UNIVERSITY OF CAMBRIDGE

Institute of Continuing Education

Genomic Medicine Programme:

Further Information and Module Descriptions

Postgraduate Certificate in Genomic Medicine
Postgraduate Diploma in Genomic Medicine
Master of Studies (MSt) in Genomic Medicine
Modular Study on Genomic Medicine

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Contents

The Genomic Medicine Programme

The Genomic Medicine Programme is designed to be flexible and accessible to working healthcare professionals, who are typically studying in addition to working full time. The programme allows students to develop their professional and academic interests for career progression, professional diversification and/or personal development.

The course is modular in structure and delivered through a combination of in-person and online sessions, self-directed learning and is supported through a virtual learning environment [VLE].

Please note: in the event that covid-19 restrictions are in place during the delivery of the course the methods of delivery will be reviewed in line with the relevant public health, Government and University guidance available at the time. If required, we may subsequently use alternative teaching formats and will contact students as soon as possible under the circumstances present.

Details of the courses and modules available to study as part of the Cambridge Genomics programme are detailed in this document:

Overall Aims of the Programme

The overall aims of the programme are to:

- provide professionally relevant teaching and learning informed by research in an integrated clinical and research environment;
- develop and create a cohort of doctors and other professionals allied to medicine able to pursue and develop their roles in the rapidly-changing and challenging environment of genomic medicine;
- prepare healthcare professionals for the adoption of genomic technologies and the increasing use of genomic information as part of the diagnostic and treatment pathway;
- develop a cohort of doctors and other professionals allied to medicine with the confidence to lead service improvement for safe and high-quality patient care, and with the required knowledge, skills and capability to have a positive personal impact on the work of others.
- develop a cohort of doctors and other professionals allied to medicine with an understanding of research methodologies and clinical opportunities relevant to genomic medicine.
- encourage a commitment to intellectual challenge and evidence-based clinical practice informed by the latest conceptual and theoretical knowledge of genomic medicine;
- develop students' intellectual, practical and transferable skills related to genomic medicine;
- encourage critical thinking related to genomic medicine;
- for the MSt, to conduct systematic research relevant to their professional practice;
- Equip students for entry into health care professional training schemes including graduate entry medicine courses;
- Prepare students for undertaking research degrees (PhD) in genomic medicine-related research fields;
- Provide students from the pharmaceutical, biotechnology and other industries with an understanding of the relevance of advances in genomics for current and future health care.

Key Partners and People

There are three Institutions (University of Cambridge, Wellcome Trust Sanger Institute (WTSI) and European Bioinformatics Institute (EMBL-EBI) associated with the Cambridge Genomic Medicine Programme. The Programme is run in collaboration with the Institute of Continuing Education (ICE) and The Department of Clinical Medicine.

The Programme Director is Prof Eamonn Maher, Professor of Medical Genetics and Genomic Medicine, Department of Medical Genetics, University of Cambridge

The Course Director for MSt/Part-time students is Dr Gemma Chandratillake, Education and Training Lead for the East of England Genomic Medicine Centre (EE GMC)

The Course Director for MPhil students is Assistant Professor Dr Timothy Hearn, Department of Medical Genetics, University of Cambridge.

The Academic Director is Dr Tom Monie, Deputy Director of Academic Centres (Academic), University of Cambridge Institute of Continuing Education.

Programme Structure

The programme leads to the following University of Cambridge degrees or awards and also provides options for studying individual modules and progression pathways from one award to the next. Each module is equally weighted providing 15 FHEQ-7 credits if successfully completed.

Postgraduate Certificate in Genomic Medicine

The Postgraduate Certificate in Genomic Medicine is a one-year part-time programme resulting in 60 FHEQ level-7 credits. Students are required to take **four modules** with additional between-module reflection, study and assignment work.

Postgraduate Diploma in Genomic Medicine

The Postgraduate Diploma in Genomic Medicine is a two-year part-time programme resulting in 120 FHEQ-7 credits. Students must complete **eight modules** with additional between-module reflection, study and assignment work.

Master of Studies (MSt) in Genomic Medicine

The MSt in Genomic Medicine is a two-year part-time master's degree resulting in 180 FHEQ level-7 credits. The MSt in Genomic Medicine builds on the generic platform of taught Modules provided by the Postgraduate Certificate and the Postgraduate Diploma in Genomic Medicine.

The MSt comprises either:

- **eight taught modules** plus a 60 credit research project/dissertation of 10,000-12,000 words or the equivalent on an agreed topic in genomic medicine;
  or
- **ten taught modules** plus a 30 credit literature-based research project/dissertation of 5,000-6,000 words or the equivalent on an agreed topic in genomic medicine.

Modular Study

Individual modules of the Genomic Medicine Programme may be studied as standalone modules, for Credit or for Continuing Professional and Personal Development [CPPD] or as a platform for further study (see below for further details). Each module is worth 15 FHEQ, Level 7 credits.

Progression pathways in Genomic Medicine

The Genomic Medicine programme is of a modular structure which allows for students to progress through various study pathways:

- **Individual modules** of the Genomic Medicine Programme carry 15 FHEQ Level 7 credits and may be studied as standalone modules for Credit, or as a platform for further study:
    - 1 module at 15 credits may be transferred forward into the PG Certificate
    - 2 modules at a total of 30 credits may be transferred forward into the PG Diploma or MSt

    NB: Modules being transferred into an award can only be brought forward from the previous academic year and can only be modules studied at Cambridge.

- **The Postgraduate Certificate in Genomic Medicine** can be taken as a stand-alone award or as a platform for further study of the Postgraduate Diploma and Master of Studies in Genomic Medicine.
    - **Certificate to Diploma:** A student who has successfully completed the Postgraduate Certificate and wishes to progress to the PG Diploma (if admitted) will be required to complete an additional 4 modules in one year.
    - **Certificate to MSt:** A student who has successfully completed the Postgraduate Certificate and wishes then to complete the MSt will, if admitted be required to complete a further 4 modules and the 60 credit research project or a further 6 modules and the 30 credit literature based project in the second year of study.

- **The Postgraduate Diploma in Genomic Medicine** can be taken as a standalone award or as a platform for further study of the Master of Studies in Genomic Medicine.
    - **Diploma to MSt:** A student who has successfully completed the Postgraduate Diploma in Genomic Medicine who wishes then to complete the MSt will, if admitted, be required to complete the research project in one year.

Please note that progression:

- Is subject to application and successful admission to the course and is not automatic.
- Would normally need to be within two years of completing the Postgraduate Certificate or Diploma.

The final award (on successful completion) subsumes any previous award(s), which are withdrawn in favour of the final award. E.g. If a student holding a Postgraduate Certificate progresses to the Postgraduate Diploma, the prior award of the Postgraduate Certificate is withdrawn in favour of the Postgraduate Diploma.

For more information about all of the courses and awards above please see our website here: https://www.ice.cam.ac.uk/ under 'Courses'.

Course Modules Summary

Dates for the Programme starting in October 2022 will be confirmed on the ICE website here: https://www.ice.cam.ac.uk/

Introduction to human genetics and genomics (GM1) *Gateway part 1*
Omics techniques and the application to genomic medicine (GM2)
Bioinformatics, interpretation, and data quality assurance in genome analysis (GM7)
Application of genomics to infectious disease (GM5)
Introduction to human genetics and genomics (GM1b) *Gateway part 1*
Molecular pathology of cancer and application in cancer diagnosis, screening, and treatment (GM4)
Pharmacogenetics and stratified healthcare (GM6)
Counselling skills for genomics (GMO2) *Gateway part 2*
Advanced Bioinformatics - Option Module (GMO4)
Epigenetics and Epigenomics (GMO5)
Genomics of common and rare disease (GM3)
Research and statistical skills for Genomic Medicine (GMO7)
Workplace based module (GM3)

Each 15 credits of study is roughly equivalent to 150 hours of study which will consist of face-to-face teaching, blended, and self-directed learning. This is an indicative amount and it is recognised that individuals may engage in greater or lesser amounts of study for each unit.

Module Descriptions

The following modules are offered for study as part of the Cambridge Genomics Programme

GM1 - An introduction to human genetics and genomics

Content Description

This module consists of approximately 30 hours of contact time. This introductory module aims to provide the student with an introduction to the key areas of genomics, human genetics and genetic variation. It will prepare participants to understand disease genetics and how genomic medicine can be utilised to elucidate disease mechanisms and biology. In addition, this module will also cover the fundamentals of information governance in the context of genomic medicine and its applications providing underpinning knowledge for later modules in bioinformatics and statistics. This module will serve as a foundation for those wishing to advance their careers within the NHS in genomic medicine. This module provides clear understanding of the structure and variations in genetic material. Covering basic genetics and genomics, it will prepare students to understand the role of genetics in disease and how genomic information can be utilised to elucidate disease mechanisms and biology.

Content

In GM1 you will learn about:

- Structure and function of nucleic acids and chromosomes
- Architecture and organisation of the human genome and genetic variation within it
- DNA sequence variation, type and frequency e.g. single nucleotide variants, small insertions and deletions, copy number variation, rearrangements and tandem repeats
- How variation arises and its extent in populations (e.g. HapMap)
- Gene regulation: enhancers, promoters, transcription factors, silencers
- Epigenetics and imprinting
- Mutational mechanisms: how different types of DNA variants affect gene function or expression to cause disease; correlation of genotype with phenotype
- Concepts of penetrance, expressivity, heterogeneity and pleiotropy
- Modes of inheritance for clinical manifestation of human variation
- Types of genetic testing (prenatal, carrier, predictive, diagnostic, cascade, screening, etc)
- Germline, mitochondrial and somatic mutations
- Chromosomal abnormalities and disease
- Mechanisms of Mendelian disorders
- Interpretation of genetic variation
- Basic Bayesian approach to calculating disease probabilities
- Overview of key ethical, legal and social implications of genomics
- Introduction to some of the principles underlying application of genomic data in clinical practice
- Legislation, Codes of Practise, Caldicott Guardian and Information Commissioner
- Patient identifiable data and information, relationship between data and information
- Information system risks to patient safety, electronic and paper copies, safe havens, encryption, secondary uses of data, audit and research
- Secure information exchange between professionals
- Sharing and communication with patients and careers, consent
- Handling requests for information about patients /clients.

Learning Outcomes
By the end of this module students will be able to:

- Discuss the human genome structure and the properties of DNA
- Critique genome architecture and its variation across human populations
- Critically evaluate the regulation of gene expression, transcription and translation
- Appraise and interpret variation in genome structure and sequence in the context of physiological function and disease
- Discuss and analyse epigenetic modifications and imprinting and its role in disease
- Correlate genetic markers to phenotype and interpret output of association studies both for dichotomous and quantitative traits
- Discuss different disease mechanisms and modes of inheritance
- Apply concepts of inheritance and calculate genetic risks for Mendelian conditions
- Discuss and justify the ethical and governance frameworks in place within the NHS and how they apply to medical genomics including patient safety, data sharing and confidentiality
- Identify the range, purposes, benefits and potential risks of sharing, integrating and aggregating clinical data and information.
- Describe and evaluate the purpose, structures, use and storage of health records.

GM2 - Omics techniques and their application to genomic medicine

Content Description
This module explores the state of the art genomics techniques used for DNA sequencing (targeted approaches, whole exome and whole genome sequencing) and RNA sequencing, using highly parallel techniques, together with current technologies routinely used to investigate genomic variation in the clinical setting. This module will introduce the bioinformatics approaches required for the analysis of genomic data, which together with data governance covered in GM1 will provide a solid foundation for the Bioinformatics and Statistics modules. The module will also cover the use of array-based methodologies and RNA sequencing in estimating levels of protein expression, micro RNAs and long non–coding RNAs. A comprehensive introduction to metabolomics and proteomics, which are important for the functional interpretation of genomic data and discovery of disease biomarkers will also be included. Students will also learn about the strategies employed to evaluate pathogenicity of variants for clinical reporting.
Teaching of these core technologies and introductory bioinformatics will be facilitated in part by hands-on production of genomic data in which students will take DNA samples through an entire ‘omics’ workflow.

Content
In GM2 you will learn about:

- Basis of genotyping and detection of genetic variation
- Whole exome and whole genome sequencing, including library preparation methods, sequencing chemistries and platforms
- Hands-on practical experience of an ‘omics’ workflow from sample to analysed data

- Brief overview of methodologies for detecting base substitutions (SNV), small insertions and deletions (indels), copy number variants (CNV) or rearrangements, to include Sanger sequencing, pyrosequencing, ARMS, MLPA, qFPCR, microarray
- Genomic testing strategies as: gene focused, multiple genes, or whole genome or exome, and for detection of sequence, copy number or rearrangements
- RNA expression profiling (expression array) and RNA sequencing
- Metabolomics and proteomics techniques
- Overview of bioinformatics approaches to the analysis of genomic data using Galaxy

Learning Outcomes
By the end of this module students will be able to:

- Describe and critically evaluate a range of up-to-date genomic technologies and platforms used to sequence targeted parts of the genome or whole genomes
- Discuss the application of other techniques (for example array comparative genome hybridisation, qPCR) commonly used to interrogate genomic variation in the clinical setting using examples in cancer and rare inherited diseases and infectious diseases
- Acquire the knowledge of selecting appropriate technology platforms for applications in medical genomics either for research or medical diagnostic purposes
- Critique how these techniques and their applications in RNA expression can be applied to metabolomics and proteomic analysis
- Discuss and critically appraise approaches to the bioinformatics analysis and interpretation of 'omics' data
- Critically evaluate the different 'omics' technologies and platforms and their application to genomic medicine and the impact of personalised medicine

GM3 - Genomics of common and rare inherited diseases

The number of rare monogenic disorders is estimated to be greater than 7000, but only in approximately half of these are the underlying genes known. Common conditions such as intellectual disability, diabetes, and schizophrenia are thought to arise from a complex interplay of genetic and environmental factors but deeper understanding of the genetic and mechanistic basis of these conditions is necessary for clinical translation.

The module offers a comprehensive overview of the traditional and current strategies and techniques used to identify genes responsible for both common multifactorial and rare inherited diseases, focusing mainly on the latter. This module will initially explore the clinical presentation and course of a range of common and rare inherited diseases. The principles and practise of medical genetics, and the management and treatment of probands and their families will be discussed. In addition, the role of genomics in a care pathway will be examined including the patient and family perspective. Building on knowledge gained in GM2, students will further explore the analytical challenges in genomics as applied to rare inherited diseases.

Content
In GM3 you will learn about:

- Clinical presentation and course of a range of rare inherited and common diseases
- Principles and practise of medical genetics; risk stratification and management of patients and their families

- Approaches and techniques used to identify genes responsible for common and rare inherited diseases (e.g. candidate gene, positional mapping, genome wide association studies, exome/whole genome sequencing, use of population data sets)
- An overview of the techniques used for functional validation of putative disease- associated mutations
- Basic statistics to aid interpretation of Genome Wide Associated Studies (GWAS) and analysis of populations
- The Genomics England 100,000 Genomes Project and data infrastructure
- Selection of tractable cases with unmet diagnostic need suitable for whole genome analysis
- Analytical challenges in genomics as applied to rare inherited diseases including; the potential of electronic health records to enrich patient data, the importance of phenotyping and use of databases such as ClinVar, the use of large population datasets and sharing information e.g. Human Variome Project
- Impact of patient on-line access to their health records, test results etc. on medical genomics.

Learning Outcomes
By the end of this module students will be able to:

- Examine the landscape of common and rare inherited diseases
- Explain the genetic architecture of common and rare inherited diseases
- Critically evaluate traditional and current approaches used to identify genes for common and rare inherited diseases
- Synthesise information gained from exome/whole genome analysis with patient information / medical records to determine diagnosis, penetrance or prognosis for a number of examples of common and rare inherited conditions
- Discuss and evaluate the Genomics England Programme and the Data Infrastructure
- Identify phenotype, select cases and relevant family information for whole exome or whole genome based approaches for hypothesis free whole exome or whole genome sequencing
- Discuss and critically evaluate the implications of patient access to their medical records and clinical information for medical genomics, inter- professional practice and multidisciplinary care
- Have an understanding of the range of methodologies that can be used to functionally validate putative disease mutations.

GM4 - Molecular pathology of cancer and application in cancer diagnosis, screening, and treatment

This module aims to equip the student with detailed knowledge and understanding of the molecular mechanisms involved in cancer development. This will include the ways in which interrogation of a person's own genome and the genome of tumour cells can facilitate the diagnosis and treatment of cancer. This module covers the molecular mechanisms that underlie cancer development, growth and metastasis, and the differences between different cancers. It will explore the different molecular and cellular actions of anti-cancer treatments, the genomic factors affecting response and resistance to treatment, and the research approaches to anti-cancer drug design and development. Broad situations which confer a high cancer risk to a person and/or to other members of the same family will be discussed in the context of how genomic information may be integrated into cancer screening programmes.

Content

In GM4 you will learn about:

- Tumour classification systems
- Cellular properties of tumours: growth, division, invasion, aberrant hormone or toxin production, immunogenicity
- Molecular and functional classification of somatic DNA mutations
- Clonal evolution and subclonal architecture of cancer
- Factors in tumour formation: molecular mechanisms and role of microenvironment, mutagens, mutational processes, molecular signatures & changing classification
- Diagnosis, molecular sub-classification, aggressiveness (prognosis) characterisation of metastases
- Monitoring disease following treatment (medical, surgical or bone marrow transplant)
- Genomic testing of cell free tumour DNA in blood, for diagnosis and monitoring of solid cancers
- Importance of sample quality for tumour genomic analysis
- Understanding the molecular effects of single and the synergy between multiple oncogenic mutations
- Computational/internet resources on Cancer Genomics (COSMIC, mutational calling algorithms, genome browsers, medical/scientific literature)
- The basis of heritable predisposition to cancer
- The role of environmental factors, microorganisms and lifestyle choices on cancer predisposition and protection
- Genomic and cellular markers and choice of treatment regimes in haematological cancer and in solid tumours
- Companion diagnostics in cancer
- Breakthrough tumour, relapse, metastasis and molecular mechanisms

Learning Outcomes
By the end of this module students will be able to:

- Understand the mutational processes driving cancer and how these manifest themselves as mutational signatures in cancer genomes
- Appreciate the concepts driving the clonal evolution of different cancers and its parallels to Darwinian natural selection
- Understand the concepts of driver and passenger mutations, as well as the basis of acquired resistance to cancer therapies
- Apply the principles of cancer development and emerging changes in classification
- Compare and contrast the genomic basis of cancer predisposition, and how this is used to identify people and families at higher risk of cancer
- Critically evaluate the impact of genomic advances for the diagnosis, classification, treatment selection and monitoring of cancer (e.g. leukaemia, breast, melanoma, lung cancers)
- Analyse how information from exome and whole genome analysis of tumour tissue can be used to investigate the molecular and cellular processes leading to cancer and inform strategies for drug development.

GM5 - Application of genomics in infectious disease

From this module the student will understand how genomics can be used to better understand the nature, diversity and mechanisms of evolution of microbes causing human disease, provide more accurate diagnosis, predict which drugs are likely to be more effective and monitor treatment and control of infectious disease in individuals and populations.

The student will learn about the genomic structure of infectious agents, implication of acquisition or loss of nucleotides, genes and plasmids on pathogenicity, sensitivity of a pathogen to drug treatment and response to the host. Students will also be taught about current typing approaches for diagnostics and epidemiology of infectious agents, the surveillance systems operating in the UK and abroad and how genome-based approaches can complement/replace these existing methodologies both locally and internationally.

This module may be particularly interesting to students studying in ACY 2020-21 as it covers viral genomics and some of the work around Sars-Cov-2.

Content
In GM5 you will learn about:

- Infection as a cause of national and global morbidity and mortality
- Transmission of human infections: person to person, food and waterborne, sexually transmitted, vector-borne, zoonosis
- Prokaryotes, their genome, replication and population genetics
- Genomic characterisation of viruses: DNA and RNA genomes, single-stranded, double stranded, segmented
- Genomic comparisons of microbial strains in the context of outbreaks and transmissions in hospitals and the community
- Anti-infective drug action
- Mutation rate and drug resistance
- Genomic evidence of individual susceptibility to specific infection
- Methods and systems for typing and tracking infectious disease locally and internationally.
- Role of genomics in: infectious disease diagnosis, prognosis, drug selection, resistance, monitoring, epidemic control, drug research

Learning Outcomes
By the end of this module students will be able to:

- Explain the differences between prokaryote and eukaryote genomes
- Discuss and appraise how the genome sequence of pathogens can be used to track cross infection and outbreaks of infections among the population
- Critically evaluate the emerging action of drugs in controlling infection e.g. Shigella, E-coli, HIV, TB
- Critically evaluate the molecular basis of organism drug resistance in some infections and how this directs drug research
- Evaluate how sequencing of the genome of infective organisms can be used in infectious disease for assessing: diagnosis, sub-classification and strain identity, pathogenicity, drug resistance and drug selection; and for epidemic control

GM6 - Pharmacogenomics and stratified healthcare

Pharmacogenomics is playing a key role in our health care system. Pharmacogenomics and stratified health care ensure that healthcare professionals tailor the 'right treatment, for the right person, at the right time' and is a fast developing area. This module provides a comprehensive overview of the analytical strategies and techniques used in pharmacogenomics and explore some of the challenges and limitations in this field (availability of patient material for studies of adverse drug reactions which tend to be rare, allelic heterogeneity between different ethnic groups, patient compliance etc.). Biomarkers are the predictive tools for optimising drug response and preventing adverse drug reactions thus this module will also provide an overview of the different type of genomic biomarkers currently in use or emerging. This module describes the complexity of pharmacogenomics and the effect of medication on individuals based on their genetic make-up i.e. tailoring drug treatment to improve patient response and techniques to stratify patients at risk of adverse drug reactions. The module uses examples of known validated pharmacogenomic tests relevant to the use of drug treatments and also use the expertise provided by the major clinical- and academic- industrial research cluster in biomedical science that is developing locally. The module provides a focus to develop interactions with industrial partners and academic groups developing research programs in stratified medicine across a broad range of diseases.

Content
In GM6 you will learn about:

- Genomic basis of: drug reaction, drug efficacy, ethnic differences in both these; and how these are applied in prescribing practice
- Use of genomic information, for targeted drug development
- Companion diagnostics and options for NHS service delivery models
- Different types and examples of genomic-targeted intervention (examples of genomically-targeted clinical, therapeutic or lifestyle choices)
- Genomic biomarkers: SNPs, variability of short sequence repeats, haplotypes, DNA modifications, e.g. methylation, deletions or insertions, copy number variants, RNA expression levels, RNA splicing, microRNA levels
- Use of biomarkers in treatments other than cancer.
- The role of academic-industrial partnerships in clinical drug development and clinical trials.

Learning Outcomes
By the end of this module students will be able to:

- Discuss and evaluate the mechanism of several examples of genome-determined differential drug response, and drug reaction
- Appraise the strategies and analytical approaches for stratifying patients for optimal drug response or adverse drug reactions including ethnic differences, and how these translate into 'companion diagnostics'
- Identify and analyse the challenges and limitations of pharmacogenetic studies
- Identify and evaluate the different types of current and emerging biomarkers used in personalised medicine
- Discuss and critically evaluate how genomic information can enable development of drugs targeted for particular genotypes

- Identify the ethical, legal and social issues (ELSI) that could accompany patient stratification for healthcare advice or intervention and defend the use of patient stratification to improve the diagnosis and treatment of disease

GM7 - Bioinformatics, interpretation, and data quality assurance in genome analysis

The module covers the fundamental principles of informatics and bioinformatics applied to clinical genomics. Students are taught to find and use major genomic and genetic data resources; use software packages, *in silico* tools, databases and literature searches to align sequence data to the reference genome, critically assess, annotate and interpret findings from genetic and genomic analyses. Theoretical sessions are coupled with practical assignments of analysing and annotating predefined data sets. This module is central to the Genomic Medicine Programme as it provides students with the skills to begin to analyse genomic data. This module is suitable for beginners and does not involve the use of the Unix command line or R. Students with previous bioinformatics experience are advised to take the advanced bioinformatics module.

Content
In GM7 you will learn about:

- Methods of alignment of sequencing data to the reference genome using state of the art alignment programmes
- Assessment of data quality through application of quality control measures
- How to determine the analytical sensitivity and specificity of genomic tests
- Use of tools to call sequence variants (e.g. GATK) and annotate variant-call files using established databases
- Filtering strategies for variants, in the context of clinical data, and using publicly available control data sets
- Use of multiple database sources, in silico tools and literature for pathogenicity evaluation, and familiarity with the statistical programmes to support this
- Principles of integration of laboratory and clinical information, and place of best- practice guidelines for indicating the clinical significance of results
- Principles of biomedical ontologies (e.g. HPO, SNOMED, ICD) and how to use them for the annotation of clinical phenotypes

Learning Outcomes
By the end of this module students will be able to:

- Understand the principles applied to quality control of sequencing data, alignment of sequence to the reference genome, calling and annotating sequence variants, and filtering strategies to identify pathogenic mutations in sequencing data
- Understand the challenges associated with the analysis of variation data, how to treat candidate variants given known false positive/negative rates and population frequencies as well as the implications for disease diagnosis
- Interrogate major database sources of genomic sequence (e.g. Ensembl), protein sequences (e.g. Uniprot), short variations (e.g. 1000 Genomes, dbSNP, HapMap, EVA), structural variation (e.g. dbVar), variant-disease association (e.g. ClinVar, OMIM, Decipher), GWAS and other association studies (e.g. dbGAP, EGA, GWAS catalogue), pathways (e.g. Reactome), cancer genes and variants (e.g. ICGC, COSMIC, TCGA) and be able to integrate this

information with clinical data, to assess the potential pathogenic and clinical significance of the identified sequence variants
- Identify and critically evaluate biomedical ontologies for the annotation of clinical phenotypes
- Acquire relevant basic computational skills for handling and analysing sequencing data for application in both diagnostic and research settings
- Discuss and critically evaluate statistical methods for handling and analysing sequencing data
- Gain practical experience of the bioinformatics pipeline for variant calling through the Genomics England programme.
- Justify and defend the place of Professional Best Practice Guidelines in the diagnostic setting for the reporting of genomic variation.

GMO2 - Counselling skills for genomics

This is an introduction to counselling skills for genomics. The aim of this module is to equip students with the knowledge, communication and counselling skills and appropriate attitudes and behaviours towards the diagnosis and management of patients whose care will be influenced by genomic investigations. Students undertaking this module are taught how to communicate and provide appropriate support to individuals and their families. Development of counselling skills is achieved via theoretical and practical sessions. Students are taught to understand the importance of a family history and communication of pathogenic and/or uncertain results. Patient involvement is an integral feature of this module. The patient perspective will also be considered extensively within the role play delivery.

Content
In GMO2 you will learn about:

- Communication and counselling skills
- Consent and what it means in relation to the 100,000 Genomes Project
- Ethical and social implications of genomic testing
- How to record and interpret a family history, recognising what is or may be relevant
- How to verify personal and family history information; consent, confidentiality, access to records
- Different purposes of genomic testing
- Approaches to prenatal testing, pre-implantation testing (PGD) and pre-conception carrier screening in relation to new technologies
- Strategies of approach to lifelong patient management of whole genome information
- Managing and explaining complex genome results
- Sources for patient support: patient support groups, on-line resources, other resources

Learning Outcomes
By the end of this module students will be able to:

- Explain and justify the importance of and application of informed consent in the field of genomic medicine
- Explain the different purposes of genomic testing in patients with rare inherited diseases, cancer and infectious diseases
- Explain genomic results in terms of diagnosis prediction and uncertainty
- Describe and evaluate the skills necessary to support individuals who have genomic results that affect their care including the underpinning evidence base and patient perspective

- Discuss the concepts of genetic and genomic predispositions to illnesses
- Discuss the consequences of genomic test results on the patient and the wider family including incidental findings drawing on the published evidence base and personal experiences of patients, carers and the wider family
- Evaluate and discuss the communication and counselling skills needed to engage and communicate effectively in a compassionate manner with patients, their carers and the wider family
- Explain the range of screening pathways used to test for inherited and acquired disorders and evaluate their effectiveness including how they support clinical decision making
- Discuss and critically evaluate current and potential future ethical, legal and social issues (ELSI) of genome testing and whole genome sequencing

GM07 - Research and statistical skills for Genomic Medicine

This module aims to provide and equip students with the knowledge of statistics and computational tools needed to independently complete genomic medicine research. This module complements the knowledge from the wider course to ensure all students are competent in planning research, and can perform appropriate statistical analysis in R. The module is designed to prepare students for research projects and presents material in this context. This module serves as an informatics foundation for students learning bioinformatics and statistical languages. In particular, the module introduces students to the Genomics England Research Environment, and provides both self-directed, and supervised learning of the Unix command line environment and the R statistics language. This module provides an excellent foundation for performing a research project on the Genomics England 100,000 genomes data, and for students considering undertaking a PhD in future years.

Course content
In GMO7 you will learn about:

- How to write a research grant proposal
- Up to date computational and experimental tools for genomic medicine research projects
- The Genomics England research environment and how to perform research on the 100,000 genomes dataset.
- How to use the Unix command line and Galaxy to perform basic genomic analysis
- Fundamental concepts in statistics offering students a foundation and framework for understanding more complex methods.
- Implementation of the statistical methods illustrated during the course using the R environment.
- Basic concepts in using R
- Basic statistical and mathematical concepts including correlation, regression, model selection, and generalized linear models
- Exploration of bayesian statistics and tools applied for haplotype estimation and Machine Learning tools for non-linear regression will also be explored

Learning Outcomes
By the end of this module students will be able to:

- Demonstrate a rounded knowledge of the classic and modern tools and technologies used in research projects. Emphasis will be placed on the overlap between modern and traditional approaches and the type of data they might be presented within a research project

- Understand the conceptual basis for statistical tests, and be aware of the various tools that they can implement when exploring either genomic or expression data
- Choose the correct statistical test based on the data source and experimental design and implement the test in R
- Have a thorough understanding of the types of computational tool available for use in research projects, and the best platform to use them on (Galaxy, command line, HPC etc.)
- Have a good understanding of how to access the central University Linux cluster from an external computer, in preparation for accessing remote High Performance Computing services.

GMO4 - Advanced bioinformatics – from genomes to systems

This module introduces students to bioinformatics approaches that can provide a system level understanding of disease associated processes, using a combination of 'omics' data types (e.g. genomic, transcriptomic, epigenomic, and proteomic).

This module builds upon the basic bioinformatics techniques introduced in GM7 or GMO7 along with the disease and subject specific knowledge gained in other modules. Students with no prior bioinformatics experience are encouraged to take this module following GM7. This module uses the Unix command line and R to analyse genomic medicine data.

The module is delivered through both lectures and hands-on practical sessions, and employs real data to illustrate the application of systems biomedicine approaches in genomic medicine.

Content:
In GMO4 you will learn about:

- Principles and practical experience of implementing bioinformatics pipelines for the analysis of genomic data.
- Principle of basic programming (e.g. Unix, R) and statistical methodologies needed to carry out analysis of variants
- How to use programmes and tools on the Unix command line to go from raw NGS sequence reads to calling variants.
- How to use Jupyter notebooks for bioinformatics applications
- Proteomics data, with a particular focus on protein-protein interaction networks
- Genetic interaction networks
- Methods and tools for network analysis and disease network re-construction
- Mathematical modelling approaches for integrating different data sources and understanding the deregulation of signalling networks in diseases
- Clinical use cases relating to the disease areas covered in previous modules e.g. cancer, infectious diseases.

Learning Outcomes:
By the end of this module students will be able to:

- Discuss the challenges, promises and pitfalls of moving from genome to whole systems analyses
- Access and handle appropriately a range of biological data types
- Implement analysis pipelines and perform basic statistical analysis
- Employ basic tools for network analysis, network visualisation and mathematical modelling of biological processes

- Critically analyse use cases where system approaches have been used to provide new insights into disease associated processes, across a range of disease areas

GMO5 - Epigenetics and epigenomics

The completion of the human genome project has paved the way for major advances in our understanding of human genetic disease and the pathogenesis of cancer. Nevertheless, these advances have also revealed that genetics is only part of the story and there is increasing recognition that epigenetics will be critical for understanding human disease and the practice of genomic medicine. Cambridge is the leading European centre for epigenetic research and this module will draw on world-leading local scientists to provide expert coverage of this fascinating topic.

Content
In GMO5 you will learn about:

- Definition and history of epigenetics
- Elements of epigenetic gene regulation: chromatin packaging, nucleosomes, histone marks, establishment and maintenance of DNA methylation, non-coding RNAs etc.
- Methodologies for investigating epigenetics regulation in health and disease
- Genomic resources for epigenetic research and interpretation. The Epigenome Project
- Role of model organisms in elucidating epigenetic control mechanisms
- Mechanisms of epigenetic regulation of gene expression in normal development (including nuclear reprogramming, X-chromosome inactivation and genomic imprinting)
- Epigenetics and inherited disease: inherited disorders caused by mutations in genes regulating epigenetic processes, human imprinting disorders, assisted reproductive technologies
- Epigenetics and acquired disease: epigenetics and cancer, epigenetics and gene/environmental interactions, epigenetics and ageing
- Epigenetics and therapeutics

Learning Outcomes
By the end of this module students will be able to:

- Understand the role of epigenetic factors in regulating gene expression
- Appreciate the critical role of epigenetics in normal development and human health
- Critically appraise methodologies for epigenetic studies of human disease
- Understand the role of epigenetic abnormalities in human disease, and in particular, the role in inherited disorders and neoplasia
- Describe the relevance of epigenetics for gene-environment interactions and the significance of epigenetics for therapeutic strategies for human diseases such as cancer

GMO6 - Expanding the content of genomic medicine with a workplace-based module

There is the potential opportunity to complete a work-based module which could, for example, explore clinical genomic practice in the NHS Regional Genetics Department at the student's workplace. The NHS Laboratory at CUH is the first diagnostic laboratory to implement "clinical exome" sequencing in the NHS, and has applied a variety of next generation sequencing technologies to a number of diagnostic applications. The mass of data resulting from clinical exome

sequencing alone offers many possibilities on which projects can be based. Examples of suitable projects might include a short case- based portfolio of study, completion and analysis of a clinical audit project, or an analysis of pathogenic genetic variation in specific clinical cohorts.

Suitable projects might involve:

- Critically evaluate existing practice in genomic medicine
- Devise and critique methods and approaches in genomic medicine
- Apply technical expertise to a range of cases, then evaluate and reflect on the utility of these technologies to the practise of genomic medicine techniques
- Apply clinical expertise to a range of cases and reflect on the utility of the genomic testing.

This module is primarily intended for NHS-funded students on the part-time MSt. MPhil students interested in this module should discuss the possibility with Prof Eamonn Maher at the earliest opportunity.

Further information

For additional information about the Genomic Medicine Programme, including; entry requirements, how to apply and assessment, please see the course web pages at: https://www.ice.cam.ac.uk/

Whilst every effort is made to avoid changes to this programme, published details may be altered without notice at any time. The Institute reserves the right to withdraw or amend any part of this programme without prior notice