



PA4005

**Molecular
Pharmacology**

**Course Handbook
2019-20**

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Cover image:

Confocal micrograph of fluorescently labelled HeLa cells.

Nuclei are labelled in blue, tubulin in green and actin fibres in red.

Courtesy of:

Kevin Mackenzie

Microscopy and Histology Core Facility

Institute of Medical Sciences

University of Aberdeen

<http://www.abdn.ac.uk/ims/microscopy-histology>

Course Summary

This course is concerned with the pharmacology of receptors and drug discovery. It deals with the criteria that should be used to characterize and classify drugs and receptors. Receptor effector systems are also examined in depth. Theory is supplemented throughout by practical exercises involving data handling and interpretation and the presentation of information by students.

Course Co-ordinator: Dr James Hislop (james.hislop@abdn.ac.uk), IMS, Foresterhill.

Course Aims & Learning Outcomes

The purpose of this course is to cover in depth areas of molecular pharmacology that are particularly relevant to the discovery and characterization of receptors and their ligands. Theory is supplemented throughout by practical exercises both to improve understanding of the material covered and to develop important transferable skills.

The detailed course objectives are:

1. To consider the criteria that must be satisfied to establish the existence of a new receptor or transmitter.
2. To consider strategies for discovering new drugs
3. To consider strategies for characterizing pharmacological receptors
4. To gain a detailed understanding of receptor signal transduction processes.
5. To gain expertise in the use of computer software packages for the handling of the kind of data by which drugs or receptors are classified and in the interpretation of these data.
6. To gain expertise in selective reading and in the objective and critical interpretation of data and in the oral and written presentation of a hypothesis and its underlying evidence.

Course Teaching Staff

Course Co-ordinator(s):

Dr James Hislop (JH), Medicine, Medical Sciences and Nutrition (Course Co-ordinator)

Other Staff:

Dr Caroline Barelle (CB), Elasmogen

Professor Mirela Delibegovic (MD), Medicine, Medical Sciences and Nutrition

Dr Wael Houssen (WH), Medicine, Medical Sciences and Nutrition

Dr David Lyons (DL), Medicine, Medical Sciences and Nutrition

Dr Fiona Murray (FM), Medicine, Medical Sciences and Nutrition

Professor Graeme Nixon (GFN), Medicine, Medical Sciences and Nutrition

Dr Derek Scott (DS), Medicine, Medical Sciences and Nutrition

Dr Obinna Ubah (OU), Elasmogen

Dr Neil Vargesson (NV), Medicine, Medical Sciences and Nutrition

Assessments & Examinations

(a) Continuous assessment - 30% of the total assessment will be based on the OSPE (20%) and presentations (10%) during the course

(b) Examination - This will take place in the summer diet, April/May. It will take the form of an essay-based examination, which will comprise 70% of the assessment for PA4005. The format will be a two-hour paper with a choice of 2 questions from a total of 4. All components of the course including the content of tutorials and presentations are examinable. All assessments (continuous and examined) will be made using the University Common Grading Scale (copy attached).

(c) Satisfactory performance - Students are expected to attend all elements of the course and to complete all class exercises. The minimum performance acceptable for the granting of a class certificate is attendance at 75% of the course and presentation of all course work.

Class Representatives

We value students' opinions in regard to enhancing the quality of teaching and its delivery; therefore, in conjunction with the Students' Association we support the Class Representative system.

In the School of Medicine, Medical Sciences & Nutrition we operate a system of course representatives, who are elected from within each course. Any student registered within a course that wishes to represent a given group of students can stand for election as a class representative. You will be informed when the elections for class representative will take place.

What will it involve?

It will involve speaking to your fellow students about the course you represent. This can include any comments that they may have. You will attend a Staff-Student Liaison Committee and you should represent the views and concerns of the students within this meeting. As a representative you will also be able to contribute to the agenda. You will then feedback to the students after this meeting with any actions that are being taken.

Training

Training for class representatives will be run by the Students Association. Training will take place within each half-session. For more information about the Class representative system visit www.ausa.org.uk or email the VP Education & Employability vped@abdn.ac.uk. Class representatives are also eligible to undertake the STAR (Students Taking Active Roles) Award with further information about this co-curricular award being available at: www.abdn.ac.uk/careers.

Problems with Coursework

If students have difficulties with any part of the course that they cannot cope with alone they should notify the course coordinator immediately. If the problem relates to the subject matter

general, advice would be to contact the member of staff who is teaching that part of the course. Students with registered disabilities should contact Mrs Jenna Reynolds (medsci@abdn.ac.uk) in the School Office (based in the IMS, Foresterhill), or Mrs Sheila Jones (s.jones@abdn.ac.uk) in the Old Aberdeen office associated with the teaching laboratories, to ensure that the appropriate facilities have been made available. Otherwise, you are strongly encouraged to contact any of the following as you see appropriate:

- Course student representatives
- Course co-ordinator
- Convenor of the Medical Sciences Staff/Student Liaison Committee (Professor Gordon McEwan)
- Personal Tutor
- Medical Sciences Disabilities Co-ordinator (Dr Derryck Shewan)

All staff are based at Foresterhill and we strongly encourage the use of email or telephone the Medical Sciences Office. You may have a wasted journey travelling to Foresterhill only to find staff unavailable.

If a course has been completed and students are no longer on campus (i.e. work from second semester during the summer vacation), coursework will be kept until the end of Fresher's Week, during the new academic year. After that point, unclaimed student work will be securely destroyed.

Course Reading List

The basics of Molecular Pharmacology are covered in the usual Pharmacology text books available in the library.

Rang & Dales Pharmacology. Ed. H.P.Rang, J.M.Ritter, R.J.Flower, G.Henderson

Netters Illustrated Pharmacology. Ed. R.B.Raffa, S.M.Rawls, E.Portyansky Beyzarov

As this is the final year, lectures will focus on more up-to-date aspects of pharmacological research, with specific focus on the research interests of the faculty. These are often not covered by general text books therefore students are required to rely more on primary sources for reading (e.g. review articles and peer-reviewed papers). Recommendations for advanced reading will be indicated by individual lecturers for their teaching sessions.

Lecture Synopsis

Lecture 1: Introduction to PA4005 & Molecular Pharmacology Basics - Dr J Hislop

This lecture will introduce the students to the course. It will also comprise a refresher lecture to reintroduce the concepts, types of analyses and terminology used by molecular pharmacologists, with focus on receptor pharmacology.

Lecture 2: Pharmacogenomics – Dr F Murray

Why do some drugs seem to work in certain individuals and not in others? One reason for interindividual variability in drug response is pharmacogenomics. The lecture will review data regarding the genetic variation of G protein-coupled receptor dependent signalling pathways and their biochemical consequences.

Lecture 3: Gs Signalling and Compartmentalisation of cAMP - Dr F Murray

The Gs heterotrimeric G proteins transduce signals from G protein-coupled receptors to increase intracellular levels of cAMP. This lecture will cover the molecular aspects by which the level of this critical second messenger is controlled to maintain fidelity of signalling. The lecture will also discuss the importance of signalling components that tightly control the level of cAMP and those that help to generate spatially discrete signalling complexes

Lecture 4: The Role of cAMP Signalling in Disease - Dr F Murray

The lecture will discuss the importance of cyclic AMP in the physiological progression of a number of disease states, including hypertension.

Lecture 5: GPCRs – Dimerization and Allosteric Modulation – Dr J Hislop

This lecture will introduce the important G-protein-coupled Receptor (GPCR) class of membrane receptors, and their important role in cellular and physiological function. Heterotrimeric G proteins transduce signals from G protein-coupled receptors to effector proteins to modulate cellular function. G protein signalling constitutes a fundamental mechanism of intercellular communication used by all eukaryotes. This lecture aims to highlight the physiological role of the G α proteins and describe recent advances in their function, regulation and downstream signalling. This lecture will also cover the concept of receptor dimerization and its expanding role in both receptor function and as drug targets. Many receptors and ion channels contain allosteric binding sites. These are important drug targets. This lecture will introduce the concept and mechanisms of allosteric modulation.

Lecture 6: GPCRs Desensitisation and Ligand Bias- Dr J Hislop

How is GPCR signalling controlled? The mechanism of GPCR desensitisation will be discussed including the role of GRK and 2nd messenger kinases. This lecture will also introduce the molecule arrestin and its central role in both receptor desensitisation and novel aspects of G-protein independent signalling will be discussed (Ligand Bias).

Lecture 9: GPCR Trafficking - Dr J Hislop

What are the control mechanisms and cellular events that control and maintain receptor expression? This lecture discusses the cellular mechanisms responsible for GPCR internalisation and recycling/downregulation, focussing the functional importance of these processes

Lecture 7-8: Biologic and Antibody Therapy – Dr C Barelle and Dr O Ubah, Elasmogen

The inherent ability of monoclonal antibodies (mAbs) to specifically bind target and intervene in disease-related biological processes, whilst reducing off-site toxicity, makes them an effective, potent and now proven class of therapeutics. These clinical benefits are also reflected in their commercial value as they currently dominate the top ten revenue-generating drugs. The purpose of these two lectures is to i) illustrate the molecular mechanisms underlying the action of an approved mAb; ii) discuss the emerging world of immuno-oncology – combining the action of mAbs and our own immune systems and iii) explore the next generation of biologics – how can we improve on mAbs?

Lecture 10: Gastrointestinal Pharmacology - Dr D Scott

This lecture will introduce the various targets for therapeutic molecules in the gastrointestinal tract. We will focus specifically on drugs used to treat peptic/duodenal ulcers and inflammatory bowel disease. The development of new drugs to treat these conditions has evolved immensely over the past 50 years, and they have generated large amounts of revenue for pharmaceutical companies. The classes of drugs summarised briefly will include antacids, H₂ antagonists, proton pump inhibitors, ulcer triple therapy, laxatives, antidiarrhoeal agents, corticosteroids, immunosuppressants and aminosalicylates. Students will be issued with a case study on this topic, which they will revise in their own time. Their answers will be presented at the second session.

Lecture 11: Molecular Biology of Addiction – Dr J Hislop

Using the examples of psychostimulant and opiate addiction, this lecture will give practical examples of some of the concepts described in Lectures 1-4. This will focus on how molecular changes in receptor trafficking and signalling may underlie the addictive qualities of a number of drugs of abuse.

Lecture 12-13: The Molecular Pharmacology of Ion Channel Function – Dr D Lyons

Ion channels are the molecular basis of neuronal excitability – facilitating numerous processes including signal transduction, action potential discharge and synaptic transmission. This Lecture will demonstrate how the pharmacological manipulation of ion channel activity and transductional regulation can induce functional changes in neuronal excitability and rhythmogenesis, network function and synaptic plasticity.

Lecture 14 & 16: Diabetes and Insulin Resistance: current therapies - Prof M Delibegovic

This set of lectures will cover the aetiology of diabetes mellitus (type 1 and type 2 DM), with particular emphasis on causes and consequences of T2DM, insulin action and defects in post-insulin receptor signalling pathway. The lectures will address insulin's effects on regulation of whole body glucose homeostasis, 2 phases of insulin secretion, central and peripheral actions on carbohydrate and lipid metabolism. In depth analysis of up-to-date mouse genetic research as well as translational aspects/drug therapies will be covered. Finally changes in insulin sensitivity will be put into context in relation to aetiology of other diseases such as cardiovascular and Alzheimer's disease.

Lecture 15: Thalidomide - Dr N Vargesson

These lectures will cover an introduction to the history of Thalidomide, teratogenesis and type of defects, current uses/trials and a review of recent research into the mechanism of teratogenesis.

Lecture 17: Marine Natural Products Lecture - Dr W Housen

The lecture will cover the drug discovery from natural products with special emphasis on drugs derived from marine organisms. Natural products in general have a long history of being an important source of new medicines. Extreme environmental conditions such as high salinity, low light intensity and high pressure may trigger marine organisms to produce novel chemical structures to help them survive within their niches. Many of these chemicals have unique pharmacological properties. Examples of these compounds and their pharmacological properties will also be discussed.

Lecture 18 & 19: SIP Receptor Signalling - Professor G Nixon

In these lectures, novel intercellular and intracellular signalling through sphingosine-1-phosphate in health and disease will be discussed.

Practical/Lab/Tutorial Work

Tutorials

Students will be divided into two groups (numbered 1 & 2). Each student will be given material in advance of tutorials. They must study this material as instructed before attending the tutorials. The purpose of these is to improve expertise in the interpretation of scientific data relating to the discovery and characterization of pharmacological receptors and their ligands. The tutorials provide preparation for the data analysis exam paper.

Practical

The practical work for PA4005 will take the form of an Objective Structured Practical Examination (OSPE for short!), which some of you may have experienced before. However, this style of assessment at multiple stations during a strict time limit is also similar to the job interviewing methods used by many employers.

The practical runs over 2 days spread throughout the course (see timetable). An online video is available to MyAberdeen to explain the basis of the OSPE and the details of the practical skills tested.

Thursday morning of week 1 (see timetable) will be available for students to have an opportunity to practice the skills which will be assessed. During this morning, staff will be on hand to demonstrate and answer any questions. This will give the opportunity to ask questions and then students will be directed towards what they should revise for the assessment. Given that students will have little other coursework at this time, their

preparation for the assessment should not be too onerous. Many of you will be already familiar with some of the practical skills assessed. Please note – IT IS ESSENTIAL THAT YOU ATTEND THIS LABORATORY PRACTICAL SESSION.

On the Thursday morning of week 3, students will be scheduled to attend the practical laboratory for a one hour long slot, during which time they will undertake their assessment. Students cannot pick and choose when they attend, appointments will be issued by staff. Allocated groups will be available on the MyAberdeen course website. Attending at the correct time is one of the professional skills that will be assessed! During your one hour slot, you will be assessed at several stations on how well you complete the practical skills. In addition, the students' professionalism as scientists and potential employees will be graded and students will also have to submit a short written assignment.

A major benefit of this practical is that, in addition to brushing up your practical skills, it can also provide practice for future interviews for jobs or academic positions. It will also prepare you in the generic skills needed for the Honours projects you will all be undertaking in the second half-session after Christmas.

The practical coordinators for PA4005 are Dr Derek Scott (d.scott@abdn.ac.uk), and Dr James Hislop. The OSPE will contribute 20% towards your final course mark.

For these classes a laboratory coat should be worn at all times in the laboratory. The University and Department safety rules must be adhered to at all times. Students may find it useful to bring a calculator to the laboratories in order that the required calculations can be made.

PowerPoint Presentations

On Thursday of week 5 (see timetable), students (in groups of 2) will be required to present a scientific paper related to molecular pharmacology. ALL STUDENTS ARE REQUIRED TO ATTEND THE WHOLE SESSION. Students will be randomly paired, and a research paper assigned by the end of the first week. Each pair will be required to collaborate and present their paper to the assembled class using MS PowerPoint presentation software. Each presentation will be of 10 minutes duration and will be followed by a 5-minute discussion period. Papers and groups will be assigned at random and instruction will be provided on the basic construction of a PowerPoint presentation. Individual presentations will be assessed for delivery and content and this will contribute towards the continuous assessment. Peer marking from your fellow students will account for 10% of the final assessment.

Each presentation should:

- Set the background to the work described in the paper
- Identify the aims of the paper
- Outline the methodological approach adopted

- Describe the main results presented
- Discuss the physiological relevance of the main results
- Assess whether the aims of the paper have been achieved
- Assess the scientific quality of the paper
- A time limit of 10 minutes for each presentation will be strictly adhered to.

Presentations will contribute 10% towards your final exam mark.

University Policies

Students are asked to make themselves familiar with the information on key institutional policies which have been made available within MyAberdeen (<https://abdn.blackboard.com/bbcswebdav/institution/Policies>). These policies are relevant to all students and will be useful to you throughout your studies. They contain important information and address issues such as what to do if you are absent, how to raise an appeal or a complaint and indicate how seriously the University takes your feedback.

These institutional policies should be read in conjunction with this programme and/or course handbook, in which School and College specific policies are detailed. Further information can be found on the [University's Infohub webpage](#) or by visiting the Infohub.

The information included in the institutional area for 2019/20 includes the following:

- Absence
- Appeals & Complaints
- Student Discipline
- Class Certificates
- MyAberdeen
- Originality Checking
- Feedback
- Communication
- Graduate Attributes
- The Co-Curriculum

Medical Sciences Common Grading Scale

Grade	Grade Point	Category	Honours Class	Description
A1	22	Excellent	First	<ul style="list-style-type: none"> Outstanding ability and critical thought Evidence of extensive reading Superior understanding The best performance that can be expected from a student at this level
A2	21			
A3	20			
A4	19			
A5	18			
B1	17	Very Good	Upper Second	<ul style="list-style-type: none"> Able to argue logically and organise answers well Shows a thorough grasp of concepts Good use of examples to illustrate points and justify arguments Evidence of reading and wide appreciation of subject
B2	16			
B3	15			
C1	14	Good	Lower Second	<ul style="list-style-type: none"> Repetition of lecture notes without evidence of further appreciation of subject Lacking illustrative examples and originality Basic level of understanding
C2	13			
C3	12			
D1	11	Pass	Third	<ul style="list-style-type: none"> Limited ability to argue logically and organise answers Failure to develop or illustrate points The minimum level of performance required for a student to be awarded a pass
D2	10			
D3	9			
E1	8	Fail	Fail	<ul style="list-style-type: none"> Weak presentation Tendency to irrelevance Some attempt at an answer but seriously lacking in content and/or ability to organise thoughts
E2	7			
E3	6			
F1	5	Clear Fail	Not used for Honours	<ul style="list-style-type: none"> Contains major errors or misconceptions Poor presentation
F2	4			
F3	3			
G1	2	Clear Fail/ Abysmal	-	<ul style="list-style-type: none"> Token or no submission
G2	1			
G3	0			

Course Timetable - PA4005: 2019-2020

Date	Time	Place	Subject	Session	Staff
Week 7					
Mon 9 Sep	12.00-13.00	1:143/144	Molecular Pharmacology Basics	Lecture	JH
Tue 10 Sep					
Wed 11 Sep	12:00-13:00	1:147	Pharmacogenomics	Lecture	FM
Thu 12 Sep	09:00-13:00	2.054	Introduction and Practice for OSPE	Practical	JH/FM/DS/ST
	14.00-15.00	1M:003	Data Analysis Tutorial: Group 1	Tutorial	ST
	15.00-16.00	1:154	Data Analysis Tutorial: Group 2	Tutorial	ST
Fri 13 Sep	10:00-11:00	1:147	Gs Signalling and Compartmentalisation of cAMP	Lecture	FM
	12.00-13.00	1:147	Role of cAMP Signalling in Disease	Lecture	FM
Week 8					
Mon 16 Sep	11.00-12.00	1:143/144	GPCRs, Dimerization and Allosteric Modulation	Lecture	JH
Tue 17 Sep					
Wed 18 Sep	11.00-12.00	1:147	GPCR Desensitisation and Bias	Lecture	JH
Thu 19 Sep	12:00-13:00	1:143/144	Antibody Therapeutics 1	Lecture	CB
	14:00-15:00	1M:003	Tutorial: Group 1	Tutorial	JH
	15:00-16:00	1:154	Tutorial: Group 2	Tutorial	JH
Fri 20 Sep	10.00-11.00	1:147	Antibody Therapeutics 2	Lecture	OU
Week 9					
Mon 23 Sep	11.00-12.00	1:143/144	GPCR Trafficking	Lecture	JH
Tue 24 Sep					
Wed 25 Sep	12.00-13.00	1:147	GI Pharmacology and Therapeutics	Lecture	DS
Thu 26 Sep	09:00-13:00	2.054	OSPE	Practical	JH/FM/DS/ST
	14.00-15.00	1M:003	GI Tutorials Group 1	Tutorial	DS
	15.00-16.00	1:154	GI Tutorials Group 2	Tutorial	DS
Fri 27 Sep	11.00 -12.00	1:143/144	Molecular Pharmacology of Addiction	Lecture	JH
Week 10					
Mon 30 Sep	11.00-12.00	1:143/144	Molecular Pharmacology of Ion Channels 1	Lecture	DL
Tue 1 Oct					
Wed 2 Oct	09.00-10.00	1:032/033	Molecular Pharmacology of Ion Channels 1	Lecture	DL
Thu 3 Oct	11.00-12.00	1:147	Diabetes and Insulin Resistance: Current Therapies	Lecture	MD
	15:00-16:00	1:032/033	Thalidomide	Lecture	NV
Fri 4 Oct	09.00-10:00	1:147	Diabetes and Insulin Resistance: New Research	Lecture	MD
Week 11					
Mon 7 Oct	11.00-12.00	1:143/144	Marine Products	Lecture	WH
Tue 8 Oct					
Wed 9 Oct	09.00-10.00	1:032/033	S1P Receptor Signalling 1	Lecture	GFN
Thu 10 Oct	10:00-12:00	Aud	Presentations	Presentation	JH/FM
	12:00-17:00	BMP LT			
Fri 11 Oct	11.00-12.00	1:143/144	S1P Receptor Signalling 2	Lecture	GFN

Staff

Dr Caroline Barelle (CB), Elasmogen
Professor Mirela Delibegovic (MD), Medicine, Medical Sciences and Nutrition
Dr James Hislop (JH), Medicine, Medical Sciences and Nutrition
Dr Wael Houssen (WH), Medicine, Medical Sciences and Nutrition
Dr David Lyons (DL), Medicine, Medical Sciences and Nutrition
Dr Fiona Murray (FM), Medicine, Medical Sciences and Nutrition
Professor Graeme Nixon (GFN), Medicine, Medical Sciences and Nutrition
Dr Derek Scott (DS), Medicine, Medical Sciences and Nutrition
Dr Steven Tucker (ST), Medicine, Medical Sciences and Nutrition
Dr Obinna Ubah (OU), Elasmogen
Dr Neil Vargesson (NV), Medicine, Medical Sciences and Nutrition

Venues

1:154, 1:147, 1M:003, 1:032/033, 1:143/144 and 2.054 are all found in the Polworth Building at Foresterhill.

L5 CR – Level 5 Conference room can be found in the IMS Building at Foresterhill