

系所組別： 細胞生物與解剖學研究所

考試科目： 生命科學

考試日期：0308，節次：3

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There are 5 essays in this test. Please read each of the articles and answer the following questions accordingly.

I. Ozone is perhaps best known for its role in protecting the earth from solar radiation. But scientists recently discovered that the extremely reactive form of oxygen is produced by the human immune system as part of its defense strategy. New findings suggest that such ozone production could contribute to atherosclerosis, the disease commonly known as hardening of the arteries that increases the risk of heart attacks and strokes.

As atherosclerosis develops, inflammation fuels the growth of plaques in the arteries. Paul Wentworth, Jr. and Richard Lerner of the Scripps Research Institute and their colleagues theorized that the fat-laden deposits that are hallmarks of the disease have all the necessary ingredients to manufacture ozone. "Ozone is damaging, and it is really a problem that we are going to have to think about in the next few years," Wentworth notes. "There may be a whole slew of molecules that ozone generates that we have never thought about before." The researchers analyzed plaque samples removed from patients suffering from coronary artery disease and found two compounds—dubbed atheronals by the authors—that are signature byproducts of ozone's interaction with cholesterol, forms of which have long been associated with atherosclerosis. The team writes that "it seems likely that ozone is generated throughout the evolution of the disease."

1. Does ozone protect both the earth and our bodies based on the new finding? Why or why not? (10%)
2. Where in our bodies did the researchers find the substances derived from ozone?(5%)  
What condition in humans can be linked to these substances? (5%)

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II. Germany's Harald zur Hausen and France's Luc Montagnier and Françoise Barre-Sinoussi share the 2008 Nobel Prize in Physiology or Medicine, awarded October 6th.

Barre-Sinoussi and Montagnier discovered HIV. Shortly after reports in the early 1980s of a new immunodeficiency syndrome, researchers all over the world raced to find the cause. The two French scientists cultured cells from lymph nodes of patients. They first detected the enzyme reverse transcriptase, which meant that a retrovirus was active. Further searching

(背面仍有題目,請繼續作答)

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turned up retroviral particles, which could kill white blood cells and which also reacted with antibodies from infected patients. These discoveries made possible unprecedented rapid development of blood screening techniques and of new antiviral therapies.

Zur Hausen defied the medical establishment and postulated in the 1970s that cervical cancer was caused by the human papilloma virus. He was able to isolate viral DNA in tumors. He also determined that there were multiple kinds of papilloma viruses, and that only some caused cancer. His discovery led to the development of a vaccine against cervical cancer.

3. Please briefly describe the contributions from these 3 Nobel laureates.(10%)

4. HIV was first discovered from which tissue? (5%) How was HIV discovered? (5%)

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III. Like a ship preparing for a long voyage, the brain forms its neurons and glia during early development and must survive life's tempests without the benefit of extensive cell replacement. Nevertheless, dividing cells have been observed throughout the mature CNS, suggesting that neural circuits are not formed exclusively from a fixed complement of cells. Progenitors located in the subventricular zone (SVZ) continually supply the rodent olfactory bulb with new interneurons and new hippocampal granule neurons are constantly formed from dividing cells in the subgranular zone (SGZ) of the dentate gyrus. Proliferating cells in the adult CNS are not, however, restricted to these small niches, as the proliferation marker bromodeoxyuridine (BrdU) is also readily incorporated by small, highly ramified non-neuronal cells that are scattered throughout the adult white and gray matter. Dr. Rivers *et al.* track the fate of these cycling glial cells in the adult brain using genetically modified mice and find that they can develop into both oligodendrocytes and excitatory projection neurons.

5. Are the neuron cells replaceable in mature CNS? Can you describe the evidence provided here?(20%)

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IV. The enduring presence of a mother's cells in her children, referred to as maternal microchimerism, seems to have both good and bad effects, explains Lee Nelson of the Fred Hutchinson Cancer Research Center in Seattle. Scientists suspect that a mother's cells gain

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access to the fetus via the placenta, and the small percentage of those cells lingering in the tissues after birth may contribute to some autoimmune diseases. Nelson's team found maternal cells lurking in the hearts of infants who died of cardiac failure caused by neonatal lupus. They suspect that the immune system of the growing fetus attacks the maternal cells. In some cases, however, a mother's cells might help regenerate diseased tissue. It turns out that children with type 1 diabetes tend to have higher-than-average numbers of maternal cells dwelling in the blood and pancreas. "There are indications that in the pancreas these cells might be serving a repair function," says Kathleen Gillespie of the University of Bristol, who is currently leading an autopsy study of pancreatic maternal cells in diabetic and nondiabetic children.

6. Is the existence of maternal microchimerism good or bad to the offsprings? Can you give examples to support your statement? (20%)

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V. Macroautophagy is an evolutionarily conserved vacuolar, self-digesting mechanism for cellular components, which end up in the lysosomal compartment. In mammalian cells, macroautophagy is cytoprotective, and protects the cells against the accumulation of damaged organelles or protein aggregates, the loss of interaction with the extracellular matrix, and the toxicity of cancer therapies. During periods of nutrient starvation, stimulating macroautophagy provides the fuel required to maintain an active metabolism and the production of ATP. Macroautophagy can inhibit the induction of several forms of cell death, such as apoptosis and necrosis. However, it can also be part of the cascades of events that lead to cell death, either by collaborating with other cell death mechanisms or by causing cell death on its own. Loss of the regulation of bulk macroautophagy can prime self-destruction by cells, and some forms of selective autophagy and non-canonical forms of macroautophagy have been shown to be associated with cell demise. There is now mounting evidence that autophagy and apoptosis share several common regulatory elements that are crucial in any attempt to understand the dual role of autophagy in cell survival and cell death.

7. Based on the description above, is autophagy adaptive or detrimental to cell survival? Explain. (20%)