BCMB2001 unit outline

The unit is designed to provide medical and life sciences students with a solid grounding in human and other eukaryotic biochemistry and molecular biology that can be applied to a wide range of disciplines and Majors. The key themes will be the flow of energy on a cellular and organismal level, and the flow of information within cells and between generations. These principles, introduced in first year, will be substantially expanded upon here through the lens of molecular mechanisms. An important focus in this unit will be the regulation of metabolic and genetic processes at the molecular level, equipping students with the ability to discern how disruptions to biochemical pathways in cells affect health and trigger disease as a result of diet, environment and genetic mutation. A key feature of this course will be the introduction to students, in terms of both theory and hands-on experience, of the molecular biology tools and techniques that are integral to all modern life sciences and are becoming increasingly important in modern medicine.

The course will build on the quantitative approaches introduced in first year Chemistry and Biology, fostering scientific rigour in experimental design, data collection and interpretation, with the additional exposure to modern analytical tools including mining databases and the analysis and presentation of complex data. In order to address the breadth of content that is required to achieve the aims of this unit, regular tutorials will be included to reinforce the acquisition of core concepts; each tutorial will incorporate a quiz as a study aid.

How is this material related to your Majors

When you complete this unit, you will have a thorough understanding of the key concepts that underpin Biochemistry and Molecular Biology and be able to apply and integrate this conceptual framework into other related disciplines within the medical and life sciences. From this knowledge base, gained from lectures, tutorials, laboratory investigations and other enquiry-based learning activities, you will explore the biochemical consequences of common medical challenges, such as cancer, obesity and diabetes. Your knowledge of Biochemistry and Molecular Biology will be developed and extended to include the regulation of complex multi-cellular organisms. This enlarged perspective will enable you to select and apply practical and/or theoretical techniques to conduct relevant investigations.

From the laboratory component you will gain experience designing and planning an investigation. Further, you will analyse raw data, reflect on the significance of these results and present conclusions that are well-reasoned and supported by experimental evidence. In completing these tasks, you will need to gather, synthesise and critically evaluate information from a range of sources, including both experimental and published material. These findings will be communicated by a

variety of modes to a range of audiences. This experience will help you develop creative and innovative approaches to addressing and communicating scientific issues.

Unit Learning Outcomes:

1	Describe in detail the main anabolic and catabolic processes in the cell and discuss how variations in energy demand and supply affect these processes.
2	Compare and contrast the integration of anabolic and catabolic processes in the cells and predict how perturbations to these processes, including fuel selection and genetic mutation, affect the cell and whole organism.
3	Summarise the catabolic and anabolic fates of dietary nitrogen and predict how the synthesis and degradation of nitrogenous biopolymers are affected in contexts such as starvation, diabetes and cancer.
4	Describe the complexity of the eukaryotic genome and its structure in detail and identify the key constituent elements.
5	Outline the specific processes by which genetic information is transmitted from one generation to the next and analyse the flow of this information within the cell
6	Describe and evaluate the steps involved in gene transcription and translation and evaluate the different ways by which gene expression can be regulated
7	Evaluate the main concepts and power of modern molecular biology techniques and select the appropriate technique for specific applications in life science and medical research
8	Explain, with examples, the difference between qualitative and quantitative measurements; obtain quantitative measurements of metabolite concentrations and enzyme activities, in an accurate and reproducible manner
9	Adapt, develop and trouble-shoot recognised procedures for novel contexts and requirements
10	Assess the quality of, interpret and draw conclusions from data obtained in the laboratory.
11	Summarise and identify the key points from topical biochemical data from a number of published sources; synthesise and communicate the findings.

Lecture topics:

Lecture Titles	Description	Lecturer
Molecular Biology (15 lectures and 3 tutorials)		
1. Introduction	Introduction, administration and revision of the structure of nucleic acids, prokaryotic genomes and central dogma	DH
2. Prokaryotic replication	This lecture will start with the basic concepts of replication covered in BIOL1XX7 and present the example of the E. coli replication fork. The challenges of bi-directional replication and fidelity in copying will be covered in the context of this model.	HN
3. Applications to Molecular Biology	How different DNA polymerases (eg Klenow and Taq) are used in molecular biology: PCR, DNA sequencing, cloning, producing labelled oligonucleotide probes	HN
4. The Eukaryotic genome	Then enter the world of the eukaryotic genome and explore how the genome is packaged into chromosomes, considering the coding and non-coding regions.	HN
5 Eukaryotic DNA replication	Starting with the E. coli replication fork, consider eukaryotic replication with multiple, linear chromosomes, the eukaryotic cell cycle, the link between DNA replication and the cell cycle; both prokaryotic and eukaryotic. Mitotic cell division revisited.	HN
6 Eukaryotic DNA replication		HN
Tutorial	**Tutorial** covering genome organisation and synthesis in the context of normal cell cycle and cancer.	HN & DH
7. Prokaryotic transcription	**Lecture 7:** review of transcription and the regulation of transcription in prokaryotes; lac and trp operons	ASW
8. Eukaryotic transcription	**Lecture 8**: Introduction into eukaryotic transcription: promoters, RNA polymerases and transcription factors. Basal transcription, elongation, enhancers.	ASW
9. Post-transcriptional processing	**Lecture 9:** Splicing (alternative splice sites), cleavage, poly-adenylation, transport, stability of mRNA, control of aberrant transcripts.	ASW
10. Translation in Prokaryotes	**Lecture 10:** From the concepts of genetic code covered in BIOL1XX7, the redundancy is extended and prokaryotic translation revisited.	MH
11. Translation in eukaryotes	**Lecture 11**: Translation of mRNA in eukaryotes and comparison with prokaryotes. Ribosomes, assembly of the translational complex and	MH

	initiation, elongation and termination of translation	
12. Translational Regulation	**Lecture12.** Pre- and post-translational control. Control of translation in eukaryotes: alternative start sites, Iron-responsive elements, Control of protein stability and degradation.	MH
Tutorial	**Tutorial:** Review the flow of information inside cells from DNA to action molecules. There is a difference between genome (DNA, which is the same in nearly every cell) and expressed genes (RNA and protein), which give rise to different cell types. How do we measure gene expression? Identifying and quantifying mRNA (e.g. reverse transcription, Northern Blots, microarrays, Quantitative PCR)	MH & DH
13 & 14. Gene cloning techniques and in vitro expression	**Lectures:** Introduce fundamental and modern methods of cloning, recombinant DNA technology and stripping down the central dogma of DNA into its most fundamental components	HN
15. Future aspirations	The future directions of molecular biology **Advanced**: Use of transgenetic animals	HN MH
Tutorial	**Tutorial:** Review of cloning and molecular biology techniques in experimental contexts	HN, MH & DH
Metabolism (16 lectures and 2 tutorials)		
16. Principles of energy balance and fuel oxidation	Introduce students to concepts of anabolism and catabolism, generation of ATP to meet demand. Application of regulatory themes to whole body energy balance, weight	GSD
17. Oxidative Phosphorylation: Demand and supply		GSD
18. Oxidative Phosphorylation: Demand and supply		GSD
19. Central Catabolic Pathways	Introduce students to the key catabolic pathways: glycolysis, beta oxidation and Krebs cycle. Focus on the structural and regulatory features of one enzyme in each pathway.	GSD
20. Central Catabolic Pathways		GSD

21. Central Catabolic Pathways		GSD
22. Integration of Catabolism: Fuel selection	Illustration of the regulation and integration of carbohydrate and fatty acid oxidation by reference to muscle fuel utilization during walking, jogging, running and sprinting.	GSD
23. Integration of Catabolism:		GSD
24. Integration of Catabolism:	These 2 lectures explores the demand for glucose by the brain and mechanisms for blood glucose homeostasis: liver glycogenolysis and control of glycogen phosphorylase. The integrated breakdown and catabolism of glycogen, fat and protein stores during the post-prandial period, short-term fasting and long term food deprivation is considered. Detailed treatment gluconeogenesis and ketone body formation and usage.	GSD
25. Integration of Catabolism: Fuel Selection during starvation		GSD
Tutorial: Integration of catabolism	**Tutorial Molecular extrapolation**: the regulation of gluconeogenesis and glycogenolysis at allosteric, covalent modification and gene expression levels.	GSD & DH
26. Anabolic Strategies: Disposal of dietary carbohydrate	This lecture introduces students to the chemistry of carbohydrates and sources of dietary carbohydrates. This leads to the processing of ingested carbohydrates and the importance of the regulation of blood glucose by insulin.	GSD
27. Anabolic Strategies: Disposal of dietary carbohydrate	This lecture focuses on the control of the post-prandial glucose response and the fate of excess dietary carbohydrate through the formation of glycogen in muscle and liver (glycogenesis) and fat in adipose tissue and liver (lipogenesis).	GSD
28. Anabolic Strategies: Disposal of dietary carbohydrate	The regulation of fatty acid synthesis and triacylglycerol formation is investigated with reference to Glyceroneogenesis and the pathways including alternative fates of glucose.	GSD
29. Anabolic Strategies: Disposal of dietary fat and storage	Chemistry of fatty acids and triacylglycerols and sources and types of dietary fats. The fate of ingested fats and cholesterol. Digestion of fat and repackaging as chylomicrons in the gut.	GSD

30. Anabolic Strategies: Disposal of dietary fat and storage	Processing of lipoproteins by the liver. Transport of fats and cholesterol to the peripheral tissues. Endogenous formation of cholesterol.	GSD
Tutorial: Anabolic Strategies	**Research extrapolation:** examination of the usefulness or hype around the glycemic index *Medical extrapolation: Strategies to regulate blood cholesterol concentration.*	GSD & DH
31. Protein and nucleic acid metabolism	Overview of nitrogen metabolism. The processing of amino acids and formation of urea. Pathways of amino acid backbone synthesis and degradation. Overview of nucleotide formation and degradation.	GSD
32. Revision and Catch Up as required	This could be used to cover a bit more metabolism if you wanted to do more on nitrogen metabolism…linking nucleotide synthesis to cancer???	GSD

Laboratory Sessions

Practicals	Description	Weeks
Introductory techniques	Using spectrophotometry to produce a spectrum, a standard curve and to determine the concentration of an unknown.	2 and 3
DNA fingerprinting I	Pipette challenge…has your pipetting improved? Using student's own cheek cells, DNA is isolated and amplified by PCR at a locus, D1S80, used in crime scene investigations.	4 and 5
DNA fingerprinting II	The number of copies of the VNTR at this locus is determined from the amplified DNA for each student by agarose gel electrophoresis.	**6 and 7**
Plasmid isolation	Plasmid DNA, from a number of cultures, is isolated using a commonly used commercial kit. The plasmid DNA is then digested with specific restriction endonucleases ready for next week.	**6 and 7**
Plasmid	The digested plasmid DNA is separated by agarose gel electrophoresis and the identity of the plasmid	**8 and 9**

identification	determined by the sizes of the digestion products. The properties of restriction enzymes and their uses in cloning are explored.	
Enzyme kinetics	The fundamental parameters of an enzyme catalyzed reaction (Vmax and K_M) are determined and explored.	**8 and 9**
Enzyme –linked Metabolite Assay (ELMA)	The estimation of serum glucose in a number of patients is used to introduce the principles of an ELMA.	**10 and 11**
Design assay	Students use the principles explored in the previous prac session to design an ELMA to measure another metabolite or glucose in another context.	**12 and 13**

Assessment

Assessment	**Schedule**	**% final mark**
Data Analysis and presentation: • Poster for advanced on their cloning • Powerpoint for regular students	Friday week 11	5
ELN, including laboratory calculations	Every fortnight	25
PeerWise MCQ design 2% per fortnight	On alternate weeks	10
ELMA design assay and interpretation	weeks 12 and 13	10
Final Exam		**50**
Mark Breakdown		
Theory		50
Practical		50