OCR
Oxford Cambridge and RSA

Cambridge **TECHNICALS LEVEL 3**

Cambridge TECHNICALS 2016

APPLIED SCIENCE

A PROJECT APPROACH TO DELIVERY
DEVELOPING A GENOMICS PIPELINE

Version 2

wellcome sanger institute

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CONTENTS

INTRODUCTION

The purpose of this guide is to give you an overview of how you could holistically deliver a range of units from Cambridge Technicals in Applied Science Level 3 (Human Science Pathway) in conjunction with The Wellcome Sanger Institute.

Link to qualification: https://www.ocr.org.uk/qualifications/vocational-education-and-skills/cambridge-technicals-applied-science-level-3-certificate-extended-certificate-foundation-diploma-diploma-extended-diploma-05847-05849-05879-05874--2016-suite/

For the purpose of this guide the intention is for learners to undertake a series of investigative tasks relevant to developing a high throughput genomics pipeline. Genomics pipelines can be developed for a range of different areas, with considerable emphasis on health and monitoring disease.

This project approach has been developed in partnership with The Wellcome Sanger Institute. The Institute was founded to use genome analysis and sequencing to enhance our understanding of biology and disease. Areas of research include cancer, human diseases, and pathogens, drug resistance and gene modification.

Some pipelines can be used for diagnostic purposes, for example identifying mutations in cancer samples or identifying bacteria in the human microbiome. Other pipelines produce biomaterials, such as genome-modification vectors for targeted manipulation of genomes for research purposes. The Sanger Institute is involved in several large-scale projects, producing such resources that are being used by research centres across the world to learn more about the function of specific genes in several organisms, including humans, mice and malarial parasites.

Developing a laboratory procedure into a scalable pipeline poses many challenges, which represent valuable learning opportunities. Setting up a pipeline requires in-depth understanding of the biological concepts behind each step of the procedure as well as skills in information-management and communication, to build and manage a robust industrial process at scale.

Learners will use concepts in biochemistry, genetics and genomics in a number of areas, including:

- DNA structure, the genetic code and protein synthesis.
- DNA sequencing and developing genomics pipelines.
- How DNA sequencing can be used to fight specific diseases, from cancer to malaria, and other infectious diseases.

Learners will examine these areas in work they undertake, understand the different processes and approaches that may be necessary to achieve their research goals, and also look at wider aspects of the work of scientists involved in these fields.

The research areas within this project are not intended to be exhaustive, and when delivering any qualification it is always useful to be able to look at the full range of units in the course and consider areas that are, or could be, linked together, i.e. adopt a holistic approach. A holistic approach will provide you with a structured plan to teach the learners how a range of topics can work together across a number of units, providing them with some understanding of how skills and knowledge link together in a working environment.

When delivering any qualification it is always useful to be able to look at the full range of units selected and consider how they are or could be linked together – a holistic approach.

A holistic approach will provide you with a structured plan to teach the learners how a range of topics work together across a number of units, providing them with some understanding of how skills and knowledge link together in a working environment.

Please note that this Project Approach MUST NOT be used directly for assessment purposes. It is intended to support the teaching and learning of the units specified.

THE WELLCOME SANGER INSTITUTE AND OCR

The Wellcome Sanger Institute at the Wellcome Genome Campus in Cambridgeshire is a world leader in genomics research with a mission to use genome sequences to pioneer new understanding of human and pathogen biology to improve human health.

The Sanger Institute hosts a range of staff with diverse expertise in biology, genetics, medicine, pathology, technology, informatics, computational science, mathematics and statistics. Working together, and with colleagues across the wider Wellcome Genome Campus, this creative community is developing and testing bold ideas and translating them into practical interventions for health and wellbeing.

Genomics is a rapidly expanding field offering many future career opportunities for students studying today. Partnering with OCR on the Cambridge Technical in Applied Science, the Sanger Institute and Wellcome Genome Campus Public Engagement team have committed to developing an extensive range of curriculum relevant activities and resources to support the teaching of modules in the classroom. The activities provide students with an insight into the work carried out the institute and an understanding of the broad range of skills and knowledge necessary to work in this rapidly developing scientific area.

We believe the project approach to learning encourages students to think differently about how to apply their knowledge of science, technology, engineering and maths to "real life" challenges that they are likely to face in the workplace. It offers students a real opportunity to engage in independent thinking and problem solving - key attributes for successful young scientists.

wellcome sanger institute

THIS PROJECT APPROACH ENABLES THE DELIVERY AND FACILITATION OF LEARNING OF THE FOLLOWING UNITS:

Unit		LO	
Unit 1	Science fundamentals	LO1	Understand the chemical structures of elements and compounds
		LO2	Understand reactions in chemical and biological systems
		LO3	Understand cell organisation and structures
		LO4	Understand the principles of carbon chemistry
		LO5	Understand the importance of inorganic chemistry in living systems
		LO6	Understand the structures, properties and uses of materials
Unit 2	Laboratory techniques	LO1	Understand the importance of health and safety and quality systems to industry
		LO2	Be able to separate, identify and quantify the amount of substances present in a mixture
		LO3	Be able to determine the concentration of an acid or base using titration
		LO4	Be able to examine and record features of biological samples
		LO5	Be able to identify cations and anions in samples
		LO6	Be able to use aseptic technique
Unit 3	Scientific analysis and reporting	LO1	Be able to use mathematical techniques to analyse data
		LO2	Be able to use graphical techniques to analyse data
		LO3	Be able to use keys for analysis
		LO4	Be able to analyse and evaluate the quality of data
		LO5	Be able to draw justified conclusions from data
		LO6	Be able to use modified, extended or combined laboratory techniques in analytical procedures
		LO7	Be able to record, report on and review scientific analyses

Unit		LO	
Unit 5	Genetics	LO1	Understand the importance of meiosis
		LO2	Be able to apply techniques used in genetics crosses
		LO3	Understand the techniques of DNA mapping and genomics
		LO4	Understand the impact of an innovation in an application of genomics
Unit 6	Control of hazards in the laboratory	LO1	Understand the types of hazard that may be encountered in a laboratory
		LO2	Be able to use health and safety procedures to minimise the risk presented by hazards in a laboratory
		LO3	Be able to design a safe functioning laboratory to manage the risk presented by hazards
Unit 10	Testing consumer products	LO1	Understand the influence of regulatory bodies on development of consumer products
		LO2	Understand how product testing determines the development of consumer products
		LO3	Be able to use quantitative titration techniques on consumer products
		LO4	Be able to use extraction and separation techniques on consumer products
		LO5	Be able to test the effectiveness of consumer product tests

ABOUT THE MODULES AND ACTIVITIES

The guide is divided into six modules which may be sub-divided or combined according to the teaching time available.

The tables below show where each of the modules in this project provides delivery approaches and learning opportunities to ensure a thorough review of skills and understanding, prior to final assessment and evidencing by the learner.

Please note that should assessment be presented in a similar holistic way, learners must be able to present clearly-mapped evidence for each of the centre-assessed units (Units 5, 6 and 10).

BY UNIT/LEARNING OUTCOME (LO)

	LO1	LO2	LO3	LO4	LO5	LO6	LO7
Unit 1	Module 1 Activity 1	Module 1 Activity 1	Module 1 Activity 1 Module 3 Activity 1 to 4, 6 Module 4 Activity 2 Module 5 Activity 1 to 5	Module 1 Activity 1 to 3 Module 2 Activity 1 to 2 Module 3 Activity 3 Module 5 Activity 1 to 5	Module 3 Activity 5	Module 3 Activity 6	
Unit 2	Module 1 Activity 3 Module 2 Activity 3 to 4 Module 3 Activity 1, 6, 7 Module 4 Activity 2,5 Module 5 Activity 2	Module 1 Activity 2 to 3 Module 2 Activity 1 to 2 Module 3 Activity 4 Module 4 Activity 2 to 4 Module 5 Activity 1 to 5	Module 1 Activity 3	Module 3 Activity 1	Module 3 Activity 5	Module 3 Activity 5	
Unit 3	Module 1 Activity 2 Module 2 Activity 5 Module 4 Activity 5	Module 1 Activity 2 Module 4 Activity 5	Module 3 Activity 2	Module 4 Activity 5 Module 5 Activity 1 to 5	Module 1 Activity 2 Module 4 Activity 5 Module 5 Activity 3 to 4	Module 1 Activity 4 Module 3 Activity 8 Module 4 Activity 1	Reports from all activities

Unit 5	Module 3 Activity 1	Module 3 Activity 8	Module 1 Activity 1 to 3 Module 2 Activity 1 to 4 Module 3 Activity 3, 4 Module 4 Activity 2 Module 5 Activity 1 to 5	Module 1 Activity 1 to 2 Module 3 Activity 3, 4 Module 4 Activity 2 Module 5 Activity 1 to 5			
Unit 6	Module 1 Activity 3 Module 2 Activity 1, 4 Module 3 Activity 1, 5, 6 Module 4 Activity 2, 5 Module 5 Activity 2	Module 1 Activity 3 Module 2 Activity 4 Module 3 Activity 6 Module 4 Activity 2 Module 5 Activity 2	Module 2 Activity 3 to 4 Module 3 Activity 4 to 5				
Unit 10	Module 3 Activity 3, 4, 7	Module 3 Activity 3, 4, 7 Module 4 Activity 5	Module 1 Activity 3 Module 3 Activity 5		Module 4 Activity 5		

BY MODULE

	Unit	LO
Module 1	Unit 1	LO1 Activity 1 LO2 Activity 1 LO3 Activity 1 LO4 Activity 1 to 3
	Unit 2	LO1 Activity 3 LO2 Activity 2 to 3 LO3 Activity 3
	Unit 3	LO1 Activity 2 LO2 Activity 2 LO5 Activity 2 LO6 Activity 4 LO7 Activity 1 to 3
	Unit 5	LO3 Activity 1 to 3 LO4 Activity 1 to 2
	Unit 6	LO1 Activity 3 LO2 Activity 3
	Unit 10	LO3 Activity 3
Module 2	Unit 1	LO4 Activity 1 to 2
	Unit 2	LO1 Activity 3 to 4 LO2 Activity 1 to 2
	Unit 3	LO1 Activity 5 LO7 Activity 1 to 5
	Unit 5	LO3 Activity 1 to 4
	Unit 6	LO1 Activity 1, 4 LO2 Activity 4 LO3 Activity 3 to 4

	Unit	LO
Module 3	Unit 1	LO3 Activity 1 to 4, 6 LO4 Activity 3 LO5 Activity 5 LO6 Activity 6
	Unit 2	LO1 Activity 1, 6, 7 LO2 Activity 4 LO4 Activity 6
	Unit 3	LO3 Activity 2 LO6 Activity 8 LO7 Activity 1 to 5
	Unit 5	LO1 Activity 1 LO2 Activity 8 LO3 Activity 3, 4 LO4 Activity 3, 4
	Unit 6	LO1 Activity 1, 5, 6 LO2 Activity 6 LO3 Activity 4 to 5
	Unit 10	LO1 Activity 3, 4, 7 LO2 Activity 3, 4, 7 LO3 Activity 5
Module 4	Unit 1	LO3 Activity 2
	Unit 2	LO1 Activity 2, 5 LO2 Activity 2 to 4
	Unit 3	LO1 Activity 5 LO2 Activity 5 LO4 Activity 5 LO5 Activity 5 LO6 Activity 1 LO7 Activity 2 to 5
	Unit 5	LO3 Activity 3 LO4 Activity 3
	Unit 6	LO1 Activity 2, 5 LO2 Activity 2
	Unit 10	LO2 Activity 5 LO5 Activity 5
Module 5	Unit 1	LO3 Activity 1 to 5 LO4 Activity 1 to 5
	Unit 2	LO1 Activity 2 LO2 Activity 1 to 5
	Unit 3	LO4 Activity 1 to 5 LO5 Activity 3 to 4 LO7 Activity 1 to 5
	Unit 5	LO3 Activity 1 to 5 LO4 Activity 1 to 5
	Unit 6	LO1 Activity 2 LO2 Activity 2
Module 6	Unit 3	LO7 Activity 1

The intention is that the learners will be taught a range of knowledge and skills within each of the units and then carry out relevant review activities at various stages. Each of the review activities (once successfully completed by the learner) will provide all the required underpinning knowledge for their final assessment.

The practice review activities within the modules must not be used for final assessment purposes of Cambridge Technicals in Applied Science Level 3.

Model assignments for each of the mandatory centre-assessed units (Units 4, 5, 6, 7, 8, 10, 13, 14, 16, 17 and 18, 21 for Cambridge Technicals in Applied Science Level 3 units or can be found at http://www.ocr.org.uk/qualifications/vocational-education-and-skills/cambridge-technicals-laboratory-skills-level-3-introductory-diploma-diploma-05847-05849-2016-suite/

It is assumed that the learners will be given the opportunity to carry out activities that will enable them to practice the skills they have learned within each module prior to being given final assessment activities.

When considering a holistic approach to delivery and learning it is important to consider the overall objectives. In this guide the objectives are to:

- Deliver six units of Cambridge Technicals in Applied Science Level 3.
- Structure a programme of learning and reviews which is exciting and engaging for learners.
- Provide learners with an overview of how the knowledge and skills gained in one unit, support the knowledge and skills used within other units
- Provides the learners with an opportunity to consider how they would use their social and communication skills holistically within the working environment.

ASSESSMENT OF UNITS

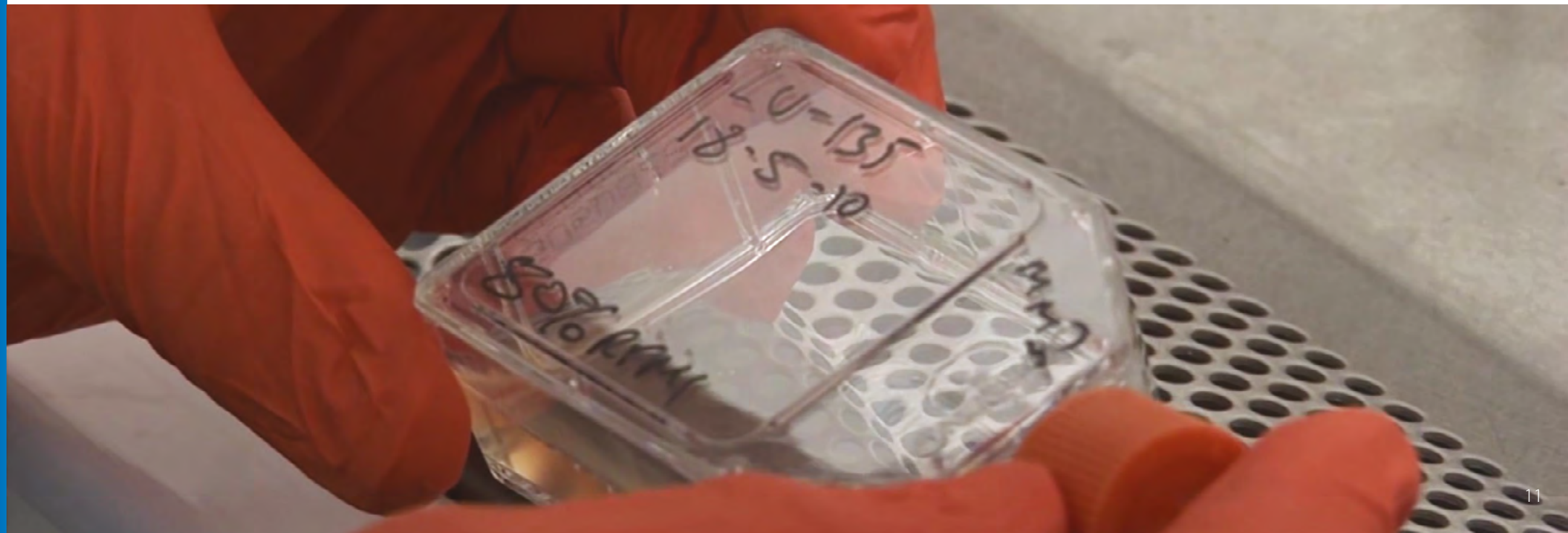
The table below shows how each unit is assessment

Completion of the modules does not guarantee all criteria have been met; this is entirely dependent on the quality of the evidence produced.

This Project Approach should be read in conjunction with the published grading criteria in the unit documents.

Methods of assessment

Unit No	Unit title	How are they assessed?
Unit 1	Science fundamentals	External = OCR set and marked exam
Unit 2	Laboratory techniques	External = OCR set and marked exam
Unit 3	Scientific analysis and reporting	External = OCR set and marked exam
Unit 5	Genetics	Internal = Centre assessed and moderated by OCR
Unit 6	Control of hazards in the laboratory	Internal = Centre assessed and moderated by OCR
Unit 10	Testing consumer products	Internal = Centre assessed and moderated by OCR



THE PROJECT BRIEF

The learner version of the Project Brief is available from http://www.ocr.org.uk/qualifications/vocational-education-and-skills/cambridge-technicals-laboratory-skills-level-3-introductorydiploma-diploma-05847-05849-2016-suite/

THE WELLCOME SANGER INSTITUTE

The Wellcome Sanger Institute is one of the premier centres of genomic discovery and understanding in the world. It was founded to sequence the first human genome. The research to improve understanding of biology and disease developed later, when sequencing became more common. The Wellcome Sanger Institute currently leads ambitious collaborations across the globe to provide the foundations for further research and transformative healthcare innovations. With its work in the field of genomics, the Institute seeks to deliver diagnostic and therapeutic benefits in areas such as cancer, immunology, public health and personalised treatment.

Building and running industrial-scale pipelines for DNA sequencing and computational analysis has been fundamental to operations from the very beginning and constitutes a core expertise around which many of today's research programmes are built. Developing a successful pipeline at scale involves much more than performing a lab procedure repetitively. There are unique challenges in building robust systems, organising the work in teams of scientists and technicians and managing data and data analysis.

You are to undertake an investigation into the background to, and some of the activities involved in or related to areas of research at the Wellcome Sanger Institute.

The investigation will involve you:

- Demonstrating an understanding of cell division, Mendelian genetics, the biochemistry of DNA and protein synthesis.
- Explaining the process of DNA sequencing and how it can be applied.
- Producing a process map for a DNA sequencing pipeline and a method within the pipeline, incorporating feedback loops and tracking procedures to exercise quality control.
- Assessing and managing risk in the laboratory and producing a Risk Assessment.
- Designing the laboratory space so that the pipeline, or part of it, can be carried out.
- Following a protocol for one stage in the pipeline.
- Making up and standardising solutions.
- Understanding how DNA sequencing can be used in the fields of cancer and malaria research and the role that microorganisms play in our everyday lives.
- Culturing cells and organisms.
- Investigating scientific, legal, e.g. Material Transfer Agreements – MTAs – and ethical issues with the transfer of vectors and plasmids.

Some aspects of this work can be undertaken as an individual or in a team. If working within a team, learners are expected to contribute to each of the areas (and be able to provide evidence of this contribution) in order to gain the experience and knowledge required to successfully complete the Cambridge Technicals Level 3 (Applied Science) units.

The challenges posed by the activities vary in levels of difficulty and complexity. In most instances, LOs are addressed several times by activities (see pages 7 to 10), so tutors can be selective in terms of those chosen.

MODULE 1

THE STRUCTURE OF DNA

Link to qualification:
https://www.ocr.org.uk/qualifications/vocational-education-and-skills/cambridge-technicals-applied-science-level-3-certificate-extended-certificate-foundation-diploma-diploma-extended-diploma-05847-05849-05879-05874-2016-suite/

Before learners can develop a laboratory pipeline, they first need to have a good understanding of:

- DNA and the genetic code
- The principles of DNA sequencing, including recent changes in sequencing technology and how it affects the scale of genomic research
- The different ways in which DNA sequencing can be carried out, eg targeted sequencing or whole genome sequencing.

Tutors need to ensure that learners are familiar with the technique of electrophoresis, and understand the principles of the Polymerase Chain Reaction (PCR), and could carry out practical work based on DNA extraction, PCR and DNA analysis.

Contained within the following assessment criteria/units/LOs:

Learning Outcome	LO number	Unit number
Understand the chemical structures of elements and compounds	LO1	Unit 1
Understand reactions in chemical and biological systems.	LO2	Unit 1
Understand cell organisation and structures	LO3	Unit 1
Understand the principles of carbon chemistry	LO4	Unit 1
Understand the importance of health and safety and quality systems to industry	LO1	Unit 2
Be able to separate, identify and quantify the amount of substances present in a mixture	LO2	Unit 2
Be able to determine the concentration of an acid or base using titration	LO3	Unit 2
Be able to use mathematical techniques to analyse data	LO1	Unit 3
Be able to use graphical techniques to analyse data	LO2	Unit 3
Be able to draw justified conclusions from data	LO5	Unit 3
Be able to use modified, extended or combined laboratory techniques in analytical procedures	LO6	Unit 3
Be able to record, report on and review scientific analyses	LO7	Unit 3
Understand the techniques of DNA mapping and genomics	LO3	Unit 5
Understand the impact of an innovation in an application of genomics	LO4	Unit 5
Understand the types of hazard that may be encountered in a laboratory	LO1	Unit 6
Be able to use health and safety procedures to minimise the risk presented by hazards in a laboratory	LO2	Unit 6
Be able to use quantitative titration techniques on consumer products	LO3	Unit 10

During the delivery of the units, the learners should carry out a range of activities to demonstrate and check their knowledge and understanding. They should also undertake review activities as they work through the programme of learning.

PRACTICE REVIEW ACTIVITIES FOR MODULE 1

ACTIVITY 1: DNA AND THE GENETIC CODE

Learners could begin by describing:

- The structure of DNA in detail.
- The discovery and the elucidation of its structure; see, for instance, http://www.yourgenome.org/stories/the-discovery-of-dna and http://www.yourgenome.org/stories/unravelling-the-double-helix, webpages on Francis Crick, http://www.yourgenome.org/stories/giants-in-genomics-francis-crick and James Watson, http://www.yourgenome.org/stories/giants-in-genomics-james-watson, and similar pages on Rosalind Franklin, http://www.yourgenome.org/stories/giants-in-genomics-rosalind-franklin and Maurice Wilkins, http://www.yourgenome.org/stories/giants-in-genomics-maurice-wilkins. They could discuss the importance of X-ray crystallography in determining the helical structure of the DNA molecule.
- Learners could also extend their research to the subsequent work of Francis Crick, Sydney Brenner and other workers in deciphering the genetic code. See https://profiles.nlm.nih.gov/ps/retrieve/Narrative/SC/p-nid/144 and http://scarc.library.oregonstate.edu/coll/pauling/dna/materials/index.html. Learners could describe in detail how the genetic code works in the synthesis of proteins. They could include the stages in protein synthesis, the nature of the peptide bond, and how the conformation of the resultant protein is dependent on the constituent amino acids.

Learners could demonstrate an understanding of heredity and how the DNA code determines the characteristics of individuals. Learners could then go on to investigate the nature of the human genome and how scientists' ideas of the nature of this have changed. An introduction to the structure of the genome can be found at yourgenome http://www.yourgenome.org/facts/what-is-a-genome.

ACTIVITY 2: THE PRINCIPLES OF DNA SEQUENCING

DNA sequencing has come a long way since it was first invented the 1970s, through automated capillary electrophoresis sequencing in the 1980s, the 'first generation' instruments that were involved in the Human Genome Project, to the introduction of next-generation sequencing (NGS) in the mid-2000s, which has completely transformed the way in which scientists work with genomes. This last transition is key, as it has enabled the comparison of large number of either human or pathogen genomes, laying the foundation for personalised genomic medicine and many of the research topics to be studied here.

While the first complete sequence of a human genome took more than a decade to produce, the latest technology can deliver a whole genome in a day. Whole population genomics are now possible, and the foundations have been laid for personalised genomic medicine.

Learners could:

- Produce a timeline to illustrate the evolution of DNA sequencing.
- Describe numerically how the data output has changed and compare this with Moore's Law.
- Describe numerically and discuss how the cost of sequencing has changed.

Learners could discuss the implications of these changes.

Learners could then look in more detail on the changes in technology and produce a report. An introduction to the history of genomics can be found at http://www.yourgenome.org/facts/timeline-history-of-genomics. Next Generation Sequencing (NGS) platforms offer a wide variety of applications, including DNA sequencing, RNA sequencing and transcriptomics (see http://www.nature.com/subjects/transcriptomics for a definition and latest news), that allow the assessment of different problems. Increasingly, these are being targeted to single cells. Downstream applications include sequencing DNA to trace evolution, identifying variation between individuals, and examining gene structure and regulation.

Additional information on techniques can be found at http://www.yourgenome.org/facts/what-is-the-illumina-method-of-dna-sequencing, which gives an excellent summary of the Illumina method of DNA sequencing. The resources http://www.illumina.com/technology/next-generation-sequencing.html and http://www.illumina.com/content/dam/illumina-marketing/documents/products/illumina_sequencing_introduction.pdf provide detail at a higher level.

Leaners could compare the underlying principles behind the current technologies as well as upcoming devices such as the nanopore long-read sequencing – https://nanoporetech.com/applications/dna-nanopore-sequencing.

PRACTICE REVIEW ACTIVITIES FOR MODULE 1

ACTIVITY 3: DNA EXTRACTION, PCR (POLYMERASE CHAIN REACTION) AMPLIFICATION AND ELECTROPHORESIS

Learners could extract DNA from their hair follicles or cheek cells, and the use PCR amplification and electrophoresis to fingerprint their own DNA at a specific locus. A suitable protocol for use at this level can be found on the BioRad website – http://www.bio-rad.com/en-uk/product/pv92-pcr-informatics-kit?pcp_loc=catprod (this technique investigates the Alu element – a short, interspersed repeat – at one specific location – the PV92 locus – on Chromosome 16). An alternative is the amplification of the 221-nucleotide region of the phenylthiocarbamide (PTC) taste receptor gene. Learners could begin with a tasting activity – adapt the activity at https://www.genome.gov/pages/education/modules/ptctastetestactivity.pdf – followed by DNA extraction, PCR amplification and electrophoresis. See http://www.carolina.com/pcr-kits/ptc-extraction-amplification-and-electrophoresis-kit-with-carolinablu-and-05-ml-tubes-with-perishables/211380P.pr, https://fog.ccsf.edu/~cpogge/Lab/12_PTC.pdf and http://bioinformatics.dnalc.org/ptc/animation/pdf/ptc.pdf.

Alternatively, extractions of DNA can be carried out using plant material. If using human cells, Centres are advised that appropriate protocols should be used/appropriate loci are used that do not have ethical implications in terms of underlying medical conditions or investigations carried out on siblings.

The protocols and accompanying kits detail techniques, along with providing reagents at appropriate concentrations. Learners could investigate alternative extraction techniques, e.g. by carrying out an extraction of DNA using an simple salting out technique, for instance, Miller, Dykes and Polesky (1988) – A simple salting out procedure for extracting DNA from human nucleated cells https://www.ncbi.nlm.nih.gov/pmc/articles/PMC334765/pdf/nar00145-0424.pdf or on the Access Excellence website – http://www.accessexcellence.org/AE/AEC/AEF/1994/dollard_onionDNA.html.

Learners could also be conversant with how reagents could be prepared and standardised.

Extraction techniques might use TE buffer (Tris-HCl buffer; Ethylenediaminetetraacetic acid [EDTA]), sodium dodecyl sulfate (SDS), protease K solution and sodium chloride solution.

Learners could:

- Prepare and standardise the EDTA solution concentration: (1 mmol dm_{-3}) by titration.
- Prepare the Tris-HCl buffer concentration: (10 mmol dm_{-3}, pH 8.0) using a pH meter they have calibrated.
- Make up the SDS e.g. 0.5 % and sodium chloride (saturated) solutions.
- Prepare dilutions of the enzyme solutions according to requirements.

Learners could extract and compare qualitatively DNA from a number of sources.

Learners should carry out a Risk Assessment before undertaking any practical work.

MODULE 2

A GENOMICS WORKFLOW

Link to qualification: https://www.ocr.org.uk/qualifications/vocational-education-and-skills/cambridge-technicals-applied-science-level-3-certificate-extended-certificate-foundation-diploma-diploma-extended-diploma-05847-05849-05879-05874-2016-suite/

This module synthesises knowledge, understanding and skills across a range of units, but focused on Units 2 (LO2) and Unit 5 (LO3 and LO4).

The Wellcome Sanger Institute receives DNA samples for sequencing from across the world. The Institute has one of the largest sequencing facilities in the world, and is currently capable of producing 1700 terabases (1700 × 1012 base pairs) of DNA sequence per year. Its next generation sequencing capacity currently consists of Illumina HiSeqs as well as a set of HiSeq X machines ('X Ten'), Illumina MiSeqs and two Pacific Biosciences machines. For large-scale genotyping, there are Illumina iScan machines and three Agina mass spectrometers.

Before learners can begin their work on a genomics workflow, they first need to have a good understanding of:

- The structure of DNA.
- The separation of fragments of DNA by electrophoresis.
- The principles of DNA sequencing (comparisons should be made between NGS technologies – see http://www.yourgenome.org/stories/next-generation-sequencing – which do not rely on electrophoresis, and Sanger (dideoxynucleotide) sequencing, which does – see http://www.yourgenome.org/video/sanger-dna-sequencing). See also https://www.gatc-biotech.com/en/expertise/sanger-sequencing.html, https://www.thermofisher.com/uk/en/home/life-science/sequencing/sanger-sequencing/sanger_sequencing_method.html and https://www.thermofisher.com/uk/en/home/life-science/sequencing/sanger-sequencing/next-generation-sequencing-validation.html.
- Health and Safety procedures.
- The use of analytical techniques.

They will apply this knowledge, understanding and skills to develop a genomics workflow.

Contained within the following assessment criteria/LO(s)/units:

Learning Outcome	LO number	Unit number
Understand the principles of carbon chemistry	LO4	Unit 1
Understand the importance of health and safety and quality systems to industry	LO1	Unit 2
Be able to separate, identify and quantify the amount of substances present in a mixture	LO2	Unit 2
Be able to use mathematical techniques to analyse data	LO1	Unit 3
Be able to record, report on and review scientific analyses	LO7	Unit 3
Understand the techniques of DNA mapping and genomics	LO3	Unit 5
Understand the impact of an innovation in an application of genomics	LO4	Unit 5
Understand the types of hazard that may be encountered in a laboratory	LO1	Unit 6
Be able to use health and safety procedures to minimise the risk presented by hazards in a laboratory	LO2	Unit 6
Be able to design a safe functioning laboratory to manage the risk presented by hazards	LO3	Unit 6

During the delivery of the units, the learners should carry out a range of activities to demonstrate and check their knowledge and understanding. They should also undertake review activities as they work through the programme of learning.

PRACTICE REVIEW ACTIVITIES FOR MODULE 2

ACTIVITY 1: EXTRACTION OF DNA

The Wellcome Sanger Institute receives DNA samples from all over the world for analysis. The DNA must be suitable for analysis – in quantity and quality – it must not be degraded and should be isolated from other cellular components e.g. protein

The sample management pipeline registers and processes more than 240 000 samples per year. The team isolates DNA and RNA from biological materials e.g. blood, formats the samples for downstream processes such as next generation sequencing.

Learners could review and evaluate:

- The rationale for, and means of registration of samples, and the types of data that should, or should not, be recorded (consider ethical issues).
- Procedures for the extraction of the DNA and RNA, in terms of the techniques available and principles. Learners should limit their evaluation to one or two extraction techniques. They could also discuss preserving the integrity of the samples and avoiding contamination.

PRACTICE REVIEW ACTIVITIES FOR MODULE 2

ACTIVITY 2

Fundamental to NGS is the preparation of the nucleic acid sample, RNA or DNA, into a form that is compatible with the sequencing system to be used. This process is called library construction.

The process that the Wellcome Sanger Institute would carry out for Illumina sequencing is typically, in outline:

- DNA library construction – the DNA is broken into fragments, ligating specialised adapters to both fragment ends. The ligated fragments are amplified. Learners could also review how library construction differs between DNA and RNA.
- Cluster amplification – the library is loaded into a flow cell. The fragments hybridise to the flow cell surface. Each bound fragment is amplified into a clonal cluster through a technique called bridge amplification.
- Sequencing – fluorescently-labelled nucleotides are added. The first base becomes incorporated. The flow cell is imaged and the emission from each cluster recorded. The base is identified and the process is repeated according to the number of bases.
- Analysis – the reads are aligned to a reference sequence with computer software, for instance to identify mutations in coding sequences in cancer samples.

A simple illustration of the process:

The Wellcome Genome Campus Public Engagement website, www.yourgenome.org, provides suitable information at

http://www.yourgenome.org/video/sequencing-at-speed.
More detail can be found at https://www.youtube.com/watch?v=HMyCqWhwB8E and https://www.youtube.com/watch?v=fCd6B5HRaZ8, The following documents are also helpful: http://www.illumina.com/content/dam/illumina-marketing/documents/products/illumina_sequencing_introduction.pdf and http://www.biotechniques.com/BiotechniquesJournal/2014/February/Library-construction-for-next-generation-sequencing-Overviews-and-challenges/biotechniques-349889.html.

Learners could research these stages and construct a genomics pipeline. The pipeline should incorporate appropriate feedback loops intended as quality control steps.

The Wellcome Sanger Institute has produced a short behind the scenes video to help support this module.

www.yourgenome.org/video/life-in-the-lab-a-dna-sequencing-pipeline

PRACTICE REVIEW ACTIVITIES FOR MODULE 2

ACTIVITY 3: DESIGNING A WORKSPACE

Learners could suggest a layout for the laboratory, or laboratories required, from their genomics pipeline. They should include measures designed to preclude or minimise contamination of the samples and also pay close attention to Health and Safety.

Learners could go on to design a workstation within one of the laboratories/the laboratory for a specific stage of the process e.g. library construction.

Some information on laboratory design is at:

- https://www.ase.org.uk/documents/lab-design-designing-and-planning-laboratories/designing-and-planning-laboratories.pdf (the information is targeted at schools and colleges, but it is a useful starting point)
- http://www.nerc.ac.uk/about/policy/safety/procedures/guidance-laboratories/.

The Lab Manager website is also helpful – http://www.labmanager.com/laboratory-technology/2010/11/five-common-mistakes-in-lab-labeling?fw1pk=1#.V3uwo7grL4Y/rd/yes/ – although it approaches the topic of labelling samples using a 'mistakes' approach.

An effective sample tracking system must also be in place, e.g. a LIMS (Laboratory Information Management System), or tracking managed using proformas or tracking sheets. Learners could consider the key feature of an appropriate system. An introduction to LIMS can be found at https://en.wikipedia.org/wiki/Laboratory_information_management_system.

This will be a challenging activity for learners. The Wellcome Sanger Institute is producing a video to help support this module.

www.yourgenome.org/video/life-in-the-lab-a-dna-sequencing-pipeline

PRACTICE REVIEW ACTIVITIES FOR MODULE 2

ACTIVITY 4: HEALTH AND SAFETY PROCEDURES

Genomics pipelines involve comparatively safe procedures. However, learners should be conversant with Health and Safety procedures, including the development of a Risk Assessment.

Learners should design a Risk Assessment proforma or use an existing industry protocol. They could prepare an example Risk Assessment for a stage of the procedure.

An example could be for selected reagents/components in the DNA fragmentation process, to include:

- TE buffer.
- Nuclease-free water.
- AMPure XP beads (contain sodium azide).
- 70% ethanol.

ACTIVITY 5: QUANTIFYING THE DNA AND DNA FRAGMENTS

This activity provides the opportunity to put into perspective the quantities of DNA scientists have to deal with, and for learners to demonstrate their understanding of DNA structure and sequencing and apply some maths.

Learners could make appropriate calculations based on genomics pipelines, for instance:

- The concentration of DNA in a sample prepared for fragmentation.
- Numbers of copies of a genome in the sample.
- Following fragmentation of the DNA, the number of fragments in their sample.

These calculations could be based on the following data. Typically:

- The mass of the human genome in diploid cell is 6 pg.
- The length of a diploid genome is 6×10^9 base pairs (bp).
- Samples for fragmentation contain 500 ng DNA made up to 120 µl with buffer.
- Following fragmentation, the average length of a fragment is 150 bp.

MODULE 3

COMBATTING MALARIA

Link to qualification: https://www.ocr.org.uk/qualifications/vocational-education-and-skills/cambridge-technicals-applied-science-level-3-certificate-extended-certificate-foundation-diploma-diploma-extended-diploma-05847-05849-05879-05874-2016-suite/

The delivery develops and synthesises knowledge, understanding and skills from Unit 5: Genetics (LOs 1 to 4), Unit 1 (LO3 and LO4) Unit 2 (LO1 and LO4).

The number of cases of malaria was estimated at 214 million in 2015, resulting in 438 000 deaths. These numbers are falling, but in 2015, 3.2 billion people – almost half the world's population – remain at risk.

Malaria is transmitted by around 200 species of a protist called *Plasmodium*, which can infect many animal species, including other mammals, birds and reptiles. All species of malarial parasites have a mosquito vector that transmits the parasite from one host to the next.

Plasmodium species are dependent on different mosquito species for transmission. *Anopheles gambiae*, for instance, is one of the vectors of *Plasmodium falciparum*, one of the species that causes malaria in humans.

The species of malarial parasite that infect humans spend part of their life cycles in humans, and part in the mosquito.

Before learners begin, they need to have a good understanding of:

- Groups of microorganisms.
- The role of microorganisms in causing of disease.
- The role of vectors in disease.
- The anatomy and life cycle of insects.
- The life cycle of parasites, particularly malaria.
- The blood system and liver.

Some familiarity with malaria as a disease would be desirable

MODULE 3

Contained within the following assessment criteria/LO(s)/units:

Learning Outcome	LO number	Unit number
Understand cell organisation and structures	LO3	Unit 1
Understand the principles of carbon chemistry	LO4	Unit 1
Understand the importance of inorganic chemistry in living systems	LO5	Unit 1
Understand the structures, properties and uses of materials	LO6	Unit 1
Understand the importance of health and safety and quality systems to industry	LO1	Unit 2
Be able to separate, identify and quantify the amount of substances present in a mixture	LO2	Unit 2
Be able to examine and record features of biological samples	LO4	Unit 2
Be able to identify cations and anions in samples	LO5	Unit 2
Be able to use aseptic technique	LO6	Unit 2
Be able to use keys for analysis	LO3	Unit 3
Be able to use modified, extended or combined laboratory techniques in analytical procedures	LO6	Unit 3
Be able to record, report on and review scientific analyses	LO7	Unit 3
Understand the importance of meiosis	LO6	Unit 5
Be able to apply techniques used in genetics crosses	LO7	Unit 5
Understand the techniques of DNA mapping and genomics	LO3	Unit 5
Understand the impact of an innovation in an application of genomics	LO4	Unit 5
Understand the types of hazard that may be encountered in a laboratory	LO1	Unit 6
Be able to use health and safety procedures to minimise the risk presented by hazards in a laboratory	LO2	Unit 6
Be able to design a safe functioning laboratory to manage the risk presented by hazards	LO3	Unit 6
Understand the influence of regulatory bodies on development of consumer products	LO1	Unit 10
Understand how product testing determines the development of consumer products	LO2	Unit 10
Be able to use quantitative titration techniques on consumer products	LO3	Unit 10

This module also provides opportunities to address aspects of Unit 8: Cell Biology (LO2), and Unit 18: Microbiology (LO1).

During the delivery of the units, the learners should carry out a range of activities to demonstrate and check their knowledge and understanding. They should also undertake review activities as they work through the programme of learning.

PRACTICE REVIEW ACTIVITIES FOR MODULE 3

ACTIVITY 1: THE NATURE OF THE DISEASE

There are five species of *Plasmodium* that cause malaria in humans, with two – *P. falciparum* and *P. vivax* – causing most cases. Learners could consider the prevalence and relative importance of these. See http://www.yourgenome.org/video/malaria-an-introduction.

Learners could access the World health Organization (WHO) website - http://www.who.int/mediacentre/factsheets/fs094/en/ - to obtain an overview of the disease and its current status.

Learners could then research and describe the life cycle of *Plasmodium spp*. They should describe the different forms of the parasite and the involvement of mitotic and meiotic divisions, and discuss the adaptations and possible selective advantages of asexual and sexual phases in the life cycle. The Malaria Challenge resource will help learners with this – http://www.yourgenome.org/interactives/malaria-challenge.

Learners will be unable to culture and observe live *Plasmodium spp*., but could examine prepared slides of different stages of the malaria parasite and could produce blood smears stained, for instance, with Giemsa stain. Centres should refer to their internal Health and Safety policy or local authority policy before working with blood.

For the staining procedure using Giemsa stain, one suitable resource is

https://www.beiresources.org/portals/2/MR4/Methods_In_Malaria_Research-6th_edition.pdf. Learners could prepare their own stain, which would give them the opportunity to prepare standard solutions, including phosphate buffer at pH 7.1 (which could involve learners making up solutions and calibrating pH meters).

Learners could try identifying the different stages of the parasites in the prepared blood smears. Learners could also estimate the percentage of infected erythrocytes in prepared slides, using oil immersion microscopy. They could record detailed images drawn or reproduced digitally with magnification and/or scale clearly indicated.

Learners should carry out a Risk Assessment before undertaking any practical work.

This activity provides the background to Activity 3, which considers areas where human intervention could best effect control.

PRACTICE REVIEW ACTIVITIES FOR MODULE 3

ACTIVITY 2: IDENTIFICATION OF MOSQUITOES

There are approximately 3500 species of mosquitoes, grouped into 41 genera. Human malaria is transmitted only by females of the genus *Anopheles*. Of the approximately 430 *Anopheles* species, only 30-40 transmit malarial parasites in nature. Several genera of mosquitoes are involved in the transmission of other human diseases, e.g. *Aedes aegypti* and other species for dengue fever, Zika fever, yellow fever and chikungunya; *Culex spp*. for West Nile fever. Several mosquito vectors are involved in the transmission of different types of encephalitis.

Learners could construct and/or use simple keys for mosquito identification, either for:

- different species of *Anopheles*, see https://www.cdc.gov/malaria/about/biology/mosquitoes/, http://www.cdc.gov/nceh/ehs/Docs/Pictorial_Keys/Mosquitoes.pdf for guidance or
- different genera; see - https://www.cdc.gov/nceh/ehs/docs/pictorial_keys/mosquitoes.pdf.

The latter document contains some keys, and learners could work on producing simplified versions. The University of Texas at El Paso Biodiversity Collections website provides a very good starting point for the identification of mosquito imagoes and larvae - https://www.utep.edu/LEB/mosquito/index.htm.

The website http://vectormap.si.edu/Mosquito_Keys.htm and http://www.tm.mahidol.ac.th/seameo/journal_37_2_2006_spp.html provide links to websites with detailed information on mosquitoes, including anatomical diagrams, along with some keys.

ACTIVITY 3: CONTROLLING MALARIA

Learners should evaluate current and past control measures for the disease, which involve both prevention and treatment of the condition.

The yourgenome website has an activity – Malaria Challenge: Managing Malaria – where learners have to plan a control programme for different countries with different challenges – http://www.yourgenome.org/activities/malaria-challenge-managing-malaria.

Learners should evaluate the methods of **prevention** of malaria (in terms of efficacy and organisms developing resistance; effectiveness in different countries; **control measures**, including the regulatory bodies involved and how assessment of safety might change over time), including:

- Appropriate clothing, insect repellents and insecticide-treated mosquito nets.
- Vector control, using and indoor spraying with insecticides; wider vector control including drainage of bodies of water.
- Prophylaxis using antimalarials to control the parasite, if infected, including drugs such as atovaquone with proguanil (Malarone®), chloroquine, doxycycline, mefloquine (Lariam®), sulfadoxine-pyrimethamine (SP), e.g. Fansidar®.
- Development of vaccines.
- Genomic methods of control.

Learners should evaluate the various preventative measures of malaria and discuss their development.

Learners could evaluate the current treatments available, including quinine, chloroquine, SP and artemisinin-based combination therapy (ACT), and discuss the evolution of antimalarial drug resistance and the development of future treatments.

Learners could review the current status of ACT. A number of websites is available, including http://www.malariaconsortium.org/pages/112.htm, http://www.wwarn.org/about-us/malaria-drug-resistance, http://malariajournal.biomedcentral.com/articles/10.1186/1475-2875-13-452, http://malariajournal.biomedcentral.com/articles/10.1186/1475-2875-13-S1-P87, with updates on the World Health Organization (WHO) website, e.g. http://www.who.int/malaria/publications/atoz/update-artemisinin-resistance-jan2014/en/, and in other sources, including the Malaria Journal, http://malariajournal.biomedcentral.com/.

Learners could evaluate responses on a national through to international level, including a consideration of the WHO Global Technical Strategy for Malaria 2016-2030, adopted by the World Health Assembly in May 2015 to provide a technical framework for all malaria-endemic countries. See http://www.who.int/malaria/areas/global_technical_strategy/en/.

Key interventions reduce malaria transmission and burden. Transmission depends on a number of factors – see http://www.ivcc.com/who-malaria-fact-sheet for an introduction-learners could discuss these, and also investigate mathematical models used to discuss the effects of malaria transmission and burden. See, for example, http://www.thelancet.com/pdfs/journals/laninf/PIIS1473-3099(15)00423-5.pdf.

Learners could define the term eradication and evaluate malaria eradication programmes. They might review these historically, see, for instance, https://www.cdc.gov/malaria/about/history/#mcwa, http://www.who.int/bulletin/volumes/86/2/07-050633/en/, http://www.malariaeradication.org/#block-views-front-page-promo-block, www.malariaeradication.org/download/file/fid/580, http://www.makingmalariahistory.org/eliminate-malaria/elimination-approaches/.

PRACTICE REVIEW ACTIVITIES FOR MODULE 3

ACTIVITY 4: A GENOMIC APPROACH TO CONTROL – *PLASMODIUM* GENETIC MODIFICATION

The numbers of deaths caused by malaria, along with the lack of clinically-approved vaccines and the reliance on a limited number of anti-malarial drugs, makes it critical to develop new approaches to malaria control. The use of genomic methods forms part of these approaches.

Learners may be familiar with genetic manipulation of organisms through recombinant DNA technology from earlier studies. They could research the ways in which plasmid vectors are used in the case of a communicable or non-communicable disease.

An introduction to plasmid vectors can be found at https://en.wikipedia.org/wiki/Vector_%28molecular_biology%29 and https://highered.mheducation.com/sites/9834092339/student_view0/chapter17/construction_of_a_plasmid_vector.html.

The Plasmodium Genetic Modification (PlasmoGEM) Project distributes free tools for the manipulation of the malarial parasites for research purposes. PlasmoGEM currently has a genomic library covering over 90 % of the genes of *Plasmodium berghei*, a malarial parasite of rodents, and over 2600 gene-targeting vectors.

Learners could:

- Discuss and suggest how a genomic approach is/could be used in the fight against malaria.
- Describe how the construction of vectors to modify the genome of Plasmodium has presented major technical hurdles. See, for instance, https://malariajournal.biomedcentral.com/articles/10.1186/1475-2875-12-373
- Research the current molecular biology techniques involved, including enzymatic restriction, ligation, the Gateway Strategy® and Gibson assembly.
- Describe a vector production pipeline for PlasmoGEM gene targeting vectors; see http://plasmogem.sanger.ac.uk/info/vectors, and illustrated in https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4362957/.
- Discuss the support of the vector production pipeline by a customised software suite in automating both the vector design process and quality control of the sequencing of the finished vectors.
- Discuss the use of molecular biology techniques involved in vector quality control.
- Explore aspects of cost-effectiveness, including issues in the trade-off between time, and the money investment involved in completing vectors.

Learners could review the production process of vectors and suggest ways in which the project could be extended, and future goals.

The Wellcome Sanger Institute has produced a video to help support this module.

www.yourgenome.org/video/life-in-the-lab-a-malaria-genome-modification-pipeline

This activity also provides learners with an opportunity to investigate and report on legal issues concerning material transfer, e.g. in the setting up of material transfer agreements (MTAs). The Association of Research managers and Administrators (ARMA) provides some information. https://arma.ac.uk/brunswick-agreements/

Learners could also investigate the nature of MTAs from different research institutions. Another issue that learners could research is the regulations applying to the transport and receipt of mail containing DNA samples within/to/from different countries.

PRACTICE REVIEW ACTIVITIES FOR MODULE 3

ACTIVITY 5: CULTURING THE *PLASMODIUM* PARASITE AND *ANOPHELES* MOSQUITO

Culture of *Plasmodium spp*. is complicated because of alternation of the parasite between mosquito and host – human, or another organism, such as a mouse in the case of *P. berghei*. A supply of *Anopheles gambiae* mosquitoes infected with the malarial parasite involves the propagation of parasite and vector life cycles in parallel. There must be a consistent supply of infected mosquitoes for the purposes of research.

The production of different sexual stages of *Plasmodium* and their isolation from infected mosquitoes requires a number of scientific techniques, including the procedures needed to:

- Rear mosquitoes – handling the mosquitoes; housing, feeding; temperature and humidity; egg laying; larval development; dissection techniques to isolate parasites, where appropriate.
- Culture the parasites – in-vitro culture, and in-vivo culture in rodents; nutrient composition (organic and inorganic components) of media for in-vitro culture. Learners could explain the composition of the media used.
- Synchronise the life cycles to generate sufficient parasites for research.

Preparation of a medium/media provides an opportunity for learners to describe, appreciate the need for, and be able to carry out aseptic technique. Learners could out qualitative (or quantitative) analyses of the cations and anions present in some commercial media, e.g. RPMI 1640 tissue culture medium.

Details of procedures are given at https://en.wikipedia.org/wiki/Vector_%28molecular_biology%29

From their research into parasite and host life cycles and culture techniques, learners could develop an organisational tool for the culture of Plasmodium, defining the tasks to be carried out on a day-to-day basis. This could also involve some number work.

The Wellcome Sanger Institute has produced a video to show how malaria parasites are cultured and stained on a microscope.

www.yourgenome.org/video/life-in-the-lab-working-in-a-malaria-lab

ACTIVITY 6: HANDLING THE MOSQUITOES

Mosquitoes capable of transmitting *Plasmodium spp*. need to be maintained in dedicated insectaries.

Learners could use their knowledge and understanding of the structure and properties of materials (metals, polymers, ceramics and composites) to design and/or construct insectaries. Equipment required will include:

Equipment for the blood-feeding of mosquitoes:

- A pooter for transferring mosquitoes.
- A mosquito container, designed to minimise mosquito escape or injury and the scientist being bitten.
- A glass, temperature-controlled membrane blood feeder for feeding the mosquitoes.

Equipment for rearing mosquitoes:

- Suitably enclosed cages for the imagoes.
- Containers for rearing the larvae.

Numerous websites are available for reference, including https://www.beiresources.org/portals/2/MR4/Methods_In_Malaria_Research-6th_edition.pdf.

Learners could justify the use of materials and size of the insectaries.

PRACTICE REVIEW ACTIVITIES FOR MODULE 3

ACTIVITY 7: HEALTH AND SAFETY WHEN WORKING WITH PATHOGENS

P. falciparum is a Group 3 pathogen and premises for its culture are derogated Containment Level 3 (CL3). The Health & safety Executive (HSE) provides information on biological hazards – http://www.hse.gov.uk/biosafety/information.htm and http://www.hse.gov.uk/pubns/misc208.pdf and BBSRC/MRC document provides information on standards for containment level 3 facilities – https://www.mrc.ac.uk/documents/pdf/ssr/standards-for-containment-level-3-facilities/

Learners could review the health and safety procedures required when working with *Plasmodium* spp. and infected *Anopheles* mosquitoes, from their culturing, research and handling, storage, through to disposal of infected organisms after use.

ACTIVITY 8: SICKLE CELL DISEASE

Sickle cell disease is caused by a mutation that leads to the change in a single amino acid in the β-chain of the haemoglobin molecule. People with sickle cell disease have a lower life expectancy, but carriers, i.e. those with a single sickle cell allele, have some protection against malaria. Learners could discuss possible explanations for the resistance the allele confers.

Learners could:

- Explain how a change in the base sequence of the HBB gene leads to the change in the haemoglobin molecule.
- Describe the location on Chromosome 11, and explain how this was determined.
- Describe the inheritance of the gene and the sickle cell allele and discuss its frequency in different populations, compared to the intensity of *Plasmodium falciparum* transmission.

The websites https://www.cdc.gov/malaria/about/biology/sickle_cell.html and https://ghr.nlm.nih.gov/condition/sickle-cell-disease#inheritance provide good starting points for learners' research.

Learners could go on to investigate other haemoglobinopathies and effects of these on infection of an individual by the parasite. They could discuss the implications of these in terms of potential strategies to interfere with the parasite and therefore prevent or control the disease. A suitable introduction is provided at http://www.uptodate.com/contents/protection-against-malaria-in-the-hemoglobinopathies?source=see_link and a more detailed discussion at http://www.thelancet.com/pdfs/journals/laninf/PIIS1473-3099(12)70055-5.pdf.

Another possible extension activity is to explore and compare protein structure – see the video from Khan Academy on the four levels of protein structure: https://www.khanacademy.org/test-prep/mcat/biomolecules/amino-acids-and-proteins1/v/four-levels-of-protein-structure

MODULE 4

THE HUMAN MICROBIOME

Link to qualification: https://www.ocr.org.uk/qualifications/vocational-education-and-skills/cambridge-technicals-applied-science-level-3-certificate-extended-certificate-foundation-diploma-diploma-extended-diploma-05847-05849-05879-05874-2016-suite/

This module synthesises knowledge and understanding from Unit 1, Science fundamentals (LO3), Unit 2 (LO4).

The human microbiome is made up largely of bacterial species, along with archaea, viruses and fungi, which colonise the human body. Most of these microorganisms are in the small and large intestine. The gut microbiome contains thousands of bacterial species, with up to 1014 bacteria. There are wide variations in species from person to person, with the mix becoming established in early childhood.

The effect of the microbiome on health is becoming increasingly well-documented, including its link with the immune system and in cardiovascular disease, diabetes, inflammatory bowel disease, multiple sclerosis and obesity.

Researchers have also begun to develop therapies targeted towards obtaining or restoring the optimum balance between microbial populations in individuals. These may include transfer of faecal matter and strain supplementation. Some commercial products, such as yogurt-based drinks, list effects on the microbiome as part of their beneficial properties.

Learners could begin by investigating methods of isolating bacteria, including individual species, from samples and mixed cultures, and methods used in bacterial identification. They could investigate the nature of the human microbiome, including but not limited to the microorganisms of the gut, the identification of species using genomic techniques, its effects on human health and opportunities for improving health and perhaps controlling inflammatory diseases.

The Wellcome Sanger Institute has produced a video to show how scientists culture bacteria from the microbiome and analyse genomic data.

www.yourgenome.org/video/life-in-the-lab-working-with-human-gut-microbiota

MODULE 4

Contained within the following assessment criteria/units/LOs:

Learning Outcome	LO number	Unit number
Understand cell organisation and structures	LO3	Unit 1
Understand the importance of health and safety and quality systems to industry	LO1	Unit 2
Be able to separate, identify and quantify the amount of substances present in a mixture	LO2	Unit 2
Be able to use mathematical techniques to analyse data	LO1	Unit 3
Be able to use graphical techniques to analyse data	LO2	Unit 3
Be able to analyse and evaluate the quality of data	LO4	Unit 3
Be able to draw justified conclusions from data	LO5	Unit 3
Be able to use modified, extended or combined laboratory techniques in analytical procedures	LO6	Unit 3
Be able to record, report on and review scientific analyses	LO7	Unit 3
Understand the techniques of DNA mapping and genomics	LO3	Unit 5
Understand the impact of an innovation in an application of genomics	LO4	Unit 5
Understand the types of hazard that may be encountered in a laboratory	LO1	Unit 6
Be able to use health and safety procedures to minimise the risk presented by hazards in a laboratory	LO2	Unit 6
Understand how product testing determines the development of consumer products	LO2	Unit 10
Be able to test the effectiveness of consumer product tests	LO5	Unit 10

This module also provides opportunities to address aspects of Unit 4: Human Physiology (LO1, LO5, LO6) and Unit 18: Microbiology (LO1).

During the delivery of the units, the learners should carry out a range of activities to demonstrate and check their knowledge and understanding. They should also undertake review activities as they work through the programme of learning.

PRACTICE REVIEW ACTIVITIES FOR MODULE 4

ACTIVITY 1: ISOLATION AND CULTURE OF BACTERIA FROM THE HUMAN MICROBIOME

Learners could be given the opportunity of culturing bacteria from a sample and isolating an individual species from a mixed culture on an agar plate to produce a pure culture. They should develop skills in the use of aseptic technique, see http://www.biotopics.co.uk/microbes/tech1.html, http://www.nuffieldfoundation.org/practical-biology/aseptic-techniques, http://microbiologyonline.org/teachers/resources.

There are numerous websites that give an overview of the technques involved, e.g. http://www.nios.ac.in/media/documents/dmlt/Microbiology/Lesson-10.pdf, http://www.sas.upenn.edu/LabManuals/biol275/Table_of_Contents_files/5-PureCulture.pdf.

A suitable basic activity is given at http://www.tmcc.edu/microbiology-resource-center/lab-protocols/bacterial-isolation/.

In terms of isolation of bacteria from the human microbiome, the use of human skin or hair is suitable, but the use of other human samples is not recommended because of possible cultivation of human pathogens. Alternatively, samples from air, water or soil could be used, but again, samples could be contaminated with pathogens.

The Wellcome Sanger Institute has produced a video on bacterial culture.

www.yourgenome.org/video/life-in-the-lab-working-with-human-gut-microbiota

The isolation of pure cultures provides learners with establishing a tentative identification of a bacterial species using a range of techniques based on colony morphology, staining technques, and bacterial metabolism, including the use of general, selective and differential culture media. Again, a number of resources is available; see, for instance, http://www.sas.upenn.edu/LabManuals/biol275/Table_of_Contents_files/5-PureCulture.pdf, http://vlab.amrita.edu/?sub=3&brch=73&sim=208&cnt=1, http://microrao.com/simple_staining.htm.

PRACTICE REVIEW ACTIVITIES FOR MODULE 4

ACTIVITY 2: EXTRACTION OF DNA

The cells of the human body are outnumbered ten to one by bacteria, but large-scale surveys of the human microbiome were not feasible until the development of next-generation sequencing.

A fundamental challenge has been to isolate DNA representative of the microbial community.

Information on extraction procedures of DNA from faeces can be found on the websites of commercial suppliers of DNA extraction kits, eg http://uk.werfen.com/~/media/il%20uk/docs/diasorin/ifu%20120602%20%20stool%20dna%20english.pdf, including comparison of techniques, eg https://norgenbiotek.com/product/stool-dna-isolation-kit#informationsheetanchor and http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0033865. Using the latter resource, learners could carry out and discuss statistical comparisons.

Learners could review Health and Safety considerations and develop Risk Assessments for the procedure. Examples of Material Safety Data Sheets (MSDS) can be found on suppliers' websites, eg http://www.stratec.com/share/molecular/Manuals/Single/Pathogens/PSPSpinStool_StoolPlusKit.pdf.

ACTIVITY 3: THE DIVERSITY OF THE HUMAN MICROBIOME

The Common Fund's Human Microbiome Project (HMP) is developing research resources to enable the study of the microbial communities that live in and on our bodies and the roles they play in human health and disease.

Learners could research the biodiversity and:

- Discuss the DNA sequencing technologies used in human microbiome studies.
- Define how are data from DNA analyses used to identify organisms belonging to the microbiome?
- Review the diversity of organisms within the human microbiome.
- Discuss intraspecific variation of organisms within the human microbiome.
- Review the variation from person to person/degree of uniqueness and discuss explanations for this.

The Common Fund's Human Microbiome Project website – https://commonfund.nih.gov/hmp, https://blog.wellcome.ac.uk/2015/05/20/invisible-you-the-human-microbiome/ and http://www.illumina.com/areas-of-interest/microbiology/human-microbiome-analysis.html are good starting points.

ACTIVITY 4: THE HUMAN MICROBIOME AND HEALTH

Learners could begin by describing the diversity of the human microbiome. Learners could discuss the presence of symbiotic microorganisms in the microbiome and their effects in excluding and out-competing pathogens.

During infection, and often in low levels in the healthy body, pathogenic bacteria may be present in or on the human body. The overuse and inappropriate use of antibiotics has led to the rise in 'superbugs', for instance MRSA (Methicillin-resistant *Staphylococcus aureus*, though the term is now used to describe resistance to antibiotics in addition to methicillin). Learners could discuss the mechanism by which this resistance to antibiotics has developed, the implications, including models of antibiotic resistance. Genomic analysis of these superbugs will lead to the development of a greater understanding of the microorganism's pathogenicity, identification of the strain causing a particular outbreak, and therefore the possibility of rapid treatment or personalised medicine.

See http://www.yourgenome.org/activities/mrsa-gene-hunt and other websites, e.g. http://www.dnadarwin.org/casestudies/9/, http://www.dnadarwin.org/casestudies/9/FILES/MRSASG1.1.pdf

Learners could also consider the links between the human microbiome and various human conditions, in particular inflammatory diseases, to include.

- Cardiovascular disease.
- Diabetes, Types 1 and 2.
- Inflammatory bowel disease (IBD).
- Multiple sclerosis.
- Obesity.

Learners could evaluate correlations and consider correlation and cause – they could review the evidence and question whether a modification in the human microbiome is the causal mechanism of a condition or modified because of it.

The Wellcome Sanger Institute has produced a video to help support this module.

www.yourgenome.org/video/life-in-the-lab-working-with-human-gut-microbiota

PRACTICE REVIEW ACTIVITIES FOR MODULE 4

ACTIVITY 5: CHANGING THE COMPOSITION OF THE HUMAN MICROBIOME

Certain human conditions and medications such as antibiotics can modify the human microbiome. See the press release - http://www.sanger.ac.uk/news/view/bugs-drugs, and/or the original scientific paper – http://www.nature.com/nature/journal/v533/n7604/full/nature17645.html.

The Gut Stuff video series provides an introduction to the topic – see http://thegutstuff.com/, also on YouTube – https://www.youtube.com/channel/UCxoAYjySUP4TK-RB2VAnmyw?spfreload=10; for example https://www.youtube.com/watch?v=iKhQ_qTTbUQ. Learners could research and discuss these.

Learners could go on to research and evaluate the claims made on various websites that prebiotic foods and probiotic preparations could be used to enhance a person's microbiomes.

Learners could consider the effects of transfer of faecal matter to patients and strain supplementation – see http://thefecaltransplantfoundation.org/what-is-fecal-transplant/.

Learners should consider the types of trials being made, eg:

- The nature of the condition, where appropriate; types of patient, age, sex, medical histories and other characteristics.
- The nature of the microbiota used.
- Safety considerations.
- The inoculum and transfer.
- The number of treatments in the investigation.
- The duration of the investigation.
- Number of research centres involved, eg single or multicentre, and implications.
- Selection of participants.
- Type of clinical trial, including the use of placebos, randomised controlled studies, blind trials, double-blind trials.

Learners could access clinical data from scientific papers, where possible (or tutors may want to supply this), consider the statistical significance of the data obtained, and evaluate the claims made. See, for instance, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4071888/. They could consider the reporting of any claims made for the efficacy of treatments, from the scientific literature to the media.

MODULE 5

CANCER

Link to qualification: https://www.ocr.org.uk/qualifications/vocational-education-and-skills/cambridge-technicals-applied-science-level-3-certificate-extended-certificate-foundation-diploma-diploma-extended-diploma-05847-05849-05879-05874-2016-suite/

The delivery begins with Unit 1, Science fundamentals (LO3) and draws in analytical methods from Unit 3 (LO4, LO5).

Cancer is caused by the genetic changes – mutations – acquired by our cells as we go through life.

The Wellcome Sanger Institute uses cutting-edge DNA sequencing methods to identify these mutations from human cancer samples.

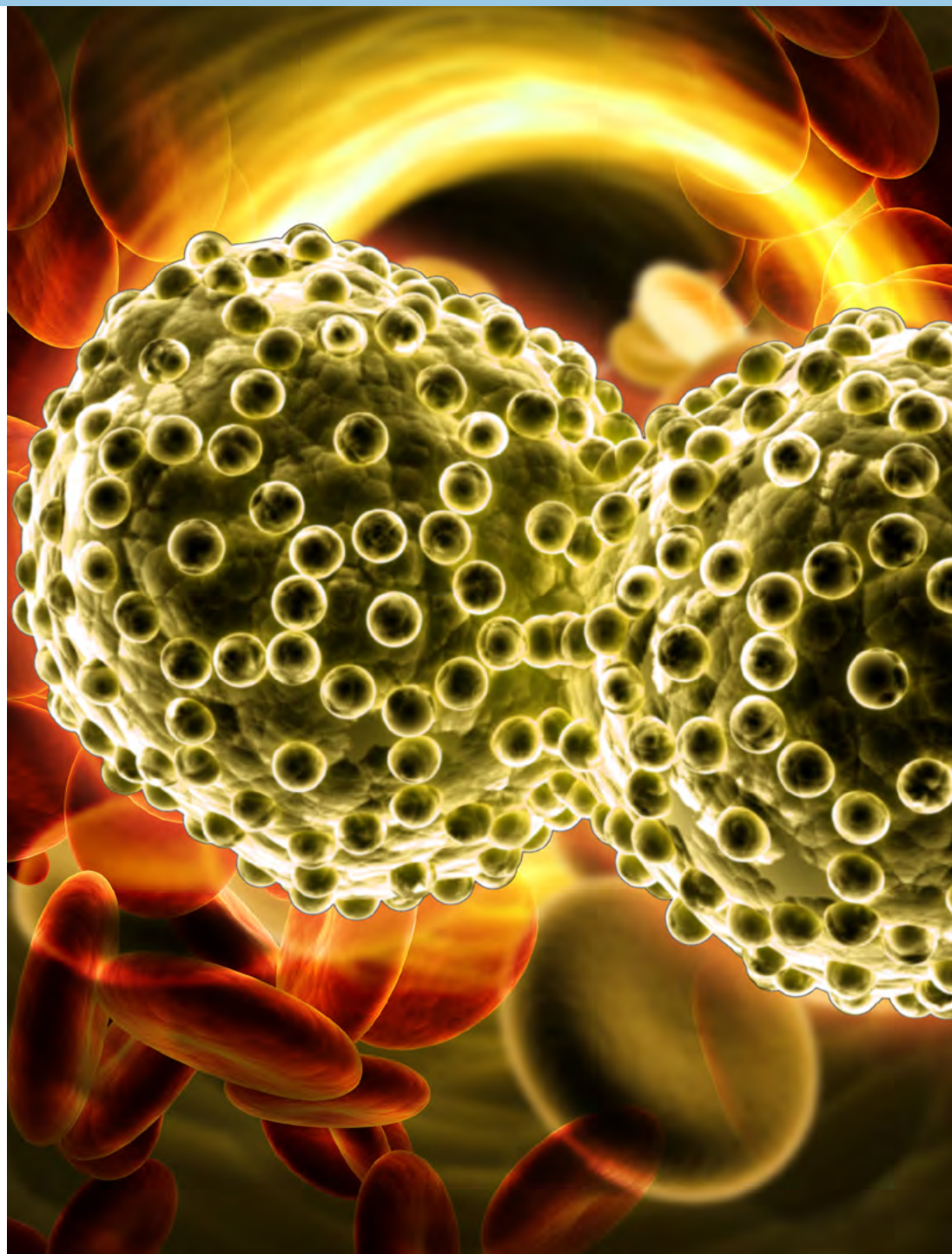
The aim is to discover:

- the genes that are frequently mutated in tumours, since these provide important insights into the biology of cancer
- the patterns of mutations in cancer cells. These patterns represent a record of the cancer's life history. They can illustrate the damaging factors the genome has been exposed to as the cancer cell has developed from a normal cell.

Learners should have a knowledge and/or understanding of cell division by mitosis and differentiation, and a basic understanding of cancer.

Some useful press releases that give context to these aspects include:

- http://www.sanger.ac.uk/news/view/smoking-pack-day-year-causes-150-mutations-lung-cells
- http://www.sanger.ac.uk/news/view/red-hair-gene-variant-drives-skin-cancer-mutations.
- http://www.sanger.ac.uk/news/view/vulnerabilities-leukaemia-cells-revealed-using-genome-editing-technique
- http://www.sanger.ac.uk/news/view/five-new-breast-cancer-genes-found.



MODULE 5

Contained within the following assessment criteria/units/LOs:

Learning Outcome	LO number	Unit number
Understand cell organisation and structures	LO3	Unit 1
Understand the principles of carbon chemistry	LO4	Unit 1
Understand the importance of health and safety and quality systems to industry	LO1	Unit 2
Be able to separate, identify and quantify the amount of substances present in a mixture	LO2	Unit 2
Be able to examine and record features of biological samples	LO4	Unit 2
Be able to analyse and evaluate the quality of data	LO4	Unit 3
Be able to draw justified conclusions from data	LO5	Unit 3
Be able to record, report on and review scientific analyses	LO7	Unit 3
Understand the techniques of DNA mapping and genomics	LO3	Unit 5
Understand the impact of an innovation in an application of genomics	LO4	Unit 5
Understand the types of hazard that may be encountered in a laboratory	LO1	Unit 6
Be able to use health and safety procedures to minimise the risk presented by hazards in a laboratory	LO2	Unit 6

This module also provides opportunities to address aspects of Unit 8: Cell Biology (LO3, LO4).

During the delivery of the units, the learners should carry out a range of activities to demonstrate and check their knowledge and understanding. They should also undertake review activities as they work through the programme of learning.

PRACTICE REVIEW ACTIVITIES FOR MODULE 5

ACTIVITY 1: GENES AND CANCER

Learners could investigate the latest research how genes are involved in cancer. The Cancer Genome Project uses human genome sequence and mutation detection techniques to find changes in DNA involved in the development of human cancers. The project aims to develop tools and identify new treatment targets for tackling cancer.

Learners could investigate and report on the cell cycle, cancer and the function of the genes frequently mutated in cancer. They could discuss the involvement of proto-oncogenes and tumour suppressor genes. They could use the video clips at http://www.yourgenome.org/video/cancer-rogue-cells and http://www.sanger.ac.uk/news/view/vulnerabilities-leukaemia-cells-revealed-using-genome-editing-technique and refer to http://www.nature.com/scitable/topicpage/Proto-oncogenes-to-Oncogenes-to-Cancer-883 to develop these ideas. The use of http://www.yourgenome.org/facts/what-is-a-mutation and http://www.yourgenome.org/facts/is-cancer-a-genetic-disease is also recommended.

COSMIC – the Catalogue Of Somatic Mutations in Cancer – is the world's largest and most comprehensive resource for exploring the impact of somatic mutations in cancer; see http://cancer.sanger.ac.uk/cosmic (see Activity 3).

As possible extension material, learners could investigate how these mechanisms are utilised in the most recent technologies to understand gene function, i.e. CRISPR cas-9. This is based on introducing changes to the DNA and relies on the repair machinery to establish the desired changes

Learners could describe the progression of the disease, including cytological, biochemical, anatomical and behavioural changes to cells, and mechanisms used by the body to respond to these changes.

ACTIVITY 2: DNA EXTRACTION AND ANALYSIS

Learners could investigate how blood samples, and samples produced from biopsy from cancer patients, are collected, handled and processed for DNA extraction.

Documents on the Newcastle University and University of York websites are helpful in describing Health and Safety procedures - http://www.ncl.ac.uk/ohss/assets/documents/301.4_G_Human_Samples.pdf and http://www.york.ac.uk/biology/intranet/health-safety/biological-safety/blood/#tab-1. Information on biopsy and DNA process control can be found at https://www.horizondiscovery.com/reference-standards/what-are-reference-standards/biopsy-process-control.

In a video clip at http://www.yourgenome.org/video/my-career-in-genomics-cancer-biology, Niki Patel, a Research Assistant in the Cancer Genome Project at the Wellcome Trust Sanger Institute, describes her day-to-day role in the laboratory, processing tumour samples and setting up experiments to analyse DNA.

ACTIVITY 3: DETECTING MUTATIONS

Large numbers of mutations – not all of which are involved in oncogenesis – are found in cancer cells.

Mutations of the KRAS gene are present in many types of cancer, including pancreatic. The KRAS gene codes for a signalling molecule.

Learners could work through the activity at http://www.yourgenome.org/activities/kras-cancer-mutation, then illustrate how to look for mutations by comparing healthy DNA sequence and a tumour DNA sequence. They should illustrate how this comparison can be made against databases, e.g. COSMIC database, http://cancer.sanger.ac.uk/cancergenome/projects/cosmic/.

PRACTICE REVIEW ACTIVITIES FOR MODULE 5

ACTIVITY 4: FROM GENOME DATA TO CANCER THERAPY

In this activity, learners could take on the role of genome researchers, and envisage the journey from cancer gene discovery to drug development.

Learners could explore data sequenced on next generation sequencing machines to identify changes in sequences or mutations in particular genes, and discuss the significance of these changes in the development of cancer. Some mutations will be involved directly in cancer development; others may be present but have no obvious impact in cancer development. These 'cancer signatures' increase understanding of cancer and lead to the possibilities of patient-specific therapy.

An example, which focuses on the BRAF gene is at http://www.yourgenome.org/activities/braf-from-gene-to-cancer-therapy. BRAF mutations are commonly found in the thyroid gland, large intestine, skin and ovary. The BRAF gene is the most commonly mutated in malignant melanoma.

Using the example on the yourgenome website, learners could:

- explore and describe how a mutated gene could have an impact on cell division.
- discuss and suggest how findings of scientists could lead to anti-cancer therapies.

ACTIVITY 5: FINDINGS FROM GENOMIC ANALYSIS

Learners could consider the ethics of some of these genomic analyses. For instance, what happens if findings are made during genomic research that have implications for a patient's health? This raises the questions concerning pertinent findings – findings sought out and generated by the research – vs. incidental findings – additional findings of the research that could have implications for a patient's health.

The PHG Foundation in Cambridge deals with such ethical issues, and produced a detailed report on managing incidental and pertinent findings from WGS in the 100,000 Genomes Project – http://www.phgfoundation.org/file/13772/.

Learners could produce a report on pertinent vs. incidental findings and make recommendations on how these should be managed. Genome Generation, Scenario 8, provides a scenario with fact cards and issue cards for learners to discuss; see http://www.yourgenome.org/activities/genome-generation.

MODULE 6

PRESENTING YOUR IDEAS

Link to qualification: https://www.ocr.org.uk/qualifications/vocational-education-and-skills/cambridge-technicals-applied-science-level-3-certificate-extended-certificate-foundation-diploma-diploma-extended-diploma-05847-05849-05879-05874-2016-suite/

The completion of the project draws on methods of reporting science from Unit 3 (LO7).

Learners will have completed a project in which they have undertaken a series of investigative tasks relevant to the development of a high throughput genomics pipeline. They will have seen how these pipelines can be developed for a range of different areas related to health and monitoring disease.

Learners could conclude by devising means of reporting and presenting the outcomes of their investigations and developments within the field of genomics and health. They should consider their prospective audience and the purposes of the communication undertaken.

Possible audiences include:

- The public.
- The government.
- Scientific regulatory bodies.
- The medical profession.

Possible purposes include:

- Public information and raising awareness of scientific developments.
- Providing information for regulators of genomic research.
- Keeping those involved in healthcare up to date with developments in genomic medicine.

Contained within the following assessment criteria/units/LOs:

Learning Outcome	LO number	Unit number
Be able to record, report on and review scientific analyses	LO7	Unit 3

During the delivery of the units, the learners should carry out a range of activities to demonstrate and check their knowledge and understanding. They should also undertake review activities as they work through the programme of learning.

PRACTICE REVIEW ACTIVITIES FOR MODULE 6

ACTIVITY 1: REPORTING ON ONE ASPECT OF GENOMICS AND HEALTH

Reporting to the public and scientific community is an important part of science.

Learners could produce and present to peers a scientific report based on one of the modules undertaken. The presentation must be developed to be presented to an audience specified by the learner. It could draw on the information and examples developed in the previous activities, providing learners with the opportunity to re-purpose information, and to interpret and evaluate information and data in context, or it could be related to developments in an area of genomics or health science in which they have developed a particular interest.

This activity should give learners opportunities to review and reflect on what they have learnt, and why this is important, and how this can be applied to improve their everyday lives, as well as those of their audience. These improvements could be related to their well-being, and/or academic and work-related goals.

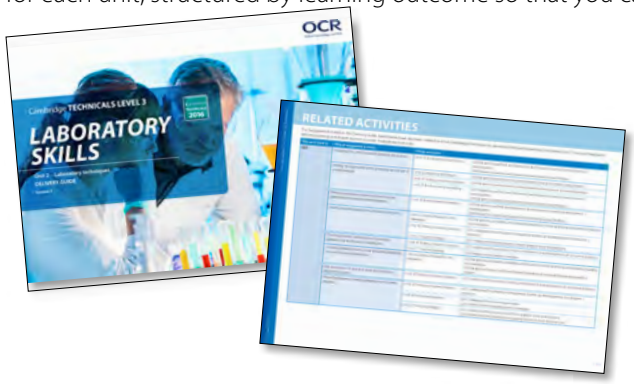
OTHER RESOURCES

Below is a list of resources available from the OCR website which can support the delivery of this project.

https://www.ocr.org.uk/qualifications/vocational-education-and-skills/cambridge-technicals-applied-science-level-3-certificate-extended-certificate-foundation-diploma-diploma-extended-diploma-05847-05849-05879-05874-2016-suite/

Delivery Guides

Delivery Guides contains suggestions for activities for lessons. There is a Delivery Guide for each unit, structured by learning outcome so that you can see how each activity helps



learners cover the unit. We've also included links to other resources you might find useful.

Lesson Elements

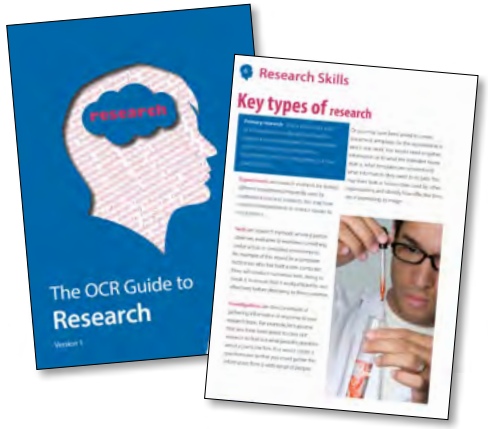
There are a number of Lesson Elements for some of the units. Each Lesson Element contains fully worked-up activities with tutor instructions and answers along with learner task sheets.

Resources Links

There are a number of Resources Links for some of the units. Resources Links provide a range of other resources you might find useful – videos, data sets and other online content.

Skills Guides

We have produced a range of skills guides covering a variety of topics, including research, communication skills, managing projects, problem solving.



www.ocr.org.uk/i-want-to/skills-guides/

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