MRes Translational Medicine 2020/21

Introduction

Translational medicine' refers to multidisciplinary research aimed at of exploiting discoveries in basic research to improve health - by developing new therapies, diagnostics or community practices.

The MRes Translational Medicine strives to help students develop into confident and self-reliant researchers who are skilled at self-directed learning, laboratory investigation, data analysis and scientific communication. The programme has been designed to equip students with an expert understanding of the relevant bioscience, "bench-to-bedside-to-community" development pathways and with the technical knowledge that would prepare them to progress to a PhD-level programme or to participate in research and development of a pharmaceutical/biotechnology setting.

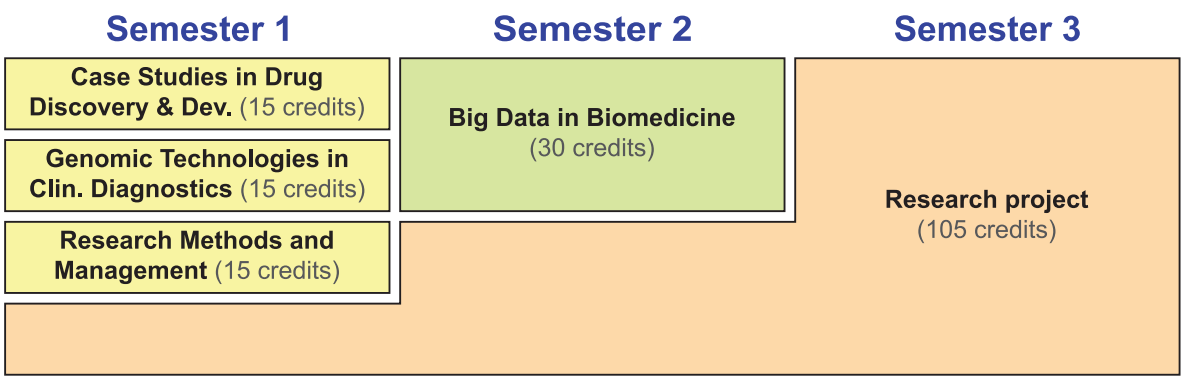

Figure 1. Course structure.

Course modules

As most translational research activities are directed toward drug development, an entire module (*"Case Studies in Drug Discovery and Development", CSDDD*) is dedicated to this area. In the CSDDD module, emphasis is placed on internationalising the curriculum by deliberately choosing learning topics on drug development on diseases of global importance.

The *"Genomic Technologies in Clinical Diagnostics"* module, which provides in-depth coverage of genomic technologies and their applications, is part of the curriculum based on the pivotal role of genomics in various areas of current translational medicine such as diagnostics, pharmacogenetics / precision medicine, and public health genomics.

The course further includes a 30-credit module on data analysis (*"Big Data in Biomedicine"*), which will enable students to acquire skills that are now required at all stages of the translational research continuum and thus are in great demand by potential employers.

The *"Research Methods and Management"* module and the research project add qualifications key to the MRes degree by expanding into the design, planning, completion and documentation of translational research.

Learning objectives and indicative curriculum content for each module are listed on the subsequent pages:

Module title: **"Case Studies in Drug Discovery & Development"**

BRIEF DESCRIPTION OF THE MODULE

The first part of this module focuses on malaria, a disease of global importance. Sessions go through a series of case studies that explore very comprehensively the pathophysiology of malaria, plus preclinical and clinical studies that led to the development of antimalarials. The second half consists of presentations and workshops by translational scientists at St. George's discussing their own research.

MODULE-SPECIFIC LEARNING OUTCOMES

On completion of this module, students should be able to:

1. Discuss the pathophysiology of disease processes and the life cycle of infectious agents; give examples of how such understanding can uncover targets for chemotherapeutic intervention.
2. Recognise the features of potential targets for chemotherapeutic intervention ("druggable" targets).
3. Explain how multiple disciplines, including chemistry, biology, cell and molecular biology, pharmacological sciences and medicine, must collaborative in the development of new drugs to improve human health.
4. Critically evaluate preclinical and clinical research studies.
5. Select and explain appropriate common laboratory techniques used to answer questions and solve problems in the preclinical screening of investigational new drugs.
6. Access and process evidence-based information, working independently and as a team.
7. Engage in and/or contribute to scientific discussions both orally and in writing using evidence-based knowledge.
8. Coherently present scientific information, both orally and in writing.

INDICATIVE CURRICULUM CONTENT

- The natural history of malaria, life cycle and drug targets.
- Overview of the discovery and development of early antimalarials
- Preclinical and clinical studies of antimalarial drugs
- Chloroquine resistance and resistance reversal strategies
- Basic Principles of drug discovery and design
- DNA enzymology and drug design
- Sudden cardiac death - abnormal electric activity and channels within the hear
- Recombinant monoclonal antibodies for prevention of infectious diseases
- Herpes, life cycle and drug targets
- Antimicrobial peptides versus multi-drug resistant bacteria
- Trying to solve problems in early pregnancy
- Immunotherapy of multi-drug resistant tuberculosis
- Viral interferon antagonists as potential therapeutic agents

Module title: **"Genomic Technologies in Clinical Diagnostics"**

BRIEF DESCRIPTION OF THE MODULE

Powerful new technologies are transforming healthcare. Over the last decade technologies have emerged that allow scientists to interrogate the genome at the chromosome or single nucleotide level in just a few days, resulting in greater availability of genomic data, which is increasingly being used to determine health management. Genomics have become pivotal in various areas of current translational medicine such as diagnostics, pharmacogenetics / precision medicine, and population genetics.

This online module focuses upon these fundamental genomic technologies. Students will familiarise themselves with the molecular and cytogenetic techniques currently employed in the diagnostic laboratories and, using their knowledge, develop testing stratagems for particular clinical condition(s). Students will also gain an in-depth understanding of genetic technologies currently undertaken in the research setting, and the challenges involved in the implementation of novel technologies in the diagnostic setting.

MODULE-SPECIFIC LEARNING OUTCOMES

On successful completion of the module students should be able to:

Part (1): "Molecular Techniques"

1. Demonstrate knowledge and applicability of the molecular principles behind PCR/Sanger sequencing; next generation sequencing; MLPA/MS_MLPA; Southern blotting; array CGH; FISH; karyotyping; the extraction and analysis of cell free fetal DNA and QF-PCR
2. Evaluate which laboratory investigation(s) is(are) most suitable for a given clinical scenario
3. Demonstrate an in-depth understanding of the methodology of at least four molecular genetic techniques

Part (2): "Next Generation Sequencing"

1. Demonstrate an understanding of the molecular principles underlying Next Generation Sequencing (NGS) technologies
2. Identify appropriate applications of these technologies to clinical scenarios within both the diagnostic and research settings
3. Design a panel of genes for analysis using Next Generation Sequencing technologies applicable to a specific clinical phenotype

INDICATIVE CURRICULUM CONTENT

Part (1): "Molecular Techniques"

- Array comparative genomic hybridisation (array CGH)
- Karyotyping
- Fluorescent in situ hybridisation (FISH)
- Southern blotting
- Multiplex ligation probe amplification (MLPA)
- Polymerase chain reaction (PCR) and Sanger sequencing
- Quantitative fluorescent PCR (QF-PCR)
- Single nucleotide polymorphism (SNP) genotyping and genome-wide association studies (GWAS)
- Extraction and analysis of cell free foetal DNA, including non-invasive prenatal testing (NIPT)

Part (2): "Next Generation Sequencing"

- The changing landscape of genomics: From Sanger sequencing to next generation sequencing

- Overview of next generation sequencing platforms and their methodology
- Targeted re-sequencing
- Alignment, variant calling and annotation
- Other applications of Next Generation Sequencing beyond DNA sequencing
- Next Generation Sequencing in gene discovery
- Gene discovery in the research and diagnostics
- Next generation sequencing in clinical diagnostics: single gene, gene panel sequencing, exome and genome sequencing
- How to design a gene panel
- The 100,000 Genomes project
- The transforming NHS: genomics in mainstream practice

Module title: **"Research Methods and Management"**

BRIEF DESCRIPTION OF THE MODULE

The Research Methods and Management module tightly integrates with the research project by introducing students to the conceptual, technical, regulatory and ethical aspects of conducting research. The module also covers a number of transferable skills related to self-directed learning, literature analysis, communication, and time management. Teaching strategies will include a "flipped classroom" approach involving self-directed learning followed by class presentations, discussions and tutorials. The principal assessment is a research proposal on the subject of students' laboratory project.

MODULE-SPECIFIC LEARNING OUTCOMES

On successful completion of the module students should be able to:

1. Appraise the framework for research governance and legislation affecting research
2. Examine the need for ethical and other approval before commencing research
3. Critically evaluate the implications for their work of health and safety and intellectual property legislation and guidelines
4. Demonstrate an awareness of personal responsibility and professional codes of conduct
5. Demonstrate effective written and oral communication skills
6. Set up a realistic timetable for research work and monitor progress towards achieving deadlines
7. Demonstrate self-awareness and reflect on action
8. Critically evaluate the characteristics of high quality, ethical research
9. Set realistic and appropriate aims, objectives and research questions for research projects
10. Write a compelling research proposal in the area of their research project that incorporates a critical appraisal of the literature, well defined and achievable research aims, appropriate experimental approaches, an appraisal of possible ethical and regulatory considerations, a realistic time line, and an overview of costings.

INDICATIVE CURRICULUM CONTENT

- Writing a research protocol
- Finding, managing and evaluating literature
- Expository writing
- What is research?
- Common laboratory methods
- Fundamentals of study design
- Experimental design
- Ethics and research governance
- Risk assessment of laboratory procedures
- Regulations for handling personal information
- Research integrity
- Time management in research
- Publishing and communicating results in research

Module title: **"Big Data in Biomedicine"**

BRIEF DESCRIPTION OF THE MODULE

Understanding of large biomedical datasets and data analysis skills are now required at all stages of the translational research continuum; training in this area is thus greatly desired by potential employers.

Since the human genome was first sequenced in 2003, the biomedical sciences have experienced an explosion of DNA sequence data, functional genomics collections and epidemiological information. The exponential progress in this area was made possible by the emergence of novel technologies used to sequence DNA, investigate gene function and to store and analyse large amounts of data. New technologies, comprehensive datasets and advances in data storage have ushered in the field of 'systems biology', a catchphrase used in reference to growing efforts of using holistic approaches to study complex problems in biology and medicine. Availability of properly trained scientists who can analyse these data is now becoming the limiting factor in industry and academia.

MODULE-SPECIFIC LEARNING OUTCOMES

On successful completion of the module students should be able to:

1. Define the technical principles and discuss the specific uses of high-throughput analytical methods used in modern biomedical science.
2. Apply common principles of computer programming and solve problems using R, Python or Unix/Linux.
3. Retrieve microarray-based gene expression data from a public data depository and extract gene sets based on defined criteria.
4. Locate chromatin immunoprecipitation/sequencing (ChIPSeq) data in an online database and characterise the binding sites of DNA-associated proteins.
5. Compare DNA sequencing results with reference data to identify sequence variants.
6. Interpret and critically appraise the published "omics" literature.
7. Apply statistics to answer questions related to quantitative genomics data.

INDICATIVE CURRICULUM CONTENT

- Programming in R
- Descriptive statistics
- Statistics: hypothesis testing
- Epidemiological / population health data
- Human genomics: Linkage analyses
- Human genomics: Next generation sequencing
- Human genomics: GWAS
- Human genomics: Genetic epidemiology
- Bacterial genomics: Prediction of drug resistance
- Bacterial genomics: Outbreak investigation
- Functional genomics: Large-scale gene expression data
- Functional genomics: DNA-binding proteins

Module title: **"Research Project"**

BRIEF DESCRIPTION OF THE MODULE

The supervised research project constitutes a central learning activity by providing immersive, work-based training in translational science. A research project involves choosing a subject, formulating a specific research question or aim, devising a research strategy to address this question, performing the research and analysing the resulting data. Project background, experimental procedures, results and discussion are written up as a 15,000 to 25,000-word dissertation and presented orally to an audience with the aid of a poster.

At the beginning of the course students will be presented with a list of available research projects, and they are asked to explore possible subjects in meetings with potential supervisors. Students choose a project by the end of the first month.

The Translational Medicine MRes course has been designed such that the research project interdigitates, wherever possible, with the taught modules. The "Case Studies in Drug Development" and "Big Data in Biomedicine" modules will include assignments requiring reading and presenting scientific literature, and students will have opportunities to choose material with relevance to their project.

Following the first term, students will prepare a research proposal on the subject of their research project (assessed as part of the Research Methods and Management module; see page 5).

MODULE-SPECIFIC LEARNING OUTCOMES

On successful completion of the module students should be able to:

1. Device detailed, step-by-step experimental protocols for a variety of relevant laboratory procedures.
2. Skilfully perform laboratory techniques specific to their area of research.
3. Keep a detailed laboratory notebook and maintain well-documented records of their
4. data.
5. Expertly perform common calculations that are routine in laboratory-based biomedical research, such as e.g. unit conversions, calculation of concentrations (in various units) and dilutions.
6. Process and analyse data, often using appropriate statistics and often using computer software to prepare graphical representations of the results.
7. For projects involving analysis of large datasets, master key aspects of computer programming, including the use of variables, different types of data, data input and output, functions, relevant algorithms/workflows, debugging tools and the programmatical generation of graphics and reports.
8. Systematically trouble-shoot technical problems that might arise during laboratory experimentation or computer use.
9. Author a research report (dissertation) akin in structure and format to a publishable research article.
10. Orally present a coherent account of a projects, using visual aids such as slides or a poster.