THIS IS THE 2011 COURSE GUIDE PROVIDED TO GIVE PROSPECTIVE HCP STUDENTS AN OVERVIEW OF WHAT HCP INVOLVES.

PLEASE NOTE THAT THERE WILL BE DIFFERENCES IN SOME DETAILS OF COURSE CONTENT, ORGANISATION AND ASSESSMENT IN 2012 (yet to be finalized).

2012 HCP COURSE GUIDES WILL BE AVAILABLE IN LATE FEB 2012.

The University of Sydney

*Department of Physiology*

HUMAN CELLULAR PHYSIOLOGY: Theory (PHSI3005/3905)
and
HUMAN CELLULAR PHYSIOLOGY: Research (PHSI3006/3906)

2011 COURSE GUIDE

This document can be downloaded as a pdf from the HCP Blackboard site or purchased as a bound hardcopy from the copy centre in the sports complex.
This course guide provides an overview and lecture outlines for PHSI3005/3905 & PHSI3006/3906 plus essential material for the PBL sessions. For those undertaking PHSI3006/3906, make sure you have a hardcopy to take to every PBL session.

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GOALS AND STRUCTURE OF HUMAN CELLULAR PHYSIOLOGY

Human Cellular Physiology: Theory (PHSI3005/3905)
The central goal of Human Cellular Physiology is to introduce students to the world of cellular physiology and develop skills to understand and critically evaluate progress in this important field of human endeavor. Human Cellular Physiology is divided into two units of study (PHSI3005/3905 and PHSI3006/3906). PHSI3005/3905 lectures aim to provide an overview of our current theoretical understanding of certain aspects of the function of tissues such as nerve, kidney, gut and bone. They will also consider the mechanisms that lead to the growth and differentiation of tissues. The lecture content and ideas will be reinforced in follow-up tutorials by the various lecturers. One of the major reasons for studying physiology is to understand disease states. These will be discussed along the way. Advances in Physiology and our progress in understanding disease states are intimately intertwined. PHSI3005 can be taken alone, but we strongly recommend taking it in combination with PHSI3006. Advanced HCP can only be taken as the combination of PHSI3905 & PHSI3906.

Human Cellular Physiology: Research (PHSI3006/3906)
PHSI3006/3906 develops upon and reinforces what is learnt in PHSI3005/3905 (this is why we strongly recommend taking PHSI3006 together with PHSI3005). In PHSI3006/3906 we will delve deeply into some specific research problems to illustrate our ongoing struggle to better understand the physiological mechanisms behind particular disease states. To make sense of what is going wrong with cells in disorders such as cystic fibrosis and prostate cancer we need to understand the normal function of the particular tissue. Each week we meet twice as a group of ~12 students and a tutor for Problem Based Learning (PBL) sessions. Our discussions will focus on reading lists of original research papers. Each list addresses a current research problem such as how and why physiological regulation of cell growth fails in prostate cancer or how dysregulated B-lymphocyte growth might lead muscle weakness in myasthenia gravis. Each PBL problem will run over 3 weeks, culminating in a group oral presentation in which your group will explain the issues to a tutor, who will assess the efforts of the group and give you feedback on strengths and weaknesses. The individual contributions of group members will also be assessed to encourage every member of the group to pull their weight (see Assessment below).
The Friday Methods lecture aims to explain methodologies that appear in the research papers you read and the sorts of information that they can reveal. Textbook theory changes over time. As a science graduate you should have at least begun to develop the ability to read and critically interpret new published experimental results in the light of pre-existing theory (those who undertake the Honours year will further develop these skills). In PHSI3006 you should endeavor to explain how the experimental evidence you read advances our theoretical understanding of the problem.

There will be two practical classes (see Web-ct for timetable information). These involve cell growth control in mammalian cell culture (coordinating academic: Dr Steve Assinder) and measuring transport of ions across membranes (coordinating academic: Dr Margot Day).

**Human Cellular Physiology (Advanced)**

Students who qualify, and wish to take HCP (Advanced) take the combination of PHSI3905 with PHSI3906. You will attend the same lectures and prac classes as students in PHSI3005 and PHSI3006. The Advanced PBL group will undertake problems 1 & 2 but not 3. This is to provide a little more time for your individual research report. Advanced students will also be relieved of the need to hand in practical reports, giving them more time for their chosen library- or laboratory-based research project. Please see the list of Library or laboratory based projects accessible via the Physiology website at [http://www.physiol.usyd.edu.au/students/prospective/](http://www.physiol.usyd.edu.au/students/prospective/) (and follow the links to Advanced projects). The lecturer offering the project will be your mentor and you should arrange to meet her/him regularly throughout the semester (fortnightly for library-based projects).

**What you need to do to set up your PHSI3905/PHSI3906 (Advanced) research project:**

1. Please contact the Unit of Study coordinator, Bill Phillips (contact details above) to get permission to enroll. You will need a form from the Faculty office and your academic transcript.
2. Choose a preferred topic from the Physiology website (see url above)
3. Contact the lecturer/s who wrote the topic to learn more about what it involves, whether the topic is still available and organize a time for fortnightly mentorship/progress meetings. In the case of lab-based projects you must be sure that your time constraints will allow you to complete the work. This means you must talk through these issues with the lab head concerned.
4. Tell Louise Harrison (Physiology Office) the name of your intended mentor and which project. Louise will be the person to organize your PBL group.
5. Meet fortnightly with your mentor with the papers and summaries of the reading you have done and with a list of questions to actively elicit helpful feedback.
6. Submit a Research Plan for your project no later than the Monday of week 6. It must be submitted via Louise Harrison in the Physiology office. See “Assessments” section of this course guide for format details.

**TEXTBOOK FOR HCP:** Molecular Biology Of The Cell / ed. Alberts
Publisher: Taylor & Francis, 5th Edn. This book should be of broad use to you in all the biomedical disciplines that you study. If you can’t afford to buy it (new or second hand), the Library has copies in the Reserve collections of the Medical & Badham Libraries, as well as multiple copies in their general collections, and copies are also held in the Dentistry and Scitech Libraries.
Frank Cotton Prize
The Frank Cotton Prize recognizes the student who achieves the overall top score in Human Cellular Physiology each year. Frank Cotton was a cardiovascular physiologist and pioneer in the field of sports science. During the Second World War he used his human centrifuge (then located in what is now the Cotton Practical Lab) to develop the anti-gravity suits used by Allied fighter pilots to prevent them blacking out under high G-forces.

Frank Cotton Prize Winners:
2005 Lauren Ferris
2006 Arabella Lindsay-Walker
2007 Lucia Hong Van Nguyen
2008 Claire Francis Dickson
2009 Jana Ludmila Vitesnikova
2010 Fallon Brielle Noon

TEACHERS IN HUMAN CELLULAR PHYSIOLOGY:
*Human Cellular Physiology* is presented by the Discipline of Physiology, School of Medical Sciences

Lecturers:
Prof Rebecca Mason
Dr Colin Dunstan
Dr Stephen Assinder
Dr Margot Day
Dr Stuart Fraser
A/Prof Chris O'Neill
Dr Michael Morris
A/Prof Bill Phillips (Unit of Study Coordinator) william.phillips@sydney.edu.au

PHYSIOLOGY RESEARCH OPTIONS
Physiology is an experimental science. To learn more about gaining research experience in Physiology:  http://www.physiol.usyd.edu.au/research/labs/index.html
For information on Physiology Honours research options  http://www.physiol.usyd.edu.au/students/honours/honours_projects.html

The biovideo project: people talk about their Honours and PhD experience  http://www.physiol.usyd.edu.au/~billp/biovideo/library.php

CHANGES MADE TO THESE UNITS OF STUDY IN RESPONSE TO STUDENT FEEDBACK
Recent changes made in response to student feedback include:
• Tutorials and quizzes introduced to provide feedback (2007)
• Model answers to quiz questions provided on line 24hrs after the quiz (2009)
• Lectopia lecture recordings (2009)
• Video "how to do PBLs" available via web-ct (2009)
• More explanation of our expectations and how to do well in HCP (2010)
• New PBL topic Regulation of potassium homeostasis by the kidneys (2010)
**TIMETABLES**

**PHSI3005/3905**

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<thead>
<tr>
<th>Lecture Times</th>
<th>Locations</th>
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<tr>
<td>Mondays 11am-12 noon</td>
<td>Chemistry LT 3</td>
</tr>
<tr>
<td>Tuesdays 12noon-1 pm</td>
<td>Carslaw LT 159</td>
</tr>
<tr>
<td>Thursdays 3pm-4pm</td>
<td>Chemistry LT 1</td>
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**Tutorial time (not every week)***

| Thursday 11am-12 noon | Education Room 424 OR |
| Thursday 2pm – 3pm    | Chemistry LT 2 |

*NB tutorials provide follow-up to lecture material, half the class each session. Your personal timetable should direct you when to attend these. If in doubt consult Louise Harrison in the Physiology office, Rm E201, Anderson Stuart Bldg.

**PHSI3006/3906**

<table>
<thead>
<tr>
<th>Lecture Time</th>
<th>Locations*</th>
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<tr>
<td>Fridays 12-1pm</td>
<td>Carslaw LT 157</td>
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**Problem based learning (PBL) sessions**

<table>
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<th>Locations*</th>
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<td>Refer to personal timetable OR</td>
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| Tuesdays 11am and Friday 11am |
| Tuesdays 1pm and Fridays 9am |

**Practicals (not every week)**

| Mondays 2-5pm and Tuesdays 2-5pm | Anderson Stuart Building |

‡ Changes in venue and time sometimes occur after this courseguide and your personal timetable are printed. Our definitive timetable is at: [http://www.physiol.usyd.edu.au/students/current/timetables/](http://www.physiol.usyd.edu.au/students/current/timetables/)  

Practical Class timetables and prac class groups will be determined when enrollments have been finalized. Details will be released via the PHSI3006 web-CT site and notices in the Physiology Department. The Cell growth and differentiation practical class requires some follow-up examination of cell cultures on the days following the practical class.

Some practical classes use animal tissue: The *Epithelial Transport* practical classes in PHSI3006/3906 involve students working with tissue dissected from cane toads. The toads are first humanely killed and the tissue dissected by a skilled technician under a protocol approved by the University of Sydney Animal Ethics Committee. If you have ethical objections to participating in such practical classes you should either change your enrolment now (before the end of week 3) or do all of the following: 1/ go to the Physiology office to complete a form explaining your ethical concerns then 2/ contact the unit of study coordinator to obtain an alternative assessment task and 3/ complete and submit the alternative assessment task.

**ASSESSMENT**

**PHSI3005:**

- **Quizzes** 40%. There will be a quiz (closed-book) given by the lecturer after most blocks of lectures. Quizzes will consist of short answer questions (SAQ; 15min each) ± single best answer
questions (SBA; 3min each). The style of questions asked and marking criteria inevitably vary somewhat from lecturer to lecturer. For this reason it is in your interest to attend the tutorial session that precedes each quiz. You will get more out of the tutorial, and better marks in the quiz and final exam, if you study the lecture material in advance, and ask questions at the tutorial. Quizzes will be invigilated under semi-exam conditions (no written matter to be taken from bags, phones and other digital devices must be switched off). The marks from these quizzes will total 40% of the final assessment mark for PHSI3005 students.

- **Examination 2hr 60%**: SAQ and SBA (closed book). This covers the lecture material. No written material will be allowed in the exam. The numbers of questions on each topic will be roughly in proportion to the number of lectures given by the relevant lecturer/s.

### PHSI3006
- PBL assessment by tutors (see Criteria below)- 20%
- 2 x Prac reports*- totaling to 20%
- 1.5h Consisting of SAQ (6 x 15min) + SBA (10 x 3min) exam 60%. No written material will be allowed in the exam. The PHSI3006 exam will test the material in the PBLs and Methods lectures. It is not the intention of lecturers to test your memory of fine technical details contained in individual papers covered during the PBLs. Nevertheless you need to study the material covered in the PBLs as you go. One of the goals of the PBL stream is to develop skills in analyzing and synthesizing biomedical information. Another goal is to teach students approaches to problem solving in cell physiology/cell biology. In reading the papers and in your PBL sessions you should consider the experimental approaches, their application and interpretation in relation to emerging theory. Thus, some PHSI3006 exam questions will ask you to explain, in broad terms, how you might apply methods described in the methods lectures to address specific scientific questions of the sort raised in one or other of the PBL problems. What we are seeking to assess is how well you can extend and apply what you have learnt. Read the question carefully and try to answer it specifically.

### PBL attendance and your duty to your colleagues
Students in Human Cellular Physiology are in their final year of undergraduate studies before graduating or progressing to the research environment (Honours). In either case we expect our soon-to-be graduates to take their personal and professional responsibilities seriously, in a way that will reflect well on them self, on the Discipline of Physiology and on the University. In PBLs, each member is responsible for contributing to the overall work and achievement of their group, as in a team-work environment.

Every PBL session is preparation for the group presentation and the final PHSI3006 exam. Thus, if you become sick, or for some other reason are unable to attend a PBL session, you should make contact with your group members and tutor to explain ASAP. If you suspect that your sickness will prevent your attendance at more than one PBL meeting you will need to apply formally for special consideration via the Faculty of Science. Contact the presenters and offer to make amends for your absence (eg by preparing an extra paper summary or overhead). If you don’t make the effort and simply miss several sessions you are unlikely to score well in the individual participation mark. In the event of repeated non-attendance without an acceptable Special Consideration, or repeated failure to actively participate in PBL sessions, a student will not be credited with the shared group-presentation mark.

### Criteria for PBL Assessment (PHSI3006/3906; total 20%)
Criteria for marking individual contributions to the PBL (10% of final mark)
This will be assessed by tutors with the aid of written summaries and overheads prepared by students for each PBL. The following criteria (mark out of 5)
Mark awarded
0 absent without excuse or apology; or severely disruptive
1 present but not useful contribution (totally unprepared, no evidence of reading done); or somewhat disruptive
2 present but minimal contribution, not well-prepared
average expectation: is well prepared, they circulate to the group and tutor a clear and helpful 1-2 page summary of the research paper/s that they have been assigned to read and, a diagram or flow chart that is likely to be useful to the students responsible for the presentation

evidence of good understanding, thorough reading as judged by thoughtful written and spoken contributions during the first 5 sessions

exceptional contribution, real insight into the problem, superb summaries and diagrams

Criteria for assessing group oral presentations
-Group presentation (10% of final mark) These marks are awarded to the group on the basis of the quality of the group presentation at the end of each topic. This will be assessed in session 6 of each problem by a tutor other than the one who normally has the group. In session 5, the group's own tutor will provide feedback to the group on their rehearsal talk. The marks awarded for each of the PBL presentations will count equally. Each talk is marked out of 9. The talks should run for not more than 45 minutes.

Information content 1/3rd (marked out of 10)
• Clear and thorough description of the normal physiology of the system in question.
• Succinct description of the abnormalities focusing on the ways in which normal physiology is known to be disturbed.
• Clear explanation of well established cellular and molecular pathways involved in the normal physiology, pointing out steps that have been proposed to be disrupted in the disorder.

Critical development of ideas 1/3rd (marked out of 10)
• Clear delineation of the boundaries between what has been well established (through experimental and other evidence) and hypotheses that have been put forward in the literature.
• Explicit description of relevant current hypotheses. This should explain what the hypothesis proposes about the cellular and molecular mechanisms behind the normal physiology and about how these might be disrupted in the disorder.
• A rational line of argument explaining how specific types of experimental and other evidence provide support for a particular hypothesis.
• Raise any evidence that may argue against a particular hypothesis explaining why it does.

Effective Communication 1/3rd (marked out of 10)
• Clear, easy to follow speech.
• Effective use of overheads and drawings.
• Speakers coordinated amongst themselves such that the sequential development of the key ideas is obvious to the listener.

How can you do well in the presentations? The key to this is that as a group you work together to gain a deep understanding of the issues. It will then be necessary for the 2-3 people who are assigned by the group to do the presentation to work together to plan the talk. They should take responsibility for organizing the meetings. Everyone will contribute to the success of the presentation. Everyone in the group should be a presenter for one of the PBL problems as this is an important skill for a graduate.

NB: In the event of repeated non-attendance without an acceptable Special Consideration, or repeated failure to actively participate in PBL sessions, a student will not be credited with the shared group-presentation mark. No one should freeload off the work of their colleagues.
In consultation with your mentor choose an original research paper that is based largely upon animal experiments? (<200wds)

In the case of lab projects). While the plan must be concise it must also be clear, so your mentor can easily follow your intentions. Please do discuss a draft of your plan with your mentor well before you hand it in. The aim is to get you on track in your project early on. Their mark will reflect their ability to see that you have done some reading, have scoped out the issues of interest to you and have a clear plan for your ongoing reading and/or experiments.

• Final Research Report*- 30% This 2,000wd report must be submitted to Louise Harrison (Physiology Office) by 4:30pm on the Monday of WEEK 12 (or the Tuesday if a public holiday). It will be written in the scholarly form with citations to original research papers and occasional review articles in the Harvard format (eg Smith et al 2004). Well-chosen figures from original published works may be included (with proper citation) where they help you to explain the issues. In this case write your own legend. Mentors have been told not to read drafts of your final report. Instead you should critically re-read your own draft report (after putting it aside for several days). This will help you identify areas of weaknesses that you can then raise with your mentor for advice, prior to final submission. Do it early to give your self enough time. The research report and essay plan will replace the PHSI3005 quizzes. If you want feedback on how you are going with the lecture material you are welcome to sit the PHSI3005 quizzes (voluntary), but the marks will not count toward your final assessment.

PHSI3906
• PBL assessment by tutors- 20%
• SAQ exam based upon PBL problems- 60%
• PHSI3906 Report on the animal ethical implications of research* (1,500wd) - 20% The use of animals in experiments is strictly regulated in Australia. Committees comprised of scientists, veterinarians and lay people consider a detailed written research proposal for each project before it can begin (see for example http://sydney.edu.au/research_support/ethics/animal/ ). The purpose of the PHSI3906 report is to deconstruct the experimental animal usage from a single graph from one published original research article of your choice, to identify the key animal ethical issues associated with the experiments undertaken and to consider the ethical justifications for the use of animals in this way. The PHSI3906 ethics report must be submitted to Louise Harrison in the Physiology office in hard copy by 4:30pm on the Friday of Week 13 (or 24h earlier if the Friday is a public holiday).

Format and expectations for PHSI3906 ethics Report (1,500wd)
In consultation with your mentor choose an original research paper that is based largely upon animal experiments. Consider the ethical issues arising from the research reported in that paper under the following subheadings (word limits are only suggestions):

1. Title: of paper you have chosen to analyse (Include authors, year, journal, volume &pages)

2. Lay summary: Describe the project in lay terms (so your mother would understand) indicating in broad terms what has been done, what new information it provides, and how this new information may, in the long term, benefit humankind and/or animals so as to justify the use of the animals. This means you must relate the particular experiments to the bigger picture of the research field you have been studying for your project (Suggested maximum 500wds).

3. Why was it necessary to use animals in these experiments? (Suggested max 50wds)

4. Alternatives: What alternatives to animals might have been considered (eg use of cultured cell lines, computer modelling) what limitations might have prevented these from being adequate substitutes for animal experiments? (<200wds)

5. Data Figure: Reproduce ONE set of results from the paper: having read the whole paper select just one set of experiments to 'deconstruct' (eg Fig 3A). By 'set of experiments' I mean the same experiment repeated "n" times, where n= the number of animals or samples of tissue for which a parameter or parameters were measured. The quantitative results will often be presented as a histogram or some other form of graph showing the mean value obtained for the samples tested and some measure of variability.
among the “n” animals (a commonly used measures of variability include the standard deviation/SD). Alternatively they might have presented the standard error of the mean (SEM). Include a copy of the figure you have chosen and its original legend (not counted in word total).

6. **Explanation of results:** Write in your own words an explanation of what the particular graphs shows. The graph may be just one panel from the figure. Explain what was done, what was measured, what the axes show and broadly what is the interpretation? (<200wds).

7. **Sequence of events:** Describe the Sequence of events for each animal: for the experiment presented in point 5 above outline what would have happened to the animal (eg given general anaesthetic, briefly describe any surgery, recovery from anaesthesia, experimental analysis of dissected tissues etc). This information should be contained in the figure legend, the Results and the Methods sections of the paper but may require some digging and following citations to earlier papers. Different countries differ in the laws and regulations that govern animal experimentation. Since the rules for the country where your paper was written may not be easily accessible or may not be in English, I recommend that you assess what was done in terms of Australian practise, taking account of the relevant NSW Government Animal Act (see [http://www.usyd.edu.au/ethics/animal/AEtechniques.html](http://www.usyd.edu.au/ethics/animal/AEtechniques.html)). Would it or should it be approved if it were to be put to a NSW Animal Ethics Committee? Identify each step in the treatment of the animal that may have adverse physical or psychological effects on the animal and any ways you can think of in which these might have been minimized. Such details are not normally included in a published paper due to space constraints but the authors would have needed to provide them to their ethics committee (<500wds).

8. **Justifying replication of experiments:** The biological sciences are mostly empirical rather than relying upon deductive logic. To establish that a particular ion channel has a characteristic conductance, of say 9 picoSiemens, it is necessary to measure the conductance not just once but multiple times, ideally on different samples on different days. Each time the measured value will likely be a little different due to error in the measurement and **biological variability**. A mean value and a measure of variability within the sample can give other scientists confidence that the conductance measurement you have made is **reproducible** and that it really represents a fundamental property of the channel. They might expect that if they were to repeat the experiments in their own lab with tissue from the same strain of mouse they should obtain the same mean value. Looking again at the graph shown in section 5, identify the measure of variability. There should also be some statistical test for any differences between means (a measure of the probability that differing means obtained might have occurred simply as a result of random biological variability within the sample). By consulting a basic biometry textbook describe the nature of the statistical analysis that the authors of the paper have used. The justification needs to be specifically for your data (max 200 wds).

9. **Holding and monitoring of animals in animal houses:** It is the responsibility of the investigating scientist to monitor animals in her/his charge both before during and after experiments. There are guidelines for this ([http://www.usyd.edu.au/ethics/animal/AEtechniques.html](http://www.usyd.edu.au/ethics/animal/AEtechniques.html)). In a few lines give some thought to animal welfare issues of general relevance to holding the type of animals used in your study in an animal house (eg how many animals per cage, health and psychological factors). Mention any special issues related to the animals dealt with in your study. Would they be weak due to the treatment or their genotype? Sensitive to pain? Any special adjustments needed? (maximum 100 wds).

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**University policy on plagiarism**

Plagiarism refers to when someone copies the written work of another and falsely presents it as their own original work. This is a serious offence for a scholar and may result in serious consequences. The relevant sections of this University policy have been included below. Please read these carefully as failure to comply can result in expulsion from the university or a failure in the unit of study. It is essential that you are aware of the University’s policy in regard to plagiarism, group work and legitimate co-operation, as stated below and advised by the Academic Board:

**POLICY/CODE OF PRACTICE**

The University is committed to the basic academic right that students receive due credit for work submitted for assessment. Integral to this is the notion that it is clearly unfair for students to submit work for assessment that is not their own. This is known as plagiarism. Such activity undermines the fabric of universities by compromising the integrity of academic work.
**Plagiarism**

Plagiarism can be broadly defined as knowingly representing another person’s ideas, findings or written work as one’s own by copying or reproducing them without due acknowledgment of the source. Within this general definition, plagiarism may take several different forms. At its worst, plagiarism is theft. Plagiarism may involve copying the work of another student, or it may involve paraphrasing or copying a published author’s text or argument without giving a reference. Procedures for dealing with plagiarism must be consistent across all faculties, and must be appropriate to the nature of the alleged offence. Less severe cases may need to be dealt with at a lower level, with the emphasis on education rather than penalties. For instance, in some students the ‘offence’ may actually be due to lack of training in academic writing skills and referencing conventions.

**Groupwork**

Groupwork is defined as a formally established project to be done by a number of students in common, resulting in a single report/essay or a number of associated reports/essays. There is a growing emphasis in the university on assessment tasks involving group assignments and projects. This has resulted from the recognition of the value of group skills as a vital component of university-based professional training.

**Legitimate Co-operation**

Legitimate co-operation can be defined as any constructive educational and intellectual practice that aims to facilitate optimal learning outcomes through interaction between students. Typical examples of these practices may include discussion of general themes and concepts; interpretation of assessment criteria; informal study/discussion groups; strengthening and development of academic writing skills through peer assistance. Legitimate co-operation is based on the principle that producing the work remains the independent responsibility of the student, while recognizing the educational value of interaction between students.”

For any material to be assessed, the most important principles which you should bear in mind are:

1) Express what you have read in your OWN words.
2) Do not quote from sources verbatim, even if using quote marks and citing your source, UNLESS the wording is so perfect that you feel that it must under no circumstances be omitted (Shakespeare falls into this category, if he’s relevant!)

To ensure your compliance with this code of ethics, you are required to affix a signed *statutory declaration* to your hard-copy submission stating the assessment is your own work. A statutory declaration is included at the back of the course guide and should be photocopied and stapled to each assessment.

**Illness and misadventure**

The School of Medical Sciences (Physiology) policy on late submission of written work or failure to attend exams as a result of illness and misadventure is posted on the web ([http://www.medsci.usyd.edu.au/students/illnessmisadventure.html](http://www.medsci.usyd.edu.au/students/illnessmisadventure.html)) Please become familiar with this policy.

**Advice on how to do well in HCP quizzes and exams**

In HCP (PHSI3005 and PHSI3006) most of your exam assessment is in the form of short answer questions (SAQs). We allow a full 15min to answer each SAQ. An SAQ format was adopted as we believe they are the best way for you to demonstrate to us as instructors how well you have understood the material, and concepts therein, covered in the course (the PHSI3005 quizzes and exam cover only the theory lecture material). In 2010 we introduced some MCQs. We allow 3min to answer the MCQs because we expect that you will need to think about what is the best answer. By adopting the advice provided in the tips below, and by employing an effective learning strategy (that is, studying as you go) should assist you in achieving good marks in the quizzes and exams.

- Answer the question you are given, not the question you prepared for. These are not open-ended essay-style questions. Examiners will not award marks for material that does not directly
address the question. Don't just spot a keyword in the question and blurt out everything you can remember. Take time to identify what is being asked of you. As senior year undergraduates we expect you to craft a thoughtful answer to address precisely what is asked. Providing material that does not directly answer the question is less useful to you than not attempting the question. You will receive no marks, AND will waste valuable time that you could have spent composing a good answer, or working on other questions that you can answer.

• PHSI3006 exam questions often ask for you to demonstrate extension or application. This is a research-based unit of study. In research we frequently need to extend from what we have learnt in one system or experiment to how we approach the next. For example, you might be asked how a particular experimental method that was outlined in a Methods lecture and was applied in a research paper that you studied, might be applied in a different experiment to answer a different question. Another question may provide you with data that you are first asked to interpret, and asked to give an example of how you might extend the research question. To prepare for such problems you first need to be familiar with the methodologies and the types of information they can yield in general terms. You should combine this with what you have learned about how such methods have previously been applied, as illustrated by the papers dealt with in your PBL sessions. This requires you to actively seek this understanding. Ask how various methodologies have been applied in your PBL reading lists. How can the kind of data a particular experimental method produces be useful in answering particular sorts of physiological questions (examples of this application are throughout your PBL readings). If you don’t understand seek the answer from your peers, tutor or the myriad of other avenues that will yield the answer. If you seek, you will learn!

• A good answer (that would gain top marks) to each SAQ should take no more than a half-page of the answer book. Any more probably means you have not addressed the question effectively and are probably wasting time with excess, irrelevant material that won’t gain any further marks.
Theme 1 Function and adaptation in the musculoskeletal system

Prof. Rebecca S Mason

Lecture 1. Overview of cell signaling
- types of signals – autocrine, paracrine, endocrine
- signal molecules
- stimulus-response coupling
- receptors – types, modularity
- intracellular actions
- receptor recycling
- what can go wrong with signalling

Lecture 2. Signaling by steroid hormones with emphasis on vitamin D hormone
- steroid receptor superfamily
- general structure of steroid receptors
- steroid binding and receptor activation
- binding to response element and recruitment of co-activators/repressors
- analogs
- receptor variants
- rapid/non-genomic mechanisms

Lecture 3. Vitamin D metabolism and actions
- Vitamin D production in skin
- Vitamin D metabolism and its regulation
- main actions
  - bone – difference between osteoporosis and osteomalacia/rickets
  - gut
  - muscle
  - parathyroid gland
  - others – auto-immune, metabolic, innate immunity, cancer

Lecture 4. Overview of bone turnover
- Bone structure:
  - Bone terminology - epiphysis, diaphysis, metaphysis, periosteum, endosteum
  - Trabecular (cancellous) and compact (compact) bone
  - Distribution of trabecular and compact bone throughout the skeleton
- Bone cells:
  - Osteoblasts, lining cells, osteocytes
  - Osteoclasts
  - Osteoclast generation require osteoblasts
- Bone matrix composition:
  - Collagen - lamellar vs woven bone
  - Non-collagenous proteins
  - Mineral
- Bone turnover: -why?
  - Resorption
  - Formation
  - Turnover in compact bone
  - Coupling
    - Growth factors
    - Calcium sensing receptor
Wnt signalling

**Lecture 5. Hormonal control of bone turnover: PTH and sex steroids**

- Parathyroid hormone
  - Mechanism of action
  - Main actions
- Hyperparathyroidism
- Intermittent parathyroid hormone
  - Mechanism of intermittent PTH on bone
  - Problems
  - Alternatives
- Sex steroids
  - Effects on bone cell function (osteoclasts and osteoblasts)
  - Effects on bone structure

**Further reading for lectures by Professor Mason:**


Mason RS. Vitamin D: a hormone for all seasons. Climacteric. Online 21 Oct 2010 (available on WebCT)


**Dr Colin Dunstan**

*Lecture 6. Paracrine and Autocrine Signaling in Skeletal Metabolism*

- Differentiation of osteoclast and osteoblast lineages
- Growth factors regulating bone formation
- Paracrine regulation of bone resorption
- Endocrine paracrine interactions in bone
- Detection and response to bone stress
- Bone fracture

**A/Prof Bill Phillips: Lectures on Neuromuscular signaling**

*Lecture 7. Presynaptic transmitter release mechanisms*

- Structure and function of the neuromuscular synapse
- Postsynaptic membrane potential recordings
- Ca^{2+} and quantal synaptic transmission
- SNAREs facilitate regulated vesicle exocytosis
- Calcium sensors regulate transmitter release and vesicle recycling

*Lecture 8. Postsynaptic mechanisms*

- Postsynaptic response to a quantum of acetylcholine
- Triggering of the Muscle action potential
- Synaptic activity and the constant renewal of the synapse
- Agrin/MuSK/rapsyn pathway of postsynaptic differentiation
- Other signaling systems that influence the health of the synapse

*Lecture 9. Myasthenia Gravis*

- Symptoms of Myasthenia Gravis (MG)
- Effects of anti-AChR antibodies on the structure and function of the neuromuscular synapse
- Autoimmune antibodies and the failure of self tolerance
- Role of T helper cells in Myasthenia gravis
- ‘Seronegative’ MG and LEMS
• Current and future treatments for MG
(Learning objectives for my three lectures above will be included at the end of the Powerpoint pdf for each lecture)

**Theme 2 Channels and transporters**

**Dr Margot Day**

**Lecture 10. Overview of ion channel characteristics**
- What is an ion channel
- Voltage-clamping and current voltage-relations
- Conductance and rectification
- Ion selectivity
- Voltage-sensitivity
- Use of drugs to characterize channels

**Lecture 11. Potassium channels and disease (i) regulation of insulin secretion**
- Overview of insulin secretion by the pancreas
- Signalling pathway involved in insulin release
- KATP channels: SUR1 and Kir6.2
- Familial persistent hyperinsulinaemic hypoglycaemia of infancy
- mutations in SUR1
- Mutations in Kir6.2

**Lecture 12. Potassium channels and disease (ii) ROMK and KCNQ**
- Characteristics of ROMK and KCNQ potassium channels
- Channel mutations
- Bartter's Syndrome
- Long QT syndrome
- Epilepsy
- Deafness

**Lecture 13. The CIC family of chloride channels: and associated diseases**
- Physiological roles of chloride channels
- Structure of voltage-gated Cl channels
- CIC-1 and myotonia
- CIC-5 and Dent's disease
- CIC-K2 and Bartter's Syndrome

**Lecture 14. Absorptive epithelia. The ENaC Na channel and renal disorders**
- Functions of the distal nephron
- Transport properties of intercalated and principal cells
- Liddle's Syndrome
- Pseudohypoaldosteronism Type II
- Endocrine related causes of ENaC overactivity

**Lecture 15. ENaC - structure and regulation**
- ENaC Structure
- Regulation by kinases, proteolytic processing and Nedd4-2
- Regulation by IGF-1 and aldosterone

**Lecture 16. Secretory epithelia. CFTR and the pathogenesis of cystic fibrosis**
- Models of transport by bicarbonate secreting epithelia, eg pancreatic ducts and bile ducts
- Respiratory epithelium
- Cystic fibrosis: pathological features

**Lecture 17. CFTR - structure and function**
- CFTR structure
- Ion selectivity of CFTR
Human Cellular Physiology 2011

• CFTR gating
• Activation of CFTR
• CFTR as a transporter regulator

Dr Stuart Fraser
Lecture 18. Anion transporters and disease
• SLC4a family of anion transporters
• Anion exchange
• Role in congenital disorders of red cell anion exchange and red cell shape changes
• Renal proximal tubular acidosis

Theme 3 Regulation of embryonic growth and development

Dr Stephen Assinder
Lecture 19. Cell proliferation 1: The Cell Cycle
• Difference between cell proliferation and cell growth
• Define when and where cell proliferation occurs (gametogenesis, development, tissue repair)
• Requirements of growth and proliferation
• Sequence of events that form the cell cycle and relationships between events
• Mechanisms of checkpoint controls that allow for correct cell cycle progression
• Define (proto) oncogenes and tumour suppressors

Lecture 20. Cell proliferation 2: Signalling events that regulate cell cycle
• Mitogens and cell cycle progression (mechanisms with specific examples)
• Interaction of signalling pathways to regulate both growth and proliferation
• Examples of hyperplastic and neoplastic pathologies to demonstrate the role of signalling pathways in modulating cell proliferation

Lecture 21: Cell proliferation 3: How to achieve immortality
• Hayflickness of cells
• Telomeres limit the of possible number of cell divisions
• Telomerase and its role in escape from senescence in transformed cells
• Alternative lengthening of telomeres and cancer

• Why is apoptosis required?
• Extrinsic mechanism of apoptosis and key factors involved
• Intrinsic mechanism of apoptosis and key factors involved
• Integration of apoptotic pathways
• Cancer cells escape apoptosis

Lecture 23: Cell survival.
• Define survival factor and describe mechanism of action
• Describe how cell/tissue quiescence is maintained in normal tissues
• Give specific examples of soluble and physical factors to demonstrate the social context in which cells exist
• Demonstrate how these factors are related to cell cycle
• Explain how inappropriate response to survival factors lead to cancer
• Demonstrate how cancer cells avoid social constraints

Dr Margot Day
Lecture 24: Early embryonic development and acquisition of social constraints on cells
• Fertilization and the zygote
• Activation of the zygotic genome - a developmental clock
• The embryonic cell cycle, survival factors and apoptosis
• Compaction, signaling due to cell-cell contact

Lecture 25: Social Impacts on Embryonic stem cells
• Totipotency and pluripotency
• Differences between embryonic and adult cells
• Differences from somatic cells
• Similarities/differences to cancer cells

Dr Michael Morris
Lecture 26: Mechanisms of cell differentiation
• Forming specialised cell types, tissues, and structures
• Epithelial-to-mesenchyme transitions
• Autocrine and paracrine mechanisms
• Signalling circuitry
• Gene expression circuitry

Lecture 27 Examples of cell differentiation
• Embryonic stem cells and early embryogenesis
• Adult stem cells - The stem cell niche and tissue renewal

Dr Stuart Fraser
Lecture 28: Regulation of embryonic growth and development I
• Gastrulation
• Formation of the embryo body plan.

Lecture 29: Regulation of embryonic growth and development II
• Development of the extra-embryonic tissues
• The role of hypoxia in regulating embryo development.
• The Warburg effect during embryogenesis

Lecture 30: Regulation of embryonic growth and development III
• What does the developing mammalian embryo require for survival and growth?
• Embryonic vascular development.
• Placenta formation in mammalian development.
• The origin of adult hematopoietic stem cells in the embryo.

A/Prof Chris O’Neill
Lecture 31: Epigenetic regulation of cellular differentiation
• Methylation in the regulation of gene expression
• Methylation in regulation of development
• Implications of gene methylation in cancer development

Suggested Reading related to Growth and differentiation lectures:
Chapter 17 The Cell Cycle.
Chapter 20 Cancer
Chapter 23 Specialised Tissues, Stem Cells, and Tissue Renewal


METHODS LECTURE SYNOPSES (PHSI3006/3906)

Methods lectures
These lectures are held Fridays at noon and provide support to the PBL Stream. The research papers within the reading lists for each PBL present experimental evidence for particular hypotheses. Sometimes two or more papers may differ in their conclusions and in the hypothesis they put forward to explain how cells and tissues function. Thus, for a scientist it is important to critically evaluate the evidence authors present. The aim of these lectures is to familiarise you with the sorts of analytical techniques in common use in cellular physiology. We will outline what is done, the nature of the data that can be obtained, how it can be interpreted and the strengths and weaknesses of different experimental approaches.

Please note that, due to lecturer timetable constraints, the sequence in which the lectures below are actually delivered may differ a little. If in doubt consult Physiology master timetables: http://www.physiol.usyd.edu.au/students/current/timetables/

Methods Lecture (i) - Dr Stephen Assinder
*In vivo* gene analysis: transgenic approaches to determine protein function
- Define “transgene” and “transgenic”.
- Why use this technology?
- Describe the approaches used to generate gain of function and loss of function phenotypes.
- Discuss conditional transgenic models in tissue and time specific gene targeting.
- Transgenics are not restricted to mice. Discuss the implications of cloning and common transgenic animals.

Methods Lecture (ii) – Dr Margot Day
Studying ion channels
- Ussing chambers
- Patch-clamping
- Characterisation of ion channels
- Xenopus oocyte expression system
- Site-directed mutagenesis
- Biochemical methods

Methods Lecture (iii) – Dr Colin Dunstan
*In vivo* models
Ethical considerations
Choice of animal
Choice of Challenge
Methods of assessment
Biochemical
Histological
Histomorphometry, immunohistochemistry, in situ hybridization
Molecular
Interpretation
Advantages and Disadvantages

Methods Lecture (iv) - Dr Bill Phillips
Interpreting protein-protein interaction results
- Immunoprecipitation and western blots to study protein interactions in tissue
- Studying interactions between recombinant proteins made in bacteria
- Studying protein-protein interactions genetically- two-hybrid studies
- Studying protein interactions in cultured cells by immunostaining and other techniques
- Fluorescent techniques for studying interactions of proteins in living cells

Methods Lecture (v) Dr Stephen Assinder
Analysing cell proliferation, cell cycle and cancer cell phenotypes.
• Cell culture and the requirements for cell growth and proliferation.
• Describe methods for measuring cell growth and proliferation.
• Introduce cell sorting and FRACS analysis.
• Discuss methods of cell synchronisation.
• Transgenic mice in the investigation of cell cycle regulation.
• Discuss and understand culture methods that assess the cancer cell phenotype.

Methods Lecture (vi) Dr Bill Phillips
Immunolocalisation techniques
• Immunohistochemistry
• Immunoperoxidase
• Immunoelectron microscopy
• Immunocytochemistry
• Immunofluorescence microscopy

Methods Lecture (vii) Christine Napier
Analysis of telomeres and chromosome abnormalities in cancer

Methods Lecture (viii) A/Prof. Chris O'Neill
Stem Cell Therapy
• How do you make stem cells
• Embryonic and adult stem cell
• Relationship between stem cells and cloning
What are the likely therapeutic options

Methods Lecture (ix) Dr Stuart Fraser
Genetic manipulation of stem cells
• Different methods for transfecting nucleic acids into cells
• Assessing gene transfer in cells
• Gene transfer into stem cells
• Manipulation of gene expression by RNA transfection
• Gene transfer by viruses into stem cell populations
PROBLEM BASED LEARNING (PHSI3006/3906)
The problem based learning (PBL) sessions of Human Cellular Physiology focus on specific questions in the current research literature in cellular physiology and illustrate the intimate relationship between basic research and progress in understanding and treating disease.
Students work in small groups to interpret recent research findings and integrate these ideas into a working understanding of the issues.

Goals of the Problem based learning stream are to:
1. Develop students’ capacity for independent self-learning
2. Develop students’ skills in literature research and evaluation
3. Develop students’ skills in analysing and synthesising biomedical information
4. Develop students’ skills in oral presentation
5. Develop students’ skills in written presentation
6. Teach students approaches to problem solving in cell biology
7. Enhance students’ knowledge and understanding of cell biology
8. Develop students’ capacities to work co-operatively
9. Stimulate curiosity

The acquisition, analysis and presentation of scientific information is a major component of many jobs in the biomedical field. The PBL stream is intended to ensure that students have the necessary skills to do it well. Student surveys in previous years have shown that the PBL approach is very successful in meeting this objective.

Structure of the PBL stream
There are 3 ‘Problems’ or topics. Each topic lasts 3 weeks. There are 5 group sessions lasting 1 hour each, over the 3 weeks. In the second session each student should orally summarise the paper that they have been assigned. Sessions 3-4 should be used to discuss and integrate the ideas. A subset of students will chair these sessions and organise a group presentation. In the last (6th) group session of the topic, each group presents a seminar giving the outcome of their research on the topic. Session 5 will be a practice talk.

Background reference/s: A review article or chapter will be assigned by the problem setter and must be read by every member of the group before the first PBL session for the problem. These compulsory papers are included in the appendix of this course guide. In addition there may be other recommended background reading such as text chapters. These introductory references will provide you with an important overview of the problem- not all the answers. At the first meeting of the PBL 2-3 members will volunteer to be the organizers for the PBL topic and the speakers for the group presentation (everyone should take a turn at this during the course of the semester). Apart from the background reference/s there is a list of ~12 papers that are highly relevant to the topic and that between them contain all the information and ideas needed to successfully grapple with the PBL topic. The organizers/presenters need to ensure during the first session all of the papers in the reading list are assigned to at least one member of the group to read and summarize.

It is the responsibility of each member of the group to read the paper or papers that they are assigned between the first and second PBL session. They must write a 1-2 page summary. In addition, having read the paper and the PBL questions they must prepare a diagram or figure that will be useful to be used as an overhead for explaining how the work described in the paper is relevant to the PBL question/s. Each member of the group is then responsible for distributing both the summary and the diagram (either as hard-copy or electronically) to all members of the group and to the tutor. Each member of the group will be assessed on the clarity and thought they have
put into the summary and the diagram as well as on their verbal contributions to the PBL sessions (see assessment criteria).

**Tutors**
Each group has a tutor. The role of the tutor is to assist the group in organising its activities. The tutors do not necessarily have expert knowledge of the individual topics and it is not intended that they provide specialist information. Each of the tutors has some years of experience in science in a cooperative research environment. The tutors should provide you with:
- guidance on how to structure your investigations.
- feedback on strengths and weaknesses in your cooperative work as a group.
- feedback on your development of ideas and presentations during sessions 1-4.
- (in session 5) a clear critique outlining the strengths and weaknesses of your rehearsal talk. This should help you improve your presentation skills and to highlight areas of deficiency that can be fixed before the final talk.

**Motivation**
Many students find PBL the most stimulating part of their undergraduate studies. However some people are more reserved and might find PBL challenging. If you do find it hard to contribute orally to group discussion, discuss it with your tutor. Chances are that this is one area of where a bit of practice will make the biggest contribution to improving your overall skill-base as a future graduate.

Assessment for the PBL stream is intended encourage you to contribute actively to the discussion of papers and to cooperate within your small group with the goal of preparing a group oral presentation. As an individual you will gain marks in two ways by actively contributing to the PBL work 1/ your individual paper summaries and the intelligent comments that you make will boost your participation mark, 2/ the group presentation will be improved, a mark that you share with your group, 3/ You will be preparing your mind (and study notes) for the PHSI3006 exam.
Problem 1  Prof R.S. Mason (01/11)

Vitamin D actions and bone

Your laboratory is sent blood from a 2-year old child who presented to their family doctor with short stature, bowed legs and bone tenderness. Simple biochemical tests had been done and showed low calcium and somewhat low blood phosphate concentrations along with raised alkaline phosphatase of bone origin. The doctor sent the blood to you with a request for 25hydroxyvitamin D and 1,25dihydroxyvitamin D analyses. The provisional diagnosis of "rickets?" was written on the form. The doctor also noted on the request form that the child had alopecia and that the parents were first cousins.

After measuring these vitamin D metabolites, you find that the 25hydroxy vitamin D values are normal, which rules out simple vitamin D deficiency, but the 1,25dihydroxyvitamin D concentrations are very high indeed.

Questions:

1. What are 25hydroxyvitamin D and 1,25dihydroxyvitamin D and why are they measured?

2. What mechanisms can you think of to explain why the child presents with what seems like rickets, but is not apparently vitamin D deficient? What do you understand by the term hormone resistance?

3. Recalling the metabolism and actions of vitamin D, why would you expect subjects with end organ resistance to 1,25dihydroxyvitamin D to develop hypocalcemia, secondary hyperparathyroidism, rickets, impaired bone mineralization and alopecia? (Malloy et al, 1999 – reference included in course guide) Can you work out why the blood 1,25 dihydroxyvitamin D concentrations are high? (Hint: There are at least 3 reasons). What does that tell you about the likelihood of a problem with the 1α-hydroxylase enzyme?

4. Can you find reasons to explain the low phosphate concentrations in this child? (Hint: There are at least 2)

5. Considering steroid hormone mechanisms of action, suggest a possible list of structural problems which might result in defective function. (Malloy et al, 1999, McEwan, 2009) What is the significance of the consanguinous marriage?

Your laboratory’s assistance is now requested to help sort out the problem.

6. In brief, how would you go about detecting the vitamin D receptor in tissues and testing its functionality (Consider in vivo and in vitro studies)? (Malloy et al., 1999, Liberman, 2007)

7. You are now asked to consider how you would go about finding the mutations responsible for resistance in your family. How would you do this? You are successful in finding a mutation in the vitamin D receptor gene of your affected subject. How do you go about proving as far as possible that this mutation is the cause of the clinical problem? (Hughes et al, 1988).

8. What can be learnt about the physiological roles of vitamin D from vitamin D-resistant experiments of nature and transgenic mice? (Bouillon et al, 2008)


REFERENCES

General:

Specific References:


Problem 2  
Dr Margot Day (01/10)  
Regulation of potassium homeostasis by the kidneys

Bartter's Syndrome is an autosomal recessive disorder with four genotypes (called type I-IV Bartter's disease). The disease is characterized by salt wasting, metabolic alkalosis, hyperreninism, secondary hyperaldosteronism, hypokalemia and hypercalciuria. Most patients present early in life with symptoms such as polyuria and muscle weakness, which may be attributed to potassium depletion. Despite the hyperaldosteronism, most patients tend to have normal blood pressure.

In type II Bartter's disease the mutated gene is KCNJ1, which encodes the inwardly rectifying K⁺ channel ROMK. ROMK is expressed in the apical membrane of epithelial cells in the renal tubule. An interesting feature of type II Bartter's disease is transitory hyperkalaemia in the neonatal period.

The aim of this PBL is for you to gain a deeper understanding of epithelial ion transport. This will be achieved by investigating the mechanisms by which a mutation in a single K⁺ channel, in one segment of the renal tubule, interferes with ion transport not only in that segment but also in other parts of the nephron.

Before the first session:
All group members should read the following article and answer the introductory questions.


Introductory questions
1. How is K⁺ transported by each of the segments of the renal tubule?
2. Which segments are important for K⁺ homeostasis and why?
3. What hormone plays an important role in K⁺ homeostasis?
4. What is a K⁺ channel?
5. What is an inwardly rectifying K⁺ channel?

Session 1:
Discuss your answers to the introductory questions. Using your current knowledge of K⁺ transport by the kidneys devise a list of topics to be addressed and questions to be answered in your presentation. Assign papers to each member of the group to read and summarise before session 2.

Sessions 2, 3 and 4:
Each member of the group should report back on their readings outlining the work in the paper and relating it to the specific topics and questions that your group devised in session 1. Your oral summary should take about 5 min.

As a group you will develop a 45 min presentation that demonstrates your understanding of the physiology of epithelial transport in the nephron and how this relates to potassium homeostasis. Your presentation will also discuss the properties of inwardly rectifying K⁺ channels and how ROMK is regulated in the renal tubule. Finally, you should discuss how mutations in KCNJ1 result in the phenotypes of Type II Bartter's disease. Thus your list of topics should encompass the molecular aspects of channel function, K⁺ transport across a single epithelial cell and the function of the kidney tubule and the whole-body aspects of potassium homeostasis.
References


Problem 3  
Dr Steve Assinder (01/11)  
Molecular mechanisms of prostate cancer development.

Prostate cancer is the most commonly diagnosed cancer in men and is second only to lung cancer in cancer-related deaths. In Australia alone over 2400 men die of prostate cancer per year (i.e. a death approximately every 4 hours. Worldwide this equates to a death every 4 minutes). The transformation of normal human cells into malignant cells is a multi-step process by which traits (capabilities) are acquired. These steps in tumourigenesis reflect the genetic alterations that drive the progressive transformation of a ‘normal’ cell to a highly tumourigenic derivative. This is reflected in vitro where transformation of cells in culture requires at least two genetic changes before they become neoplastic. Tumour development, therefore, can be described as following a Darwinian evolution. Each successive genetic change produces an acquired trait that confers a growth advantage, leading to progressive change from a normal cell phenotype to a cancer cell phenotype.

The object of this exercise is to appreciate, using examples from prostate cancer, how the acquisition of mutations leads to the classic “hallmarks of cancer” of Hanahan and Weinberg (2000). These traits represent an escape from the social behavior/constraints of normal somatic cells, including dysregulation of the cell cycle.

Your Tasks:  
All students will read the introductory references (Hanahan D, Weinberg RA (2000) Cell 100: 57-70; Sampson et al. (2007). Journal of Pathology 211: 206-218 (NB. Pgs 209-212 are most relevant) prior to the first session and answer the introductory questions.

Each student will be assigned a paper to read from the reference list. They will read, understand and present both an oral summary and provide a 1 page paper summary to the rest of the group. A portion of the individual contribution for each group member will be assessed on the basis of this task by the tutor. The 1 page summary should be self-explanatory and relate the paper to the overall goal of the PBL (below). The summary will be accompanied by a figure that is useful to the presenters. This could be a key data figure that clearly explains/supports the take-home message or flow chart/diagram or concept map. The figure will have a legend that explains the figure and relates it to an aspect/question regarding the PBL. Copies of summary and figure must be distributed to all members of the group and tutor in hard copy. You must do this by session 3. Failure to do so will result in lost marks.

Your Goal  
A 45 min presentation that provides a model of events that could lead to the development of prostate cancer. You should provide examples of known alterations, presenting supporting experimental data where available and appropriate, that contribute to alterations that collectively dictate malignancy. In so doing, your presentation should demonstrate an understanding of the integrated physiology of the normal cell. Always try to answer “why would a change/loss etc. in x lead to y?”

NB. You will find regular reference to your PHSI3005 lecture material regarding cell cycle and cancer cell biology extremely helpful in understanding and integrating the reading material, and in constructing your model.

Introductory Questions  
1) Which cell type is prostate cancer thought to originate from? (Sampson et al. 2007).
2) What are the general stages of prostate cancer development? (Sampson et al. 2007)
3) What are the 6 hallmarks of cancer? How do they relate to the general stages of prostate cancer? (Hanahan and Weinberg 2000, Sampson et al. 2007)
4) Do they occur in any specific order? (Hanahan and Weinberg 2000).

**Specific reading to achieve your goal**
A list of references is given that should be distributed for reading amongst the tutorial group. Each reference is relevant to at least one of the hallmarks.

**Organising your time and tips to achieving the goal**

**Session 1:** Discuss your answers to the preliminary questions and devise a list of topics to be addressed in your presentation.
Using your current knowledge of the cell cycle and social constraints of the cell determine how the acquisition of each of the traits confers a growth advantage.
Assign papers to each member of the group to read and summarise prior to session 2.

**Sessions 2 and 3:** Report back on your readings. Identify which hallmark/s of cancer your reading is relevant to. Remember to try to address "why would a change/loss etc. in x lead to y?"
Describe the mechanisms and types of mutations/genetic events that lead to these changes.

**Session 4:**
- Develop a hypothetical model of the development of a prostate cancer. Remember this should be an integrated model. Consider what alternative hypothetical models would also result in the development of prostate cancer.
- Devise a plan for your 45min presentation. Use your model to describe the likely genetic events that cause aberrations of normal cellular processes to explain the onset and development of prostate cancer. Also draw on alternative models to illustrate how the same outcome might be achieved.
- **Do not** consider diagnosis, prognosis or treatment of the disease.

**Session 5:** Run through your presentation with your tutor. They will provide feedback. Ensure that the timing of the presentation is correct (45 mins), if not refine. Discuss as a group, and with your tutor, any shortcomings in the presentation. Identify areas that require further information.

**Session 6:** Presentation.

**Reading:**

**Introductory References**

**Specific**


