Module - Introduction to Clinical Bioinformatics and Genetics (SBI104)

STP

Aim of this module

This rotation will provide trainees with background knowledge of genetics and a knowledge and understanding of bioinformatics tools and infrastructure. They will understand the aims and operation of a genetics laboratory service. They will understand the role of bioinformatics and the bioinformatician in supporting the laboratory service, and the effect of data and its analysis on patient care. In particular it will show how bioinformatics strategies can be used and applied to genomic and genetic data to generate information and knowledge that contributes to patient care and care pathways within a clinical setting. It will also introduce the ethical and governance framework appropriate for working with patient data in an NHS setting.

Work-based learning outcomes

1. Perform analysis on DNA data and protein sequence data to infer function.
2. Perform sequence alignment tasks followed by clustering and phylogeny.
3. Select and apply appropriate bioinformatic tools and resources from a core subset to typical diagnostic laboratory cases, contextualised to the scope and practice of a clinical genetics laboratory.
4. Compare major bioinformatics resources or pathogen typing and identification for clinical diagnostics and how their results can be summarised and integrated with other lines of evidence to produce clinically valid reports.
5. Interpret evidence from bioinformatic tools and resources and integrate this into the sum of genetic information for the interpretation and reporting of test results from patients.
6. Perform the recording of building or version numbers of resources used on a given date, including those of linked data sources, and understand the clinical relevance of this data.

Work-based Competencies

	Learning outcome	Title	Knowledge
1	1,2	Take a protein sequence and use standard bioinformatic tools to locate within a genome, annotate and infer function.	• Theoretical basis of function prediction in bioinformatics. • Tools for protein function prediction based on sequence similarity. • Tools for protein function prediction based on conserved motifs and patterns. • The use of gene ontology to annotate function. • The use of literature resources to support function prediction. • The processes of combining predictive tools to provide evidenced protein function. • Best practice guidelines and quality assurance (QA; both internal and external).
2	1,2	Take a DNA sequence and use standard bioinformatic tools to locate within a genome, annotate and infer function, including gene prediction, transcription factor (TF) analysis, splice-site boundaries potential for copy number variants (CNVs).	• The genome sequence resources available. • The annotations provided by genome resources. • The different types of DNA sequence in databases – complete genome, cDNA,

			expressed sequenced tags (ESTs), function non-coding sequences. • Tools for DNA sequence alignment, including those for matching large genomic sequences. • Resources for non-coding functional genomic regions (databases of transcription factor binding sites, CNVs etc.) • Resources for alternatively spliced genes. • Tools for exon prediction – sequence based. • Tools for exon prediction – signal based. • Tools for transcription factor (TF) prediction. • The use of literature resources to support function prediction. • The processes of combining predictive tools to provide evidenced protein function. • Best practice guidelines and QA (both internal and external).

3	3	Use three clinical cases to demonstrate the application of bioinformatic tools to common genetic scenarios.	• Application of bioinformatics tools within a clinical genetics service. • Typical care pathways for patients with a genetic disorder. • Tools for single-nucleotide polymorphism (SNP) prediction. • The genome sequence resources available. • Potentials for errors in SNP prediction methods. • Validating SNP predictions.
4	2,3	Identify variation within genetic sequence data captured from various sources.	• Application of bioinformatics tools within a clinical genetics service. • Typical care pathways for patients with a genetic disorder. • Tools for single-nucleotide polymorphism (SNP) prediction. • The genome sequence resources available. • Potentials for errors in SNP prediction methods. • Validating SNP predictions.

5	2	Reconstruct and interpret the relationship between individual sequences using phylogenetic analysis.	• Alignment and clustering algorithms. • Phylogenetic tree building. • How to interpret phylogenetic analysis.
6	3,4,5	Analyse variants using literature and bioinformatic tools or resources to predict consequence and determine significance within patient care.	• The aims and operation of a genetics laboratory service. • The principal referral reasons that would indicate testing for common genetic conditions. • Modes of inheritance. • The clinical and scientific basis for the repertoire of genomic testing available to investigate the common range of clinical referrals. • The reasons for pathogen samples to be sent to hospital or reference microbiology laboratories for sequencing. • The role of bioinformatics and the bioinformatician in supporting the laboratory service in the context of clinical diagnosis, the effect of data and its analysis on patient care. • How to search the literature for information on the consequences of

			variation in genetic loci of the human genome or the pathogens infecting a host. • Correct interpretation of the genetics literature on variation. • Location of resources relating to the consequences of variation including antimicrobial resistance databases. • How to search variation databases for information on variants. • Correct application of interpretation tools. • Correct use of data from databases or interpretation tools. • Collation of data from different sources on variation consequences to infer potential effects on patient care. • The influence of user interfaces on results. • The implications of the genomics investigations (including ethical, legal and social implications) on the patient and patient care.

7	1,2,3,4,5,6	Follow standard protocols or agreed procedures for sequence annotation and analysis.	• How to locate and follow local protocols. • How to identify applicable standard protocols for analysis made available through professional genetics organisations. • How to identify standards within the hospital and public health settings. • Ethical issues associated with patient consent. • Clinical and information technology (IT) governance rules for analysis of patient data.

8	6	Make accurate records of all work carried out.	• The reasons for keeping accurate records. • Minimum data sets for describing the analysis process. • Identify local and national guidelines for record keeping. • Applicable NHS or public health function requirements for record keeping. • Provision of evidence that quality standard operating procedures (SOPs) have been followed. • The location of relevant metadata within bioinformatic resources.

9	4,5,6	Communicate results in a way that is useful to the clinical team, highlighting their findings.	• The information needs of clinical genetics and other healthcare teams. • Local policies for clinical reporting and differences between centres. • Relevance and limitations of data from specific sources to the case(s) of interest. • The operation of laboratory information systems for recording results and generating reports. • The process for generation and validation of clinical reports.

Work-based assessment

Complete 1 Case-Based Discussion(s)	
Complete 1 of the following DOPS and/or OCEs	
Type	**Title**
DOPS	Using available tools take a fragment of DNA sequence and translate into protein sequence, search within a protein database to find matches and determine function
DOPS	Annotate DNA sequence data, and for the longest transcript of the chosen gene identify the exon boundaries.
DOPS	For a given gene, obtain protein sequences and use sequence alignment tools to produce a multiple sequence alignment.
DOPS	Find the population frequency of a variant
DOPS	Given an example of a structural variant, identify the genes and their functions, including CMVs of no clinical significance
OCE	Participate in MDT meetings with other health professionals
OCE	Attend a clinic as an observer and explain your role to the patient