENTS EVALUATED ?

- **Presentation/Critique of Research Paper in Fall Term 10%**
- **Mid-Term Exam (10 Dec 2004) 30%**
- **Presentation/Critique of Research Paper in Winter Term 10%**
- **Grant Proposal (Due: 11 Mar 2005) 30%**
- **Review of a Grant Proposal (Due: 8 Apr 2005) 10%**
- **Participation and Contribution to Class Discussions 10%**

CRITICAL ANALYSIS OF A RESEARCH PAPER

The Assignment

- **student receives the paper citation one week before presentation**
- **student locates paper via U of T Library e-journal collection**
- **student reads and critically analyzes paper**
- **consultation with faculty member is permitted**
- **student gives 10-min oral presentation + 15 min discussion**

Critical Reading of the Scientific Literature

- **What are the authors' conclusions?**
- **Are the conclusions justified by the experimental evidence provided in the paper? [i.e. Do we believe?]**
- **Are the conclusions of any significance? [i.e. Do we care?]**

THE MID-TERM EXAM

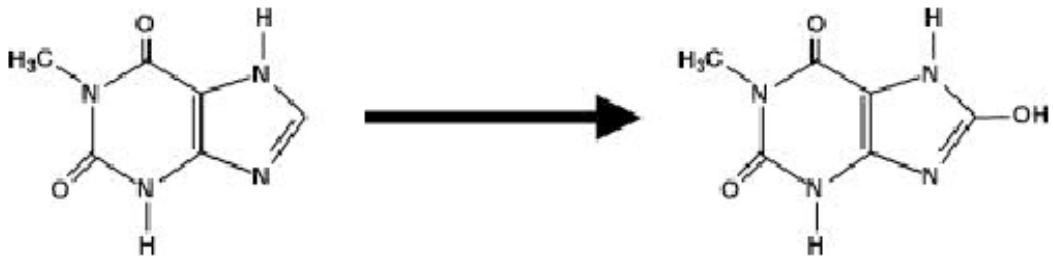
- **a written in-class 3-hour exam**
- **requires knowledge of lecture materials and research papers**
- **questions require application of knowledge to solve problems**
- **short answer, essay-style, diagrams and flow-charts, etc.**

Let's look at a sample question from the Dec 2004 exam…

[Just don't expect me to answer it !!]

1-Methylxanthine and 1-methyluric acid are major metabolites of caffeine, both of which are readily and easily measured at similar levels in the urine of coffee, tea and caffeinated cola beverage drinkers. 1-Methyluric acid is produced via the biotransformation of 1-methylxanthine, as shown below:

1-methylxanthine ***1-methyluric acid***



You perform a series of *in vitro* enzyme assays to measure 1-methylxanthine 8-oxidation to 1-methyluric acid using cytosols isolated from the livers of 40 (previously healthy) deceased motor vehicle accident victims. You detect high levels of enzyme-dependent formation of 1-methyluric acid (mean activity = 2.3 ± 0.4 nmol of product formed per minute per mg protein; range from 0.8 to 3.4) in 37 of the 40 samples. In each of the remaining 3 samples, however, levels of product formation are below the detection limit for the assay (<0.2 nmol/min/mg).

(a) Discuss the possible biochemical and/or genetic mechanisms that could produce this variation in the activities that you have observed among the 40 liver samples in your *in vitro* assays. [15 marks]

(b) How would you design and carry out experiments to distinguish from among the possible mechanisms? [20 marks]

(c) Based on the structural and functional information you have been provided above, what type of enzyme could be responsible for the conversion of 1-methylxanthine to 1-methyluric acid? [5 marks]

(d) Discuss the potential clinical and toxicological consequences of your discovery, and how you would assess these. [15 marks]

(e) Under what circumstances would you recommend predictive testing for the observed defect, and what test method would you recommend? [10 marks]

Subsequent clinical studies of patients suffering from a rare but severe form of the disease gout reveal that they have dramatically elevated levels of 1-methyluric acid in their urine after caffeine ingestion, and very low levels of 1-methylxanthine.

(f) What mechanism(s) could produce this observation? [10 marks]

(g) Describe how you could develop a useful diagnostic test to predict the occurrence of this severe form of gout. [10 marks]

(h) Discuss possible strategies that you could use to discover and develop potential therapies for the treatment of this disorder. [15 marks]

PREPARATION OF A CIHR-STYLE GRANT APPLICATION

The Assignment

- **student assigned to a general topic area under a faculty member**
  [distinct from their own thesis research **]**
- **student selects their own specific topic of interest**
- **consultation with faculty member is permitted**
- **one-page "letter of intent" submitted after 4 weeks…feed-back**
- **full proposal submitted after an additional 5 weeks**

The Benefits of this Demanding Exercise?

- **in science, a continual need to convince others of the merit of our work**
- **having to explain our goals and methods to others sharpens and clarifies our own understanding of our research**
- **the need for feed-back on strengths and weaknesses of our research before "it is too late"**

REVIEWING ANOTHER STUDENT'S GRANT APPLICATION

The Assignment

- **each student receives one other student's proposal to review**
- **consultation with faculty member is permitted**
- **written critical evaluation of the significance and strengths & weaknesses submitted after 3 weeks**

The Essential Elements of a Grant Review

- **What does the researcher plan to do? [goals, hypotheses]**
- **Does it make sense? [rationale]**
- **Is the work important? [originality, significance, impact]**
- **How will the researcher do the work? [research plan]**
- **Is the work feasible? [track record, time-line, contingency plan]**

CONTRIBUTION TO CLASS DISCUSSIONS

- **course coordinators evaluate every student presentation**

- **monitor and evaluate each student's contribution to class discussions of research papers**
  [Both QUANTITY and QUALITY of comments!!]

- **the full range (0 to 10) used to grade this component**

WE EVALUATE THE STUDENTS…

Final course grades for 2004-05 academic year:

A+ = 4	**A- = 5**	**B = 7**
A = 6	**B+ = 1**	**F = 1**

THE STUDENTS EVALUATE US…

- **written survey:** **7 questions about the course**
  7 questions about each faculty member

How well do you think that the course serves its goal of training graduate students towards a research degree??
[Very well (4) Quite well (3) Adequately (2) Inadequately (1)]…3.26

Overall assessment of teaching ability of a faculty member??
[Excellent (5) Very good (4) Good (3) Fair (2) Poor (1)]
…eight faculty: mean ± SD = 4.15 ± 0.54 , range = 3.09 to 4.70