

**Monday 3 June 2013 – Morning**

**AS GCE HUMAN BIOLOGY**

**F222/01/ADVANCE NOTICE** Growth, Development and Disease

For issue on or after:  
**13 MARCH 2013**

**Duration: 1 hour 45 minutes**



#### **INSTRUCTIONS TO EXAMINATION OFFICER/INVIGILATOR**

Do not send this Insert for marking; it should be retained in the centre or destroyed.

#### **NOTES FOR GUIDANCE (CANDIDATES)**

- 1** This Advance Notice contains two case studies, which are needed in preparation for questions 1 and 2 in the externally assessed examination **F222/01**.
- 2** You will need to read the case studies carefully and also have covered the learning outcomes for Unit F222/01 (Growth, Development and Disease). The examination paper will contain questions on the two case studies. You will be expected to apply your knowledge and understanding of the work covered in F222/01 to answer these questions. There are 100 marks available on the paper.
- 3** You can seek advice from your teacher about the content of the case studies and you can discuss them with others in your class. You may also investigate the topics yourself using any resources available to you.
- 4** You will **not** be able to take your copy of the case studies, or other materials, into the examination. The examination paper will contain fresh copies of the two case studies as an insert.
- 5** You will not have time to read the case studies for the first time in the examination if you are to complete the examination paper within the specified time. However, you should refer to the case studies when answering the questions.

This document consists of **4** pages. Any blank pages are indicated.

## Case Study 1

### **BRAF MUTATION TRIGGERS MOST MELANOMAS**

Scientists have pinpointed a genetic mutation of the BRAF gene which may trigger up to approximately 70 percent of cases of malignant melanoma. Malignant melanoma, which is mainly caused by over-exposure to sunlight, accounts for just 11 percent of skin cancers, but almost all of the deaths. The incidence of malignant melanoma has doubled in the past decade. Each year, in the UK, about 6000 new cases are diagnosed and more than 1600 people die of the disease.

It was previously known that the BRAF gene was often damaged or mutated in malignant melanomas but it was not known if this was a cause or a result of the cancer. A recent study shows that acquiring a particular BRAF mutation can be the first in a cascade of changes leading to malignant melanoma.

Researchers took DNA samples from cancerous cells and healthy cells. They compared the DNA sequence of the BRAF gene in the samples. They then went on to determine how the faults in the mutated BRAF gene might lead to cancer.

Remarkably, they found that approximately 97 percent of the mutations in the BRAF gene were the same point mutation (known as V600E). The BRAF gene codes for the BRAF protein and this point mutation results in the amino acid valine being replaced by glutamate in the amino acid sequence.

The BRAF protein is an enzyme in a pathway that transmits signals from the cell surface to the nucleus of the cell. The pathway is normally activated by the presence of growth factors on the cell surface membrane. The BRAF protein is a kinase enzyme that activates other proteins in order to pass on signals in the cell. The BRAF V600E gene mutation increases the activity of the BRAF protein by locking it in its active form. This permanently active BRAF protein sends signals that are passed from protein to protein within the cell in a 'signalling cascade' even when there are no growth factors present. These signals eventually reach the nucleus, where they switch genes on or off, causing the cell to multiply.

The high frequency of BRAF V600E mutations in malignant melanoma, and the relative lack of effective therapies for advanced stages of the disease, suggest that inhibition of BRAF protein activity may be an important new strategy for the treatment of malignant melanoma. The altered BRAF protein has a significantly different shape to the normal protein. This makes it an excellent candidate for drug targeting. Vemurafenib is a new drug specifically designed to inhibit the activity of this mutant BRAF protein.

A research team tested this new drug in a phase 3 clinical trial involving 672 adult patients with late stage, inoperable malignant melanoma and the V600E mutation in the BRAF gene. Patients were given either the new vemurafenib pill or injections of dacarbazine, the only licensed chemotherapy drug for advanced melanoma. Scientists found that vemurafenib reduced the risk of a person's disease progressing and improved overall short-term survival. At six months, 84 percent of those who received vemurafenib were still alive, compared to 64 percent of those who took dacarbazine. The average survival with vemurafenib was estimated to be 5.3 months, compared to 1.6 months with dacarbazine.

Vemurafenib has shown promising results in slowing the progression of melanoma that has spread to other parts of the body. This drug, together with a diagnostic test that will help determine whether a patient's melanoma cells have the BRAF V600E mutation, was approved for use by the US Food and Drug Administration (FDA) in August 2011.

**PLEASE SEE PAGE 4 FOR REFERENCES**

## Case Study 2

### THE BURDEN OF CHRONIC DISEASE

The health of the world's population is generally improving. Fewer people are dying from infectious diseases and therefore, in many cases, are living long enough to develop chronic diseases, such as chronic respiratory diseases. Chronic diseases are a major cause of death in all regions of the world but 80 percent of deaths due to chronic diseases occur in low and middle income countries. Over the next 10 years, deaths attributable to chronic diseases are projected to increase by 17 percent.

Chronic diseases not only cause premature death but also result in people spending time disabled by their condition and this needs to be taken into account when measuring the overall health burden on a country. One health indicator that has been developed for the monitoring and evaluation of the overall health of a country is the disability-adjusted life year (DALY). This is a measure of both the time lost due to premature death and the time spent disabled by the disease. One DALY is therefore equal to one year of *healthy* life lost. When DALY information is provided for different countries, for example by the World Health Organisation (WHO), the data needs to be age-standardised.

Chronic respiratory diseases are chronic diseases of the airways and the lungs. Major preventable chronic respiratory diseases include asthma, respiratory allergies, occupational lung disease and chronic obstructive pulmonary disease (COPD). Chronic respiratory diseases are increasingly contributing to the health burden of a country.

- In 1990, COPD was the twelfth leading cause of DALYs worldwide.
- By 2020, it is estimated that COPD will become the fifth leading cause of DALYs worldwide.

In almost all countries the poorest people are more likely to develop chronic respiratory diseases because of greater exposure to risk factors and decreased access to health services. The direct and indirect exposure to tobacco smoke is the principal risk factor for the development of chronic respiratory diseases. Other important factors include high exposure to air pollution (derived from indoor and outdoor sources), occupational related disorders, malnutrition, low birth weight and multiple early lung infections. These diseases erode the health and well-being of people and have a negative impact on families and societies. Women and children are particularly vulnerable, especially in low and middle income countries, where they are exposed on a daily basis to indoor air pollution from solid fuels used for cooking and heating.

The Global Alliance against Chronic Respiratory Diseases (GARD) is a voluntary alliance of national and international organisations aiming to combat chronic respiratory diseases. GARD's goal is to reduce the health burden of chronic respiratory diseases by:

- developing a standard way of obtaining relevant data on chronic respiratory disease risk factors
- encouraging countries to implement health promotion and chronic respiratory disease prevention policies
- recommending affordable strategies for the management of chronic respiratory diseases.

GARD is providing a comprehensive approach to raising awareness of the huge impact of chronic respiratory diseases worldwide by highlighting both the risk factors and the ways to prevent and treat these diseases.

**PLEASE SEE PAGE 4 FOR REFERENCES**

**References:****Case Study 1****BRAF MUTATION TRIGGERS MOST MELANOMAS**

1. Skin cancer drug research

<http://www.nhs.uk/news/2011/06June/Pages/vemurafenib-skin-cancer-drug.aspx>

**Case Study 2****THE BURDEN OF CHRONIC DISEASE**

1. Publications by the Global Alliance against Chronic Respiratory Diseases (GARD)

<http://www.who.int/gard/publications/en/>

2. Chronic diseases research

[http://www.who.int/chp/chronic\\_disease\\_report/en/](http://www.who.int/chp/chronic_disease_report/en/)

*All web references correct at time of production*

*Other references should also be researched*

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