



Table of Contents:

SS Molecular Medicine	60 ECTS of compulsory modules	3-4
Module List		
Personnel	Contact Details	4
Academic Matters	Explanation of ECTS, Assessment & Examinations	4-10
	and List of tutorial groups and assigned staff	
	members	
Small Group Tutorials	Detail of Groups	10
Prizes	Explanation of awards by the School	11
Health & Safety Matters,	Regulations concerning Health & Safety	11-13
Emergency Procedures &		
Covid-19 Regulations		
Student Disability Service	Information on services and contact details	13
Plagiarism	College regulations concerning plagiarism	14-18
Academic progress	College calendar rules	17-18
Class descriptors	Each grade and what is expected	19
Exam Papers	Information on layout of the 3 semester 2 exam	20-21
	papers	
Molecular Medicine Modules	Module codes, learning outcomes, course	22-48
	descriptions, key reading	
Grading Rubrics	Forms used for marking Capstone Project elements	49-53
Careers Advisory Service	Information on services, workshops, opening hours	54-55
	etc.	

Dear SS Molecular Medicine students,

Welcome to the Senior Sophister year, the culmination of your Molecular Medicine degree. It is a chance to really engage with Molecular Medicine as a subject and to graduate as well-rounded scientists with the ability to follow a wide range of career paths.

Covid-19 had an impact on how last year operated, particularly with respect to the semester one examinations (which were run on-line) and the layout of the semester two examination papers. However, we successfully reverted to in person exams at the end of semester two and the hope is that we will be able to return fully to our normal pre-Covid schedule this year. If this has to change for any reason, we have contingency plans in place, and you will be updated. We do however need to continue to exercise caution with respect to Covid-19 and while mask wearing is not currently mandatory, we recommend wearing them in lecture settings, library and other venues where people may be in close quarters. We know this mitigation is effective in limiting transmission. If

you cannot attend lectures in person due to being positive for Covid-19, you will be offered access to the learning resources and opportunities necessary to fulfil the learning outcomes, for example access to pre-recorded lectures, supplementary reading resources or detailed notes. As was the case last year, it will be sufficient for students to self-certify that they have Covid-19 through provision of a screen shot of a positive PCR or Antigen test.

For now, please take your time going through the booklet and the information therein. It contains important information including deadlines for various activities. A copy of the booklet can also be found on Blackboard under Module BIU44390.

If you have any problems during the year which affect your academic studies, please speak to me in confidence. I am here to help. Looking forward to working with you over the coming year.

Prof. Gareth Brady

SS Course Co-ordinator: bradyg1@tcd.ie

Senior Sophister Molecular Medicine

(60 ECTS)

BIU44390 CAPSTONE PROJECT IN MOLECULAR MEDICINE (S1)

20 credits

The module comprises of an original research project in molecular medicine and a research thesis.

BIU44010 ADVANCED RESEARCH SKILLS (S1)

10 credits

The purpose of this module is to further develop research, critical analysis and communication skills that are essential for a Molecular Medicine scientist. Students will be trained in data handling as well as solving quantitative problems in biochemistry and immunology. In addition, this module will introduce students to a wide array of cutting-edge techniques and strategies used in molecular medicine.

BIU44310 NEUROBIOLOGY & IMMUNOLOGY (S2)

10 credits

This module covers the structure, function and pharmacology of neurotransmitters, neuron-glia interactions, intraneuronal signalling and the neurobiology of behaviour and neurodegenerative disorders. This module also covers regional immunology (e.g. gastrointestinal immunology, respiratory immunology etc), autophagy, virology and immunometabolism.

BIU44320 MICROBIAL DISEASES & IMMUNE SYSTEM DISORDERS (S2) 10 credits

The first part of this module will focus on microbial diseases. Bacterial and viral pathogens of medical importance will be covered in detail. Parasitic protozoa such as trypanosomes and helminths will be introduced. This module will also cover the basic and clinical aspects of auto-inflammatory and autoimmune conditions, including rheumatoid arthritis, multiple sclerosis and immunodeficiency syndromes.

BIU44330 CELL CYCLE, CANCER BIOLOGY AND THERAPEUTICS (S2) 10 credits

This module will provide an in-depth analysis of the cell cycle, cancer and metastasis. It will focus on the progression of disease and current therapeutic interventions. This module will also provide a detailed overview of the meiotic and mitotic cell cycle and its regulation and the molecular biology of cancer.

NOTE: Learning outcomes for each of the modules can be found in the detailed module descriptors (from page 22).

Staff contact details:

As course co-ordinator for SS year, I am the first point of contact for students (email bradyg1@tcd.ie). The Head of School is Prof. Derek Nolan (phone extension 2455, email denolan@tcd.ie) and Prof. Vincent Kelly is the Director of Undergraduate Teaching and Learning (kellyvp@tcd.ie). Please use biochem@tcd.ie to contact the School office on Level 3 TBSI. Remember that you also have a college tutor that you can contact at any time. The names of small group tutorial tutors are provided further in the booklet. A complete list of the Biochemistry and Immunology Staff can be found at https://www.tcd.ie/Biochemistry/people/ and School of Medicine Staff can be found at https://www.tcd.ie/medicine/staff/.

Timetable, face-to-face and remote learning:

As you know, CMIS is the official college timetable but in all likelihood we will rely on locally produced information for Semester One. Small group tutorials may be face to face or remote via Teams or zoom. It is important this year that students actively engage with academic staff to enrich your education experience.

Attendance:

All students are expected to attend lectures, workshops, in-course assessments and examinations, either on-line or face to face. Tutorials, lectures and workshops play an important role in supporting progress through the academic year in particular course assignment work. Students are therefore expected to keep up a consistent rate of good participation so that performance later in the year will not be adversely affected. In the event of not being able to participate in classes due to illness, **please inform the Course Co-ordinator**. Medical certificates are required for absences of more than a few days OR if the absence means a deadline or an assessment will be missed. Details of medical certificates and other personal information will be treated confidentially.

The School operates the College procedure in relation to 'Non-satisfactory attendance and course work' (Calendar). That is, any student who misses more than a third of a course in any semester or fails to complete assignments may be declared 'non-satisfactory'. Non-satisfactory returns are made to the Senior Lecturer; such students may be refused permission to take the end of semester examinations and may be required by the Senior Lecturer to repeat the year.

From College Calendar General Regulations: 2022-23

Non-satisfactory attendance

24 All students must fulfil the course requirements of the school or department, as appropriate, with regard to attendance. Where specific requirements are not stated, students may be deemed non-satisfactory if they miss more than a third of their course of study in any term. Calendar 2022-23 33

25 At the end of the teaching term, students who have not satisfied the school or department requirements, as set out in §§19 and 24 above, may be reported as non-satisfactory for that term. Students reported as non-satisfactory for the Michaelmas and Hilary terms of a given year may be refused permission to take their semester two assessment/examinations and may be required by the Senior Lecturer to repeat their year. Further details of procedures for reporting a student as non-satisfactory are given on the College website at www.tcd.ie/academic registry/studentcases.

Explanation of ECTS:

The European Credit Transfer and Accumulation System (ECTS) is an academic credit system based on the estimated student workload required to achieve the objectives of a module or programme of study. It is designed to enable academic recognition for periods of study, to facilitate student mobility and credit accumulation and transfer. The ECTS is the recommended credit system for higher education in Ireland and across the European Higher Education Area.

The ECTS weighting for a module is a **measure of the student input or workload** required for that module, based on factors such as the number of contact hours, the number and length of written or verbally presented assessment exercises, class preparation and private study time, laboratory classes, examinations, clinical attendance, professional training placements, and so on as appropriate. There is no intrinsic relationship between the credit volume of a module and its level of difficulty.

The European norm for full-time study over one academic year is 60 credits. The Trinity academic year is 40 weeks from the start of Semester one to the end of Semester 2. 1 ECTS credit represents 20-25 hours estimated student input, so a 10-credit module will be designed to require 200-250 hours of student input including class contact time and assessments.

ECTS credits are awarded to a student only upon successful completion of the course year. Progression from one year to the next is determined by the course regulations. Students who fail a year of their course will not obtain credit for that year even if they have passed certain component courses. Exceptions to this rule are one-year and part-year visiting students, who are awarded credit for individual modules successfully completed.

For additional details see: https://www.tcd.ie/teaching-learning/NC Proposal/ECTS/ects.php

Annual Year Structure:

Information is available at https://www.tcd.ie/calendar/academic-year-structure/

Examinations/Assessments and Breakdown of Marks:

Senior Sophister Module Name ECTS Weighting 1) Capstone Project in Molecular Medicine BIU44390 20 ECTS 2) Advanced Research Skills BIU44010 10 ECTS 3) Neurobiology & Immunology BIU44310 10 ECTS 4) Microbial Disease & Immune System Disorders BIU44320 10 ECTS

SS year is broken down into a total of **60** credits.

5) Cell Cycle, Cancer Biology & Therapeutics

Capstone Project in Molecular Medicine (BIU44390) Value: 20 ECTS

10 ECTS

BIU44330

An 11-week research project and thesis. **Project laboratory work will start on Monday September 12**th and **terminate** on **Friday 25**th **November**. In general, students will finish in the laboratory by 6pm each day. Occasionally, experiments may run longer but this should not be the norm – please contact your supervisor if you need further information. In order to be fair to other students, no student is allowed to work in the laboratory after the 25th November (even to finish one last experiment). Please contact your course coordinator if you need further information.

After the completion of laboratory work, you will be required to submit a draft of your project thesis to your supervisor. The absolute deadline for submission of **thesis 1**st **draft is Monday 23**rd **January 2023.** We would strongly recommend that you submit your first draft at an earlier date in January in order to give you time to incorporate suggested revisions. Your supervisor should only see one or possibly two drafts of the thesis prior to submission. Listen carefully to their feedback and incorporate it. **There is a word limit of 3000 words for the introduction and a total of 10,000 words for the entire thesis (excluding bibliography and legends).**

A deadline for handing in final revised project thesis will operate. It is 4.00 pm on Monday 6th February. For every working day that your thesis is late 2% will be deducted from your mark. Please submit your thesis to Blackboard under module BIU44390. More details will follow.

Following submission of your project thesis you will give a 15 min oral presentation (10 min plus 5 min for questions) that explains your project, its aims, your experimental approach, your results and conclusions (**Monday 6**th **March**). Your presentation and your ability to answer questions will be assessed by a panel of three members of academic staff. Your classmates will also be present at this session. It is advisable to arrange at least one practise session with your project supervisor. This **oral presentation will account for 15% of the project mark.**

You will also present a **Project Poster** to the School at a poster session (**Friday 10**th **March**). All members of the School, both staff and students, are invited to attend and they may ask you questions about your research project. Your poster will be judged by 2 members of staff and you

will be asked questions by these judges. This poster presentation will account for 5% of the project mark.

Ms Roisin Cleere and Dr Audrey Carroll (Preparation Room) will advise you about the presentation of your poster and print it for you. Further details on Project write-ups and poster presentations will be given at the end of semester 1.

Project Marking Scheme:

Lab performance: 15% (awarded by supervisor)

Thesis: 65% (awarded by supervisor & 1 other staff member) **Oral presentation: 15%** (awarded by panel of 3 staff members)

Poster presentation: 5% (awarded by 2 staff members)

Copy of mark sheets and criteria for SS project, thesis and poster can be found below (from page 49)

- Lab performance report (supervisor only; 15%)
- Project thesis (supervisor's report made available without mark to 2nd marker)
- Project thesis (2nd marker) marks independently, meets and agrees mark with supervisor (65% of the project mark)

Note: if the supervisor and the 2nd markers are more than 10% apart, the thesis will be given to a third marker before a final mark is agreed.

Advanced Research Skills (BIU44010)

This module covers quantitative biochemical problems, bioinformatics (sequence analysis), comparative medicine and a series of group presentations by students on various biochemical techniques. A series of 18 lectures will also introduce students to a wide array of cutting-edge techniques and strategies used in biochemistry. Marks (100) for this module are awarded through continual assessment and exams as follows:

- Quantitative Problems: 4 in total, assessed by two 1 hour in-person exams of equal weighting; one compulsory question, from one of two problems, on each exam.
 Problem Exam 1 Friday 21st October and Problem Exam 2 Monday 12th December (30 marks in total)
- Bioinformatics-Sequence Analysis: 3 in total of equal weighting, assessed by assignments submitted on-line (10 marks in total)
- Comparative Medicine: assessed by a 1 hour in-person exam on 13th December; answer one compulsory essay style question. (5 marks)
- Group BioTechniques: assessed in part by oral presentation (5 marks) and a summary report (5 marks) (10 marks in total). Presentations will take place on 26th and 27th October.

Value: 10 ECTS

• **BioTechniques Exam:** Both the material delivered in lectures and material covered in the group BioTechniques will be assessed by a 2.5h in-person exam on 14th December; answer 3 out of 4 essay style questions. (**45 marks** in total).

Quantitative Problem Tutorials:

An introductory session to each of the **four** Quantitative Problems will be delivered by four assigned staff members (*e.g.* **Prb 1 Intro** on timetable). Following the introductory session, you will be asked to attempt a quantitative problem circulated by that staff member before the next tutorial session (*e.g.* **Prb 1 Tutorial**). In this session, the staff member will go through the solution to the problem. There will be two exams of equal weighting with one compulsory question on each exam. Problem Exam 1 will cover material from Problem 1 or Problem 2, and Problem Exam 2 will cover material from Problem 3 or Problem 4.

Sequence Analysis Sessions:

There will be three Sequence Analysis Exercises (Dr Jerrard Hayes). A tutorial will be delivered by Dr Hayes. He will show you how to use the required software and provide you with some worked examples. He will also advise you how and where to submit and of their submission deadlines.

Semester 2 Examination Papers

We are planning for in-person exams on campus. However, this may change depending on public health guidelines.

There are three exam papers at the end of semester 2, each with equal weighting as follows:

Paper 1 (BIU44310) Neurobiology & Immunology	Value: 10 ECTS
Exam paper (100 marks) divided into 4 sections of equal weighting:	
Section 1: Neurobiology (Answer 1 out of 2 questions)	25marks
Section 2: Immunology (Answer 1 out of 2 questions)	25marks
Section 3: General (Integrative/philosophical)	
(Answer 1 out of 3 questions)	25marks
Section 4: Quickie/Short questions (Answer 4 out of 7 questions)	25marks
Paper 2 (BIU44320) Microbial Diseases & Immune System Disorders Exam paper (100 marks) divided into 4 sections of equal weighting.	Value: 10 ECTS
• • • •	Value: 10 ECTS 25marks
Exam paper (100 marks) divided into 4 sections of equal weighting.	
Exam paper (100 marks) divided into 4 sections of equal weighting. Section 1: Microbial Disease (Answer 1 out of 2 questions) Section 2: Immune System Disorders (Answer 1 out of 2 questions)	25marks
Exam paper (100 marks) divided into 4 sections of equal weighting. Section 1: Microbial Disease (Answer 1 out of 2 questions) Section 2: Immune System Disorders (Answer 1 out of 2 questions) Section 3: General (Integrative/philosophical)	25marks 25marks

Value: 30 ECTS

Paper 3 (BIU44330) Cell Cycle, Cancer Biology & Therapeutics Value: 10 ECTS

Exam paper (100 marks) divided into 4 sections of equal weighting.

Section 1: Cell cycle & Cancer (Answer 1 out of 2 questions) 25marks Section 2: Cancer Biology & Therapeutics (Answer 1 of 2 questions) 25marks

Section 3: General (Integrative/philosophical)

(Answer 1 out of 3 questions) 25marks Section 4: Quickie/Short questions (Answer 4 out of 7 questions) 25marks

The overall degree mark is comprised of 70% of SS year and 30% of JS year.

Vivas:

On completion of their annual examinations, students may be required to sit a *viva voce* examination with the **External Examiner** (Prof. Bill Paxton, University of Liverpool, UK). Students are considered **'borderline'** if they are 1% or less off a grade and following the *viva voce* examination the External Examiner may recommend at the Examiners' meeting that the students' degree mark be brought up to the next grade. Note: not all students called for viva are borderline and additional students may be included as controls. You will not be told which category you are in. You cannot be marked down by a viva. You will not know your mark before sitting the viva. Finally, vivas will be held in-person only so please ensure you are in the country and available if called. **Requests for remote online vivas will not be granted.**

How can you prepare for the viva?

If you are called for a viva in the summer, you should read over your project thesis as the Extern often starts off by asking you about your project. He/she will want to relax you and will generally start you off on a topic you know a lot about. The Extern will probably cover about 4-6 topics during the viva and it is impossible to second guess what they will ask. However, if you feel you did badly in one particular exam question, it is a good idea to revise this topic. The Extern has access to all your marks and if he/she sees a poor mark in an otherwise very consistent good set of marks they may wish to follow this up. The Extern may also ask you if there is a topic in Biochemistry that you find particularly interesting and that you wish to talk about. It is therefore a good idea to have something prepared but ensure that it is a specific topic. Do not be too general and say that you're interested in protein structure! The Extern may also ask you on your views of the course; was there a part of the course you really enjoyed or not as the case may be. The role of the Extern is not only to assess your performance but also to assess our teaching capabilities and to identify strengths/weaknesses and even omissions in the course so that they can make recommendations for the following year.

Tutorials:

Tutors have been chosen randomly. Please contact your tutor during the first week of the first semester. You are typically expected to attend a tutorial every fortnight. Your tutor will set various exercises and these should help you in your final examinations.

SS Molecular Medicine Staff Tutorial Groups 2022-23

Student	Tutor
Alali, Fatmah Sultan Mohamed Majed Ashe, John Davies Harold, Zara Elizabeth	Prof. Vincent Kelly (KELLYVP@tcd.ie)
Delimata May, Kai Doran, Stephen Gregory Fenton, James	Prof. Jean Fletcher (FLETCHJ@tcd.ie)
Ghiba, Stephanie Hopkins, Kian Thomas James, Steven	Prof. Gareth Brady (BRADYG1@tcd.ie)
Kenny, Niamh Mary Murphy, Faye O Rourke, Aisling	Prof. Fred Sheedy (FSHEEDY@tcd.ie)
O Sullivan, Nicole Perrem, Patrick Power, Shauna	Prof. Sarah Doyle (DOYLES8@tcd.ie)
Rojas, Alexandra Sofia Walsh, Amy White, Adam	Dr Michael Carty (CARTYMI@tcd.ie)

Addresses and Phone Numbers: Please send your College based address, e-mail address and telephone number (if any) to biochem@tcd.ie. Please also include a home (or other contact) address and telephone number. This will enable us to contact you in an emergency or with important changes. If you do not enter these details you may not be informed of any changes.

Prizes:

The **Ciotti Orsi Prize** prize was founded in 1996 by the late Dr. Bruno A. Orsi in honour of his wife, Margaret Ciotti, and, from 1999 as a memorial to her. It is awarded each year by an annual gift

to the final year biochemistry, immunology or molecular medicine student who has shown excellence in research during their project and, in this way, reflects Margaret's scientific career in the U.S. Since the passing of Dr. Bruno A. Orsi in May 2020, the prize is now being given in memory of them both, reflecting their joint contributions to the world of Biochemistry. Dr. Bruno A. Orsi was professor emeritus and will be particularly remembered for his exuberant and enthusiastic teaching style. Value, €400 and a commemorative bronze medal.

Gold Medal: Gold Medals are awarded on the basis of the final, overall degree award mark (which will be calculated on a 30/70 basis over the final two years). If you achieve an overall degree mark of 75% or above you will be awarded a Gold Medal at graduation.

Health and Safety Matters:

1) Registration with Safety Officer

Preliminary safety registration takes place during two mandatory health and safety briefing sessions scheduled on the first day of term September12th. You must register, by E-mail or if required in person, with the Safety Officer once you commence your project. This is necessary in order to record your next-of-kin details in the unlikely event of an accident, to record where you will be working, to ascertain whether or not you have to work with major hazards during your project work (carcinogens, mutagens, cyto-toxics, biological agents, GMOs, radioactivity, *etc*), and to ensure that you and your supervisor understand that you have to conduct a HIRAC review (hazard identification, risk assessment and risk control) of the proposed work. (see below).

2) Formal Health and Safety Briefings

Mr Liam McCarthy (Chief Technical Officer) will describe the general management and security features of the building at an introductory briefing. Dr Darren Fayne, the School Safety Officer will give you two formal Health and Safety briefings. ATTENDANCE OF THESE BRIEFINGS ANY ADDITIONAL TRAINING SESSIONS (e.g. Radiological Protection Workshop, viewing safety videos, etc.) IS MANDATORY. Some of these actions are legal, license or College's insurer's requirements that have to be complied with.

3) Safety Lab Coat & Spectacles

You must have at least one Howie-style laboratory safety coat, conforming to the NISO 1993, or better, standard, along with a pair of safety spectacles with you at all stages during active laboratory work.

4) Specific Aspects of Health and Safety Associated with Project Work.

You are required to complete a 'Personnel Training Form' to ensure that you have been trained in all techniques/equipment that you will be using during your project, that you understand any risks associated with your project and that you understand how to minimize them. Any hazardous materials, steps or procedures (including off-site work connected with your research such as collecting samples from other laboratories, etc.) involved in your project will have been identified by, and discussed with you by your project supervisor. He/she is required, by law, to perform this hazard identification, risk assessment and risk control (HIRAC) on every experiment undertaken by you, but you have a role to play as well in making sure that you record the conclusions of this procedure in your notebook. The control measures necessary to reduce or eliminate risk must be written in your notebook for each hazardous step or procedure. The law requires this to be done. You are still in training so you cannot be classed as a competent scientist and thus able to do this yourself to ensure your safety. If in doubt about the proper procedures for any experiment, do not perform that experiment.

Senior Sophisters must make themselves aware of the College's and School's Safety Statement which is displayed prominently in every laboratory in the School. It can be downloaded from the School's Local Home-Page at this URL: www.tcd.ie/biochemistry/. You are still bound by the 'Science Faculty's Health and Safety Guidance Manual' and the associated Health Questionnaire which you completed at the start of JF year. If your health status has changed since then in terms of the categories listed (including pregnancy or lactation) you have to complete a new Health Questionnaire. If your health status again changes during the year you must consult, in confidence, with the Safety Officer. [This particularly applies in the case of pregnancy.]

If you intend working with radioactivity during your project you must first contact the School Radiological Protection Supervisor, Dr Darren Fayne (fayned@tcd.ie). You are not permitted to work with unsealed radionuclide sources.

Any student working with human materials (blood, buffy coats, semen, CSF, dialysis fluid, primary explants, etc.) <u>must</u> be vaccinated against Hepatitis B prior to commencing your project. You are not permitted to work with any risk group 3 or class 3 biological agents such as HIV, Hepatitis B and C, COVID-19, etc. or to culture Category 3 (or higher) pathogens.

You must request or otherwise obtain Material Safety Data Sheets (MSDS) for any toxic or dangerous chemicals or preparations that you are using in your project. These MSDS's have to be requested at the point of ordering any material. The MSDS must be stuck into your laboratory notebook. The guidance must be followed.

After 6:00 pm on working days, and at all times on weekends and public holidays, no Senior Sophister may work in any laboratory without the close presence of a member of the academic staff. It is the Senior Sophister's responsibility to ask that staff member if he/she will consent to act in a supervisory capacity for the time the student is working. During normal working hours, no student may work alone in any laboratory.

Failure to observe these rules/procedures will cause the offenders to be officially warned, and be reported to the Head of School, school safety officer and project supervisor. Normal College disciplinary procedures can be invoked (including fines being levied as well as withdrawal of student ID card, *etc.*) Persistent failure to observe these rules may result in that student being banned from laboratory work with loss of those marks available for project work.

All the necessary forms are available to download on the local safety pages at

https://www.tcd.ie/Biochemistry/local/safety_info.php

Once you have completed all the forms and safety briefings, E-mail them to the Safety officer, Darren Fayne (fayned@tcd.ie).

5) Emergency Procedure

In the event of an emergency, **dial Security Services on extension 1999**. Security Services provide a 24-hour service to the college community, 365 days a year. They are the liaison to the Fire, Garda and Ambulance services and all staff and students are advised to always telephone extension 1999 (+353 1 8961999) in case of an emergency, should you require any emergency or rescues services on campus, you must contact Security Services. This includes chemical spills, personal injury or first aid assistance. It is recommended that all students save at least one emergency contact in their phone under ICE (In Case of Emergency).

Students with Disabilities: The University Policy Relating to students with disabilities is available at www.tcd.ie/disability. The Student Disability Service is located in Room 2054 Arts Building, phone = 8963111, email = disab@tcd.ie. The Student Disability Services Committee provides the formal channel for raising issues affecting students with disabilities. Martha Motherway (motherm@tcd.ie) is the liaison officer for the disability services in our school.

Support Provision for Students with Disabilities: Trinity has adopted a Reasonable Accommodation Policy that outlines how supports are implemented in Trinity. Student seeking reasonable accommodation while studying in Trinity must apply for reasonable accommodations online with the Disability Service in their student portal my.tcd.ie. Based on appropriate evidence of a disability and information obtained from the student on the impact of their disability and their academic course requirements, the Disability Staff member will identify supports designed to meet the student's disability support needs. Following the Needs Assessment, the student's Disability Officer prepares an Individual Learning Educational Needs Summary (LENS) detailing the Reasonable Accommodations to be implemented. The information outlined in the LENS is communicated to the relevant School via the student record in SITS.

<u>Student responsibilities for departmental assessments/course tests:</u> Students are required to initiate contact with the School/Department and request reasonable accommodations **as per their LENS report, or email received following their needs assessment** for particular assessments for School/ Department administered assessment. Students are advised to make

13

contact at least two weeks prior to the assessment date to enable adjustments to be implemented.

Plagiarism: NB - READ THIS SECTION PROPERLY

While plagiarism has always been a serious offense (as detailed in the College Calendar-see excerpt below), the incidence of plagiarism has increased, in part due to remote and electronic submissions. It is your responsibility to understand what plagiarism is and avoid it. It can include the following:

Substantial or direct duplication of text/content:

- · from material previously submitted during your degree.
- · from published online sources without appropriate quotation and citation.
- from lecture slides.

Self-plagiarism (using materials prepared by you and previously submitted) is still plagiarism.

Care needs to be taken when paraphrasing from an article/source. Paraphrasing does not indicate that you understand the material and depending on the scale, can be considered plagiarism. For you to demonstrate understanding (and get better marks), you need to use your own words.

The full statement of College's policy on plagiarism (see Calendar, General Regulations and Information, at http://tcd-ie.libguides.com/plagiarism are reproduced below. Your capstone project thesis will be submitted through plagiarism-detecting software such as Turnitin (additional information for which can be found at: http://turnitin.com/static/index.html). It is your responsibility to educate yourself about what exactly constitutes plagiarism. Ignorance is not an acceptable defence.

It is a college requirement that all students must complete an online tutorial on avoiding plagiarism 'Ready, Steady, Write', located at http://tcd-ie.libguides.com/plagiarism/ready-steady-write.

In addition, students must complete cover sheets or include text containing the following declaration when submitting assessed work in hard or soft copy or via Blackboard:

I have read and I understand the plagiarism provisions in the General Regulations of the University Calendar for the current year, found at: http://www.tcd.ie/calendar

I have also completed the Online Tutorial on avoiding plagiarism 'Ready, Steady, Write', located at http://tcd-ie.libguides.com/plagiarism/ready-steady-write

Calendar regulations on plagiarism 2022/23

95 General It is clearly understood that all members of the academic community use and build on the work and ideas of others. It is commonly accepted also, however, that we build on the work and ideas of others in an open and explicit manner, and with due acknowledgement. Plagiarism is the act of presenting the work or ideas of others as one's own, without due acknowledgement. Plagiarism can arise from deliberate actions and also through careless thinking and/or methodology. The offence lies not in the attitude or intention of the perpetrator, but in the action and in its consequences. It is the responsibility of the author of any work to ensure that he/she does not commit plagiarism. Plagiarism is considered to be academically fraudulent, and an offence against academic integrity that is subject to the disciplinary procedures of the University.

96 Examples of Plagiarism Plagiarism can arise from actions such as: (a) copying another student's work; (b) enlisting another person or persons to complete an assignment on the student's behalf; (c) procuring, whether with payment or otherwise, the work or ideas of another; (d) quoting directly, without acknowledgement, from books, articles or other sources, either in printed, recorded or electronic format, including websites and social media; (e) paraphrasing, without acknowledgement, the writings of other authors. Examples (d) and (e) in particular can arise through careless thinking and/or methodology where students: (i) fail to distinguish between their own ideas and those of others; (ii) fail to take proper notes during preliminary research and therefore lose track of the sources from which the notes were drawn; 48 Calendar 2020-21 (iii) fail to distinguish between information which needs no acknowledgement because it is firmly in the public domain, and information which might be widely known, but which nevertheless requires some sort of acknowledgement; (iv) come across a distinctive methodology or idea and fail to record its source. All the above serve only as examples and are not exhaustive.

97 Plagiarism in the context of group work Students should normally submit work done in cooperation with other students only when it is done with the full knowledge and permission of the lecturer concerned. Without this, submitting work which is the product of collaboration with other students may be considered to be plagiarism. When work is submitted as the result of a group project, it is the responsibility of all students in the group to ensure, so far as is possible, that no work submitted by the group is plagiarised. In order to avoid plagiarism in the context of collaboration and group work, it is particularly important to ensure that each student appropriately attributes work that is not their own.

98 Self plagiarism No work can normally be submitted for more than one assessment for credit. Resubmitting the same work for more than one assessment for credit is normally considered self-plagiarism.

99 Avoiding plagiarism Students should ensure the integrity of their work by seeking advice from their lecturers, tutor or supervisor on avoiding plagiarism. All schools and departments must include, in their handbooks or other literature given to students, guidelines on the appropriate methodology for the kind of work that students will be expected to undertake. In addition, a general set of guidelines for students on avoiding plagiarism is available on http://libguides.tcd.ie/plagiarism.

100 If plagiarism as referred to in §95 above is suspected, in the first instance, the Director of Teaching and Learning (Undergraduate), or their designate, will write to the student, and the student's tutor advising them of the concerns raised. The student and tutor (as an alternative to the tutor, students may nominate a representative from the Students' Union) will be invited to attend an informal meeting with the Director of Teaching and Learning (Undergraduate), or their designate, and the lecturer concerned, in order to put their suspicions to the student and give the student the opportunity to respond. The student will be requested to respond in writing stating his/her agreement to attend such a meeting and confirming on which of the suggested dates and times it

will be possible for them to attend. If the student does not in this manner agree to attend such a meeting, the Director of Teaching and Learning (Undergraduate), or designate, may refer the case directly to the Junior Dean, who will interview the student and may implement the procedures as referred to under CONDUCT AND COLLEGE REGULATIONS §2.

101 If the Director of Teaching and Learning (Undergraduate), or designate, forms the view that plagiarism has taken place, he/she must decide if the offence can be dealt with under the summary procedure set out below. In order for this summary procedure to be followed, all parties attending the informal meeting as noted in §100 above must state their agreement in writing to the Director of Teaching and Learning (Undergraduate), or designate. If one of the parties to the informal meeting withholds his/her written agreement to the application of the summary procedure, or if the facts of the case are in dispute, or if the Director of Teaching and Learning (Undergraduate), or designate, feels that the penalties provided for under the summary procedure below are inappropriate given the circumstances of the case, he/she will refer the case directly to the Junior Dean, who will interview the student and may implement the procedures as referred to under CONDUCT AND COLLEGE REGULATIONS §2.

102 If the offence can be dealt with under the summary procedure, the Director of Teaching and Learning (Undergraduate), or designate, will recommend one of the following penalties: (a) Level 1: Student receives an informal verbal warning. The piece of work in question is inadmissible. The student is required to rephrase and correctly reference all plagiarised Calendar 2020-21 49 elements. Other content should not be altered. The resubmitted work will be assessed and marked without penalty; (b) Level 2: Student receives a formal written warning. The piece of work in question is inadmissible. The student is required to rephrase and correctly reference all plagiarised elements. Other content should not be altered. The resubmitted work will receive a reduced or capped mark depending on the seriousness/extent of plagiarism; (c) Level 3: Student receives a formal written warning. The piece of work in question is inadmissible. There is no opportunity for resubmission with corrections. Instead, the student is required to submit a new piece of work as a reassessment during the next available session. Provided the work is of a passing standard, both the assessment mark and the overall module mark will be capped at the pass mark. Discretion lies with the Senior Lecturer in cases where there is no standard opportunity for a reassessment under applicable course regulations.

103 Provided that the appropriate procedure has been followed and all parties in §100 above are in agreement with the proposed penalty, the Director of Teaching and Learning (Undergraduate) should in the case of a Level 1 offence, inform the course director and where appropriate the course office. In the case of a Level 2 or Level 3 offence, the Senior Lecturer must be notified and requested to approve the recommended penalty. The Senior Lecturer may approve, reject, or vary the recommended penalty, or seek further information before making a decision. If the Senior Lecturer considers that the penalties provided for under the summary procedure are inappropriate given the circumstances of the case, he/she may also refer the matter directly to the Junior Dean who will interview the student and may implement the procedures as referred to under CONDUCT AND COLLEGE REGULATIONS §2. Notwithstanding his/her decision, the Senior Lecturer will inform the Junior Dean of all notified cases of Level 2 and Level 3 offences accordingly. The Junior Dean may nevertheless implement the procedures as referred to under CONDUCT AND COLLEGE REGULATIONS §2.

104 If the case cannot normally be dealt with under the summary procedures, it is deemed to be a Level 4 offence and will be referred directly to the Junior Dean. Nothing provided for under the summary procedure diminishes or prejudices the disciplinary powers of the Junior Dean under the 2010 Consolidated Statutes.

Please note in the event of remote exams there will be increased vigilance of possible plagiarism. For each exam answer, examiners will be provided with similarity reports generated from the plagiarism detection software. You should never answer questions verbatim from notes provided by a lecturer or learn pre-prepared essays off by heart. One of the criteria by which we mark students is by their demonstrating understanding of a topic. Therefore, you should always aim to put things into your own words. Inevitably, there is technical jargon and phrases that are commonly used – these will obviously not be held against you.

College regulations on Academic Progress and Progression 2022-2023

Progression regulations: Bachelor programmes3

58 Some programmes with professional accreditation have received a derogation from specific regulations on progression by the University Council. The relevant programme entry provides these details. In order to rise with their class, students must obtain credit for the academic year by satisfactory attendance at lectures and tutorials and by carrying out, submitting and sitting the 3See individual entries for applicable certificate and diploma course progression regulations. 38 Calendar 2020-21 required assessment components. In addition, students must pass the year by achieving, at a minimum, an overall credit-weighted average pass mark for the year (40 per cent or 50 per cent, as per programme regulations) and either: (a) accumulate 60 credits by achieving at least the pass mark in all modules or (b) pass by compensation. All modules and components within modules are compensatable (except in particular professional programmes where compensation does not apply). To pass a year by compensation, in programmes that locate the pass mark at 40 per cent, a student must achieve the pass mark in modules carrying a minimum of 50 credits and obtain a module mark of at least 35 per cent in any remaining module(s). A student may accumulate a maximum of 10 credits at qualified pass where the mark lies between 35-39 per cent. To pass a year by compensation, in programmes that locate the pass mark at 50 per cent, a student must achieve the pass mark in modules carrying a minimum of 50 credits and obtain a module mark of at least 45 per cent in any remaining module(s). A student may accumulate a maximum of 10 credits at qualified pass where the mark lies between 45-49 per cent.

59 Progression is on an annual basis. Within a year students may carry failed modules from one semester to the next but not from one academic year to another; that is, they will not be able to rise to the next year of their programme until they have successfully completed the preceding year(s). Students who have not passed their year are required to present for reassessment when: (a) they obtain in excess of 10 credits at qualified pass (i.e. marks between 35-39 per cent where the pass mark is 40 per cent; or 45-49 per cent where the pass mark is 50 per cent); (b) they fail any module (i.e. achieving marks below 35 per cent where the pass mark is 40 per cent; or below 45 per cent where the pass mark is 50 per cent); (c) they do not obtain an overall pass mark for the year; (d) any combination of (a) - (c) occurs.

60 If a student has achieved both fail and qualified pass grades at the first sitting or has exceeded the 10 credit limit allowed for compensation and is not permitted to rise with their year, they must present for reassessment in all failed components of all modules for which they obtained a fail and/or a qualified pass.

61 Different modalities of assessment to the first sitting are permitted in the reassessment session as determined by the programme.

- 62 The same progression and compensation regulations as outlined above apply at the reassessment session. The overall credit-weighted average for the academic year will be calculated using the most recent marks achieved.
- 63 Students who fail to satisfy the requirements of their year at the reassessment session are required to repeat the year in full (i.e. all modules and all assessment components).
- 64 Students are permitted to repeat any year of an undergraduate programme subject to not repeating the same year more than once and not repeating more than two academic years within a degree course, except by special permission of the University Council.
- 65 The maximum number of years to complete an undergraduate degree is six years for a standard four-year programme and seven years for a five-year programme.

Class Descriptors: These Science Faculty Descriptors are given as a guide to the qualities that assessors are seeking in relation to the grades usually awarded. A grade is the anticipated degree class based on the consistent performance at the level indicated by an individual answer. In addition to the criteria listed, the Department's examiners will also give credit for evidence of critical discussion of the facts or evidence.

Guidelines on Grades for Sophisters' Essays and Examination Answers

Class	Range	Criteria
I	90 - 100	IDEAL ANSWER; showing insight and originality and wide knowledge. Logical, accurate and concise presentation. Evidence of reading and thought beyond course content. Contains particularly apt examples. Links materials from lectures, practicals and seminars where appropriate.
	80 - 89	OUTSTANDING ANSWER; falls short of the 'Ideal' answer either on aspects of presentation or on evidence of reading and thought beyond the course. Examples, layout and details are all sound.
	70 - 79	MAINLY OUTSTANDING ANSWER; falls short on presentation and reading or thought beyond the course, but retains insight and originality typical of the first class work.
II - 1	65 - 69	VERY COMPREHENSIVE ANSWER; good understanding of concepts supported by broad knowledge of subject. Notable for synthesis of information rather than originality. Sometimes with evidence of outside reading. Mostly accurate and logical with appropriate examples. Occasionally a lapse in detail.
	60 - 64	LESS COMPREHENSIVE ANSWER; mostly confined to good recall of coursework. Some synthesis of information or ideas. Accurate and logical within a limited scope. Some lapses in detail tolerated.
II – 2 55 - 59		SOUND BUT INCOMPLETE ANSWER; based on coursework alone but suffers from a significant omission, error or misunderstanding. Usually lacks synthesis of information or ideas. Mainly logical and accurate within its limited scope and with lapses in detail.
	50 - 54	INCOMPLETE ANSWER; suffers from significant omissions, errors and misunderstanding, but still with understanding of main concepts and showing sound knowledge. Several lapses in detail.
III 45 - 49		WEAK ANSWER; limited understanding and knowledge of subject. Serious omissions, errors and misunderstandings, so that answer is no more than adequate.
	40 - 44	VERY WEAK ANSWER; a poor answer, lacking substance but giving some relevant information. Information given may not be in context or well explained, but will contain passages and words which indicate a marginally adequate understanding.
F-1	35 - 39	MARGINAL FAIL; inadequate answer, with no substance or understanding, but with a vague knowledge relevant to the question.
F - 2	30 - 34	CLEAR FAILURE; some attempt made to write something relevant to the question. Errors serious but not absurd. Could also be sound answer to the misinterpretation of the question.
F - 3	0 -29	UTTER FAILURE; with little hint of knowledge. Errors serious and absurd. Could also be a trivial response to the misinterpretation of the question.

Note: Detailed Rubrics for the year are located at the end of the handbook

19

Molecular Medicine Breakdown of Papers 1, 2, 3 2022-23

Section 1: 'Neurobiology'

Answer 1 of 2 questions

Neurochemistry (GD)

Neurodegenerative disorders (GD/DL/CC)

Section 2: 'Immunology'

Answer 1 of 2 questions

Gastrointestinal Immunology (EL) Respiratory Immunology (MA) Autophagy & Disease (ABud) Immunometabolism (DF/LON) Metabolic Inflammation (FS)

Section 3: 'General'

Answer 1 of 3 questions

Trans-subject integrative/philosophical questions

Section 4: 'Quickie/Short questions'

Answer 4 out of 7 questions

Paper 2– BIU44320 Microbial Diseases & Immune System Disorders

Section 1: 'Microbial Diseases'

Answer 1 of 2 questions

Trypanosomiasis (DN)
Helminths (PF)
Prokaryotic Pathogens (HW)
TB (FS)

Viruses and Disease (GB)
Immunity to Infection (KM)

Section 2: 'Immune System Disorders'

Answer 1 of 2 questions

Rheumatoid Arthritis (LON) MS & EAE (JF/KM)

Autoinflammatory Disease (EC)

Inflammageing (NB)

Section 3: 'General'

Answer 1 of 3 questions

Trans-subject integrative/philosophical questions

Section 4: 'Quickie/Short questions'

Answer 4 out of 7 questions

Paper 3- BIU44330 Cell Cycle, Cancer Biology & Therapeutics

Section 1: 'Cell Cycle and Cancer'

Answer 1 of 2 questions

Mitotic Cell Cycle (VK)
Initiation & Progression (VK)
Metastasis & Treatment (VK/KM)

Section 2: 'Cancer Biology & Therapeutics'

Answer 1 of 2 questions

Haematological malignancies (TMcE) Lung Cancer (GP) Obesity & Cancer (JL) Precision Medicine & Breast Cancer (KG) Cancer Epigenetics (SG)

Section 3: 'General' Answer 1 of 3 questions

Trans-subject integrative/philosophical questions

Section 4: 'Quickie/Short questions'

Answer 4 out of 7 questions

SS Module Codes, Learning Outcomes, Course Descriptions & Key Reading

2022-2023

BIU44390 CAPSTONE PROJECT IN MOLECULAR MEDICINE (S1) (20 credits)

Learning outcomes:

On successful completion of this module students will be able to:

- Pursue with a degree of independence an original research project in Molecular Medicine. Design
 and implement a wide range of experimental procedures, critically analyse and interpret
 experimental data, synthesise hypotheses from a wide range of information sources, critically
 evaluate research literature and write a research dissertation
- Demonstrate a comprehensive understanding of the theory behind the techniques used in the research project and show a critical awareness of how these techniques can be applied to biological problems
- Discuss a specialised research area of Molecular Medicine in detail
- Work effectively as an individual and in a team and exercise initiative and personal responsibility
- Display computer literacy and use advanced computer skills to aid in conducting scientific research
- Communicate results of research project effectively with the scientific community

BIU44010 Advanced Research Skills (S1) (10 credits)

This purpose of this module is to further develop research, critical analysis and communication skills that are essential for a graduate biochemist. Students will be trained in data handling as well as solving quantitative problems in biochemistry. In addition, this module will introduce students to a wide array of cutting-edge techniques and strategies used in biochemistry.

Learning outcomes:

On successful completion of this module students will be able to:

- Apply appropriate statistical tests to experimental data and evaluate the results of these tests
- Demonstrate proficiency in the application of sequence analysis algorithms
- Solve numerical biochemical problems
- Demonstrate proficiency in the application of molecular modelling software
- Display a solid foundation in the ethics of and use of animals for experimentation
- Describe the principles behind and applications of current techniques in scientific research

Sequence Analysis: Jerard Hayes

The course will provide an introduction into Bioinformatics. Topics covered include:

- DNA (including genomic) and protein databases
- Accessing sequence information from databases using the Internet
- Sequence similarity searches (i.e. BLAST, FASTA)
- Identification of homologous proteins
- Multiple sequence alignments (i.e. Clustal W)
- Searches for protein motifs, domain, patterns

Students will carry out three exercises:

- **Exercise 1:** Accessing databases from the Internet, retrieval of sequences (DNA and protein), extracting relevant sequence information, presentation and annotation of a chosen sequence
- **Exercise 2:** Sequence similarity search (BLAST), identification of homologous proteins, multiple sequence alignment (Clustal W)
- **Exercise 3:** Sequence analysis of membrane proteins, hydrophobicity plots, identification of transmembrane helices and signal peptides

Reading list:

*essential reading # recommended

*Bioinformatics: Sequence, structure, and databanks. A practical approach. D. Higgins and W. Taylor (eds.) Oxford University Press, 2000.

*Trends guide to bioinformatics. Elsevier Science, 1998

#Benson, D. A. et al. 1999. GenBank. Nucleic Acid Research, 27: 12-17

#Bairoch, A. and R. Apweiler. 2000. The SWISS-PROT protein sequence database and its supplement TrEMBL in 2000. Nucleic Acid Research, 28: 45-48.

#Altschul et al. 1990. Basic local alignment search tool. J. Mol. Biol. 215:403-410.

#Needleman, S. B. and Wunsch, C. D. 1970. A general method applicable to the search for similarities in the amino acid sequence of two proteins. J. Mol. Biol., 48: 443-453.

#Smith, T. F. and Waterman, M. S. 1981. Identification of common molecular subsequences. J. Mol. Biol., 147: 195-197.

#Kyte, J. and Doolttle, R. F. 1982. A simple method for displaying the hydropathic character of a protein. J. Mol. Biol., 157: 105-132.

#Persson, B. and Argos, P. 1994. Prediction of transmembrane segments in proteins utilising multiple sequence alignments. J. Mol. Biol., 237: 182-192.

#Rost, B. et al. 1995. Transmembrane helices predicted at 95% accuracy. Protein Science, 4: 521-533.

#Von Heijne, G. 1992. Membrane protein structure prediction. Hydrophobicity analysis and the positive-inside rule. J. Mol. Biol., 225:487-494.

#Sonnhammer, E. L. L. et al. 1998. A hidden Markov model for predicting transmembrane helices in protein sequences. In J. Glasgow et al. (eds.) Proc. Sixth Int. Conf. On Intelligent Systems for Molecular Biology, 175-182. AAAI Press.

#Von Heijne, G. 1986. A new method for predicting signal sequence cleavage sites. Nucleic Acid Research, 14: 4683-90.

#Nielsen, H. et al. 1997. Identification of prokaryotic and eukaryotic signal peptides and prediction of their cleavage sites. Protein Engineering, 10:1-6.

X-ray crystallography: Amir Khan (2 lectures)

These two lectures will provide an introduction to X-ray crystallography and will include the following:

- overview of modern X-ray and cryo-EM techniques to visualize macromolecules (proteins, DNA, RNA) and larger assemblies at atomic resolution
- concept of resolution in imaging and its relationship to X-ray and cryo-EM hardware for data collection
- principles of X-ray diffraction and cryo-EM structure determination, advantages of the techniques and their limitations

Recommended reading:

Crystallography Made Crystal Clear Gale Rhodes

Protein Crystallography: A concise guide

Eaton Lattman and Patrick Loll

Metabolomics research: Richard Porter & David Finlay (2 lectures)

Metabolic flux analysis (1 lecture) Richard Porter

Analysis of cellular oxygen consumption together with extracellular acidity rate are an excellent way to get an overview of metabolic flux in a cell. Furthermore, the use of selective inhibitors can allow a researcher to shed light on the bioenergetics and biochemical pathways that contribute to that flux. The Seahorse Flux Analyser and the Oroboros Respirometer are excellent apparati for determining such metabolic flux. The lecture will cover the principles behind the use of these apparti and will give examples of their use to researchers.

Proteomics and metabolomics (1 lecture) David Finlay

Various approaches to proteomic and metabolomic analysis will be discussed. The types of experimental question that can be addressed using these techniques will be reviewed.

Protein engineering: Jerard Hayes (2 lectures)

Protein engineering is the process of developing valuable proteins, mainly for the biopharmaceutical market with a value of approximately \$170 billion annually. This 2-lecture course will cover the production of recombinant proteins through genetic engineering and cell biology techniques for bioprocessing and biopharmaceutical manufacturing. Included in the course is upstream processing of proteins in bacterial, mammalian and insect cell lines, downstream processing in bioreactors and production of purified products, and optimisation of

26

the bioprocess for the generation of desired post translational modifications, such as glycosylation.

Flow Cytometry & Cell Sorting: Barry Moran (2 lectures)

Flow cytometry is a key technology underpinning almost all biomedical research. Using fluorescent probes to tag molecules in or on the cell, it allows high-speed, high-parameter analysis of single cells as they flow through a fluid stream. Cell sorting extends the technology, enabling any identifiable cell population to be enriched to a very high purity. These lectures will cover the fundamentals of flow cytometry and cell sorting, including novel techniques and applications.

NMR spectroscopy for biomedical scientists: Ken Hun Mok (2 lectures)

Lecture 1. Brief overview of the theories and practices; How NMR is used in structural biology and in probing the dynamics of biomolecules.

Lecture 2. Application of NMR to metabolomics; How mass spectrometry and NMR are complementary in identifying metabolites.

Reading / Viewing Materials:

- (1) Hornak JP, Web book: "The Basics of NMR", http://www.cis.rit.edu/htbooks/nmr/, 1997.
- (2) Knowbee Tutoring, "Introduction to NMR Spectroscopy" Parts 1 and
- 2, https://www.youtube.com/watch?v=TJhVotrZt9I, 2015.
- (3) Hore PJ, Jones JA, Wimperis S, "NMR: The Toolkit", Oxford Chemistry Primers 92, Oxford University Press, 2000.
- (4) Wong F, "NMR Made Easy!" Parts 1-
- 6, https://www.youtube.com/watch?v=9orcRVTKcS0&list=PLP0TLbeMObSy4izlkMlC2QOpJCzNJ pC17, 2012.
- (5) Larive CK, Barding Jr GA, Dinges MM, "NMR Spectroscopy for Metabolomics and Metabolic Profiling", *Anal. Chem 87* (1): 133–146, 2015.
- (6) Markley JL et al, "The future of NMR-based metabolomics", *Curr Opin Biotech* 43: 34-40, 2017.
- (7) Jang C, Chen L, Rabinowitz JD, "Metabolomics and Isotope Tracing", *Cell* 173(4): 822-837, 2018.

Cellular Imaging: Derek Nolan (3 lectures)

Lecture 1: Introduction to imaging and the concept of resolution. Application of electron microscopy in cell imaging. EM tomography and specialized techniques. Introduction to light microscopy.

Lecture 2: Advanced light microscopy: wide field and confocal microscopy.

Lecture 3: Application of fluorescent proteins and probes in multidimensional imaging in fixed and live cells.

Suggested reading and references.

http://www.nature.com/milestones/milelight/index.html

An excellent resource available on line. This series highlights the most influential developments in light microscopy in a series of short articles, each describing a major achievement. Almost a one stop shop

http://www.olympusmicro.com/

The Olympus Microscopy Resource Center.

This site covers a wide range of topics in light microscopy: basic to advanced topics with primers and interactive tutorials in some sections.

Principles and Techniques of Biochemistry and Molecular Biology. 7th Edition. Wilson K & Walker J Eds. Chapter 4 Microscopy. Brief overview of field.

Correlative cryo-light microscopy and cryo-electron tomography: from cellular territories to molecular landscapes. Current Opinion in Biotechnology, Volume 20, 2009, Pages 83-89 From nano to micrometre scale in cells.

Transgenics: Vincent Kelly & Derek Nolan (5 lectures)

Lecture 1. Mutagenic, transgenic & cloning technology (VK): The concept of forward and reverse genetics in understanding gene function will be considered and how these mutations are physically introduced into the genome through random mutagenesis, viral mutagenesis, gene replacement and gene-targeting strategies. The process of microinjection to create transgenic animals, gene knockouts and cloned animal will be covered and the generation and use of induced pluripotant stem cells (iPS) in biomedical research applications.

Lecture 2. Design and development of transgenic constructs (VK): The design of targeting vectors relies on a detailed structural/functional understanding of the gene under study. Various strategies for controlling the activity of the gene are available including the creation of knockouts, knock-ins, conditional knockout and reporter systems. Gene-trap technology has, in recent times, gained significantly in popularity and the methodology will be examined in some detail.

Lecture 3. Zinc Finger Nucleases and Talen Nucleases(VK): These state-of-the-art technologies have the potential to revolutionise the manipulation of the eukaryotic genome, from cells in culture to mice, rats, rabbits, pigs etc. This lecture will cover the principles of this technology and how it is being currently exploited in research.

Lectures 4 & 5. RNA interference (DN): The discovery of the classical RNA interference pathway involving siRNA will be described. The lectures will consider the concept of regulation of expression through siRNA and microRNAs along with the use and design of RNAi based approaches in functional genomics. The advantages and limitation of such approaches will investigated through the use of specific examples. The potential use of RNAi in therapeutic approaches will be outlined.

Reading List:

Lectures 1-3:

** Highly relevant material

Papers relate to the endothelin B receptor and conditional mouse. These papers are discussed in the lectures and are given as an example of the power of inducible transgenics.

** Molecular Cell Biology, Lodish et al., Sixth Edition. W. H. FREEMAN, New York. (Good general overview of genetic techniques)

*Baneyx F (1999) Recombinant protein expression in E. coli. Current opinion in Biotechnology 10:411-421. (Detailed review of the plasmid/E.coli features that direct recombinant expression)

**Bockamp et al. 2002. Of mice and models: improved animal models for biomedical research. Physiol. Genomics. 11:115-132 (*Very good overview of mouse transgenics, covers the endothelin receptor B example described in lectures*)

Fields, S. and Sternglanz. 1994. The yeast two-hybrid system: an assay for protein-protein interactions. Trends in Genetics 10: 286-292

**Vidan S, Snyder M. (2001) Large-scale mutagenesis: yeast genetics in the genome era. Curr Opin Biotechnol. 12:28-34.

Beutler B, Poltorak A. (2000) The search for Lps: 1993-1998.

J Endotoxin Res. 6:269-93. (An amusing and personal account of Bruce Beutlers discovery of TLR4 by positional cloning)

*Wang B. and Zhou J. 2003. Specific genetic modifications of domestic animals by gene targeting and animal cloning. Reproductive Biology and Endocrinology, 1:103

#Masaki T. (2004) Historical review: Endothelin. Trends Pharmacol Sci. 25(4):219-24.

#Shin et al. 1999. The temporal requirement for endothelinreceptor-B signalling during neural crest development. Nature. 402: 496-501

#Lee et al. 2003. The endothelin receptor-B is required for the migration of neural crest-derived melanocyte and enteric neuron precursors. Developmental Biology 259; 162–175

Lectures 4-5

- (1) Cogoni C, and Macino G. (2000) Post-transcriptional gene silencing across kingdoms. *Genes Dev* **10**: 638-643.
- (2) Guru T. (2000). A silence that speaks volumes. *Nature* **404**, 804-808.
- (3) Sharp PA. RNA Interference-2001. (2001) Genes Dev 15: 485-490.
- (4) Ullu E., Tschudi C. and Chakraborty T. (2004) RNA interference in protozoan parasites *Cellular Microbiol.* **6**: 509-519

Comparative Medicine: Peter Nowlan

The purpose of this lecture course is to introduce students to the basic requirements for working with animals. This is necessary if a full appreciation of animal related work is to be got from the projects. It is also a legal requirement that anybody involved in the use of animals for scientific purposes has appropriate training (EC directive 86/609)

This module is not intended to be a comprehensive training course. To do this would require a much more detailed and extensive series of talks. Most of the training which will be required by students will be obtained by working in close contact with a technician and with experienced supervisors.

The golden rule should be always 'if you don't know ask somebody'.

The welfare of the animal and often the success of your Project will depend on using a correct approach to animals involved in your project.

Even if you are not undertaking a SS project which involves live animals you may do so in your future career.

- Introduction to Laboratory Animal Science
- The Law and Application for a licence
- Animal House Design; Its effect on Research
- Characteristics of Individual species
- Experimental design Choice of species
- Injections and tissue sampling
- Health Considerations
- Alternatives to live animal experimentation
- Handling Video, Safety, Local arrangements
- Video and discussion 'Ethics of Animal research'
- The Scientists Viewpoint
- Assessment

Reading List:

Laboratory animals an introduction for new experimenters. A. A. Tuffery
Handbook of laboratory animal management and care. S. Wolefensohn, M. Lloyd
Introduction to laboratory animal science and technology. J. Inglis
Humane experimental technique. W. Russell, R. Burch
Experimental and surgical technique in the rat. H. Wayneforth, P. Flecknell

Animals and alternatives in toxicology; present and future prospects. M. Balls, J. Bridges, J. Southee

In vitro toxicology. S. Cox Gad

UFAW handbook on the care & management of laboratory animals. T. Poole Laboratory animals anaesthesia. P. Flecknell

Handbook of rodent and rabbit medicine. K Laber-Laird, M. Swindle, P. Flecknell

The biology and medicine of rabbits and rodents. J. Harkness J. Wagner

The laboratory animals, principles and practice. W. Lane-Petter, A. Pearson

Man and mouse, animals in medical research. W. Paton

Lives in the balance. J. Smith, K. Boyd

The ethics of using animals in biomedical research, Vivisection in historical prospective. R. Rupke

BIU44310 NEUROBIOLOGY & IMMUNOLOGY (S2) (10 credits)

This module covers the structure, function and pharmacology of neurotransmitters, neuron-glia interactions, intraneuronal signalling and the neurobiology of behaviour and neurodegenerative disorders. This module also covers the molecular basis of immune mediated responses.

Learning outcomes:

On successful completion of this module students will be able to:

- Recall and integrate key knowledge on structure of cell types in the brain and how they control
 neurotransmission and critically evaluate how various chemicals (biogenic amines, amino acids,
 peptides & labile gases) in the brain fulfill the criteria for characterisation as neurotransmitters
- Employ an understanding of the molecular mechanisms that are involved in the major neurodegenerative disorders and the medical advances that are in development
- Demonstrate an understanding of the complexities and unique aspects of immunology in organs such as GI tract and respiratory system.

• Integrate biochemistry and immunology analyses to critically understand the impact of immunometabolism and autophagy on the immune response.

PART 1: NEUROBIOLOGY & NEURODEGENERATIVE DISORDERS

Neurochemistry: Brain Biochemistry & CNS Acting Drugs: Prof Gavin Davey (5 lectures).

Lecture 1:

- Energy substrates for the brain
- Glucose/lactate transporters
- What uses ATP in the brain?
- Astrocytes-neuron lactate shuttle hypothesis
- Glucose sensing neurons
- What controls blood flow in the brain?

Lecture 2:

- · Energy thresholds in the brain
- Mitochondria control glutamate release
- Mitochondrial fusion/fission dynamics
- Complex I activity & mitochondrial fusion

Lecture 3:

- In vivo techniques for measuring neurotransmitter release and actions
- Microdialysis & HPLC
- Classical neurotransmitters
- Atypical neurotransmitters
- Nitric oxide

Lecture 4:

- GABA metabolism & GHB
- Polyamine NTs
- Glial cells and NT release (D-serine, taurine, NAAG & neuropeptides)

Lecture 5:

- Melatonin as a NT
- Aspartate & pheromones

References: to be supplied closer to lectures

Neurodegenerative disorders: An interdisciplinary approach: Prof David Loane (6 lectures).

Lecture 1: Aspects of energy metabolism and neurodegeneration: mitochondrial defects, reactive oxygen species, permeability transition pore, cytochrome c release — induction of apoptosis and necrosis. Aging & Proteostasis. Brain Imaging Techniques.

Lectures 2-3: Parkinson's disease-pathology, anatomy, protein aggregation, dopaminergic neuron destruction, mitochondria, ROS production, genetics, epidemiology, MPTP + neurotoxins, alpha-synuclein, prevention in animal models. Treatments – new therapies.

Lectures 3-4: Alzheimer's disease – pathology, PET scans, neurofibrillary tangles, tau protein, tangles, beta-amyloid, presenilin, apolipoprotein E. Treatments.

Lecture 5: Stroke – ischemic and hemorrhagic. Animal models. Ischemic cascade. Hypotheses – glutamate excitotoxicity, energy failure, heat shock protein expression, reactive oxygen species. Treatment.

Lecture 6: Huntington's disease, polyglutamine repeats and hungtingtin. Future therapies: Gene Therapy – somatic and germline. Retroviruses, adenoviruses, liposomes, naked DNA and adenoassociated viruses. Stem-cell research. Pharmacological intervention.

References: to be supplied closer to lectures

Reading/Learning Resources:

- Basic Neurochemistry: Molecular, Cellular, and Medical Aspects by G.J. Siegel et al.(1999). 7th Edition excellent; 6th edition freely available online through Pubmed website (https://www.ncbi.nlm.nih.gov/books/NBK20385/).
- Principles of Neural Science (5th. Edition) by E.R. Kandel et al. (2000) McGraw-Hill- A monster textbook >1600 pages but very good.
- Proteins, Transmitters and Synapses by D.G. Nicholls (1994) Blackwell, Oxford The best on synaptic bioenergetics (out of print but there is a copy in the library).
- Stahl's Essential Pschopharmacology: Neuroscientific Basis and Practical Applications by S.S. Stahl (2000). Cambridge Univ. Press. Idiosyncratic but fun.
- The Biochemical basis of neuropharmacology by JF Cooper, FE Bloom and RH Roth Oxford University Press, Eighth Edition
- Molecules and mental illness by Samuel H. Barondes Paperback 216 pages (June 1999) W H Freeman & Co.; ISBN: 0716760339- Drugs and the brain by Solomon Snyder

Neurological diseases: Prof. Colm Cunningham (4 Lectures)

Multiple Sclerosis & the brain's immune privilege

Contrast Innate and specific immunity

- explain why specific immunity in brain is different
- incomplete privilege: EAE -> MS
- blood brain barrier, Cell infiltration
- Dendritic cells, antigen drainage etc
- What is immune privilege NOT (Galea)
- Multiple sclerosis, Th1, Th17 cells
- treatments; steroids, interferon-b
- Tysabri, VCAM inhibition (natalizumab)

Alzheimer's disease, microglia, transgenic models & vaccination studies

Basal forebrain cholinergic loss, current treatments

- the amyloid hypothesis
- Discuss Tg2576 and other genetic AD models
- Microglia, inflammation and NSAID treatment
- The AD vaccination studies in vivo and in patients
- BACE inhibitors, gamma-secretase inhibitors

PART 2: IMMUNOLOGY & IMMUNOMETABOLISM

Gastrointestinal tract Immunology: Prof Ed Lavelle (3 lectures)

Lecture 1: Overview of gut associated lymphoid tissue, Peyer's patches, inductive and effector sites. Uptake of antigens across epithelial surfaces.

Lecture 2: Dendritic cells and T cells in the gastrointestinal tract. Homing of gut T cells

Lecture 3: Mucosal humoral immunity. IgA responses and their regulation.

Respiratory tract Immunology: Prof Michelle Armstrong (3 lectures)

Lecture 1: Introduction to the basic biology of the respiratory tract: conducting airways, mucosal surface, lung parenchyma and organization of the lung immune system. Understanding the concept that the lung is continually exposed to foreign antigens and must discriminate between recognition of innocuous environmental antigens and pathogenic antigens.

Lecture 2: Roles played by individual cells in regulating immune response in the lung: airway epithelial cells, alveolar macrophages, regulatory T-cells, T-cell homing to lung, innate lymphoid cells.

Lecture 3: Immunological challenges faced by the lungs: Infectious/inflammatory disease (cystic fibrosis), interstitial disease (IPF and pulmonary sarcoidosis) and allergic disease (asthma).

Autophagy: Prof Andrei Budanov (2 lectures)

Lecture 1: The mechanics of autophagy

- Early signalling events in autophagy
- Omegasomes: PI3P platforms that manufacture autophagosomes
- Sources of the autophagosome membrane
- Ubiquitin-like conjugation systems that mediate membrane formation
- Autophagosome maturation and lysosomal fusion

Lecture 2: Selective autophagy & disease

- Chaperone-mediated autophagy, macro/microautophagy & mitophagy
- Autophagy and cell death
- Autophagy and ageing: age-related neurodegenerative diseases
- Autophagy in cancer prevention, development and therapy
- Autophagy as a defence against intracellular pathogens

Reading list:

"Autophagy: molecules and mechanisms" by Jon Lane.

A list of suitable reviews will be given out during the lecture course

Immunometabolism: Profs David Finlay and Luke O'Neill (5 lectures)

Lecture 1. Cellular metabolism + immune cells (David Finlay)

Overview of metabolic pathways. Discuss why cells adopt different metabolic configurations. Outline the metabolic configurations used by different immune subsets.

Lecture 2. Macrophage immunometabolism (Luke O'Neill)

Metabolic changes during macrophage polarization, roles of key metabolites in M1 and M2 macrophages. Role of mitochondria as signal generator in macrophages.

Lecture 3. Lymphocyte immunometabolism (David Finlay)

Central role for metabolism in the control of lymphocyte activation, differentiation and function; Effector, regulatory and memory T cells, NK cells and B cells.

Lecture 4. Nutrients and the tumour microenvironment (David Finlay) Discuss nutrient availability to immune cells and nutrients as fuels and key regulators of immune signalling. Focus on how the tumour microenvronment can alter immune function through altering nutrient levels. Potential for improved anti-cancer immunotherapy through manipulation of metabolism and nutrient levels.

Lecture 5. Targeting metabolism to treat inflammatory and infectious disease (Luke O'Neill)

Prospects of targeting metabolism to treat inflammatory and infectious diseases. Current therapies that target metabolism: metformin, rapamycin and methotrexate. Solute carriers, PKM2, SDH and GAPDH as examples.

Metabolic Inflammation: Prof Fred Sheedy (3 lectures)

Lecture 1: "PAMPs & DAMPs"

Activation of the innate immune system by endogenous metabolite accumulation and danger signals

Lecture 2: "Dysfunctional Resolution"

Effectors in the immune response to metabolites, Removing danger, Resolving inflammation, Restoring homeostasis & strategies to boost this.

Lecture 3: "Inborn errors of meta-inflammation"

Genetics in metabolic inflammation. Hyperlipidemia. Lysosomal Storage Disorders. Spontanous activation of innate immunity. Environmental Factors.

BIU44320 MICROBIAL DISEASES & IMMUNE SYSTEM DISORDERS (S2) (10 credits)

This module covers the pathogenesis of infectious diseases. Bacterial pathogens of medical importance will also be covered in detail. It will provide an introduction to parasitic protozoa such as trypanosomes and helminths. The biochemical and genetic mechanisms by which bacteria, viruses and parasites evade the host immune responses will be covered. This module will also cover the pathogenesis of autoimmune and inflammatory disease.

Learning outcomes:

On successful completion of this module students will be able to:

- Relate how African trypanosomes avoid the immune response and innate immunity of their human hosts.
- Define the molecular basis of pathogenesis of various prokaryotic pathogens of medical importance including *Helicobacter pylori*
- Relate how Mycobacterium Tuberculosis avoid the immune response and innate immunity of their human hosts.

36

- Compare the strategies to control helminth infections, using specific species as examples and evaluate the global impact of helminth infections on endemic countries.
- Understand viral infections and the basis of virus-induced disease
- Critically evaluate the contribution of immunology to a range of important human diseases including autoimmunity (rheumatoid arthritis), autoinflammatory diseases, immune deficiency and inflammaging.

PART 1: MICROBIAL DISEASES

African Trypansomes : Prof Derek Nolan (8 lectures)

The aim of these lectures is to provide an introduction to African trypanosomes, parasitic protozoans that cause sleeping sickness in humans and a related disease, Nagana, in cattle. These parasites are a major problem for human and veterinary health throughout sub Saharan Africa and serious barrier to economic development of the region. Perhaps the most striking feature of these parasites is that that they are exclusively extracellular. They grow and divide in the mammalian vasculature and consequently exposed the adaptive and innate defence responses of their mammalian hosts. In addition, for a variety of reasons, African trypanosomes have been come a favourite model organism for molecular and cell biologists and many discoveries of broad significance have emerged from studies on these model unicellular eukaryotes. Areas where such discoveries have been reported will be illustrated in the lectures where appropriate. The course is organized into two parts.

Trypanosomes Part 1: Stealth strategies of an elusive parasite

- 1. How are trypanosomes, such as *Trypanosoma brucei*, able to evade the host humoral immune response given that they are constantly exposed to this arm of the immune response?
- 2. What other strategies do trypanosomes employ to circumvent the innate immune responses?
- 3. How are these parasites able to acquire essential macromolecular growth factors from their hosts without attracting a response?

Trypanosomes Part 2: What is the molecular basis of human sleeping sickness?

The focus in part II is on the innate immunity that humans and other primates have to infection by all but a few trypanosomes. In effect in this part we will consider the molecular basis of African human sleeping sickness. We will consider the nature of the trypanolytic toxin present in human serum and how this toxin kills these parasites. We will see an amazing link between the toxin and an unsuspected programmed cell death pathway. Finally, we will see how two strains of trypanosomes have responded by developing independent mechanisms to resist this toxin and how in turn certain human populations are able to overcome this resistance and the price they pay for this capacity.

Reading List:

Additional specific references for key experiments will be provided within the lectures which are available on the school website.

Trypanosomes Part I

- (1) Cross, G.A.M. (2001) African trypanosomes in the 21st century: what is their future in science and health? *Int. J. Parasitol.* **31**: 427-433
- (2) Borst, P. (2002) Antigenic variation and alleleic exclusion Cell 109: -8.
- (3) Pays, E. (2005) Regulation of antigen gene expression in *Trypanosoma brucei Trends Parasitol*. **21**: 517-520.
- (4) Pays E. (2006) The variant surface glycoprotein as a tool for adaptation in African trypanosomes. *Microbes and infection* **8**: 30-937.
- (5) Field, MC & Carrington, M. (2004) Intracellular membrane transport systems in *Trypanosoma brucei*. *Traffic* **5**:1-9
- (6) Nolan, DP, Garcia-Salcedo, J.A., Geuskens, M., Salmon, D., Paturiaux-Hanocq, F., Pays, A., Tebabi, P. and Pays, E. (2001)

Endocytosis of macromolecules by African trypanosomes. pp127-141 In "World Class Parasites Volume 1: The African Trypanosomes" Eds. Seed, R. & Black, S.J. (Kluwer Academic Publishers)

- (7) Stockdale C. et al (2008) PLoS biology Vol6 issue 7 e185 "Antigenic Variation in Trypanosoma brucei: Joining the DOTs"
- (8) Navarro M. et al (2007)TRENDS in Microbiology Vol.15 No.6 doi:10.1016/j.tim.2007.04.004

Nuclear architecture underlying gene expression in Trypanosoma brucei

Trypanosomes Part II

- (1) Pays, E. Vanhamme, L., Vanhollebeke, B., Nolan, D. P.. and Perez-Morga, D. (2006) The trypanolytic factor of human serum. *Nat Rev Microbiol.* **6**: 477-86.
- (2) Vanhollebeke B & Pays E (2010) Mol. Microbiol. **76**: 806-814 The trypanolytic factor of human serum, many ways to enter the parasites, a single way to kill it.
- (3) Pays E & Vanhollebeke B (2008) Microbes Infect **10**: 985-989Mutual self-defence: the trypanolytic story
- (4) Genovese et al. (2010) Science 329: 841-845.

Association of trypanolytic ApoL1 variants with kidney disease in African Americans

- (5) Pays E. et al. (2014) The molecular arms race between African trypanosomes and humans Nature Reviews Microbiology VOLUME 12 575-584.
- (6) Vanwalleghem G. et al. (2015) NATURE COMMUNICATIONS | 6:8078 | DOI: 10.1038/ncomms9078 Coupling of lysosomal and mitochondrial membrane permeabilization in trypanolysis by APOL1

Helminths of Human Importance. Prof Padraic Fallon (3 lectures)

A third of the world's population is infected with parasitic worms. These lectures will address the major parasitic worms that are of medical importance.

Lecture 1: Introduction to the major helminth parasites that infect man. Medical and economic impact of helminth parasites on society.

Lecture 2: Explore key concepts of biology of helminth infections. Wormy people: genetic predisposition to helminth infection. Co-evolution of man and parasitic worms: molecular and biochemical adaptation. The Helminth proteome and genome projects.

Lecture 3: Gastro-intestinal versus systemic (tissue or blood dwelling) worm infections. Modulation of immunity by helminth parasites: implications for designing vaccines. Molecular and biochemical targets for current and future drugs to treat helminth infections.

A reading list will be given out during the course

Prokaryotic pathogens: Prof Henry Windle (3 lectures)

Lecture 1: Bacterial pathogens as a paradigm for chronic infection I: Molecular mechanisms of bacterial induced disease - modulation of host cell signalling responses and pathogenesis. Procarcinogenic microorganisms.

Lecture 2: Bacterial pathogens as a paradigm for chronic infection II. Infection and cancer – the *Helicobacter pylori* connection: molecular basis of pathogenesis

Lecture 3: Mixed microbial populations and disease. The microbiome in health and disease.

General Reading:

Helicobacter pylori: A Paradigm Pathogen for Subverting Host Cell Signal Transmission. (Review article) Naumann M et al (2017) Trends in Microbiology 24 (4) 316-328 PMID:28057411

Human gut microbiome: hopes, threats and promises (Review article). Cani PD

Gut. 2018;67(9):1716-1725. PMID: 29934437

The immune response to tuberculosis: Prof Frederick Sheedy (2 lectures)

Lecture 1: The innate immune response to tuberculosis; a model for pathogen evasion of the human host response. The alveolar macrophage and recruited inflammatory cells. First contact – Phagocytosis & Pattern Recognition.

Lecture 2: The adaptive immune response to TB – the TB granuloma; prison for the live bug. T-cells, IFNy and TNF orchestrating the granulomatous response.

Viruses and Disease: Prof Gareth Brady (3 Lectures)

Lecture 1: Introduction to Viruses and Viral infections

- Classification of viruses
- Host adaptation and species barriers
- Routes of entry
- Cell, Tissue and Organ tropisms
- Virus Infection Cycles

Lecture 2: Anti-Viral Immunity, Adaptation and Disease

- Overview of anti-viral immunity and clearance
- Virus-induced inflammation and disease
- Methods of virus detection and serological assays
- Epstein Barr Virus and B cells
- Molluscum Contagiosum Virus and Human Skin

Lecture 3: Emerging viruses and Pandemics

- Influenza Virus: from seasonal infections to deadly emergent strains
- Coronaviruses: from the common cold to SARS, MERS and COVID-19

Reading list:

A list of suitable reviews will be given out during the lecture course

T cell differentiation, regulation and immunity to bacterial and viral infection: Prof. Kingston Mills (4 lectures)

T cell differentiation and regulation (2 lectures) Kingston Mills

Lecture 1. T cell subtypes, antigen presentation and T cell differentiation.

Lecture 2. Natural and induced regulatory T cells. Regulatory T cells in infectious diseases. Role of anti-inflammatory cytokines produced by innate cells and T cells in subversion of immunity to infection.

T cell immunity to bacterial and viral infection (2 lectures) Kingston Mills

Lecture 1: The bridge between innate and adaptive immunity. Pathogen activation of macrophages and dendritic cells through pattern recognition receptors. Role of dendritic cells in directing T cell subtypes.

Lecture 2: Role of Th1/Th2 cells in immunity to infection, including HIV, hepatitis C virus and Bordetella pertussis.

PART 2: IMMUNE SYSTEM DISORDERS

Rheumatoid Arthritis: Prof. Luke O'Neill (2 lectures)

Lecture 1: What is rheumatoid arthritis? Clinical, molecular and cellular definitions. Early concepts: connective tissue structure and degradation. Rheumatoid Factor. And B cells. HLA associations and the genetic component. Autoantigens. Role of inflammation – prostaglandins and tissue degrading enzymes.

Lecture 2: Key role of cytokines – IL-1, TNF, IL6. Current therapies – NSAIDs, steroids, biologic therapies (anti-TNF, anti-IL-1, anti-IL-6, anti-CD20 and CTLA-4 lg). Prospect for future therapies.

Multiple Sclerosis and EAE: Profs Jean Fletcher & Kingston Mills (3 lectures)

Lecture 1: Breakdown of tolerance in autoimmunity. Risk factors, pathogenesis, diagnosis and monitoring of MS

Lecture 2. MS therapies: Mechanisms of action, efficacy, side effects.

Lecture 3: EAE. Role of innate and adaptive immunity in pathogenesis of autoimmune diseases. Role of regulatory T cells in preventing autoimmune diseases.

Autoinflammatory diseases: Prof Emma Creagh (2 lectures)

Lecture 1: Key features of systemic autoinflammatory disorders. Classic hereditary 'Periodic Fever Syndromes' - FMF (Familial Mediterranean Fever), TRAPS (TNF Receptor Associated Periodic Syndrome) and HIDS (Hyperimmunoglobulinemia-D with periodic fever syndrome).

Lecture 2: NLRP3/Cryopyrin-associated periodic syndromes (CAPS): Familial Cold Inflammatory Syndrome (FCAS); Muckle-Wells Syndrome (MWS) and Neonatal onset multisystem inflammatory disease (NOMID). Autoinflammatory disorders associated with skin pustules, such as DIRA (deficiency of IL-1R antagonist), CARD14 mediated psoriasis (CAMPS) and early onset inflammatory bowel diseases (EO-IBD).

Immunodeficiency: Prof Derek Doherty (2 lectures)

Lecture 1: Primary immunodeficiencies. This lecture will cover the genetic bases, clinical presentations, diagnoses and treatments of primary immunodeficiencies, including antibody, complement, MHC and lymphocyte deficiencies.

Lecture 2: Acquired immunodeficiencies. This lecture will cover the different causes of acquired immunodeficiencies but will focus mainly on HIV-associated disease, including the virology, immunology, clinical features and recent progress in vaccine development. The significance of HIV in the developing world, where many other infectious disease are also endemic, will be emphasized.

Inflammaging: Prof Nollaig Bourke (2 Lectures)

Lecture 1: The mechanisms of inflammageing. Inflammageing overview. Discussion of how innate and adaptive immune responses are dysregulated with age and how this contributes to increased systemic inflammation.

Lecture 2: The consequences of inflammageing. Specific focus on the impact of inflammageing with relation to age related diseases, particularly cardiovascular disease, neuro-cognitive decline and cancers. Discussion on therapeutic targeting of inflammageing.

BIU44330 Cell Cycle, Cancer Biology & Therapeutics (S2)

This module covers the cellular and regulatory mechanisms that control the cell cycle. It Furthermore it covers the molecular basis of cancer, the progression of the disease and the therapeutic treatment strategies.

Learning outcomes:

On successful completion of this module students will be able to:

- Explain the processes of growth, proliferation, and cellular division and outline the cellular changes and regulatory mechanisms that define the stages of the cell cycle
- Critically discuss the environmental and hereditary causes of cancer and relate how alterations to the cell cycle impact on cancer development
- Describe the genetic, metabolic and cellular alterations in various types of cancer and outline the process of metastasis
- Evaluate the contribution of the immune system to cancer
- Describe the therapeutic strategies for the control of cancer such as dietary mechanisms for reducing initiation, targeting oncogenes, overcoming drug resistance and immunotherapy

42

Part 1: Cell Cycle & Cancer:

Mitotic cell cycle: Prof Vincent Kelly (4 Lectures)

Lecture 1. The cell cycle & growth. This lecture will cover some of the seminal discoveries of the cell cycle, discussing the experiments performed on frog oocytes, sea urchins and yeast. Key regulators of cell cycle progression, as determined by these early studies, MPF, Cdc2/cdc28, wee1 and Cdc25, will be covered. Components of the mammalian cell cycle, which have been discovered principally via bio-informatic approaches, will be discussed including mammalian cyclin dependant kinases (CDKs) and cyclin-dependant kinase inhibitors (CKI).

Lecture 2. Start of the cell cycle, G1. Signals for a cell to start proliferation are essential for initiation of the cell cycle. Examples will be provided of how growth signals through PI3K, AKT, mTOR and myc are co-ordinated to the uptake of amino-acids and glucose. In addition, we will discuss how cell-cell and cell-matrix contacts must be altered to permit cell cycle progression.

Lecture 3. S-phase, DNA replication & DNA repair checkpoints. The control of DNA replication is a major decision point of the cell cycle. This lecture will describe the replication licensing process, the selection of the origin(s) of replication and the proteins that make up the origin replication complex, e.g. Mcm, Cdc6. If the DNA to be replicated is not properly loaded or is damaged the cell initiates various checkpoints, i.e G1- and S-phase checkpoint. This lecture will cover the various protein complexes such as 911, the MRE11-Rad50-NBS1/PH2AX complex and the kinase pathways used to tell the cell to stop the cell cycle process including ATM & ATR, BRCA1, Chk1 Chk2 and P53.

Lecture 4. Mitosis. Chromosome cohesion/seperating sister chromatids/Overview of ubiquitin/Ubiquitin ligases and the cell cycle/SCF complex & G1 to M phase transitions/APC complex and anaphase entry/microsatellite instability (MIN) and chromosomal instability (CIN)/Centrosomes & centrosome inactivation checkpoint

- 1. The Cell Cycle: An Introduction. (1993) Andrew Murray, Tim Hunt Oxford ISBN 0-19-509529-4
- 2. Nurse P, Masui Y, Hartwell L. (1998) Understanding the cell cycle. Nat Med. 4(10):1103-6
- 3. Malumbres M, Barbacid M. (2005) Mammalian cyclin-dependent kinases. *Trends Biochem Sci.* **30**(11):630-41.
- 4. Sarbassov DD, Ali SM, Sabatini DM. (2005) Growing roles for the mTOR pathway. *Curr Opin Cell Biol.* **17**(6):596-603.
- 5. Prober DA, Edgar BA. (2001) Growth regulation by oncogenes--new insights from model organisms. *Curr Opin Genet Dev.* **11**(1):19-26.
- 6. Blow JJ, Dutta A. (2005) Preventing re-replication of chromosomal DNA. *Nat Rev Mol Cell Biol.* **6**(6):476-86.
- 7. Niida H, Nakanishi M. (2006) DNA damage checkpoints in mammals. *Mutagenesis*. 21:3-9.

Cancer and invasion: Profs Vincent Kelly & Kingston Mills (11 Lectures)

Part 1: Initiation & Progression (4 Lectures) Vincent Kelly

Lecture 1. Underlying causes of cancer (VK): The characteristics that are used to classify cancers and their stage of development will be described. A number of examples will be given of how environmental factors, i.e. xenobiotics, radiation and oxidative damage contribute to multistep carcinogenesis. The means by which cancer is limited by DNA damage sensing, DNA repair and cellular adaptation to oxygen/radical damage will be covered.

Lecture 2. Oncogenes and tumour suppressor genes (VK): Many of the original discoveries on oncogenes were derived from work on viruses. The concepts of onocgenes and proto-ocogenes will discussed such as *src* and the Rous sarcoma virus and there will be an in dept examination of the ras oncoprotein pathway and the function of other oncogenes including *abl*, *sis*, *c-myc* and how they influence cellular proliferation. Suppressor genes play an important role in limiting cancer formation and a number of models were put forward from original studies including Knodson's two-hit model and haploinsufficiency. The mode of action of tumour suppressors such as APC, MSH2, MLH1, BRCA1, p53 will be examined with particular focus on p53, Rb and APC.

Lecture 3. Cancer epigenetics (VK): Changes in the genetic code is but one means to arrive at a pre-malignant crossroads. Epigenetics changes in gene expression have been found to alter tumor suppessor gene activity through. These epigenetic changes may occur as a consequence of altered DNA methylation status at CpG promoter regions of aberrant histone modification. In fact, cooperative suppression by both mechanisms has recently become the focus of new anticancer therapies through the development of DNMT and histone deacetylase inhibitors.

Lecture 4. Cancer metabolism & the tumor microenvironment (VK): Many of the control points of cancer, oncogenes, tumor suppressor genes (including mTOR, PI3K, Akt, p53, AMPK) are intimately linked to metabolism, especially glycolysis, which provides the cancer with the building blocks for growth. The tumor cell microenvironment is invariably acidic and hypoxic causing the transcription factor HIF1a to set in place protective responses including unregulating the production of monocarboxylate transporters, VEGF, matrix metalloproteinases and angiogenic factors.

Part 2: Metastasis and Cancer Treatments

Lecture 1. Angiogenesis and metastasis (VK): The process by which cancer cells develop new blood supplies (angiogensis) is reliant on being able to remodel the tumor environment and the extracellular matrix. A discussion of how this remodelling occurs through matrix metalloproteinases and plasminogen will be given along with the cause and consequences of breaking cell-cell interactions. The means used by cancer cells to physically move from the primary tumor (e.g. epithelial-mesenchymal transition) and how the immune system promotes

this process will be described. Breast cancer will be used as a model of how cancer cells choose secondary sites for proliferation, especially the bone marrow; 'the vicious cycle'.

Lecture 2. Colon cancer, genetics and epigenetics (VK): Arguably, colon cancer is one of the best studied cancers in terms of its formation and progression. This lecture will discuss the contribution of chromosomal instability in terms of changes to APC, COX2 and Smad4 and microsatellite instability caused by epigenetic suppression of mis-match repair enzymes including MSH2 & MLH1. The contribution of inflammation to colon caner will be considered and how NSAIDS and IL-10 mediate polyp formation.

Lecture 3. Stem cell theory of cancer, focusing on colon cancer (VK): The intestinal crypt stem cells are maintained in a specialized compartment of the intestinal crypt through the Ephrin receptors. The maintenance and proliferation of these stems cells will be covered including the various signals used to control their proliferation, such as hedgehog, WNT, PDGF, Eph, NOTCH and BMP. The importance of the intestinal stems cells to cancer development and treatment will be considered.

Lecture 4. Cancer treatment (VK): Classical anti-cancer drugs such as antimetabolites, alkylating agents and antimytotic agents are still widely used in therapy today despite severe side-effects. Newer 'magic bullets, hold promise of more specific cancer treatment strategies such as Imatinab in the treatment of CML. However, drug resistance is a problem and has revealed the phenomenon of oncogene addition. Recent drug strategies have begun to focus on targeting tumor cell metabolism, its environment and the cancer initiating cells (cancer stem cells) that perpetuate proliferation even after treatment.

Lecture 5. Cellular and humoral Immune responses to tumors (KM): These lectures include the role of antibody, cytotoxic T lymphocytes, macrophages, NK cells and Th1 cells; Evasion and subversion of immune responses by tumors - anti-inflammatory cytokine production and regulatory T cell induction; Tumor-specific antigens and breaking tolerance to self antigens

Lecture 6-7. Tumor immunotherapy (KM): Antibodies, Toll-like receptor agonists and cell-based therapies; Tumor vaccines - killed tumor cells, tumor specific peptides and antigens, heat shock proteins and dendritic cell vaccines

Cancer References:

- 1. Hanahan D, Weinberg RA. (2011) Hallmarks of cancer: the next generation. Cell. 144(5):646-74.
- 2. Gibbs WW. (2003) Untangling the roots of cancer. Sci. Am. 289:56-65
- 3. Payne SR, Kemp CJ. (2005) Tumor suppressor genetics. *Carcinogenesis*. 6:2031-45.
- 4. Prochownik EV. (2005) Functional and physical communication between oncoproteins and tumor suppressors. *Cell Mol Life Sci.* 62:2438-59.
- 5. Jeggo PA, Lobrich M. (2006) Contribution of DNA repair and cell cycle checkpoint arrest to the maintenance of genomic stability. *DNA Repair (Amst)*. 5:1192-8.

- 6. Webb CP, Vande Woude GF. (2000) Genes that regulate metastasis and angiogenesis. *J Neurooncol.* 50(1-2):71-87.
- 7. Fodde R, Smits R, Clevers H. (2001) APC, signal transduction and genetic instability in colorectal cancer. *Nat Rev Cancer*. 1(1):55-67.
- 8. de Visser KE, Eichten A, Coussens LM. (2006) Paradoxical roles of the immune system during cancer development. *Nat Rev Cancer*. 6:24-37.
- 9. Crosnier C, Stamataki D, Lewis J. (2006) Organizing cell renewal in the intestine: stem cells, signals and combinatorial control. *Nat Rev Genet*. 7(5):349-59.
- 10. McDonald SA, Preston SL, Lovell MJ, Wright NA, Jankowski JA. (2006) Mechanisms of disease: from stem cells to colorectal cancer. *Nat Clin Pract Gastroenterol Hepatol*. 3(5):267-74.
- 11. Immunobiology by Janeway and Travers
- 12. Cellular and Molecular Immunology by Abbas, Lichtman and Pober

Part 2: Cancer Biology & Therapeutics:

Haematology and haematological malignancies: Prof Tony McElligott (2 Lectures)

Introduction to Haematology and haematological malignancies: Haematological malignancies are a group of neoplasms that arise through malignant transformation of bone marrow derived cells. The great diversity seen in this group of malignancies reflects of the complexity of normal haematopoeisis and the immune system. The primary basis of classification is the distinction between tumours of lymphocytes and those of myeloid lineage. Haematological malignancies include leukaemias, lymphomas and multiple myeloma, and are defined and distinguished from one another according to clinical features, microscopic morphology, immunophenotype and molecular/genetic features.

Molecular biology of haematological malignancies and leukaemia: Many molecular genetic markers have been described in haematological malignancies including chromosomal translocations and rearrangements of the immunoglobulin and T-cell receptor genes. These prognostic or predictive markers can be useful in guiding clinical management of patients and permit the development of very sensitive and specific assays for the detection of neoplastic cells. In addition, these molecular markers have provided important clues in elucidating the biological mechanisms by which haematological malignancies develop and persist. More recently, it has been recognised that epigenetic changes and aberrant expression of miRNAs are common features of some haematological malignancies and may play an important role in carcinogenesis.

Molecular basis of lung cancer & Obesity/Cancer: Profs Graham Pigeon & Joanne Lysaght (4 Lectures)

Lecture 1. Molecular biology of lung cancer: An introduction to lung cancer with a focus on molecular aspects involved in the development and progression of the disease. Focusing on genes/mutations regulating the transformation of normal bronchial epithelium to lung cancer.

Lecture 2. Novel therapeutic approaches in the treatment of lung cancer: An overview of current clinical trials / treatments focused on molecular targets in lung cancer and how this relates to research strategy.

Lecture 3. Obesity and Cancer: An overview of the epidemiology of obesity and cancer. Particular focus on the mechanisms linking central obesity and metabolic syndrome the progression of cancer, examining adipose tissue as an immunomodulatory and metabolic organ.

Lecture 4. Obesity and Immunomodulation in Cancer: A focus on central obesity as a chronic inflammatory condition, and how obesity may effect immune cell subsets and influence tumour progression and development.

Information on these lectures will be available later in the term.

Precision Medicine & Breast Cancer: Prof Kathy Gately (2 Lectures)

These lectures will focus on cancer Rates in the 21st century, Hallmarks of Cancer, Tumour Heterogeneity, mutation profiles, Precision/Personalised Medicine molecular mechanisms in breast cancer etc.

Information on these lectures will be available later in the term.

Cancer Epigenetics: Prof Steven Gray (3 lectures)

Lecture 1: The Basics. This lecture will introduce the student to both the history and current knowledge of the known mechanisms underpinning epigenetic regulation of gene expression.

Lecture 2: Epigenetics and Disease. This lecture will introduce the student to the various roles that epigenetics plays in the development of disease including cancerous and non-cancerous conditions, and will include aberrant epigenetic dysregulation, trans-generational epigenetics, and will introduce issues where epigenetics plays important roles in intra-tumoural heterogeneity and cancer stem cells.

Lecture 3: Targeting Epigenetics for the treatment of disease.

This lecture will discuss the broad implications pertaining to the potential to target disease epigenetically. It will discuss the issues with respect to the failure of many epigenetic targeting approaches and how new epigenetic targeting strategies are changing the paradigms for therapy. The potential for nutritional interventions will also be introduced.

Grading Rubrics

Senior Sophister Lab Performance Report

This mark contributes 15% to the overall project mark. It is designed to assess lab performance, independent of the thesis and based on criteria listed below.

Student Name:	Supervisor Name:		
			,
Attendance	Poor		As expected
How diligently did the student work?	Well below		Intensively
	expectation		
How well did the student plan the experiments?	Well below		Research level
How well were the experimental methods and	expectation Well below		Research level
results documented (e.g. in lab book)?	expectation		Research tevel
How well did the student observe the relevant	Never	10000	Always
safety procedures (e.g. wear lab coat)?			ř
How accurate was the student's experimental	Well below		Research level
technique?	expectation		
Quantity of work done	Very little		A great deal
Ability to trouble shoot in lab	Poor	00000	Excellent
Level of help in lab available	Very little		A great deal
Ability to work independently	Poor		Excellent
Attitude to work	Poor		Highly motivated
Ability to work with others	Poor		Excellent
Ability to respond to criticism	Poor		Excellent
Comments:			
Particular difficulties if any:			
-			
Manla and a£ 1000/ .			
Mark out of 100%:			

Senior Sophister Project Thesis - <u>Supervisor's report</u>

This mark is independent of the lab performance. The research project thesis mark is to be agreed with the second examiner (and third examiner if first/second marks are greater than 10% apart). This agreed mark contributes 65% to the overall project mark. It is designed to capture the abilities of a student to engage in an academic research project, plan experiments, critically analyse data and communicate research findings and their implications.

Student name			
Project Title			
Supervisor name			
Date			,
1st Draft submission on		Yes □	No □
time			
	Thesis	1	
Presentation	Messy, poor English		Publication standard
Abstract	Wholly inadequate		Publication standard
Introduction	Trivial		Publishable
Literature coverage	Poor		Extensive and deep
Description of aims	Wholly inadequate		Perfectly clear
Materials and methods	Wholly inadequate		Perfectly clear
Description of results	Wholly inadequate		Perfectly clear
Figures/ legends/ tables	Wholly inadequate		Perfectly clear, complete
References	Wholly inadequate		Fully accurate
Quality of data	Poor		Exemplary
Analysis of data	Poor		Comprehensive analysis
Appropriate statistical analysis	Poor		Strict
Discussion	Poor		Publication standard
Scientific rigour e.g. use of controls	Weak		Strict
Understanding/ insight	Very little		Research level
Capacity for self-direction	Poor		Outstanding
Quality of first draft	Poor		Excellent
Comments: Particular difficulties if any:			

Mark out of 100%:				
Senior Soph	nister Project Thesis	- Second Exam	<u>iiner's</u> report	
This mark is independent of the lab performance. The research project thesis mark is to be agreed with the project supervisor (and third examiner if first/second marks are greater than 10% apart). This agreed mark contributes 65% to the overall project mark. It is designed to capture the abilities of a student to engage in an academic research project, plan experiments, critically analyse data and communicate research findings and their implications.				
Student name Project Title				
Date				
Examiner's name				
Agreed mark (out of 100%):				
	Thesis			
Presentation	Messy, poor English		Publication standard	
Abstract	Wholly inadequate		Publication standard	
Introduction	Trivial		Publishable	
Literature coverage	Poor		Extensive and deep	
Description of aims	Wholly inadequate		Perfectly clear	
Materials and methods	Wholly inadequate		Perfectly clear	
Description of results	Wholly inadequate		Perfectly clear	
Figures/ legends/ tables	Wholly inadequate		Perfectly clear, complete	
References	Wholly inadequate		Fully accurate	
Quality of data	Poor		Exemplary	
Analysis of data	Poor		Comprehensive analysis	
Appropriate statistical ana	llysis Poor		Strict	
Discussion	Poor		Publication standard	

Scientific rigour e.g. use of controls	Weak				Strict	
Understanding/ insight	Very little				Research level	
Comments:						
Mark out of 100%:						
Senior Sophister Poster Mark Sheet This mark contributes 5% to the overall project mark.						
Student Name: Degree:						
Examiners: Overall Mark:						
Poster clearly communicates all kinformation	xey scientific	Stro	ngly Disagree			Strongly Agree
Information is accurate, no signif	icant errors	Strongly Disagree				Strongly Agree
Poster is logically laid-out and ea	sy to follow	Strongly Disagree				Strongly Agree
Poster is eye-catching and visuall	y appealing	Strongly Disagree				Strongly Agree
Exhibits analytical and critical th	inking	Strongly Disagree				Strongly Agree
Poster and presenter shows unde topic	rstanding of the	Strongly Disagree				Strongly Agree
Presenter explained the poster wo	ell	Strongly Disagree				Strongly Agree
Presenter answered questions ful	ly	Stro	ngly Disagree			Strongly Agree

Any Specific Comments:				
Senior Sop	hister Research	Project Oral Pr	esentation	
This presentation is to be marked independently by three examiners who will then discuss and agree a mark. This agreed mark contributes 15% to the overall capstone project mark. It is designed to capture the abilities of a student to communicate their research findings, the importance of the research and plans for future work				
Student Name				
Degree Programme				
1st Examiner's Name				
2 nd Examiner's Name				
3 rd Examiner's Name				
Date				
Broad Understanding	Shallow		Extensive	
of the Subject Area Statement of Aims	Incoherent		Very Clear	
Statement of Aims	medicient		Very Clear	
Structure of presentation	Badly Disorganised		Logical and Well Organised	
Amount of material	Too Little, Too Superficial		Appropriate	
Diagrams and Images	Irrelevant/Poor Quality		Highly Relevant/Excellent Quality	
Understanding of Methods	Shallow		Extensive	
Understanding of Results	Shallow		Extensive	
Summary/Conclusion	Absent		Concise and Appropriate	
Ideas for Further Research	None		Plenty	
Timekeeping	Poor		Excellent	
Audibility	Too Quiet, Monotone		Clear and Lively and Varied Tone	
Rapport with audience	Poor		Lively and Good Eye Contact	



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