※ 考生請注意：本試題不可使用計算機。 請於答案卷(卡)作答，於本試題紙上作答者，不予計分。
There are 5 essays in this test with a total score of 100%. Each essay contains a text followed by questions. Please **answer questions in Chinese or English pointedly according to the text.**

1. Drug that boosts nerve signals offers hope for multiple sclerosis

An experimental antibody drug aimed at protecting nerves from the ravages of multiple sclerosis offers hope for a new way to combat the neurological disease - if researchers can definitively show that it works. Its developer, Biogen of Cambridge, Massachusetts, presented results from a small clinical trial at an American Academy of Neurology meeting in 2015. The antibody, anti-LINGO-1, is intended to stimulate regrowth of the myelin sheath, the fatty protective covering on nerve cells that is damaged by multiple sclerosis. If the initial promising results from the trial are confirmed, it will be the first such myelin-regeneration therapy.

Myelin sheaths insulate and support axons, the fibres that transmit signals between nerve cells. In multiple sclerosis, immune attack destroys these sheaths. Stripped of this protective coating, the axons gradually wither away, causing the numbness and muscle spasms that are characteristic of the disease. The 12 drugs approved in the United States to treat multiple sclerosis slow this immune attack - although sometimes with dangerous side effects. But none stops it.

Anti-LINGO-1 blocks the LINGO-1 protein, which inhibits the production of myelin. In doing so, the drug spurs myelin growth. It has consistently performed well in animal models and in human cells grown in culture. Assessing multiple-sclerosis drugs is, however, challenging: symptoms are difficult to measure reliably and often progress slowly. And the benefits of remyelinating drugs are expected to manifest over years, not months.

At the neurology meeting, Biogen reported on a trial of anti-LINGO-1 in 82 patients with optic neuritis, a loss of vision common among people with multiple sclerosis. The trial found that the antibody was no better than a placebo at improving vision. But it did speed up signalling in retinal nerves - a possible sign that the myelin sheath had been rebuilt - by 41% over placebo after eight months of treatment. The trial was small, and it is too early to know whether the drug will provide tangible relief from other symptoms of multiple sclerosis, such as numbness.

Biogen is conducting another anti-LINGO-1 trial to test an experimental way (based on magnetic resonance imaging) to assess remyelination, as well as the effect of the drug on symptoms in people for whom the disease is progressing rapidly.

There is little expectation that anti-LINGO-1 or other drugs like it will cure multiple sclerosis. Instead, the hope is that the drugs can be used in combination with the available immune treatments to slow progression

of the disease.

Q1-1: What are the symptoms often seen in patients of multiple sclerosis? What are the underlying mechanisms of this disease? (10%)

Q1-2: Are there drugs available for treating multiple sclerosis now? How does anti-Lingo-1 work and why does it raise excitement as a new drug? (15%)

2. Printed body parts come alive

The advent of three-dimensional (3D) printing has generated a swell of interest in artificial organs meant to replace, or even enhance, human machinery.

Printed organs, such as a prototype outer ear developed by researchers at Princeton University in New Jersey and Johns Hopkins University in Baltimore, Maryland, was on the agenda at the Inside 3D Printing conference in New York in April, 2015. The ear is printed from a range of materials: a hydrogel to form an ear-shaped scaffold, cells that will grow to form cartilage, and silver nanoparticles to form an antenna. The device is just one example of the increasing versatility of 3D printing.

That business is currently focused on titanium replacement hip joints, which can be tailored to fit individual people, and made-to-order polymer bones to reconstruct damaged skulls and fingers. Printed body parts brought in US$537 million last year, up about 30% on the previous year.

Scientists are looking ahead to radical emerging technologies that use live cells as 'ink', assembling them layer-by-layer into rudimentary tissues. Bioprinting firm Organovo of San Diego, California, already sells such tissues to researchers aiming to test experimental drugs for toxicity to liver cells. The company's next step will be to provide printed tissue patches to repair damaged livers in humans.

Q2-1: Which body parts have been successfully made with 3D printing? (5%)

Q2-2: What purposes have tissues made from 3D printing served so far? (5%)

3. Nations adopt historic global climate accord

When the gavel came down for the final time at the climate summit in Paris on 12 December, 2015, representatives from 195 countries erupted into cheers. They had approved a landmark plan to combat climate change after two weeks of gruelling negotiations. The agreement commits most countries to reduce their greenhouse-gas emissions, while seeking to protect low-lying islands from rising seas and helping poor nations to develop their economies without relying on cheap, dirty fossil fuels.

The accord, years in the making, seeks to hold warming "well below" 2 °C above pre-industrial temperatures. Countries' current climate pledges fall short of that goal, but many scientists and governments

see the Paris agreement as the last, best hope to set the planet on a course to avoid catastrophic climate change.

The ambitious 32-page package contains a multitude of provisions to accelerate the world's transition from fossil fuels to solar, wind, nuclear, hydropower and other clean energy sources. Nearly every country is asked to play its part in ensuring that greenhouse-gas emissions peak, and then begin to decline, as soon as possible. Countries will assess their progress towards reducing emissions in 2018, and must revisit their climate pledges every five years, beginning in 2020. The aim is that these pledges will become more ambitious over time.

The long road to the Paris agreement began in Rio de Janeiro in 1992, when nations approved a general 'framework' to combat climate change that left the details for later agreements. After 20 annual meetings with little progress to curb ever-soaring emissions, representatives arrived in Paris with pledges from 187 countries that outlined the steps each would take to cut its emissions by 2030.

Never before had so many promises been on the table. Even if all of the promises were fulfilled, and were followed by substantial additional emissions reductions, the world would warm 2.7 °C by 2100. This is deep into the territory that scientists expect would prompt catastrophic, irreversible climate changes. Yet the Paris agreement seeks to limit planetary warming to well below 2 °C, urging nations to pursue an even stricter target, 1.5 °C. To put this in perspective, the average global temperature has already risen 1 °C since the start of the Industrial Revolution.

The Intergovernmental Panel on Climate Change (IPCC) has concluded that holding warming to 2 °C will probably require emissions to be cut by 40–70% by 2050 compared with 2010 levels. Achieving the 1.5 °C target would require substantially larger emissions cuts - of the order of 70–95% by 2050. The Paris agreement directs the IPCC to study scenarios for limiting warming to 1.5 °C, and to deliver a report to nations by 2018 to help them determine how much to strengthen their climate commitments.

Q3-1: What is the primary goal for the climate accord made in Paris last December? How many degree(s) of temperature is allowed to rise according to this agreement? (10%)
Q3-2: How many years earlier before Paris climate summit was the first world summit held to combat climate change? (5%)
Q3-3: How will the goal of Paris agreement be achieved based on this article? (10%)

4. Clues to ageing from short-lived fish

For the turquoise killifish, 'live fast, die young' is no cliché. The little African freshwater fish reaches sexual maturity three weeks after hatching and dies of old age a few months later. A pair of studies now hints at the

genetic basis for this abbreviated existence, providing precious information for a small but growing cadre of labs that hope that the species will help to unlock the secrets of human ageing.

Turquoise killifish (*Nothobranchius furzeri*) inhabit transient ponds that fill up during the rainy season in Mozambique and Zimbabwe. During the brief wet period, the fish rapidly develop, mate and lay eggs that go into suspended animation during the dry season, to hatch when the rains return the following year.

A favourite of fish hobbyists, killifish are now found in dozens of labs. Elderly killifish - a couple of months old - show hallmarks of ageing. Their bright scales fade and their cognition wavers; many develop tumours. Lifespan-altering experiments that take years in mice and decades in primates can be over in months in killifish, which are also more closely related to humans than are fruit flies, nematodes and other short-lived lab organisms popular in ageing research.

The turquoise killifish genome contains several clues to its peculiar, fleeting life. A group at the Max Planck Institute for Biology of Ageing in Cologne, Germany found that variations in genes involved in nutrient sensing, DNA repair and ageing have been selected for during its evolutionary history. Such genes might prove instructive for ageing in longer-lived animals. One such is *IGF1R*, which has been linked to extreme longevity in bowhead whales, naked mole-rats and Brandt's bat. Genes linked to *IGF1R* vary between an extremely short-lived killifish lab strain and a wild variety that can live for twice as long. The two strains also differ in a gene that has been linked to dementia in humans.

The ability to enter suspended animation (known as diapause) may also be linked to lifespan; genes involved in a similar stasis in nematodes influence ageing too. In the other study, a team led by Christoph Englert and Matthias Platzer at the Leibniz Institute on Ageing–Fritz Lipmann Institute in Jena, Germany, found substantial overlap in the expression patterns of genes in the killifish embryos in diapause and those in the brains of aged killifish.

Experiments that create fish lacking particular genes are needed to confirm whether the genes pinpointed in these studies truly influence ageing. These tests are already under way. While Killifish hold much promise for ageing research, they have not yet yielded the insights that have come out of simpler organisms. Scientists have a long list of genes that extend or shorten lifespan in nematodes, fruit flies and yeast, but it remains to be seen whether genes such as *IGF1R* have these pivotal roles in killifish.

Q4-1: Please list two reasons that make Killifish an attractive model for aging research. (10%)
Q4-2: Which genes were found in these two studies to be possibly linked to aging? (10%)

5. Lab staple agar runs low

Microbiology's most important reagent is in short supply, with potential consequences for research, public health and clinical labs around the world. Agar - the seaweed-derived, gelatinous substance that biologists use to culture microbes - is experiencing a global downturn.

The shortage can be traced to newly enforced trade restrictions on the seaweed, arising from environmental concerns that the algae are being overharvested. It is unclear how deeply the dearth will hit researchers, but it has already pushed wholesale prices of agar to an all-time high of around US$35–45 per kilogram — nearly triple the price before scarcities began. Individual researchers, who buy packaged agar from lab-supply companies, can pay many times this amount.

One major supplier, Thermo Fisher Scientific, says that it has stopped selling two 'raw' agar products - agar that has not been mixed with other ingredients - until 2016, so that it can prioritize more-popular products that contain a mixture of agar and growth nutrients. The company reports that about 200 of its customers have been affected. Another major lab-supply company, Millipore Sigma, has also halted sales of raw agar and it will re-evaluate its supplies early 2016. Millipore Sigma blames the shortage on competition from food companies for purified agar. The global demand from food-makers, at several thousand tonnes annually, dwarfs the 900 tonnes that go to lab-supply companies.

Formed of long chains of sugar molecules, agar is prized by microbiologists for its ability to form hard gels when mixed with water and growth nutrients. When a solution of bacteria is spread onto an agar-lined plate, individual cells grow into distinct colonies, allowing researchers to isolate each different strain in the mixture.

Since the introduction of agar plates in the 1880s - which enabled researchers to isolate tuberculosis, cholera and other disease-causing bacteria for the first time - bacteriological agar has been derived from a clutch of red seaweed species belonging to the genus *Gelidium*. Algae of this type grow atop rocky sea beds, forming vast underwater lawns of bushy, red fronds, and they favour cool, turbulent waters that provide a steady supply of oxygen and other nutrients - a preference that makes industrial-scale farming impossible. In some places, *Gelidium* is harvested by underwater divers or when the tides roll in, but the seaweed is most commonly collected when storms wash it ashore.

The geographical sources of *Gelidium* have shifted over the decades. Before the Second World War, Japan was king; Portugal was also once a leading supplier. Now, most of the world's agar derives from *Gelidium* grown in Morocco, with Spain in second place and Portugal, France, Mexico, Chile, South Africa, Japan and South Korea all contributing smaller quantities.

Current agar deficiencies are due mostly to an unsteady supply of Moroccan *Gelidium*. Throughout the 2000s, the nation regularly harvested as much as 14,000 tonnes per year, which was sold on to foreign and domestic agar producers. But citing concerns over dwindling *Gelidium* populations, the Moroccan government cut the legal annual harvest to around 6,000 tonnes, and has limited foreign exports of the algae to around 1,200 tonnes. And that means that companies such as Thermo Fisher and Millipore Sigma, which buy purified agar from producers and sell it on to researchers as packaged products, have little choice but to pay the skyrocketing prices that agar now commands.

Prospects for new sources of *Gelidium* are bleak. Agar substitutes, such as a seaweed product called carrageenan, have proved unsuitable for culturing microbes. Before a technician introduced agar to his lab, pioneering German microbiologist Robert Koch isolated bacteria on potato slices. At present, there's no real alternative other than using potato.

Q5-1: What is the major use of agar in a microbiology laboratory? Please give at least one example for its use. Is there any known substitute to agar currently? (8%)
Q5-2: What are the main causes for the current agar shortage in the market? Why can't we produce the seaweed through culture (or farming)? (12%)