RECOGNISING ACHIEVEMENT

ADVANCED SUBSIDIARY GCE **2858/01**

HUMAN BIOLOGY

Case Studies

INSERT

WEDNESDAY 9 JANUARY 2008 Morning

Time: 45 minutes

CUP/T39236

INSTRUCTIONS TO CANDIDATES

- Questions 1 and 2 are based on the articles which follow on pages 3 to 6 of this insert.

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Case Study 1

THE CHEMICAL ORIGIN OF LIFE

Since the publication of the structure of the DNA molecule by Watson and Crick, DNA and proteins have probably been the most researched macromolecules in living cells. The structure of DNA proposed by Watson and Crick certainly makes it the ideal genetic material, whereas proteins, in the form of enzymes, are responsible for catalysing the metabolic processes that occur in every cell.

RNA was thought to be limited to its roles in protein synthesis, where it was shown to exist as three 'types' – messenger RNA, transfer RNA and ribosomal RNA. However, in 1986, the phrase 'RNA World' was first used by Walter Gilbert. The basic idea behind this phrase is that RNA molecules that replicate themselves could have formed the basis of the origin of life on Earth. It is now known that a fourth type of RNA exists. This is an RNA molecule that has catalytic properties and essentially acts as an enzyme. This has been named 'ribozyme' and it is capable of catalysing the making or breaking of phosphodiester bonds which are present in the sugar-phosphate backbone of polynucleotides.

The 'RNA World' hypothesis proposes that RNA molecules which were capable of catalysing their own replication would survive in the 'primordial soup'. Some RNA chains were formed with catalytic properties that could bind amino acids together. These amino acids would then form proteins which in turn would support further synthesis of RNA. RNA molecules would work cooperatively and other macromolecules would eventually be synthesised leading to the development of the earliest prokaryotic cells.

Is there any supporting evidence for this hypothesis? Some argue that RNA polynucleotides are too easily broken down. However, ultraviolet radiation, while damaging to DNA molecules, can actually cause RNA to polymerise. If UV radiation levels were high in the 'RNA World', then RNA molecules may have had an advantage over DNA in terms of their stability.

This hypothesis received more support in 2001 when the structure of the ribosome was described and the catalytic site responsible for joining the amino acids together was found to consist only of RNA. The protein content of ribosomes has a structural role rather than an enzymic one.

However, there is plenty of criticism of this theory and the idea of an 'RNA origin of life' is still very much an hypothesis.

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Case Study 2

BLOOD TRANSFUSION LABORATORY

Anna is a 'company contact' for the National Blood Service (NBS). She promotes the work of the NBS in her company and encourages people to become donors. The number of donors from her company has risen dramatically and, as a result, Anna is receiving an award. The ceremony is preceded by a visit for Anna and other area winners to the local Blood Transfusion Laboratory, where she has a chance to see what happens to the blood which is donated. Her guide is Neil, a biomedical scientist and the laboratory manager.

Neil: Well, this is where the blood arrives. Our most productive donor sessions, as you know, happen after work so the blood units collected are stored overnight at 4 °C.

Anna: *Yes, I know how important it is to get the units into cold storage quickly.*

Neil: It certainly is. You have to slow down the metabolism in the cells, although this in itself can cause problems later with the potassium levels. As the cells are less active, they tend to lose potassium into the plasma and so this has to be monitored.

Anyway, the bags are labelled with the blood group and whether the donor is male or female.

Anna: *Blood group I can understand, but surely the sex of the donor doesn't really matter?*

Neil: It does if we use female plasma because of TRALI – Transfusion Related Acute Lung Injury. It's the second major cause of transfusion injury and can cause respiratory distress.

Anna: *Why is it only a problem with female plasma?*

Neil: It happens because anti-leucocyte antibodies in the female donor plasma react with the recipient's leucocytes. These cells agglutinate and the biggest problem seems to be in capillaries in the pulmonary circulation. Females probably have more antibodies in their plasma due to pregnancies. But don't worry, plasma is only one of the products we get from donated blood and there's no problem using female blood for other important blood products.

Anna: *Your labelling system – I see it's all electronically bar-coded.*

Neil: Oh yes. A complete audit trail is possible. We record collection session with donor details and which products the blood is used to make. The test results that we take from the sample tube are also recorded.

Anna: *I'm often asked about the tests that are done – health, lifestyle and travel questions. Obviously, people are concerned about the risks from blood transmitted diseases.*

Neil: We always check the blood group of course, and then we check for antibodies to *Treponema pallidum*. This is the bacterium which causes syphilis. We also check for the presence of antibodies to some viruses. Some you will have heard of but others are more unusual. For example, we test for antibodies to a virus called Human T-Lymphotropic Virus. This virus infects T-lymphocytes and can also cause disorders in the nervous system and a form of leukaemia. Surprisingly, it is relatively common in some populations – the virus is endemic in Japan, the Caribbean and parts of Africa, and is thought to be passed from mother to child at birth and by breast feeding.

Anna: *So do you tell donors if the results come up positive?*

Neil: If we get a positive result, we will usually inform you and offer advice. If it is significant to your health, you will be asked to discuss the results with one of our doctors and we would refer you to your own doctor – with your permission of course. Having said that, there is at least one exception – CMV or Cytomegalovirus.

Anna: *What makes this one special?*

Neil: 50% of the UK population has antibodies to this virus. It causes mild flu-like symptoms and people in good health make a full recovery and probably don't even realise they were ill, so donors are not informed if they are positive. CMV positive blood and blood products are perfectly safe for most people but they are not given to small babies or, for example, bone marrow recipients.

But we are running out of time. Let's quickly look through the other rooms.

First, the centrifuge room. Here the leucocytes are filtered out – the filter is part of the blood bag. We centrifuge at 4100 rpm for 15 minutes and the sample separates into cells and plasma. Then the bag is placed in the press and squeezed and the plasma is forced out.

Anna: *Oh, now I see why you have all these empty bags attached to the collecting bag. You never have to open the bags at all so everything is kept sterile! So what happens to the cells and what happens to the plasma?*

Neil: Well, the red blood cells are suspended in SAGM which stands for saline, adenine, glucose, mannitol. I'm sure you've heard of saline and glucose. The adenine is a stabiliser and the mannitol is a sugar alcohol that isn't absorbed by the cells. In SAGM, packed cells can be stored for up to 21 days at between 4 and 6 °C. The blood plasma is frozen quickly and stored at –60 °C for several months. Of course, sometimes we deliberately thaw some plasma to make cryoprecipitate.

Anna: *What's cryoprecipitate?*

Neil: The plasma is allowed to thaw slowly and some proteins are precipitated. This product is very useful in controlling bleeding disorders, as are platelets, of course.

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Anna: *Ah, you mentioned these before. I was curious about this. One of the girls at work has a high platelet count and she has been asked to be a platelet donor.*

Neil: I'm not surprised. Platelet requirement is what drives the blood collection – they have such a short shelf life you see – only 5 days and this has to be at 22 °C in a shaking incubator and in a gas permeable bag! She's probably been asked to consider apheresis – have you heard of this?

Anna: *I don't think so.*

Neil: Well, we can call into the Apheresis Room on the way to your presentation. Basically, the donor is connected directly to a machine with a centrifuge. Blood from a vein enters the machine and the platelets and some plasma are spun out. The remaining blood is returned directly back to the patient. Platelets and plasma regenerate really quickly so this can be done every two weeks instead of only 3 times or so each year for a blood donor.

Anna: *That's amazing! In fact, this whole tour has been amazing. I could go round again!*

Neil: Well, it's always good to explain things to someone as enthusiastic as yourself about blood donation. Come on – lets look at apheresis in action before we go on to your presentation.

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