



UNSW
AUSTRALIA

FACULTY OF MEDICINE

SCHOOL OF MEDICAL SCIENCES

DEPARTMENT OF PHARMACOLOGY

PHAR 3102

Molecular Pharmacology

COURSE OUTLINE

SEMESTER 1, 2015

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PHAR3102 Course Information

Molecular Pharmacology (PHAR3102) is a 3rd year Science Course worth six units of credit (6 UOC). The course is usually undertaken as part of a major in Pharmacology in a Bachelor of Science or Bachelor of Medical Sciences and as part of the Medicinal Chemistry Program. This course builds on the information you have already gained in Introductory Pharmacology and Toxicology (PHAR2011).

OBJECTIVES OF THE COURSE

This course will examine the molecular basis of drug action and explore how cutting edge biotechnology and biomedical research can advance pharmacological knowledge, increasing our understanding of how drugs work. The following areas will be studied in detail; genetic variability in drug action, protein structure-activity relationships, receptor-ligand interactions, signal transduction, biochemical and molecular aspects of G-protein coupled receptors and their signalling mechanisms. Research and analytical skills will be developed in practical classes.

COURSE CO-ORDINATOR and LECTURERS:

Course Coordinator:

Dr Angela Finch

Rm 326 Wallace Wurth Building East ph: 9385 1325

Co-coordinator

Dr Lu Liu

Rm 325 Wallace Wurth Building East ph: 9385 8762

Students wishing to see the course coordinators should make an appointment *via* email as our offices are not readily accessible. We will organize to meet you in a convenient location elsewhere in the building.

Lecturers in this course:

Dr Angela Finch

a.finch@unsw.edu.au

Dr Nicole Jones

n.jones@unsw.edu.au

Dr Trevor Lewis

t.lewis@unsw.edu.au

Dr Lu Liu

lu.liu@unsw.edu.au

COURSE STRUCTURE and TEACHING STRATEGIES

Learning activities occur on the following days and times:

- Lectures: Thursday 9-10 am and Friday 12-1pm
- Collaborative Learning Session: Wednesday 12-1pm or 3-4pm*
- Practicals: Monday 10 am -1 pm or 2-5pm*

* Once enrolled in one of the two sessions, students cannot change.

Students are expected to attend all scheduled activities for their full duration (2 hours of lectures per week and up to 4 hours of practical and collaborative learning sessions per week). Students are reminded that UNSW recommends that a 6 units-of-credit course should involve about 150 hours of study and learning activities. The formal learning activities are approximately 72 hours throughout the semester and students are expected (and strongly recommended) to do at least the same number of hours of additional study.

Lectures will provide you with the concepts and theory essential for an understanding of molecular pharmacology. To assist in the development of research and analytical skills

practical classes and collaborative learning sessions will be held. These classes allow students to engage in a more interactive form of learning than is possible in the lectures. The skills you will learn in practical classes are relevant to your development as professional scientists.

APPROACH TO LEARNING AND TEACHING

The learning and teaching philosophy underpinning this course is centred on student learning and aims to create an environment which interests and challenges students. The teaching is designed to be engaging and relevant in order to prepare students for future careers.

Although the primary source of information for this course is the lecture material, effective learning can be enhanced through self-directed use of other resources such as textbooks and Web based sources. Your practical classes will be directly related to the lectures and it is essential to prepare for practical classes before attendance. It is up to you to ensure you perform well in each part of the course; preparing for classes; completing assignments; studying for exams and seeking assistance to clarify your understanding.

STUDENT LEARNING OUTCOMES

PHAR3102 will develop those attributes that the Faculty of Science has identified as important for a Science Graduate to attain. These include; skills, qualities, understanding and attitudes that promote lifelong learning that students should acquire during their university experience.

Graduate Attributes

- A. Research, inquiry and analytical thinking abilities
- B. The capability and motivation for intellectual development
- C. Ethical, social and professional understanding
- D. Effective communication
- E. Teamwork, collaborative and management skills
- F. Information Literacy – the skills to locate, evaluate and use relevant information.

On completion of this course students should:

1. be able to describe the genomic regulation of drug action
2. be able to discuss the molecular pharmacology of receptors, channels and enzymes
3. have gained a knowledge of molecular biology techniques used in pharmacology
4. be able to accurately record experimental data and draw conclusions from experimental data
5. be able to demonstrate their ability to work in teams and communicate scientific information effectively

ASSESSMENT PROCEDURES

- | | |
|---|------------|
| • Progress exam (40 min duration) | 15% |
| • Laboratory notebook | 10% |
| • Molecular techniques wiki and learning activity | 10% |
| • End of session examination (2 hours duration) | 60% |
| • Formative Assessment | 5% |
-

The *practicals* are provided to support lecture material and practise analytical skills. The practical classes and collaborative learning sessions help you to develop graduate attributes A, C, D & E. At the completion of the practical course you will be required to submit your laboratory notebook covering all of the practical sessions.

In the collaborative learning sessions students will work in teams to research a technique used in molecular pharmacology. They will build a *wiki* and facilitate a *learning activity* in the collaborative learning session. This assessment task will allow you to develop your research, information literacy, communication and time management skills, as well as allowing you to demonstrate your ability to work in a team and collaborate successfully (Graduate Attributes A, D, E & F).

A penalty will apply for late submissions of assessment tasks (10% per day).

The *progress examination* will be held in the lecture slot on Thursday the 23rd of April. This exam will give you feedback on how you are succeeding in the course. The *progress examination* and *end of session examination* will test not only your knowledge of the molecular pharmacology of receptors, channels and enzymes but also your ability to apply the knowledge you have acquired from multiple lectures to molecular pharmacology scenarios. The examinations may be in the format of MCQ, short or long answer questions. The questions will be based on the material covered in the lectures, practical classes and collaborative learning sessions. Material covered prior to the progress exam may be again examined in the final exam. The examinations will address graduate attributes A and B. The end of session examination will be held during the official examination period.

TEXTBOOKS AND OTHER RESOURCES

Due to the cutting edge nature of this course and the rapid advances made in the field of Molecular Pharmacology, a single primary text which adequately covers the content of this course has not been identified. Therefore each lecturer will provide you with additional resources to supplement their lecture material. These resources will take the form of text books, journal articles or web-based resources. If available, links to the electronic form of these resources will be put on the course Moodle page.

Two textbooks have been identified that together cover the majority of the course content.

“Pharmacology in drug discovery: understanding drug response” by T. P. Kenakin, will be used as a reference text for lectures given in weeks 4, 7-12.

“Molecular Pharmacology: From DNA to Drug Design” by Dickenson, Freeman, Lloyd Mills, Thode, & Sivasubramaniam, will be used as a reference text for lectures in weeks 1, 2, 5-11.

COURSE EVALUATION AND DEVELOPMENT

Each year feedback is sought from students about the courses offered in the Department of Pharmacology and continual improvements are made based on this feedback. The Course and Teaching Evaluation and Improvement (CATEI) Process of UNSW is the way in which student feedback is evaluated and significant changes to the course will be communicated to subsequent cohorts of students. Also a staff-student liaison group will be set up and students will be invited to become class representatives to seek feedback from their colleagues and meet with academic staff to discuss any issues that arise. Based on feedback given in these meetings changes will be implemented during the course and for future years.

Based on the feedback received in 2009 and 2010 the following changes have been made: questions provided to help focus the reading of journal articles for collaborative learning sessions, reduction in the proportion of total marks for the final examination, marks to encourage participation in collaborative learning sessions, smaller practical classes and

reduction in the length of each experiment to ensure it can be completed within a three hour practical class. Based on feedback received in 2011, the journal club questions are referenced back to the lectures to a greater extent. Dr Finch has worked with Dr Kenakin to develop a textbook that covers some parts of the course. Based on feedback received in 2012, formative quizzes have been added to provide more continual feedback and a new textbook will be trialled. Based on feedback made in 2013 the practical manual has been revised. Based on feedback received in 2014, the order of the topics covered in the collaborative learning sessions has been changed to match better with lecture content.

GENERAL INFORMATION

The Department of Pharmacology is part of the School of Medical Sciences and is within the Faculty of Medicine. It is located in the Wallace Wurth building. General inquiries can be made at the BABS.SOMS.BEES (B.S.B.) Student Office, located on the Ground Floor Room G27, of the Biosciences Building. Office hours are 9.00 am - 5:00pm.

Professor Margaret Morris is Head of Department and appointments to meet with her may be made via email (m.morris@unsw.edu.au).

Departmental Vacation Scholarships: The School of Medical Sciences supports several summer vacation scholarships each year to enable good students to undertake short research projects within the school. For further details contact the Administrative Officer.

There is an honours program conducted by the School. The Honours program is coordinated by Dr Thomas Fath (t.fath@unsw.edu.au), Ph: 9385 8495. Any students considering an Honours year should discuss the requirements with the coordinator. Outstanding students may be considered for scholarships offered by the University and these are offered annually. Honours Administrator: Vicky Sawatt (v.sawatt@unsw.edu.au) Ph:9385 8195.

Postgraduate degrees

The Department of Pharmacology offers students the opportunity to enter into the following graduate programs:

Course Work Masters: Masters in Drug Development. For more information contact Dr Orin Chisholm (o.chisholm@unsw.edu.au)

Research Masters: In Pharmacology. For more information contact the post-graduate coordinator Dr Pascal Carrive (p.carrive@unsw.edu.au)

Doctorate (Ph.D): In Pharmacology. For more information contact the post-graduate coordinator Dr Pascal Carrive (p.carrive@unsw.edu.au)

The School Teaching Administrator

Ms Carmen Robinson is able to provide additional information on any courses offered by the School.

BABS.SOMS.BEES (B.S.B.) Student Office, G27 Biosciences Building.

ph:9385 2464,

Email: Carmen.Robinson@unsw.edu.au

OFFICIAL COMMUNICATION BY EMAIL

All students in the course PHAR3102 are advised that e-mail is the official means by which the School of Medical Sciences at UNSW will communicate with you. All messages will be sent to your official UNSW e-mail address (e.g. z1234567@student.unsw.edu.au) and, if you do not wish to use the University e-mail system, you MUST arrange for your official mail to

be forwarded to your chosen address. The University recommends that you check your mail at least every other day. Facilities for checking e-mail are available in the School of Medical Sciences and in the University library. Further information and assistance is available from IT at UNSW (<https://www.it.unsw.edu.au/catalogue/index.html>)

When contacting a lecturer with a query, it is essential that the following information is provided as a minimum: student name, student number, course number, course name.

ATTENDANCE REQUIREMENTS

Attendance at scheduled teaching activities is governed by the University's requirement that students attend at least 80% of all classes.

Attendance at practical classes is compulsory, and must be recorded in the class roll at the start of each class. Arrival more than 15 minutes after the start of the class will be recorded as non-attendance. It is your responsibility to ensure that the demonstrator records your attendance and no discussions will be entered into after the completion of the class. Satisfactory completion of the work set for each class is essential. It should be noted that non-attendance for other than documented medical or other serious reasons, or unsatisfactory performance, for more than 1 practical class during the session may result in an additional practical assessment exam or ineligibility to pass the course.

The University acknowledges that students are involved in many extra-curricular activities throughout their studies. The School of Medical Sciences is generally supportive of students' activities but must be confident that these do not significantly impact on attendance at scheduled teaching activities or completion of assessment requirements.

Guidelines on extra-curricular activities affecting attendance can be found on the School of Medical sciences Website. <http://medicalsciences.med.unsw.edu.au/sites/default/files/Extra-curricularActivitiesSOMS.pdf>

BEHAVIOUR IN PRACTICAL CLASSES

The practical class is an opportunity for students to develop graduate attribute C by behaving in an ethical, socially responsible and professional manner within the practical class.

- Punctual arrival is expected.
- Turn off mobile phones before entering the class.
- A lab coat must be worn when required practical classes
- Enclosed shoes are compulsory.

Students must take due care with biological and hazardous material and make sure all equipment is left clean and functional. Those who don't adhere to these basic laboratory rules will be marked absent.

PRACTICAL CLASSES

In the interests of safety, special attention should be paid to any precautionary measures recommended in the notes. If any accidents or incidents occur they should be reported immediately to the demonstrator in charge of the class who will record the incident and recommend what further action is required.

The procedures used in the laboratory classes involving *the use of animals* have been approved by Animal Care and Ethics Committee (registration number ACE04/54B). All

experiments undertaken in the Department of Pharmacology adhere to the NHMRC code of conduct for animal experimentation.

TECHNOLOGY ENABLED LEARNING AND TEACHING RESOURCES

- To access teaching materials, go to the TELT, or Technology Enabled Learning and Teaching web site <http://telt.unsw.edu.au/> or myUNSW <https://my.unsw.edu.au/portal/dt>
- Click on “Moodle” and log on using the “Web Single Sign On” page.
- After logging on to Moodle, look for the course PHAR3102. You should have access to it if you are properly enrolled.
- You can make use of lecture recordings taken of the lectures that are available on the EchoCenter via Moodle. Lecture slides will also be made available on Moodle.

HANDWRITING

Students whose writing is difficult to understand will disadvantage themselves in their written assessment. Make every effort to write clearly and legibly. Do not use your own abbreviations.

SPECIAL CONSIDERATION

Please note the following Statement regarding Special Consideration.

If you believe that your performance in a course, either during session or in an examination, has been adversely affected by sickness or for any other reason, you should notify the Registrar and ask for special consideration in the determination of your results. Such requests should be made as soon as practicable after the problem occurs. **Applications made more than three days after an examination in a course will only be considered in truly exceptional circumstances.**

Application for Special Consideration must be made via Online Services in myUNSW. When submitting a request for special consideration you should provide all possible supporting evidence (eg medical certificates). In exceptional circumstances further assessment may be given. **If you believe you might be eligible for further assessment on these grounds, you should contact the Course Authority or the relevant Course Office as soon as possible.** Please refer to <https://student.unsw.edu.au/special-consideration> for further details regarding special consideration.

MISSED EXAMS

If in any circumstances you unavoidably miss an examination, you must inform the course coordinator. Normally, if you miss an exam (without medical reasons) you will be given an absent fail. If you arrive late for an exam no time extension will be granted. It is your responsibility to check timetables and ensure that you arrive with sufficient time. **PLEASE NOTE that if you miss any examinations for medical reasons you can apply for Special Consideration must be made via Online Services in myUNSW within 3 DAYS** (refer to <https://student.unsw.edu.au/special-consideration> for further details). Your request for consideration will be assessed and a deferred exam may be granted. You cannot assume you will be granted supplementary assessment. The deferred exam may include a significant oral element.

The supplementary exams for the School of Medical Sciences in Semester 1, 2015 will be held on the 14th, 15th and 16th July, 2015.

For further details please refer to

<http://medicallsciences.med.unsw.edu.au/students/undergraduate/science>

MISSED PROGRESS EXAM

If you unavoidably miss the progress exam in PHAR3102, you must lodge an application with UNSW Student Central for special consideration within 3 DAYS.

(<https://student.unsw.edu.au/special-consideration>)

If your request for consideration is granted an alternative assessment will be organised which may take the form of a supplementary exam or increased weighting of the final exam.

MEDICAL CERTIFICATES

Students who miss practical classes due to illness or for other reasons must submit a copy of medical certificates or other acceptable documentation to the course coordinator.

Certificates should be lodged no more than 3 days after an absence. Certificates lodged after 7 days will not be accepted. The following details must be attached: Name, Subject number, Group number, Date of the class, Name of class/es missed.

STUDENT SUPPORT SERVICES

Those students who have a disability that requires some adjustment in their teaching or learning environment are encouraged to discuss their study needs with the course coordinator prior to, or at the commencement of, their course, or with the Equity Officer (Disability) in the Student Equity and Disabilities Unit. Issues to be discussed may include access to materials, signers or note-takers, the provision of services and additional exam and assessment arrangements. Early notification is essential to enable any necessary adjustments to be made.

Student Equity and Disabilities Unit, Ground Floor of the Goodsell Building

Tel: +61 2 9385 4734/5434

Email: seadu@unsw.edu.au

Website: www.studentequity.unsw.edu.au

STUDENT RIGHTS AND RESPONSIBILITIES

<https://student.unsw.edu.au/policy>

APPEAL PROCEDURES

Details can be found at MyUNSW.

To have a result reviewed (checking of mark and/or reassessment):

<https://student.unsw.edu.au/results>

To appeal academic standing or ability to progress:

https://my.unsw.edu.au/student/academiclife/assessment/finalisation_results.html

GRIEVANCE RESOLUTION OFFICER

In case you have any problems or grievance about the course, you should try to resolve it with the Course Coordinator (Dr Angela Finch ph:9385 1325) or the Head of Department (Prof Margaret Morris ph: 9385 1560). If the grievance cannot be resolved in this way, you should contact the School of Medical Sciences Grievance Officer, Dr Priti.Pandey (9385 2483, P.Pandey@unsw.edu.au).

PLAGIARISM

The School of Medical Sciences will not tolerate plagiarism in submitted written work. The University regards this as academic misconduct. Evidence of plagiarism in submitted assignments, etc. will be thoroughly investigated and may be penalised by the award of a score of zero for the assessable work. Evidence of plagiarism may result in a record being made in the Central Plagiarism Register and the Faculty Students Ethics Officer being notified.

What is Plagiarism?

Plagiarism is the presentation of the thoughts or work of another as one's own.* Examples include:

- direct duplication of the thoughts or work of another, including by copying material, ideas or concepts from a book, article, report or other written document (whether published or unpublished), composition, artwork, design, drawing, circuitry, computer program or software, web site, Internet, other electronic resource, or another person's assignment without appropriate acknowledgement;
- paraphrasing another person's work with very minor changes keeping the meaning, form and/or progression of ideas of the original;
- piecing together sections of the work of others into a new whole;
- presenting an assessment item as independent work when it has been produced in whole or part in collusion with other people, for example, another student or a tutor; and
- claiming credit for a proportion a work contributed to a group assessment item that is greater than that actually contributed.†
- For the purposes of this policy, submitting an assessment item that has already been submitted for academic credit elsewhere may be considered plagiarism.
- Knowingly permitting your work to be copied by another student may also be considered to be plagiarism.
- Note that an assessment item produced in oral, not written, form, or involving live presentation, may similarly contain plagiarised material.
- The inclusion of the thoughts or work of another with attribution appropriate to the academic discipline does *not* amount to plagiarism.
- The Learning Centre website is the main repository for resources for staff and students on plagiarism and academic honesty. These resources can be located via: <https://student.unsw.edu.au/plagiarism>

The Learning Centre also provides substantial educational written materials, workshops, and collaborative learning sessions to aid students, for example, in:

- correct referencing practices;
- paraphrasing, summarising, essay writing, and time management;
- appropriate use of, and attribution for, a range of materials including text, images, formulae and concepts.

Individual assistance is available on request from The Learning Centre.

Students are also reminded that careful time management is an important part of study and one of the identified causes of plagiarism is poor time management. Students should allow sufficient time for research, drafting, and the proper referencing of sources in preparing all assessment items.

* Based on that proposed to the University of Newcastle by the St James Ethics Centre. Used with kind permission from the University of Newcastle

† Adapted with kind permission from the University of Melbourne.

Molecular Pharmacology LECTURE and PRACTICAL OUTLINES

The course timetable is appended at the end of these notes and can also be found on Moodle.

The course is divided into 5 main themes covering the molecular basis of drug action.

- **Genomic Regulation of Drug Actions**
- **'Receptor-Ligand' Interactions and Protein Structure**
- **Molecular Pharmacology of Receptors, Channels and Enzymes**
- **Signal Transduction and Modulation**
- **Receptor Theory**

Genomic Regulation of Drug Actions

Pharmacogenetics and Pharmacogenomics

The concept of pharmacogenetics and pharmacogenomics will be covered in these lectures. The types of genetic mutations: single nucleotide polymorphisms; tandem repeat polymorphisms; gene insertion and deletion; gene duplications; alternative splicing and their effects on drug targets will be explored. The influence of genetic background on drug efficacy and the use of pharmacogenomics to individualise therapy will also be covered.

Pharmacogenetics: Practical

In this practical we will investigate the role polymorphisms of cytochrome *P450 2D6* play in inter-individual differences in drug metabolism and their contribution to either a lack of efficacy or adverse side effects of drugs. To identify these polymorphisms, we will be using publically accessible databases, other computer based techniques and data obtained from PCR.

The Regulation of Gene Transcription

This lecture will briefly discuss the process of gene transcription and go on to examine transcription factors in more detail – including their different structures and roles in biological functions such as development, responses to environmental stimuli (e.g. heat or low oxygen), and gene transcription. A number of examples of therapeutic agents that can act by modulating gene transcription – including hormones acting at nuclear receptors, will be discussed.

Pharmacological Regulation of Gene Expression: Practical

Drug induced changes of gene expression of transcription factors will be examined. Techniques learnt include tissue/cell culture, RNA isolation, RNA quantification, RT-PCR and gel electrophoresis. Primer design will also be introduced.

'Receptor-Ligand' Interactions and Protein Structure

In this lecture we will review the non-covalent interactions underlying the molecular recognition between a protein ('receptor') and a small molecule ('ligand'). We will focus on the relationships between affinity and specificity, enthalpy and entropy and these non-covalent interactions. We will also review the basics of protein structure, including the structure and properties of amino acid side chains and the four levels of protein architecture, primary through to quaternary structure. We will focus on the importance of non-covalent interactions in protein structure.

Molecular Pharmacology of Enzymes, Channels and Receptors

How Enzymes Work

This lecture will cover general principles of how enzymes work including; catalytic transition state, binding energy and reaction specificity, equilibrium constant and enzyme kinetics (the Michaelis-Menten equation).

Drug Modulation of Enzyme Function

This lecture will cover the basic principles of how drugs modulate enzyme activity including competitive, non-competitive and uncompetitive inhibition. A brief overview of analytical techniques used in enzyme activity characterisation will also be given.

Receptor Enzymes

This lecture introduces the enzyme-linked receptors, covering the five main types of enzyme-linked receptors. The main structural features of enzyme-linked receptors, and how they relate to function of these receptors will be examined. The signalling pathways of each main types of enzyme-linked receptors and how signalling is regulated will also be discussed.

Voltage-gated ion channels

This lecture introduces the families of voltage-gated channels and identifies the key organs where they have an important role (eg. nervous system, heart, skeletal muscle). The main structural domains of the voltage-gated ion channels with respect to the crystal structures that are available and how they relate to the experimental evidence for function will be discussed. We will relate these structural domains to common drug actions. Introduces the idea of ion channels as 'enzymes' where the product is the conduction of ions across the cells membrane.

Ligand-gated ion channels

This lecture introduces the families of ligand-gated ion channels. The main structural domains with respect to the crystal structures available and how they relate to the experimental evidence for function will be discussed. We will discuss some key actions of ligand-gated ion channels (eg. neurotransmission), how they are altered by common drug actions, and the kinetic mechanism of the actions.

G-Protein Coupled Receptors (GPCRs)

This lecture will provide an introduction to the six G-protein coupled receptors (GPCR) families. It will explore the structural similarities and diversity between these families. Representative members from each family will be examined in more detail. The role of receptor dimerisation and receptor activity modifying proteins (RAMPs) in producing different receptor phenotypes will also be covered.

GPCRs: Role of Structural Motifs

This lecture will take a more detail look at the key structural regions of GPCRs and their role in receptor activation and regulation. The structural regions examined will include the N-terminus, extracellular loops, specific transmembrane helices, the DRY motif, intracellular loops and tails.

Signal Transduction and Modulation

Second Messengers

This lecture will review the types of second messenger molecules. Several examples of second messenger systems, including: the phosphoinositol, Ca²⁺, cAMP, cGMP and arachidonic acid systems will be covered. The main signal transduction pathways used by

GPCR will be introduced in this lecture and the role of second messengers as drug targets will be explored.

Guanine Nucleotide-Binding Proteins (G-proteins)

This lecture will review the members of the G-protein superfamily. It will explore the structural characteristics of this family and the mechanisms of G-protein activation and regulation, including the GTPase and GTP switch. G-protein dependent signalling pathways will be covered. The role of G-proteins in disease will be discussed.

Regulation of GPCR Signalling

Mechanisms by which receptor desensitisation occurs, including internalisation, phosphorylation, binding of β -arrestins, and degradation will be covered. The role of homologous and heterologous in receptor regulation will be explored. Some of the key enzymes involved in modulation of GPCR signalling include; second messenger dependant kinases, G-protein receptor kinases and RGS proteins. The function and regulation of these enzymes will be covered.

Receptor Internalisation & Alternative Signalling Pathways

Ligand mediated endocytosis and the regulation of this process will be discussed. The classification of desensitisation of GPCRs into Class A and Class B and the role of internalisation in non-G-protein mediated receptor signalling will also be discussed.

Receptor Signalling: Practical

This practical will examine the ability of the β_2 adrenergic receptor to activate extracellular signal-regulated kinase (ERK) via G-protein dependent and independent pathways.

Receptor Theory

Advanced Pharmacodynamics

The pharmacological concept of potency, efficacy, pD_2 , pA_2 will be reviewed. The calculation of pD_2 and pA_2 values from concentration-response curves of agonists and antagonists will be covered. Factors affecting pharmacodynamic variability and the role of this variability in drug efficacy and toxicity will be discussed.

Determining Antagonist Potency: Practical

In this computer-aided practical the antagonist potency of mepyramine against histamine-induced contractile responses of guinea-pig ileum will be determined. EC_{50} values will be obtained from concentration-response curves generated by semi-log paper and Prism. The antagonist pA_2 value will be calculated using the Arunklakshana & Schild method.

Constitutively Active Receptors and Inverse Agonists:

The concept of constitutively active receptors will be discussed in this lecture. Examples of wide-type receptors, naturally occurring receptor mutants, receptor variants created by site-directed mutagenesis, showing constitutive activity will be covered. The concept of inverse agonism and its discovery through molecular pharmacology techniques will be discussed. Examples of inverse agonists will be given and their potential as therapeutics will be discussed.

Allosteric Modulators:

This lecture will cover the principles of receptor allosteric modulation. The concepts of allosteric versus orthosteric binding sites will be explored. The allosteric mechanisms in activation of enzymes, ligand-gated channels and GPCRs will be covered. The role of allosteric sites as novel drug targets will be explored.

Signalling-Bias.

Signalling-bias (also called; ligand-directed signalling, functional selectivity, agonist-directed trafficking, biased agonism, or protean agonism) describes the observation that different ligands acting on the same receptor cause different patterns of response. These observations have led to a change in the concept of the receptor as either off or on but rather existing in a spectrum of conformational states each of which gives rise to a different signalling outcome. This lecture will explore these concepts and the influence they have on drug development.

Receptor Theory

Since the 1920's models have been developed to assist in the understanding of the complex events that occur upon ligand binding to receptor. The first simple model was the two-state model, however with advances in pharmacology (such as molecular pharmacology) this model could no longer explain the results obtained, this led to the development of more complex models; including the Occupational and Operational models of agonist action followed by the Ternary complex model and the Cubic ternary complex model. These lectures will discuss the development of these models and examine specific examples of experimental results which support the receptor states described by these models. The Induction versus Conformational Selection hypotheses of ligand action will also be covered.

New concepts in Pharmacology

In this lecture we will discuss the emerging concepts in receptor pharmacology that are currently being published and debated at scientific meetings, including heteromers, bitopic ligands and signalling texture.

TIME TABLE

Wk		Practical Monday 10-1 or 2-5pm Wallace Wurth 120	Collaborative Learning Wed 12-1 or 3-4 Mat 232	Lecture Thu 9-10 Mat C	Lecture Fri 12-1 Mat D
1	2/3	Introduction to Molecular Pharmacology and Assessment Tasks		Pharmacogenetics/genomics I (L Liu)	Pharmacogenetics/genomics II (L Liu)
2	9/3	Pharmacogenetics	Microarray/ siRNA	Nuclear Receptors/Transcription Factors (N Jones)	Protein Structure & Receptor-Ligand Interactions (R Griffith)
3	16/3	Pharmacological Regulation of Gene Expression (Part A)	Journal Club	Enzymes (R Griffith)	Enzyme Modulation (R Griffith)
4	23/3	Pharmacological Regulation of Gene Expression (Part B)	Genetically Engineered Animals/ Reporter Gene Assays	Channels (T Lewis)	Channels (T Lewis)
5	30/3	Pharmacological Regulation of Gene Expression (Part C)	Journal Club	Receptor Enzymes (A Finch)	Public Holiday
Mid-semester Break					
6	13/4	Pharmacological Regulation of Gene Expression Data Analysis	Protein Crystallography/Receptor binding assays	GPCRs: Introduction to Families A, B & C (A Finch).	GPCRs: Role of Structural Motifs (A Finch)
7	20/4	Receptor Signalling (Part A)	Journal Club	Progress Exam	Second Messengers (L Liu)
8	27/4	Receptor Signalling (Part B)	Careers in Pharmacology	G-proteins (L Liu)	Regulation of GPCR Signalling (L Liu)
9	4/5	Receptor Signalling (Part C)	Bioluminescence Resonance Energy Transfer/ Confocal Microscopy	Receptor Internalisation & Alternative Signalling Pathways (A Finch)	Allosteric Modulators (A Finch)
10	11/5	Receptor Signalling Data Analysis	Journal Club	Constitutive Active Receptors (L Liu)	Advanced Pharmacodynamics (L Liu)
11	18/5	Determining Antagonist Potency	Calcium signalling/ cAMP Assays	Signalling Bias (A Finch)	Receptor Theory I (A Finch)
12	25/5	Advanced Pharmacodynamics	Journal Club	Receptor Theory II (A Finch)	New concepts in Pharmacology (A Finch)
13			Exam Revision		

Assessment Tasks

Task	Due Date
Molecular Techniques Wiki (draft)	One week before due date
Molecular Techniques Wiki	9 am the Friday prior to the week of scheduled presentation.
Learning Activity	During assigned collaborative learning session
Progress Exam	Thursday, 23 rd April, 9 am
Laboratory Notebook	Friday 22 nd May, 10am
Final Examination	Official exam period

Laboratory Notebook

You will be required to keep a laboratory notebook for all practical classes in this course. Keeping a laboratory notebook is an important skill for every scientist to develop. Laboratory notebooks are a complete record of all the procedures carried out and data collected for each experiment. Enough detail needs to be recorded so as someone could reproduce your experiment at a later date. A laboratory notebook is a legal document and as such certain conventions and procedures must be followed.

The requirements for laboratory notebooks are given below:

- The lab notebook must be a bound book and not a spiral notebook or loose sheets in a folder
- The first 2 pages should be reserved for a table of contents
- Each page is numbered
- All entries are to be made in blue or black ink.
- Never remove any pages from your laboratory notebook.
- All information should be recorded directly into your notebook. Write down in detail what you do for each step of the experiment and record your results as you obtain them. Graph, films, printouts etc should be stuck directly into your notebook. Do not record data or calculations on scraps of paper and later copy them into your book. Whilst your laboratory notebook should be legible and as neat as possible it is more important that you record all the information.
- If you make a mistake strike it through with a single line and initial and date the correction. Do not use correction fluid or scribble out the mistake. The mistake should still be readable as sometimes you will realize that the entry was not a mistake after all and will want to be able to read it.
- Do not skip pages in your laboratory notebook (for example to allow space for data that will be collected later) instead make reference such as "continued from page 2" or "continued on page 5". You can start a new a new experiment on a new page however any blank space on the preceding page must have an X put through it.
- Each entry in the laboratory notebook should begin with the date, the title and a brief description of the aims of the experiment.

- At the end of each day your laboratory notebook should be signed and dated by a witness (*i.e.* a demonstrator)

The following information should be recorded in your laboratory notebook for each experiment:

To be completed before you come to class:

1. A brief and informative title.
2. The aims of the experiment. This section should clearly and concisely describe the purpose of the experiment (two or three sentences maximum) in your own words, explaining what the question is that you are asking (your hypothesis) and the methods you are using to answer your question. *N.B. This only needs to be done once for multi-week experiments.*
3. Preparation questions for each practical done (keep this brief).

To be completed during the class:

4. A concise step by step description of what you actually do when performing the experiment (this should be in point form).

The protocol should contain enough information to allow another researcher to repeat what you've done. If you reference the lab manual, you need to be specific and record which pages you are referring to. Also, if you did the experiment differently to what is written in the lab manual, you need to indicate this. Key information such as centrifuge speeds, temperatures, master mix recipes, incubation times and concentrations, along with notes on major deviations from the manual/protocol needed to be recorded. Extraneous information like telling the reader you were labelling tubes should not be included. It is OK to note what is in each tube and its label, but you don't need to tell us you wrote a label on the tubes.

5. Record any calculations you have done
6. Any observations (*e.g.* gel has a bubble, not all the sample loaded, current not stable).
7. All data collected with correct units, titles and labelled axes on graphs, and titles and labels for all drawings, films and printouts.

To be completed at the end of the experiment:

8. A summary of your findings and conclusions (two or three sentences maximum, this can be in point form).

How do your findings relate to your original aims/hypothesis? If the results were not as expected, suggest possible reasons for this. How do your findings relate to other studies in the scientific literature? *N.B. This only needs to be done once for multi-week experiments.*

Laboratory Notebooks are due before **10am, Friday 22nd May**. Laboratory notebooks are to be submitted at the BABS.SOMS.BEES (B.S.B.) Student Office, G27 Biosciences Building. You will need to staple or use sticky-tape to attach the Assessment Cover Sheet to the front cover of your book.

Marking Criteria – Laboratory Notebook

Criteria	<i>Excellent</i> >8.5	<i>Very Good</i> 8.4-7.5	<i>Good</i> 7.4-6.5	<i>Needs Improvement</i> 6.4-5.0	<i>Unacceptable</i> <5.0
Organisation _____/10 x 0.5	Each experiment has a title and date and appears in the table of contents. Errors are neatly struck through, no correction fluid used. All entries in pen. Each page numbered. Each day is initialled.	Each experiment has a title and date and appears in the table of contents. Most errors are neatly struck through. All entries in pen. Each page numbered. Each day is initialled.	All but one experiment has a title and date and appears in the table of contents. Some errors are not neatly struck through. Some entries not in pen. Each page numbered. Each day is initialled.	Not all experiments have a title and date and appear in the table of contents. Not all errors are neatly struck through. Not all entries are in pen or each page numbered. One day not initialled.	Experiments lack a title and date and don't appear in the table of contents. Errors are not neatly struck through. Entries not in pen. Page numbers lacking. More than one day is not initialled.
Safety _____/10 x 0.5	All safety summaries attached and signed.	8-9 safety summaries attached and signed.	6-7 safety summaries attached and signed.	6-5 safety summaries attached and signed	>50% of safety summaries not attached and/or signed.
Preparation _____/10 x 1	All questions answered correctly.	All questions answered with minor errors.	Questions answered, with some errors.	Not all questions answered, some answered with errors.	Majority of questions not answered or incorrect.
Aims _____/10 x 2	The aims of each experiment or the questions to be answered is clearly identified and stated.	The aims of each experiment or the questions to be answered are stated.	The aims of most experiments or the questions to be answered are identified but more detail needed.	The aims of some experiments or the questions to be answered are partially identified, however more details are needed.	The majority of the aims of each experiment or the questions to be answered are not given.
Experimental protocol _____/10 x 2	The protocol for each experiment is succinctly described with all key information included. All calculations are correct.	The protocol for each experiment is described with all key information included. Only minor errors in calculations.	The protocol for each experiment is described however, key information missing in some experiments. A few errors in calculations.	Describes how the experiments were done, but key information missing. Errors in calculations. .	Does not accurately describe how the experiments were done. Calculations are incorrect or missing.
Data _____/10 x 2	All data collected are presented. The data are clearly labelled. Correct units are given.	All data collected are presented. The data are clearly labelled with minor omissions. Minor errors in units given.	Data collected are presented and clearly labelled but with minor omissions. Errors in units given.	Some data not presented or not labelled. Errors in units.	Most of the data collected not presented. The data are not labelled. Correct units not used.
Conclusions _____/10 x 2	Clear and concise conclusions given. Conclusions are valid and supported by appropriate reference(s).	Clear conclusions are given. Conclusions are mostly valid and supported by appropriate reference(s).	Conclusions are given. Minor errors in conclusions. Appropriate references needed.	Conclusions are given for most experiments. Some conclusions are not valid and or not supported by appropriate reference(s).	Conclusions do not accurately describe the results of the experiments or are not presented for the majority of experiments.

Molecular Techniques Collaborative Learning Session

Overview

Publishing a scientific paper is the primary way that a scientist contributes new knowledge or methods to the scientific community. Collectively, these journal articles chronicle advances in science and technology. Without this foundation of work—whether a seminal contribution or a simple finding—future experiments would have no context and scientific research could not progress. Thus, understanding the literature is vital to understanding scientific research.

To understand scientific literature, however, it is important to know what tools and techniques scientists use to ask and answer questions. Over the course of the semester, you will explore several molecular biology techniques that are essential to understanding the scientific papers publish in the area of molecular pharmacology. Each student group will design and lead an exploration of a laboratory technique that is found in the papers to be discussed in each “journal club” collaborative learning session.

Instructions for the in-class activity

Part 1: Make a wiki about the technique

To help your classmates prepare for the activity you will design, your group will write a wiki about the technique that contains the following information:

- **How the technique works.** For example, describe the materials needed or provide an annotated diagram of the important steps involved, or the molecular process that occur during each step of the technique.
- **How the technique is used.** Include a description of what type of information this technique provides and what types of questions can be answered using the technique.
- Two **Hypotheses** that could be tested using this technique and two hypotheses that could not be tested using this technique. Include an explanation of why they can or cannot be tested using this technique.
- **Benefits and limitations of the technique.**
- **References.** List any resources that your group used to develop the fact sheet or in-class activity, and highlight other important resources where your classmates can find more information.

The Wiki should not be longer than 1000 words. Each member of the group must write and/or edit a minimum of 100 words. Contributions of less than this will result in a grade of 0/5%. Each member must log onto Moodle themselves; if you use someone else’s log-on, or work collaboratively outside Moodle your contribution will not be recognised.

The course coordinators are available at any point in the planning process to answer questions about the technique or this project.

Each group must organise a meeting with the Course coordinator for the week prior to their presentation to review their wiki content and learning activity. It is recommended that these meetings are booked as earlier as possible as your preferred time may not be available.

Researching your assigned technique

Places to look for general information:

- Textbooks
- Internet: Beware that not all sites will be accurate! Good information can usually be found at university websites, textbook publishers and scientific company websites.

Places to look for specific information:

- The library has many books covering molecular biology techniques
- The Current Protocols series of books are available in the library and electronically via the library catalogue. This series includes: Current Protocols in Molecular Biology, Current Protocols in Pharmacology, Current Protocols in Nucleic Acid Chemistry, Current Protocols in Human Genetics, Current Protocols in Bioinformatics, Current Protocols in Protein Science.
- Scientific literature (hint: limit your search to reviews or methods journals)
- Journal Websites

Cell - <http://www.cell.com/>

Science - <http://www.sciencemag.org/>

Nature - <http://www.nature.com/nature/index.html>

Molecular Pharmacology - <http://molpharm.aspetjournals.org/>

Trends in Pharmaceutical Sciences

<http://www.sciencedirect.com/science/journal/01656147>

Part 2: Design and lead an in-class activity

Each group will work together to design and lead an in-class activity that will:

1. Actively engage your classmates involved in learning and understanding the technique
2. Help your classmates determine how well they understand the technique

The entire activity should take **no more than 15 minutes**. After the activity, plan to spend 5 minutes to tie everything together and answer any questions your classmates might have.

Altogether, you will have 20 minutes of collaborative learning session time, so use it wisely.

Some ideas for activities

- **Interpret data from an experiment** that employs the technique. Develop a series of key questions that will encourage discussion about what conclusions can be drawn from those data.
- **Sequence the important steps in the technique.** Diagram each step on a separate sheet of paper. Have groups of students describe what is happening at each step, arrange the diagrams into the correct order, and explain why they ordered the steps in that way.
- **Act out the important steps of the technique.** Provide materials for your classmates to serve as critical molecules, reactions, or other “players” in technique, then have each person describe what their role is, and have the entire class act out the technique. Discuss key points afterwards.
- **Solve a scenario where the technique is done or used incorrectly** (e.g. steps missing or out of order, or incorrect conclusions drawn from an experiment). Have your classmates work together to determine the correct order of the steps, propose more appropriate conclusions (and justify their answers), or answer questions about the scenario.

- **Compare and contrast.** Have classmates compare and contrast your technique with another related technique. Give your classmates a set of scientific questions and have them decide which technique to use for each and explain their decisions.

Timeline (what is due when):

The Monday one week before you present

The academic taking your collaborative learning session (either Dr Finch or Dr Liu), will review your draft of the wiki and a description of your activity (and any accompanying visual aids, quizzes, etc.) and feedback will be given in the meeting with the coordinator where suggestions for improvement will be given.

On the Monday before you present

The coordinator will open your wiki for viewing by the whole course at 9am so that your classmates can study it before the collaborative learning session.

During collaborative learning session on the day you present

- Introduce the activity, give instructions
- Guide classmates in completing the activity
- Wrap-up; tie everything together and answer questions
- Do not give a “lecture” on the topic the rest of the class will have covered that prior to the class by reading your wiki

What to do on the weeks another group will be presenting:

Study the wiki to familiarise yourself with the technique so that you can participate meaningfully in the planned activity. You should come to class prepared to discuss any of the information found in the wiki and how the technique is used in the paper for discussion in the collaborative learning session.

Formative Assessment

The goal of formative assessment is to provide ongoing feedback that you can use to improve your learning. Formative assessment tasks help students identify their strengths and weaknesses and therefore the areas they should focus on.

Journal Club

The journal article and the questions to be answered will be posted the week before the collaborative learning session. You need to come to the collaborative learning session with the questions answered. You will be given credit for attempting to answer the questions and participating in the class discussion.

Learning Activity Participation

You will get credit if you participate meaningfully in the planned activity. You should come to class prepared to discuss any of the information found in the wiki.

Spot Quizzes.

Four times in the semester, during a practical class, a 15 minute open-book quiz will be given. This quiz will be a mixture of MCQ and short answer questions. You will be able to use your lecture notes (slides and your handwritten notes) and other notes you have made from textbooks and other additional reading suggested by your lecturers.

Marking Criteria – Molecular Techniques Wiki

Criteria	Excellent (>8.5)	Very Good (8.4-7.5)	Good (7.4-6.5)	Needs Improvement (6.4-5.0)	Unacceptable (<5.0)
Completeness _____/10 x2	The wiki contains all assigned elements and all details necessary to fully explain the technique. Your wiki can stand alone for the readers to use as a comprehensive source of information on the technique.	The wiki contains all assigned elements, but lacks a few minor details. Your wiki provides readers with most of what they should know about the technique but could be more comprehensive.	The wiki contains all assigned elements, but lacks some details. Your wiki provides readers with most of what they should know about the technique but lacks a key detail.	The wiki contains all assigned elements but lacks important details. Your wiki provides a general overview, but readers would need to look elsewhere to fill in the gaps.	One or more assigned elements are missing or incomplete. Your wiki lacks key information needed to give the reader a basic understanding of the technique.
Accuracy _____/10 x2	All information included in the wiki is accurate. The reader can confidently rely on the wiki as a source of information about the technique.	The information is accurate except for a few minor errors. The wiki is useful as a resource but may mislead the readers on a few small details.	The information is accurate except for a few minor errors. The wiki is useful as a resource but may mislead the readers with some details.	The information contains several errors. While no significant errors are made, the wiki contains enough errors to detract from its usefulness as a source of information about the technique.	A significant error is made that causes confusion. The reader cannot depend on your work as a reliable source of information about the technique.
Clarity _____/10 x 2	The wiki is well written and easy to read. All terms are clearly defined and topics are fully explained. Your writing allows readers to easily understand the meaning of all points presented.	The majority of the wiki is well written and easy to read, but a few minor terms or details are unclear. Your writing allows readers to understand the meaning of all points presented.	The majority of the wiki is well written and easy to read, but some terms or details are unclear. Your writing requires readers to infer your meaning regarding a few details.	Some parts are unclear or poorly written. The lack of clarity in your writing is distracting to readers and causes them to question your meaning, but they can still draw appropriate conclusions with some effort.	Major portions or key details of the wiki are unclear or poorly written. Your writing is unclear enough to cause the reader to misinterpret your meaning, leading to confusion about the technique.
Creativity _____/10 x 2	The wiki makes optimal use of visual aids or other creative elements (pictures, drawings, flow charts, figures, etc.) to illustrate key points of the technique. Your creativity greatly enhances your wiki as a learning tool and provides additional means for the reader to gain understanding about the technique beyond what is stated in the text.	The wiki makes use of visual aids or other creative elements to illustrate key points of the technique. Your creativity enhances your wiki as a learning tool and allows the reader to gain greater understanding about the technique.	The wiki includes visual aids or other creative elements to illustrate the technique, but they are not original or inclusive of details specific to the technique. The readers gain something from the aids but may have trouble visualizing or fully understanding parts of the technique.	The wiki includes pictures or diagrams, but they do not contribute to the readers' understanding of the technique.	Visual aids or creative elements are not used. The reader does not gain a full sense of the technique from your information sheet.
Individual contribution to the wiki _____/10 x 2	Contributes extensively to the researching, writing, and editing. Shows appropriate wiki etiquette when editing and respects the work of others	Contributes equally with other group members in researching, writing, and editing. Shows appropriate wiki etiquette when editing and respects the work of others.	Contributes to the researching, writing or editing. Displays appropriate wiki etiquette most of the time and generally respects the work of others	Provides minimal contribution to the researching, writing and editing. Displays appropriate wiki etiquette some of the time but often fails to respect the work of others	Does not contribute to the researching, writing and editing (<100 words). Does not follow wiki etiquette and fails to respect the work of others

Total _____/100

Marking Criteria – Molecular Techniques Learning Activity

Criteria	<i>Excellent</i> (>8.5)	<i>Very Good</i> (8.4-7.5)	<i>Good</i> (7.4-6.5)	<i>Needs Improvement</i> (6.4-5.0)	<i>Unacceptable</i> (<5.0)
Choice of content _____/10 x3	The activity addresses key or difficult aspects of the technique. Your classmates will leave with a deeper understanding or reinforced knowledge of the technique.	The activity addresses an important aspect of the technique. Your classmates will learn about the technique but would benefit more from a more in depth choice of content.	The activity addresses an important aspect of the technique, but not the most important or difficult aspects. Your classmates will learn something about the technique but would benefit more from a different choice of content.	The activity addresses a minor or easily understood aspect of the technique. This will not help further their understanding of the technique beyond what they could easily grasp on their own.	The activity does not address any important details of the technique or its uses. Your classmates will not learn from it.
Knowledge of the technique _____/10 x3	The presenters serve as experts on the technique. The content of the activity is clear and accurate, and the group is able to provide thorough and accurate answers to all reasonable questions raised by the class. Your classmates can depend on you teach them all they need to know about the technique.	The presenters are knowledgeable about the technique. The content of the activity is clear and accurate. The group is able to accurately answer most reasonable questions raised by the class without assistance. You are able to give your classmates a sound knowledge of the technique.	The presenters have some knowledge of the technique. The content of the activity is clear and mostly accurate. The group is able to answer most reasonable questions raised by the class but requires assistance from the instructor in some cases. You are able to teach your classmates most of what they need to know about the technique.	The presenters know a little more about the technique than their classmates. Some content of the activity is unclear or inaccurate, or the group is only able to answer basic questions raised by their classmates about the technique. Your classmates cannot depend on you to teach them much about the technique.	The presenters do not understand the technique themselves. Much of the content of the activity is inaccurate or vague, or the group cannot answer basic questions about the technique. Your lack of preparation causes confusion for your classmates.
Activity design _____/10 x3	The chosen activity engages all members of the class in learning about the technique. The activity is well-designed, creative, and generates useful discussion. Your classmates will gain something from the activity beyond what they would gain from simply reading the information sheet.	The chosen activity engages all members of the class in learning about the technique and generates good discussion. Your classmates will learn from the activity, but would benefit from a more creative format.	The chosen activity engages most members of the class in learning about the technique and generates some discussion but lacks originality. Your classmates will learn from the activity, but would benefit from a more engaging format or better planned activity	The chosen activity engages the class in learning about the technique but is not well-designed or does not generate useful discussion. Poor planning reduces the effectiveness of the activity in helping your classmates learn about the technique.	The chosen activity does not engage the class in learning about the technique. Your classmates could learn the information just as well by reading the information sheet.
Group participation (group graded as a whole) _____/10 x1	All members of the presenting group work together to lead the activity and make sure it runs smoothly and all members of the group are willing and able to answer questions about the technique. Everyone contributes equally and works as a team.	All members of the presenting group participate in leading the activity and are willing and able to answer questions about the technique, but all do not contribute equally.	All members of the presenting group participate in leading the activity and are able to answer questions about the technique, however, the members of the group work independently rather than as a team.	Some members of the presenting group show little effort to participate in leading the activity or are not prepared to answer questions about the technique.	The presenting group does not work together to lead the activity and answer questions. Some members do not participate, or a lack of preparation and communication leads to confusion.

