LKCMedicine PhD Programme

Specialised Advanced Modules (SAM)

Please note that not all SAM will be offered in any one semester. Each SAM is ungraded and will be conducted over a period of up to two weeks with a maximum of 12 contact hours. Details are subject to change without prior notice.

Clinical Trials

This module will provide students with an introductory understanding of the theoretical and practical issues in study design, conduct, analysis, and interpretation of clinical trials of health interventions.

Given the complexities of diseases and epidemics, researchers and policy makers confront the challenge of disentangling the complex causal interdependencies. Reliance on administrative public health data suffers from the inherent weakness of confounding - a weakness that clinical trials address. Yet the conduct of a rigorous and successful clinical trial requires creativity and meticulous planning. Similarly, novel models of healthcare delivery, drugs and new treatment procedures are best tested with clinical trials where the potential benefits would reach thousands - or even millions - of people suffering from the same illness. Accordingly, this module will equip students with important skills for engaging in world class research.

The main learning outcomes are:

- Understand the principles of clinical trials and experimental design
- Appreciate the strengths and limitations of alternative study designs (e.g. quasi-experiments and observational studies)
- Able to write a draft protocol for a clinical trial

The syllabus will cover:

- Definition/Phases of Clinical Trials: Overview of clinical trials and ethics
- Standard Clinical Trials Designs: Parallel group, cross-over; control arms, single arms, active control, placebo; observational trials (e.g., prospective, retrospective; case-control, matching, and cohort)
- Hypotheses/Aims: Superiority, non-inferiority, equivalence, primary, secondary
- Key issues: Endpoints/measurements, treatments/interventions, randomization, stratification, blinding, sample size
Protocol design issues: Describe scientific and practical issues to consider in clinical trial design. Understand the concepts of internal and external validity and how protocol design may impact the validity of the study.

**eHealth, mHealth & Health Informatics**

Digital health, eHealth, mHealth, health informatics, and all e- are the buzzwords in health research today. This module is designed to introduce highly motivated students to these new and rapidly developing fields. It will provide students with a solid conceptual grounding in the fundamentals of the design, evaluation, and implementation of technologies related to eHealth, mHealth, and health informatics. More specifically, the module will focus on two areas of eHealth, mHealth, and health informatics: data analysis and the design of interventions.

There is a need for more healthcare practitioners to cross the innovation chasm in Singapore. Singapore has a strong healthcare infrastructure that requires more practitioners to adopt scientific and multidisciplinary mind sets in managing the complex challenges. Nevertheless, existing modules tend to narrowly focus on one domain that inhibits innovation. This module fills in this critical gap by providing a strong foundation for students of digital health, eHealth, mHealth, and health informatics. It is broader than traditional health informatics programs which cover infrastructure IT in healthcare, but not the more recent developments of digital healthcare products marketed directly to consumers in both low and high-income countries. Further distinctive characteristics of this module are the emphasis on multidisciplinary collaboration during real world projects and the global perspective taken.

At the end of the module, students will be able to:

- Demonstrate an understanding of key eHealth, mHealth, and health informatics challenges
- Basic understanding of appropriate research methods to evaluate eHealth, mHealth, and health informatics challenges
- Demonstrate skill in choosing and carrying out appropriate design techniques for building eHealth, mHealth, and health informatics applications
- Evidence an understanding of the health system, social, and commercial environments in low, medium, and high income countries that influence the design of eHealth, mHealth, and health informatics technologies

**Topics**

- Introduction to eHealth, mHealth: Overview of field
- Health, Health Systems, Policy: The nature of disease, health system structures and levers, health policy
• Designing eHealth and mHealth applications: Requirements gathering, design processes, design methods, iterative evaluation methods
• Health data analysis: Data utilisation methods, databases, ontologies, interoperability, standards
• Statistics: Basic statistical thinking, modelling and regression
• Implementing mHealth and eHealth Systems: Socio-cultural factors, change management, project management, models of innovation, procurement, managing software
• Digital Healthcare Innovation and Entrepreneurship: Commercialisation, IPR, Regulation and data standards, information governance, policy frameworks, financing, business pitches
• Research Methods: Systematic review, clinical trials, social science methods, health economics
• Global Digital Health: Exemplar technologies, implementation issues, cultures of innovation, power relationships
• Advanced topics in Health Data Analysis

There will be strong component of eLearning comprising several modules. Appropriate module and project work will supplement formal teaching. Each module lead will be supported by a junior researcher to facilitate the practical work. There will be a particular emphasis on students applying their knowledge to real problems.

Genes and Development
Modern developmental biology has transformed our understanding of human biology, revealing the cellular and molecular mechanisms that underlie cell differentiation and organogenesis as well as many of the most common human diseases. The key to this breakthrough has been the application of genetic analysis in model organisms such as the nematode, *C.elegans*, the fruitfly, *Drosophila* and the zebrafish, *Danio rerio*.

The aim of this module is to provide a grounding in the basic concepts and approach of developmental biology and an appreciation of the application of the knowledge it generates, especially in regenerative medicine but also in disease analysis. It will introduce the classic forward genetic screens that have been performed using worms, flies and fish as well as the use of reverse genetics in higher organisms, especially the mouse, and illustrate how mutations can be used to dissect complex genetic pathways. It will also cover key concepts in development, including stem cells, totipotency, pluripotency, cell fate specification, lineage restriction, inductive interactions, organisers, gene regulatory networks and morphogens.

The module will use a Team Based Learning approach with sessions focussed on the experimental evidence underpinning key concepts.
Human Genetics
The main aim of this module is to explain the main principles of human genetics and genomic medicine to the medical graduate. The skills and information gained will enable the medical graduates to continuously update their knowledge by understanding how to follow, and critically assess, the new developments in the cutting edge research into genetics and genomics. This will become a particularly important component in the application of concepts of “individualised medicine” or “personalised medicine” that the current generation of students will definitely encounter as future medical professionals. This module will make them better prepared to contribute to the research and development of this trend, as well as other basic and biomedically applied research in general.

Topics
- Single Gene disorders and gene-dose disorders
- Statistics toolbox in Human Genetics and Genomics
- Complex genetic disorders
- Chromosome biology and epigenetics
- Prenatal diagnostics and genetic counselling
- DNA damage and repair
- Genetics of cellular ageing and cancer
- Personalized genomics, population genetics, and pharmacogenetics
- Single Cell genetics

Human Metabolism and Metabolic Diseases
The metabolic disease programme will integrate basic research and a molecular approach towards a better understanding of the aetiology and treatment options of common diseases such as diabetes mellitus and its complications and fatty liver disease. A more thorough understanding of the biology and pathology in the fields of metabolic disease is becoming more and more important as the number of patients with relevant diseases steadily grows. This approach will integrate various “omics” platforms including the NTU-Phenome Centre (metabolomics, lipidomics) and promises to enlighten the research field and to develop a unique example for bench-to-beside and back research. The metabolic disease group will be led by interdisciplinary research groups (basic scientists and clinical scientists) who have already a proven track record of active interactions.

The programme themes will aim to unravel key molecular mechanisms involved in metabolic disease and will lead to
- a better understanding of the early infiltrate in islet cell autoimmunity
- address biology and pathology of islet cells as a prototypic miniorgan system
- will apply various in-vitro and animal models, non-human primates as well as humans by using the eye-model toolbox to study the islet cell functionality and the secretome
• study the impact of transcription factors on the control of liver metabolism and the milieu intérieur as a whole
• better understanding of an organ cross talk by applying the eye-model
• define the respective contributions of the brain (hypothalamus), muscle, liver, and adipose tissue in the development of metabolic disease
• pinpointing novel molecular mechanisms involved in vascular pathology
• characterize the impact of changes of the milieu intérieur (including microbiome) on the ageing process

The metabolic disease group will establish
• an environment in clinical and experimental research in metabolic disease at LKC School of Medicine together with research teams at NTU as well as the associated clinical partners and the various stakeholders in biomedical research in Singapore, and
• to foster an international scientific environment with regular exchange programs with our partner University Imperial College London.

Infectious Diseases
The goal of this module is to introduce the PhD students to the basic methods for infectious disease epidemiology and case studies of important disease syndromes and entities. The seminars will cover definitions and nomenclature, group work on outbreak investigations, disease surveillance and control (with a particular focus on dengue control in Singapore), case-control studies, practical demonstration of laboratory diagnosis, dynamics of transmission, and assessment of vaccine field effectiveness. Diseases of global health concern, such as diseases targeted for elimination (polio, Guinea worm, leprosy, measles, malaria, etc) deserve special attention to enhance awareness about infectious diseases in the global context. At the end of the module, the students will have a fundamental understanding of infectious diseases, in particular

- **The basics**: history of infectious diseases, basic concepts of disease dynamics, parasite diversity, evolution & ecology of infectious diseases
- **Emergence of diseases**: The basic reproductive number, critical community size, epidemic curve, zoonoses, spill over, globalization
- **Spread of diseases**: transmission types (droplets, vectors, sex), superspreading, diffusion, nosomical transmission, principles of surveillance and control, outbreak investigations and outbreak management
- **Control of diseases**: drug resistance, vaccination, herd immunity, quarantines, antibiotics, and antivirals
- **The future of infectious diseases**: Evolution of virulence, emergence of drug resistance, eradication of diseases.
Topics

• Epidemiology of Infectious Diseases. Workshop: web-based evaluation of WHO statistics and data on global epidemiology of infectious diseases
• Introduction to bacteriology. Laboratory exposure: diagnosing bacterial diseases in the microbiology laboratory at Tan Tock Seng Hospital
• Antibiotic resistance. Workshop: Antibiotic stewardship.
• Introduction to Vaccinology. Workshop: Vaccine impact assessment
• Diseases targeted for elimination or eradication. Workshop: global health case studies
• Emerging Infectious Diseases. Workshop: outbreak investigation case study
• Vector-borne diseases. Workshop: Control of dengue in Singapore.

Microbial Pathogenesis
This module aims at providing an introduction to the cellular and molecular biology of microbial pathogenesis and covers general aspects of bacterial, fungal, protozoan and viral pathogens. Microbial pathogenesis and host-pathogen interaction are interested in the strategies that pathogens use to attack and exploit their hosts, and how the hosts defend themselves against those attacks. Thousands of years of coevolution have seen the development of sophisticated strategies from both sides. From the pathogen’s perspective, the host can be seen as a growth medium favourable to its replication and/or long-term persistence. In that sense, the tropism of a pathogen to a given organ or compartment is constrained by virulence factors, nutrients availability and the immune system. An interesting aspect is that the most successful pathogens are not necessarily the most virulent. Some infectious agents have even deployed strategies to damper their virulence in order to optimize long-term persistence without affecting the integrity of the host. Other classes of pathogens, referred as pathobionts, are part of our normal flora that can create disease only under particular circumstances, for instance when the immune system is weaken.

Topics

• General principles of microbial pathogenesis
• Virulence mechanisms of selected infectious diseases
• Opportunistic & Hospital-acquired infections
• Contribution of immunity on microbial pathogenesis
• The microbiota as a source of infection and defence
• Current and emerging strategies to combat infections

Molecular and Cellular Immunology
The overall goal of this module is to introduce the PhD students to the cellular and molecular aspects of the immune system in human health and diseases. The module will cover the
essential concepts underlying the mechanisms of immune regulation - how complex receptor-ligand interactions and chemokines/cytokines control cellular signal transduction processes that enable the immune system to precisely respond to foreign antigens and protect the individual from infections and inflammation. Students will learn about the immune cell functioning such as T-lymphocyte adhesion, migration and polarization. Specific roles of effector T-cell subsets (Th1, Th2, Th17 and Tregs) in the immune responses, autoimmunity and immunomodulation will be explained. The advantages, limitations and challenges associated with cellular and molecular level analysis of immune regulation will be discussed. The module will also cover some of the basic and cutting-edge experimental tools and techniques, advanced methodologies and bioinformatics approaches currently implemented in the immunological research laboratories.

At the end of the module, the students will have a fundamental understanding of the cells, molecules and associated molecular processes involved in the functioning of the immune system. This will help the students in developing skills so that they will be able to read the published literature intelligently, explore major principles and concepts in immunology and immunopathology, critically interpret complex data and appraise scientific research in this rapidly advancing field. Ultimately, the student will be able to apply the knowledge to address a specific research problem.

Molecular and Cellular Oncology
Understanding the molecular and cellular signalling pathways for tumour progression and metastasis is crucial to enhance translational research, especially for development of targeted cancer therapies. The Molecular and Cellular Oncology module is directed at second- and third- year postgraduate students to provide them with core concepts in cancer biology. Topics covered will include the cancer hallmarks, cell cycle and checkpoints, DNA damage and repair, aneuploidy, telomere biology, apoptotic and autophagic pathways, cell-to-cell communication, cancer stem cell and epithelial-mesenchymal transition, metastasis and invasion, angiogenesis, cancer genomics/epigenomics, metabolic basis of cancer and the emerging field of immunotherapy. The main focus will be on how cellular dysfunction and deregulation of cell signalling contributes to the tumorigenesis process, together with insights into molecular targets and cellular responses to therapy, as well as tumour heterogeneity and drug resistance.

Molecular Motors, Muscle & Movement
This module would consist of lectures, practical classes, commentary and team-based learning (TBL) sessions to explore key papers. Depending on available time, mini experimental projects could be considered.
Neurodegenerative Disease and Psychiatric Disorders
The major objective of the module is to familiarise research students in the second and third year of their post-graduate research studies with some basic principles behind neurological and psychiatric diseases: their neurobiological bases, the most fundamental pathogenic mechanisms leading to the disorders, some techniques used to explore the human brain regarding the disease conditions (with special regard to neuroimaging), and the major clinical aspects of the disorders (symptoms, diagnosis, treatments).

The module is primarily for PhD students NOT working in the field of neurosciences (though students working in this field are also welcome), but for those who work in other fields and would like to have a general insight into the main questions behind translational neuroscience research, with special regard to neurodegenerative disorders and psychiatric disorders.

Skin Biology and Disease
Diseases of the skin, the largest organ of our bodies, are amongst the most prevalent conditions for which novel treatments are sought. The last decade has seen a rapid expansion of our knowledge of skin physiology and disease mechanisms, leading to the development of targeted treatments for diseases such as eczema, psoriasis, and skin tumours. At the same time, advances in regenerative medicine and biotechnology have underpinned the development of novel products and concepts for treating wounds, such as burns and non-
healing wounds. There is also a growing interest in the maintenance of healthy skin, with the knowledge derived from basic discoveries being applied not only to treat but also prevent disease and optimise skin longevity and function. We are thus on the verge of an exciting new era in the development of novel treatments for skin diseases as well as common skin conditions.

Research at LKCMedicine is particularly focused on translational medicine, its central mission being to bring scientific results from the bench to the bedside. Dermatology and Skin Biology at LKCMedicine focus its research efforts on three main areas, i) regenerative medicine and wounding, including non-healing ulcers and burns, ii) skin malignancies, including melanoma, and non-melanoma skin cancers, and iii) inflammatory and immune skin disorders such as atopic dermatitis and psoriasis.

**Stem Cells and Disease Modelling**
The main aim of this module is to explain the main principles of stem cell biology and induced-pluripotent-stem-cell technology and their applications in research into functions of genes and gene-mutations, disease modelling, drug discovery, drug toxicity testing, and the concepts of individualised approach to disease. The skills and information gained will enable the medical graduates to continuously update their knowledge by understanding how to follow, and critically assess, the new developments in the cutting edge research into stem cells and its applications. This will become a particularly important component in the application of concepts of stratified patient populations, regenerative medicine, “individualised medicine” and “personalized medicine” that the current generation of students will likely encounter as future medical professionals. This module will make them better prepared to contribute to the research and development of this trend, as well as other basic and biomedically applied research in general.

**Topics**
- Mouse ES cells, knockout/knock-in mice and functional genomics
- Hu-ESC, epigenetics of pluripotency
- In vitro differentiation of stem cells
- Adult tissue specific stem cells (NSC, MSC, HSC) and use in regenerative therapy
- iPSC invention and use in disease modelling, drug discovery, drug toxicity testing
- Disease Gene-repair and stem cell replacement strategies
- Direct in vivo reprogramming and Transdifferentiation of somatic cells
- Current technological limitations (DN) and Ethical issues

*Information correct as at 9 June 2015*