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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 extends your previous knowledge in the area of drug metabolism and toxicology. The process of drug development will be examined from the importance of understanding the metabolic profile of drugs and their transport to covering molecular aspects of pre-clinical toxicology. External Experts from academia and the pharmaceutical industry contribute to the teaching and assessment of this important area. This course opens up new opportunities for employability in academia and the pharmaceutical industry.

Co-ordinator: Professor Heather M Wallace (437956)

Course Aims & Learning Outcomes
The course aims to develop an understanding of molecular toxicology at an advanced level. The learning outcomes are:

- Knowledge of drug-induced toxicity including organ specific toxicity and oxidative stress
- Understanding of immunotoxicology and immunopharmacology
- Knowledge of the processes involved in cell death including apoptosis, autophagy and necrosis
- Knowledge of risk assessment
- Understanding of research and development (R & D) in the pharmaceutical industry
- Molecular carcinogenesis (genotoxic and non-genotoxic)
- Developments in stem cell research

Course Teaching Staff
Course Co-ordinator(s):
Professor HM Wallace (HMW), School of Medicine, Medical Sciences, Dentistry and Nutrition

Other Staff:
Professor H Galley (HFG), School of Medicine, Medical Sciences, Dentistry and Nutrition
Dr R Dearman (RD), University of Manchester
Professor Ruth Roberts (RR), ApconiX. Ltd
Dr R J Weaver (RW), Bioanalysis & New Technologies Division, Safety Assessment, France
Mr A Woolley, ForthTox Ltd, Linlithgow
Dr E Collie-Duguid (ECD), School of Medicine, Medical Sciences, Dentistry and Nutrition
Dr M Leek (ML), TC Biopharma

Assessments & Examinations
Students are expected to attend the lectures, practical classes and tutorials. Any period of absence must be covered by a medical certificate in accordance with University regulation (see Notice Boards). Practical reports and assignments must be handed in for marking by the
dates indicated. A 100% attendance is required at practical classes. If assignments are not handed in on time e.g. if an assignment is more than 1 week late without good cause, it will not be marked.

The distribution of assessments is as follows:

1. Degree written exam 2h paper, answer 2 questions = 70% of the grade for this course
2. Continuous assessment Practical report, editorial and problem solving = 30% of the grade for this course.

Past papers for PA4302 are available on the Web.

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](http://www.ausa.org.uk) or email the VP Education & Employability [vped@abdn.ac.uk](mailto: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](http://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 ([mailto:medsci@abdn.ac.uk](mailto:medsci@abdn.ac.uk)) in the School Office (based in the IMS, Foresterhill), or Mrs Sheila Jones ([s.jones@abdn.ac.uk](mailto: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**

**Books recommended for purchase**

Rang and Dale’s, Pharmacology 8th Edition

**The following are available at Foresterhill Library Counter (Heavy Demand)**

- Casarett & Doull’s Toxicology. (Fifth edition). ISBN. 0071054766.
- Comprehensive Toxicology (Reference Section, Foresterhill) (13 volumes)
- Boelsterli, A. Mechanistic toxicology: the molecular basis of how chemicals disrupt biological targets. ISBN. 0415284589. (4 copies FH).

Foresterhill Library holds the issues of Trends in Pharmacological Sciences, which may be very useful for reading around many topics relevant to the course.

**Lecture Synopsis**

**Toxicological significance of drug metabolism - Professor Heather Wallace**

- Understanding drug withdrawal
• Importance of inhibition and induction of drug metabolism
• Mechanisms of drug induced toxicity

Immunopharmacology - Dr I Crane

• Review the use of immunosuppressive drugs in transplantation and autoimmune diseases. Explain the rationale behind the use of immunosuppressive regimes. Discuss the different categories of immunosuppressive drugs and agents.
• Describe the structure and action of CsA, FK506 and rapamycin. Compare and contrast their side effects and pharmacology. Discuss, using examples, therapeutic efficacy and monitoring.
• Explain the mode of action of fungal immunosuppressant’s at the molecular level. Compare and contrast the calcium-dependent and -independent mechanisms
• Explore the increasing significance of monoclonal and polyclonal antibodies and their role in more specifically targeting the rejection process. As well as their role in the pre-transplantation setting in inducing transplantation tolerance. The ultimate goal in clinical transplantation.

Immunotoxicology - Dr Rebecca Dearman

• overview of the adaptive immune system
• the health consequences of impaired immune function
• consideration of allergy caused by chemicals and proteins.

Drug targeting and gene therapy I and II - Professor Heather Wallace

• Importance of drug targeting
• Barriers to drug delivery
• Issues around successful gene therapy

Molecular carcinogenesis - Professor Heather Wallace

• Proto-oncogenes, oncogenes and tumour suppressor genes
• Cell cycle regulation
• Carcinogenesis

Drug Transporters - Professor Heather Wallace

• Drug transporter families
• Toxicity issues with drug transporters
• Regulation of drug transport by nuclear receptors

Biomarkers - Dr Elaina Collie-Duguid

• Biomarkers in the management of human disease
• Types of biomarkers and their potential clinical utility
• Biomarkers in current clinical use.
Introduction to Pharmaceutical Research & Development - Dr Richard Weaver

- The lecture offers students an insight into how novel pharmacological targets are discovered, researched and candidate molecules optimized as pharmacologically active molecules with 'drug-like' properties before pre-clinical and clinical development.
- From research through to market, lectures will illustrate how the quality, safety and efficacy of candidate drugs are developed, firstly in the research discovery phase and secondly, in Development phase which guided by the expectations of the Regulatory framework.
- Scientific topics covered will include in vitro and in vivo toxicology, safety pharmacology, drug metabolism, pharmacokinetics and pharmacodynamics, and their application for the research & development of medicines.

Mechanisms of drug induced liver injury - tbc

- Detail the direct mechanisms responsible for drug-induced liver injury, using specific examples of paracetamol and inhalation anaesthetics.
- The protective mechanisms employed by hepatocytes to prevent drug-induced toxicity.
- Provide evidence for a role of immune cells for inducing liver injury and mediating reparative processes.

Mechanisms of drug induced toxicity I and II and II - Professor Heather Wallace

- Cell death: necrosis, programmed cell death, apoptosis and autophagy
- How cell death is regulated
- How drugs influence cell death

Toxicity Testing - Mr A Woolley

- Considerations and objectives of toxicity testing
- General design principles, including test systems and ethics
- Toxicity testing in specific areas

Risk assessment - Mr A Woolley

- General thoughts on interpretation and consolidation of test results; use of NOAELs
- Principles and objectives of risk assessment
- Risk assessment in practice - including exposure models and thresholds of toxicological concern

Mechanisms of drug induced toxicity oxidative stress - Professor H Galley

- Give a brief overview of the potentially damaging effects of oxidative stress.
- Describe an example of drug toxicity involving oxidative damage and strategies to prevent toxicity.
- Discuss the potential for drugs, which provide antioxidant protection inside mitochondria.

Non Genotoxic Carcinogenesis - Professor Ruth Roberts

- An overview of nongenotoxicity and key differences from genotoxicity
• Describe the main mechanisms of nongenotoxic carcinogenesis with examples and a detailed case study of PPARα agonists
• Importance of species differences and significance for human risk assessment

Alternatives to animal testing - Professor Ruth Roberts

• The challenge of drug safety testing: what is needed to ensure patient and volunteer safety?
• Look at historical and current use of in vitro methods in drug safety testing
• Consider challenges and opportunities

Practical/Lab/Tutorial Work

Practical: Dr O Ubah, Dr F Saunders

• explore the mechanisms by which cytotoxic drugs cause cell death
• distinguish between apoptosis and necrosis by applying a panel of assays to cultures of cells that have been exposed to a range of concentrations of drug
• encourage team working and data sharing
• deduce the likely mechanism of cell death induced by the drug

Practical tutorial: Dr F Saunders

• share and discuss your team data and conclusions with the rest of the class
• facilitated discussion of the advantages and disadvantages of each assay and other methods available

The details of the practical classes are given in the Practical Manual. Please ensure that you bring clean white laboratory coats to the practical and all students must read and observe the Notes on Behaviour and Safety in Laboratories enclosed with the laboratory manual.

Laboratory reports should be prepared with the aid of a word-processor and the data analysed with the aid of appropriate software packages. The DEADLINE for handing in completed laboratory reports is MONDAY 14th NOVEMBER AT 1300h.

The practical work required in this course may present difficulties to students with special educational needs. For such students, alternative arrangements will be made.
University Policies

Students are asked to make themselves familiar with the information on key institutional policies which 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 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 University¹s Infohub webpage or by visiting the Infohub.

The information included in the institutional area for 2017/18 includes the following:

- Absence
- Academic Appeals & Complaints
- Assessment (Common Grading Scale)
- Codes of Practice on Student Discipline (Academic and Non-Academic)
- Class Certificates
- Recording of Lectures
- Exam Results
- Transcripts
- MyAberdeen
- TurnitinUK
- Feedback
- Communication
- Aberdeen Graduate Attributes
- The Co-Curriculum
# Medical Sciences Common Grading Scale

<table>
<thead>
<tr>
<th>Grade</th>
<th>Grade Point</th>
<th>Category</th>
<th>Honours Class</th>
<th>Description</th>
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</table>
| A1    | 22          | Excellent   | First         | • 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  | • 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  | • 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         | • 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          | • 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           | Clear Fail  |                | • Contains major errors or misconceptions  
• Poor presentation |
| F1    | 5           | Clear Fail  | Not used for Honours | • Contains major errors or misconceptions  
• Poor presentation |
| F2    | 4           |             |               |                                                                                                                                                                                                         |
| F3    | 3           |             |               |                                                                                                                                                                                                         |
| G1    | 2           | Clear Fail/ Abysmal | - | • Token or no submission |
| G2    | 1           |             |               |                                                                                                                                                                                                         |
| G3    | 0           |             |               |                                                                                                                                                                                                         |
### Course Timetable PA4302: 2017-2018

<table>
<thead>
<tr>
<th>Date</th>
<th>Time</th>
<th>Place</th>
<th>Subject</th>
<th>Session Type</th>
<th>Staff</th>
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<tr>
<td><strong>Week 13</strong></td>
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<tr>
<td>Mon 23 Oct</td>
<td>10:00-11:00</td>
<td>1:147</td>
<td>Introduction (PA4302)</td>
<td>Lecture</td>
<td>HMW</td>
</tr>
<tr>
<td></td>
<td>11:00-12:00</td>
<td>BMP</td>
<td>Toxicological Significance of Drug Metabolism (Shared)</td>
<td>Lecture</td>
<td>HMW</td>
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<tr>
<td>Wed 25 Oct</td>
<td>11:00-13:00</td>
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<td>Drug Targeting + Gene Therapy</td>
<td>Lecture</td>
<td>HMW</td>
</tr>
<tr>
<td>Thu 26 Oct</td>
<td>1400-16:00</td>
<td>1:143/144</td>
<td>Drug Targeting + Gene Therapy (Shared)</td>
<td>Lecture</td>
<td>HMW</td>
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<tr>
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<td>16:00-17:00</td>
<td>1:032/033</td>
<td>Career Development (PA4302)</td>
<td>Lecture</td>
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<tr>
<td>Fri 27 Oct</td>
<td>10:00-13:00</td>
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<td>Practical <em>in vitro</em> toxicology (PA4302)</td>
<td>Practical</td>
<td>FRS/OCB</td>
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<td><strong>Week 14</strong></td>
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<td>Mon 30 Oct</td>
<td>10:00-12:00</td>
<td>Dugal Baird</td>
<td>Immunology Overview (Shared)</td>
<td>Lecture</td>
<td>IC</td>
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<td>Tue 31 Oct</td>
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<td>Wed 1 Nov</td>
<td>11:00-13:00</td>
<td>1:147</td>
<td>New slot requested</td>
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<tr>
<td>Thu 2 Nov</td>
<td>10:00-12:00</td>
<td>1:143/144</td>
<td>Drug Research + Development (Shared)</td>
<td>Lecture</td>
<td>RW</td>
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<tr>
<td></td>
<td>14:00-15:00</td>
<td>1:143/144</td>
<td>Pharmacokinetics + ADME w/ Q+A (Shared)</td>
<td>Lecture</td>
<td>RW</td>
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<tr>
<td>Fri 3 Nov</td>
<td>10:00-13:00</td>
<td>2:054</td>
<td>Practical <em>in vitro</em> toxicology Group 2 (PA4302)</td>
<td>Practical</td>
<td>FRS</td>
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<td><strong>Week 15</strong></td>
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<td>Mon 6 Nov</td>
<td>10:00-12:00</td>
<td>BMP LT</td>
<td>Biomarkers (Shared)</td>
<td>Lecture</td>
<td>ECD</td>
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<td>Tue 7 Nov</td>
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<td>11:00-13:00</td>
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<td>Lecture</td>
<td>HMW</td>
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<td>Thu 9 Nov</td>
<td>10:00-11:00</td>
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<td>Molecular Carcinogenesis (Shared)</td>
<td>Lecture</td>
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<td>1:143/144</td>
<td>Drug Transporters (Shared)</td>
<td>Lecture</td>
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<td>Stem Cell Therapies 1 + 2 (Shared)</td>
<td>Lecture</td>
<td>ML</td>
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<td>Fri 10 Nov</td>
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<td><strong>Week 16</strong></td>
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<td>Mon 13 Nov</td>
<td>10:00-12:00</td>
<td>BMP LT</td>
<td>Cell Death 1 + 2 (Shared)</td>
<td>Lecture</td>
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<td>Tue 14 Nov</td>
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<tr>
<td>Wed 15 Nov</td>
<td>11:00-13:00</td>
<td>1:147</td>
<td>New slot requested</td>
<td>Lecture</td>
<td>HMW</td>
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<tr>
<td>Thu 16 Nov</td>
<td>10:00-11:00</td>
<td>1:143/144</td>
<td>Tutorial – problem solving 2 groups (PA4302)</td>
<td>Tutorial</td>
<td>HMW/tbc</td>
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<td>14:00-15:00</td>
<td>1:143/144</td>
<td>Mechanisms of drug-induced toxicity 1 (Shared)</td>
<td>Lecture</td>
<td>HMW</td>
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<td>Fri 17 Nov</td>
<td>11:00-12:00</td>
<td>1:143/144</td>
<td>Toxicity Testing (Shared)</td>
<td>Lecture</td>
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<td></td>
<td>12:00-13:00</td>
<td>1:143/144</td>
<td>Risk Assessment (Shared)</td>
<td>Lecture</td>
<td>AW</td>
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<td><strong>Week 17</strong></td>
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<td>Mon 20 Nov</td>
<td>10:00-11:00</td>
<td>BMP LT</td>
<td>Non-Genotoxic Carcinogenesis (Shared)</td>
<td>Lecture</td>
<td>RR</td>
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<td></td>
<td>11:00-12:00</td>
<td>BMP LT</td>
<td>Use of In-Vitro Alternatives to Animal Testing by the Pharmaceutical Industry (Shared)</td>
<td>Lecture</td>
<td>RR</td>
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<td>Tue 21 Nov</td>
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<tr>
<td>Wed 22 Nov</td>
<td>10:00-12:00 – 11-13:00</td>
<td>012 Suttie Lecture Theatre</td>
<td>Inmuno-toxicology (Shared)</td>
<td>Lecture</td>
<td>RD</td>
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<td>Mechanisms of Drug Induced Injury - Oxidative Stress (Shared)</td>
<td>Lecture</td>
<td>HFG</td>
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<td>Fri 24 Nov</td>
<td>09:00-10:00</td>
<td>FLT</td>
<td>Unforeseen Problem (PA4302)</td>
<td>Assessment</td>
<td>HMW</td>
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<td>Professor HM Wallace (HMW), Course Co-ordinator</td>
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<td>Dr F R Saunders (FRS), School of Medicine, Medical Sciences and Nutrition</td>
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<td>Professor Ruth Roberts (RR), ApconIX Ltd</td>
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<td>Dr R J Weaver (RW), Bioanalysis &amp; New Technologies Division, Safety Assessment, France</td>
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