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RAFFLES INSTITUTION

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CANDIDATE NAME	
CIVICS GROUP	1 7 S 0 3
INDEX NUMBER	

PROTEOMICS **9815/01**

Paper 1 26 September 2017

2 hour 30 minutes

Additional materials: Answer Paper

Appendix List of Amino Acids (with Question Paper)

READ THESE INSTRUCTIONS FIRST

Write your index number, CT group & name on all the work you hand in.
Write in dark blue or black pen on both sides of the paper.
You may use a soft pencil for any diagrams, graphs or rough working.
Do not use staples, paper clips, highlighters, glue or correction fluid.

Section A
Answer **all** questions.
Section B
Answer **three** out of **four** questions.
Section C
Answer the question.

At the end of the examination, fasten all your work securely together. **Please hand in this question booklet together with your answer sheets.**

The number of marks is given in brackets [ ] at the end of each question or part question.
You may use a calculator.
You are reminded for the need for clear presentation in your answers.

This document consists of **8** printed pages.

Section A

Answer all the questions in this section.

1 A naïve B cell produces only the membrane-bound form of IgM. When it becomes activated and differentiates into a plasma B cell, it may transiently produce both membrane-bound and secreted forms of IgM, but it will eventually produce only the secreted form.

(a) (i) Describe how amino acids in solution are joined. [2]

(ii) Discuss the difference between the processes of *in vivo* (in a cell) and *in vitro* (in solution outside a cell) joining of amino acids. [2]

(b) (i) Using your knowledge of an immunoglobulin structure, compare the amino acid sequences of the membrane-bound and secreted forms of IgM. [3]

(ii) Name the process that generated the two forms of IgM. [1]

(iii) Describe how the two forms of IgM are targeted to their final destinations. [4]

(c) Immune protection is one of the biological processes in which proteins play a role. State two other biological processes in which proteins play different crucial roles. For each process, name the protein involved. [2]

[Total : 14]

2 There are 4 major classes of ATP-powered transport proteins, namely ATP-binding Cassette (ABC) family, P-class, F-class and V-class.

(a) Members of the ATP-binding Cassette (ABC) family contain two transmembrane domains and two cytosolic ATP-binding domains.

(i) Explain what is meant by *family*. [1]

(ii) The amino acid sequence of a novel protein was searched against a database for domains. It was found to have high sequence homologies with ABC family's cytosolic ATP-binding domain and part of the transmembrane domain.

Discuss whether it is possible to determine the role of the novel protein. [3]

(b) Fig. 2.1 shows an ATP synthase which is a F-class protein. It is a multimeric complex.

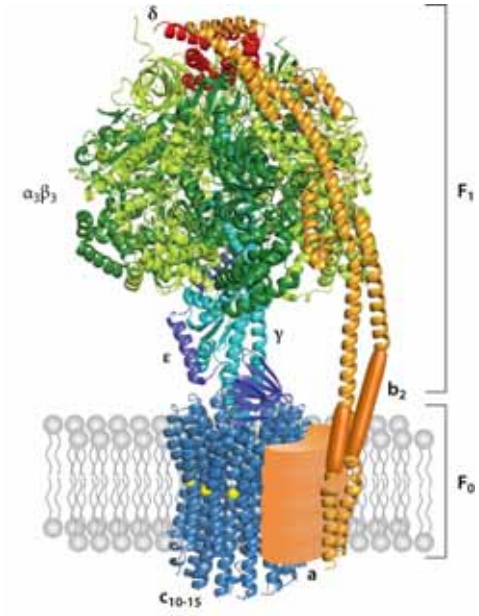


Fig. 2.1

(i) ATP synthase is associated with a gradient across a membrane. State what the gradient is and describe how the gradient is used in a cell. [3]

(ii) Explain the significance of non-covalent interactions in ATP synthase. [4]

(c) X-ray crystallography and nuclear magnetic resonance (NMR) spectroscopy are techniques that can be used to determine protein structure. Distinguish between the principles of the two techniques. [2]

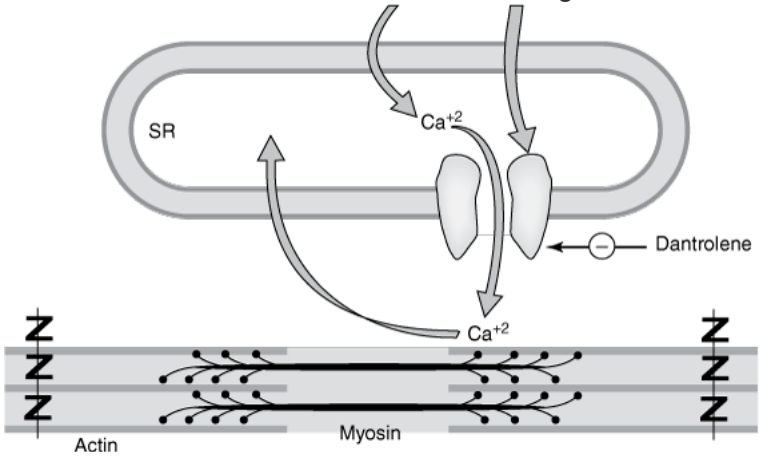
[Total : 13]

3 Describe three different ways in which two proteins can bind to each other. Suggest and explain which of these three ways gives the strongest interaction between proteins. [5]

[Total : 5]

4 Muscle spasms are involuntary muscle contractions which may result from some conditions which affect the nervous system, such as multiple sclerosis and cerebral palsy.

Muscle relaxants used to relieve muscle spasms work by causing the muscles to become less tense or stiff, which in turn reduces pain and discomfort. Dantrolene is a muscle relaxant which works directly on the muscle and its mechanism is shown in Fig. 3.1.



SR = sarcoplasmic reticulum **Fig. 3.1**

(a) Describe how dantrolene relieves muscle spasms. [5]

(b) Calcium and molecule X are important during for thin and thick filaments to slide past each other during muscle contraction. There is a loss of molecule X upon death and rigor mortis sets in whereby stiffening of the body occurs.

Identify molecule X and explain how rigor mortis occurs when molecule X is absent. [3]

[Total : 8]

5 (a) Neurofilament is a 160kDA protein that is found in neurones. It is estimated that neurofilament is made up of approximately 1940 amino acids.

(i) Outline how Edman degradation is used to determine the amino acid sequence of a protein. [3]

(ii) Explain why Edman degradation is not the method of choice for sequencing neurofilament protein and suggest an alternative method of choice. [2]

(b) Given that there is no available antibody made against neurofilament, describe how a pure sample of neurofilament protein can be obtained using column chromatography. [5]

[Total : 10]

Section B

Answer 3 out of the 4 questions in this section.

6 Haemophiliacs lack many clotting factors in the blood and this results in bleeding that last longer than normal people. The main treatment for haemophilia is called replacement therapy whereby concentrates of clotting factors such as VIII are administered.

Fig. 6.1 below shows part of the blood coagulation cascade.

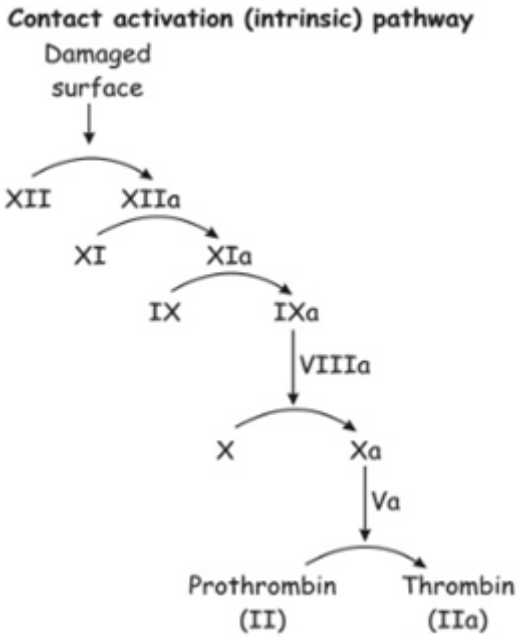


Fig. 6.1

(a) Explain how treatment with concentrates of clotting factor VIII results in blood clot formation. [4]

(b) The release of calcium ions during injury is important for blood clot formation. Explain the role of calcium ions in thrombin activation. [2]

(c) Explain the significance of protein modifications. [4]

[Total : 10]

7 (a) Using myoglobin as example, account for the following statement.

"The shapes of proteins are specified by genes." [5]

(b) Discuss the benefits and limitations of studying amino acid sequences compared to mRNA. [3]

(c) Contrast the protein helices in collagen and keratin. [2]

[Total : 10]

8 Pyruvate dehydrogenase complex is a complex of 3 enzymes and catalyses the irreversible formation of acetyl-coA from pyruvate in animals. In the cell, the activity of pyruvate dehydrogenase is stringently controlled by several ways, as shown in Fig. 8.1 below.

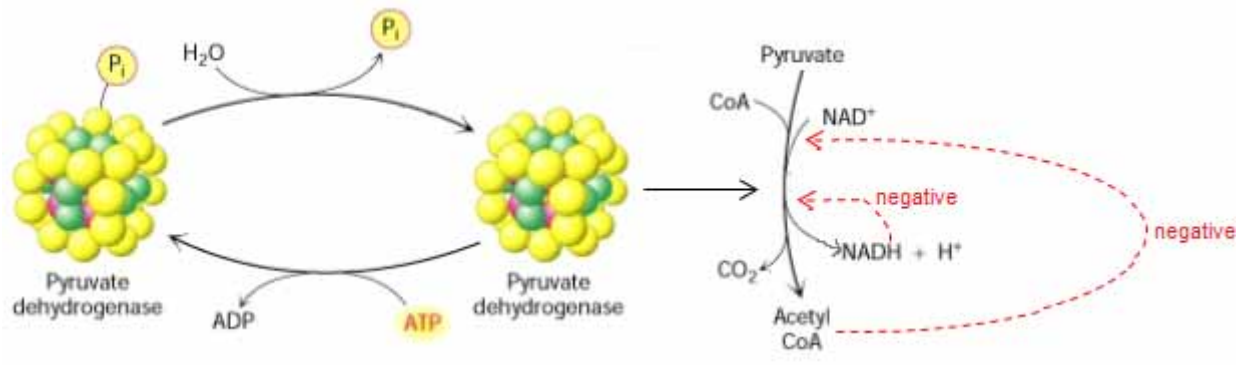


Fig. 8.1

(a) With reference to Fig. 8.1, explain how activity of pyruvate dehydrogenase is regulated. [4]

(b) Explain the importance of coenzyme A and NAD^+ in pyruvate dehydrogenase's function. [2]

(c) Explain how the structure of pyruvate dehydrogenase allows for increased rate of reaction. [4]

[Total : 10]

9 (a) NeuroD is a basic helix-loop-helix protein that is expressed in parts of the brain, pancreatic cells and entero-endocrine cells. Previous studies showed that it is involved in the differentiation of nervous system and development of pancreas.

Describe a technique using antibodies to determine the location of the neuroD protein in mouse brain tissue. [4]

(b) Describe the binding property of antibodies in localisation studies. [2]

(c) Describe **two** limitations of the method suggested in **(a)**. Suggest another method to better investigate the localisation of human neuroD protein. [4]

[Total : 10]

Section C
Answer the question in this section.

10 Pancreatic cancer arises when pancreatic cells undergo uncontrolled cell division and invade other parts of the body. The most common type of pancreatic cancer, pancreatic adenocarcinoma, accounts for about 85% of cases and involves changes to the proteome.

(a) Given tumour samples taken from pancreatic adenocarcinoma and normal pancreatic tissue, describe appropriate approaches and techniques that can be used to analyse the changes to tumour tissue proteome. [12]

(b) Cyclophilin A is a protein that was found to be upregulated in 80% of pancreatic adenocarcinoma. The nucleotide sequence of cyclophilin A gene is known but its function and interacting partners is largely unknown.

Given a cDNA library extracted from pancreatic adenocarcinoma tissue, describe an *in vivo* experiment that can be performed to identify all potential interacting partners of cyclophilin A. [8]

[Total : 20]

End of Paper

Appendix

List of Amino Acids