



Australia's
Global
University

Faculty of Medicine
School of Medical Sciences

SOMS3232

Cellular Mechanisms of Health and Disease

COURSE OUTLINE

Term 3, 2021

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Please read this manual/outline in conjunction with the following pages on the [School of Medical Sciences website](#):

- [Advice for Students](#)
- [Learning Resources](#)

(or see "STUDENTS" tab at medicallsciences.med.unsw.edu.au)

SOMS3232 Course Information

This course in molecular medicine bridges the gap between the fundamental sciences of cell biology/biochemistry/immunology and their therapeutic applications. It conveys the dynamic process of scientific discovery in areas of research strengths in biomedicine at UNSW by a focus on novel techniques bringing about paradigm shifts in our understanding of cell function and our ability to diagnose and treat diseases. Students will engage closely with researchers, and will develop a range of skills to prepare them for research-oriented careers in academia and industry.

Prerequisite: ANAT3231 or BIOC2101 or BIOC2181 or BABS2202 or (ANAT2241 and PHSL2101)

OBJECTIVES OF THE COURSE

The primary aim of the course is to teach students some of the molecular and cellular processes that drive normal cell function and how subtle changes can lead to a range of common diseases. These concepts will be presented in the context of cutting-edge research to highlight how research outcomes can inform development of technologies, drugs and clinical practice ("bench to bedside").

Secondly, the aim is to convey the recent transformation of biomedical research to a quantitative discipline, the incorporation of approaches from the physical sciences (biophysics, chemistry, mathematics, engineering) and the invention of new methodologies that have opened new fields (e.g. transgenic animals, gene editing, imaging and microscopy). Overall the course is designed to raise the students' curiosity about how a cell works, what the big questions are, how these can be addressed experimentally and how these discoveries relate to our understanding of human health and disease. Lecturers will be tasked to convey the excitement of cutting edge research including its challenges and controversies. Interaction between the lecturer and the students is desired to facilitate critical thinking.

COURSE CO-ORDINATOR and LECTURERS

Course Coordinators:

Till Böcking till.boecking@unsw.edu.au
Edna Hardeman e.hardeman@unsw.edu.au

Students wishing to see the course coordinators should make an appointment *via* email.

Lecturers in this course:

Maté Biro m.biro@unsw.edu.au
Yann Gambin y.gambin@unsw.edu.au
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Nigel Turner n.turner@unsw.edu.au

COURSE STRUCTURE and TEACHING STRATEGIES

Learning activities occur on the following days and times:

- Research lectures: Thursdays 16:00-18:00
- Collaborative Learning Session (Journal Club): Wednesdays 09:00-11:00
- Practical component (lab embedment): to be negotiated

Students are expected to attend all scheduled activities for their full duration (2 hours of research seminars per week, 2 hours of collaborative learning sessions per week, negotiated practical component). Students are reminded that UNSW recommends that a 6 units-of-credit course should involve about 150 hours of study and learning activities. The formal learning activities are approximately 60 hours throughout the term and students are expected (and strongly recommended) to allocate 90 hours of additional study.

Research seminars will provide you with the concepts and theory essential for an understanding of the cellular and molecular basis of human health. To assist in the development of research and analytical skills practical classes and collaborative learning sessions will be held. These sessions allow students to engage in a more interactive form of learning than is possible in the research seminars. The skills you will learn in practical classes are relevant to your development as professional scientists.

RESOURCES

Journal articles and web-based resources are available electronically via links on the course Moodle page.

See also medsciences.med.unsw.edu.au/students/undergraduate/learning-resources

STUDENT LEARNING OUTCOMES

On completion of this course students should be able to:

1. Describe the molecular and cellular mechanisms that underlie a range of common diseases such as cancer, metabolic disorders and immune diseases.
2. Analyse the process of scientific research and the appraise the role of transforming technologies in advancing our knowledge
3. Understand strategies for translation of research into technologies and treatments
4. Analyse scientific literature, integrate and contrast scientific data from different sources to synthesise new models and hypotheses; participate in scientific discussions.
5. Use reflective practice to integrate knowledge, skills and experience of scientific research

COURSE EVALUATION AND DEVELOPMENT

Course evaluation will be conducted using myExperience. Student feedback is taken seriously, and continual improvements are made to the course based, in part, on such feedback.

ASSESSMENT PROCEDURES

- ePortfolio/reflective journal **50%**
- Literature Oral Presentations **30%**
- Project Assignment **20%**

ePortfolio/reflective journal

Students will be required to keep a reflective journal. Entries will be guided by the material (online) and a set of questions. The entry for each topic in the course will consist of a combination of (a) questions on the online material prior to the corresponding research seminar and (b) reflection on the topic after the research seminar. Feedback will be provided by peers and academics. Peers will read and comment on each other's posts. Assessment will be based on the following components:

(1) Participation: Posting of weekly entries answering the assigned questions and comments by due date.

(2) Content: Understanding of the topic, scientifically sound response, appropriate references.

Literature Oral Presentations (Journal Club)

Students present a summary and analysis of research articles. Students will be assigned a journal articles chosen by the guest lecturer/course convenor. The presentation should highlight the main research question, key result(s) and conclusions as well as implications for research translation. The presentation (including questions time) will be held using slides (power point or similar format) for the entire class during the journal club component of the course. The presentation and subsequent class discussion will be moderated by the lecturer. Feedback will be provided by academics and peers. Criteria for Assessment: 1. CLARITY AND STRUCTURE: Oral presentation was clear, well-structured and illustrated and easily understood. 2. TIMING: Appropriate weight given to different aspects within the allocated time frame. 3. UNDERSTANDING: Presenter appeared to have a good understanding of the topic: able to answer audience questions clearly. 4. STIMULATED LEARNING: Presentation was interesting; significant issues and answered questions were highlighted.

Project Assignment

Groups of students will be teamed up with a postgraduate student in the laboratories of lecturers. The group will be given a research question and will be tasked to design an experimental plan that can address this question. This is to be worked out in the team, whereby the students can discuss their ideas with the postgraduate student they are teamed up with. Each member will then prepare a report of their proposed experiment. The report should cover the following aspects: (1) Introduction/background to the research problem. (2) Experimental design, including choice of techniques. (3) Discussion of how data should be analysed and interpreted. (4) Expected outcomes.

GENERAL INFORMATION

Your health and the health of those in your class is critically important. You must stay at home if you are sick or have been advised to self-isolate by [NSW health](#) or government authorities. Current alerts and a list of hotspots can be found [here](#). You will not be penalised for missing a face-to-face activity due to illness or a requirement to self-isolate. We will work with you to ensure continuity of learning during your isolation and have plans in place for you to catch up on any content or learning activities you may miss. Where this might not be possible, an application for fee remission may be discussed.

If you are required to self-isolate and/or need emotional or financial support, please contact the [Nucleus: Student Hub](#).

If you are unable to complete an assessment, or attend a class with an attendance or participation requirement, please let your teacher know and apply for [special consideration](#) through the [Special Consideration portal](#).

To advise the University of a positive COVID-19 test result or if you suspect you have COVID-19 and are being tested, please fill in this [form](#).

UNSW requires all staff and students to follow NSW Health advice. Any failure to act in accordance with that advice may amount to a breach of the Student Code of Conduct. Please refer to the [Safe Return to Campus](#) guide for students for more information on safe practices.

Attendance Requirements

For details on the Policy on Class Attendance and Absence see [Advice for Students](#) and the [Policy on Class Attendance and Absence](#).

Practical Classes

Groups of students will be assigned to the laboratories of lecturers participating in the course, where they will be teamed up with a postgraduate student. After a short introduction to the research focus of the lab from the group leader, the postgraduate student will introduce the group to the main techniques and experimental approaches used in the research. The team will then work on a project assignment related to the laboratory placement (see above). Completion of the course component is possible via videoconferencing.

Special Consideration

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

Student Support Services

Key Dates <https://student.unsw.edu.au/dates>

Transitioning to Online Learning <https://www.covid19studyonline.unsw.edu.au/>

Guide to Online Study <https://student.unsw.edu.au/online-study>

UNSW Student Life Hub <https://student.unsw.edu.au/hub#main-content>

Student Support and Development <https://student.unsw.edu.au/support>

IT, eLearning and Apps <https://student.unsw.edu.au/elearning>

Student Support and Success Advisors <https://student.unsw.edu.au/advisors>

Equitable Learning Services: <https://student.unsw.edu.au/els>

Academic Integrity and Plagiarism

The [UNSW Student Code](#) outlines the standard of conduct expected of students with respect to their academic integrity and plagiarism.

More details of what constitutes plagiarism can be found [here](#)

RESEARCH LECTURE OUTLINES

Infection & Immunity I/II: Molecular arms race between host cells and HIV

Till Böcking, EMBL Australia Node in Single Molecule Science, SoMS, UNSW

David Jacques, EMBL Australia Node in Single Molecule Science, SoMS, UNSW

We will summarise the basic life cycle of the human lentivirus Human immunodeficiency virus type 1 (HIV-1), from the point of cellular attachment/fusion, reverse transcription, integration and subsequent viral assembly. We will further map how our immune system has evolved to counter the passage of lentiviruses through the expression of various restriction factors and in turn how lentiviral genomes have evolved to respond to each restriction. Our discussion will highlight how basic science has enabled breakthroughs in medicine:

(1) What is the role of structural biology and new imaging technologies in providing drugs for treating HIV infection and answering question about the molecular arms race between host and virus?

(2) How can lentiviruses can be harnessed for gene delivery? We will outline the power of genetic manipulation using technologies like CRISPR in targeting disease states. We will further outline how elements of HIV used in gene delivery may in turn represent the most promising efforts towards a HIV cure.

Infection & Immunity III: T cell receptor function – from first principles to synthetic biology

Jesse Goyette, EMBL Australia Node in Single Molecule Science

T cell decision making. T cells migrate through tissues continuously monitoring for infection or neoplastic transformation (cancerous cells). To carry out this function T cells use a specialised surface receptor, the T cell receptor (TCR), to sample antigens presented on major histocompatibility complex (MHC) molecules. When activated through the TCR, T cells can lyse infected cells, secrete cytokines, and perform other effector functions that collectively allow them to initiate and regulate immune responses. Critically, T cells must be insensitive to self-antigens, which are constantly presented at high levels on MHCs, and exquisitely sensitive to foreign antigens that are often presented at very low levels. This ability to discriminate between self and non-self is central to adaptive immunity and consequences of a failure to discriminate lead to autoimmunity, uncontrolled infection or cancer. In this module we will explore how T cells use their TCR to make the decision to respond to cells they encounter or remain quiescent.

CAR receptors. We now understand the molecular mechanisms of T cell activation to the point where we can create synthetic T cell receptors, called 'chimeric antigen receptors' (CARs) that react to antigens which would otherwise not be recognisable. This has been used clinically in a strategy that involves isolating T cells from a cancer patient, rewiring them with a CAR recognising a cancer-specific antigen and returning them to the patient. Results from haematological cancers have been exciting and since the seminal work of Carl June the field has expanded rapidly. We will discuss the design principles involved in engineering CAR receptors, their clinical potential and active areas of future research.

Mechanobiology I: Cellular mechanotransduction: mechanically-activated ion channels

Kate Poole, EMBL Australia Node in Single Molecule Science, SoMS, UNSW

The ability of cells to sense and respond to mechanical inputs is an ancient sense, with ion channels that can convert mechanical inputs into electrochemical signals found in all classes of life. In multicellular organisms, such mechanically-activated ion channels are required for the function of many cells and tissues; an acute response to mechanical stimuli underpins our senses of touch and hearing, integrated sensing of changing mechanical loads is fundamental for maintaining cartilage and the vasculature, and migratory cells (such as fibroblasts in wound healing or tumour cells during metastasis) can probe the mechanical properties of their surroundings by applying forces at cell-matrix contact points.

There are a number of challenges involved in the study of mechanically-activated ion channels. It is challenging to identify new mechanically-activated ion channels and to characterise how they are activated and modulated. This lecture will discuss the technical approaches used to study mechanically-activated channel activity in different cell types and discuss how the type of mechanical input and local physical context can modulate channel activity. As an example of recent research in the field, we will discuss the identification of a new channel candidate that regulates the migration and invasion of melanoma cells.

Mechanobiology II: Immune cell search and kill strategies

Maté Biro, EMBL Australia Node in Single Molecule Science, SoMS, UNSW

The main immune cells responsible for antitumor activity are Cytotoxic T cells (CTLs). CTL can migrate rapidly and with striking versatility in a continuous search for cells to subdue. They constitutively patrol organs for cognate antigen and typically migrate using an elongated and polarised shape with a dynamic leading edge and a uropod at the rear. T cells are however able to adopt diverse migration modes depending on both extra- and intracellular cues. In order to reach their target cells, circulating CTL must first cross the endothelial barrier and then negotiate the complex interstitial space within the tumour microenvironment. Burgeoning immunotherapies against cancers attempt to harness the capacity of these T cells to navigate various barriers and organs to reach the tumour and then effectively engage and kill their targets, yet little is known of the cellular forces that underpin their movements and interactions.

We will cover aspects of immune cell-mediated antitumour responses, from the cell-intrinsic cytoskeletal machinery driving motility to the sensing of extracellular cues and population level search strategies, and killing mechanisms upon target encounter and engagement.

Cancer I: Reprogramming of metabolism in cancer**Nigel Turner**, School of Medical Sciences, UNSW

Metabolic reprogramming is now well established as a critical aberration facilitating the growth and proliferation of many cancers. While the initial description of altered metabolism in cancer cells was made over 90 years ago by the famous biochemist Otto Warburg, the last 2 decades has seen an explosion of research in this field, with a compelling body of evidence now showing that signalling pathways that drive oncogenesis also trigger major alterations in nutrient uptake and metabolism, and that several cancers can be directly caused by mutations in specific metabolic enzymes. In addition to changes in metabolism at the level of the tumour, strong links have also emerged between metabolic diseases, such as obesity and diabetes, and cancer prevalence, severity and disease progression. This extensive interplay between oncogenic signalling and intermediary metabolism has raised the possibility that targeting metabolic pathways may be an exciting therapeutic approach for preventing and treating cancer. This research seminar will explore some of the key findings in this field, the technologies that have greatly advanced this area of study and the latest developments in targeting metabolism for cancer therapy.

Cancer II: Mechanisms underlying cell architecture: the actin cytoskeleton**Edna Hardeman**, School of Medical Sciences, UNSW

The architecture of all cells underpins their function and is altered significantly in cancer. One of the challenges in biology has been to understand how cell architecture is assembled and regulated. Three major polymer systems are used in human cells to provide architectural specificity: microfilaments, intermediate filaments and microtubules. These three systems provide overlapping functional properties and collaborate to satisfy the architectural demands of the cell. The microfilaments are thin filaments, around 8nm in diameter, composed of a core polymer of actin. These microfilaments not only provide architectural information but also support most if not all functions in the cell. There are 2-3 versions (isoforms) of actin present in mammalian cells, that operate by recruiting specific 'actin binding proteins' such as the motor proteins myosin to carry out a particular function.

The conundrum has been to explain how actin filaments, with so few isoforms, can be involved in so many diverse cellular functions. Surprisingly, this has only been solved recently. It was discovered that most microfilaments of human cells (and indeed all metazoans) are composed of two polymers, actin and tropomyosin, which wrap around each other. There are many isoforms of tropomyosin - over 40 in human cells - that have fundamentally different functional properties. It is the specific isoform of tropomyosin wrapped around an actin filament that provides the cellular functional 'post code' to the filament and decides which actin binding protein(s) can interact with the actin. We will discuss how choice of experimental system, genetic technology and improvements in imaging contributed to this transformation of our thinking.

Cancer III: Targeting the actin cytoskeleton in cancer: how tropomyosin provided an unexpected opportunity**Peter Gunning**, School of Medical Sciences, UNSW

The involvement of the actin cytoskeleton in cell proliferation and migration makes it an attractive anti-cancer target. Many drugs have been developed which target the assembly of actin into filaments and several of these have progressed to pre-clinical trials in animal models. Unfortunately, all anti-actin drugs have failed because of their impact on the contraction of the heart. This could, perhaps, have been predicted because the actin in the cancer cell is almost identical to the actin used for contraction of the heart. Alternative strategies have therefore been employed in many laboratories throughout the world. These have focussed on the targeting of actin binding proteins and signalling molecules and have thus far proved disappointing. In contrast, the targeting of the major tropomyosin isoform found in cancer cells has shown promise and has proved to be well tolerated in pre-clinical animal models.

The targeting of tropomyosin has the advantage that the major cancer cell tropomyosin isoform is structurally different to the tropomyosin isoform in the human heart. This facilitated the development of drugs that target cancer cells but avoid any cardiac impact. Furthermore, the anti-tropomyosin drugs synergise with anti-microtubule drugs which are among the most widely used anti-cancer drugs. We will discuss how our understanding of fundamental biological processes informs our approach to human health and drug development and the weaknesses inherent in limited knowledge. We will also cover the interface between protein structure and drug design and the revolution in drug development in the last 5 years.

Neurodegeneration: Molecular aspects of Parkinson's disease - from pathophysiology to biomarker development

Emma Sieracki, EMBL Australia Node in Single Molecule Science, SoMS, UNSW

Yann Gambin, EMBL Australia Node in Single Molecule Science, SoMS, UNSW

Many neurodegenerative diseases are characterized by the formation of abnormal protein aggregates in neurons, nerve or glial cells. In Parkinson's disease (PD), the second most common neurodegenerative disease, these inclusions named Lewy Bodies are the main pathological feature of PD and are driven by the aggregation of alpha-synuclein (α -SYN), their main constituent. Genetic links between familial forms of PD and α Syn mutations have been identified, suggesting that α Syn aggregation played an important role in disease genesis and progression. So far, PD diagnosis is limited to recognition of clinical symptoms associated with the condition, and only detects advanced stages of the disease. Yet association of α Syn aggregation with disease progression has made it a promising target for biomarker development. Biophysical studies over the years revealed α Syn aggregation pathway.

Here we will present the models of α Syn aggregation and the biological relevance of those findings. In particular, we will introduce the concept of prion-like aggregation and propagation and discuss the implications for disease progression. α Syn aggregation is also found in other neurodegenerative diseases such as Alzheimer's disease or multiple sclerosis atrophy (MSA), often in conjunction with other proteins and we will examine the potential for cross-aggregation of proteins. Finally, we will examine how fundamental knowledge of the aggregation process is leading to the development of new biomarkers for PD.

TIMETABLE

Week	Dates	Journal Club (Wed 09:00-11:00)	Research lecture (Thurs 16:00-18:00)
1	15/09, 16/09	Introduction to journal club (Böcking)	Intro; Infection & Immunity I (Böcking)
2	22/09, 23/09	Infection & Immunity II (Böcking/Jacques)	Infection & Immunity II (Böcking/Jacques)
3	29/09, 30/09	Infection & Immunity III (Goyette)	Infection & Immunity III (Goyette)
4	06/10, 07/10	Mechanobiology I (Poole)	Mechanobiology I (Poole)
5	13/10, 14/10	Mechanobiology II (Biro)	Mechanobiology II (Biro)
6	free	-	-
7	27/10, 28/10	Cancer I (Turner)	Cancer I (Turner)
8	03/11, 04/11	Cancer II (Hardeman)	Cancer II (Hardeman)
9	10/11, 11/11	Cancer III (Gunning)	Cancer III (Gunning)
10	17/11, 18/11	Neurodegeneration (Sierecki/Gambin)	Neurodegeneration (Sierecki/Gambin)

ASSESSMENT TASKS

Task	Due date	
<i>ePortfolio</i>	<i>Entry</i>	<i>Comments</i>
Immunity & Infection II	23/09, 16:00	28/09, 12:00
Careers	30/09, 16:00	05/10, 12:00
Mechanobiology I	07/10, 16:00	12/10, 12:00
Mechanobiology II	14/10, 16:00	16/10, 18:00
Cancer I	28/10, 16:00	02/11, 12:00
Cancer II	04/11, 16:00	09/11, 12:00
Cancer III	11/11, 16:00	16/11, 12:00
Neurodegeneration	18/11, 16:00	20/11, 18:00
<i>Literature Oral Assignment</i>	to be allocated to groups	
<i>Project Assignment</i>	Can be submitted throughout the session, latest submission date: 20/11/2020	