There are 5 essays in this test with a total score of 100%. Each essay contains a text followed by questions. Please answer these questions in Chinese or English **briefly and to the point according to the text.**

Essay 1: Targeted treatment tested as potential cancer cure

After Van VanderMeer was diagnosed with advanced lung cancer, the results of a genetic test offered some hope. Last year, the 64-year-old lawyer learned that his cancer featured a genetic rearrangement that might render it vulnerable to a drug being tested in clinical trials. But because the experimental drug, crizotinib, was being given only to patients who had failed chemotherapy, VanderMeer had to wait for more than a year to gain access to the drug. Even though VanderMeer's tumours had by then spread to both of his lungs, crizotinib vaporized them within two weeks.

VanderMeer is now doing well and hoping to continue beating the disease: more than half of patients who take the drug, made by Pfizer of New York, seem to have a better prognosis than do those who didn't receive treatment. But what if VanderMeer had started taking it sooner?

Now oncologists, pathologists and geneticists are hoping to answer that question with a study that will test whether genetically targeted treatments, applied soon enough, can cure patients of lung cancer rather than buying them a few extra months of life.

Targeted therapies have now been approved for many cancers, and it has become routine for major cancer centres to genotype patients' tumours to determine whether they might benefit from targeted drugs, in case standard treatments fail. But the clinical trial, which will be conducted by the Alliance for Clinical Trials in Oncology, a nationwide group funded by the US National Cancer Institute in Bethesda, Maryland, will test whether using targeted treatments earlier can prevent patients with lung cancer from ever reaching that point.

In the trial, tumours will be genotyped after surgery to determine whether mutations are present in a gene encoding epidermal growth factor receptor (EGFR). Mutations in this gene are targeted by many molecular therapies, including erlotinib and gefitinib, which are approved for the treatment of advanced lung cancer. Some of the patients who have *EGFR* mutations will begin taking erlotinib after surgery, instead of waiting to see whether their cancer recurs.

Although similar approaches have been tested in smaller trials, yielding mixed results, organizers say that a larger, better-defined study is needed to provide a clear answer.

"We have never tested these drugs in the right population," says oncologist Ramaswamy Govindan of Washington University in St Louis, leader of the trial. "We have never tested a group of patients who have mutations in *EGFR* and then asked the question, 'could these patients be cured by gefitinib or erlotinib?'"

Q1-1: Why did VenderMeer wait for more than a year to take the drug crizotinib? (5%)

Q1-2: What's the purpose of this new drug trial? What drug(s) is/are tested? (10%)

(背面仍有題目,請繼續作答)

Essay 2 How to laugh away stress

They say that laughter is the best medicine, and now research is beginning to prove that this adage might be truer than we think. Laughter has long been known to make people happier, but a new study has shown that even anticipating a good laugh is good for your health.

When stressed out, the body constricts blood vessels, elevates the production of potentially damaging stress hormones, and raises blood pressure. Short periods of stress are normal and not dangerous, but over long periods of time stress weakens the immune system and makes heart problems more likely.

In 2005 researchers found that laughing lowers blood pressure, but the biochemical mechanism within the body remained unclear. Now Lee Berk at Loma Linda University in California and his colleagues have revealed part of the answer.

Back in 2006, Berk and his colleagues found that merely anticipating laughter boosted the production of mood-elevating hormones called β-endorphins and the immunity-enhancing human growth hormone by 27% and 87%, respectively. This led the team to wonder whether the link between lowered blood pressure and laughter could be the result of laughter somehow interfering with the production of stress hormones.

To test this, they worked with a group 16 men. Half were told that they were going to watch a humorous video that they themselves had selected earlier; the other half were told that they were going to sit in a room with magazines. The researchers monitored the men for levels of the stress hormones cortisol and adrenaline, and for dihydroxyphenylacetic acid (DOPAC) - a metabolite of dopamine that helps to produce adrenaline - throughout the experiment.

Berk and his team found that levels of all three stress chemicals decreased before, during and after the men viewed their videos. Thirty minutes after the videos were watched, cortisol was down 67%, adrenaline was down 35%, and DOPAC was down 69%. But what really shocked the team was that cortisol, adrenaline and DOPAC decreased by 39%, 70%, and 38% respectively before anything funny was seen. "It would seem that merely having a merry heart in anticipation of the happy experience lowered stress levels... they dropped before videos were even watched" says Berk.

Berk and his team are serious about the study of laughter, because the potential applications are huge. "It's no joke, we need to start prescribing humour as medication" says Berk. Immune disorders are known to be exacerbated by stress, and if getting immune-disorder patients to anticipate happiness or laughter reduces concentrations of stress chemicals in the blood, then this therapy can only serve to help, explains Berk.

Stress hormones do a lot more than regulate the immune system, they contribute to many health-related issues such as depression, high blood pressure and control of diabetes. The next step is to understand the biochemical pathways that allow communication between this humour region of the brain and the hormone-releasing section of the endocrine and immune systems.

Q2-1: Why is laughter a good medicine? (10%)

Q2-2: What's the most striking finding in this study? (5%)

Essay 3: Cigarette clampdown

Australian smokers are already confronted by graphic images and warnings of death and disease every time they pull out a packet of cigarettes. But from December 2012, the warnings will be bigger, more gruesome and on a monochrome paper backing. In its latest attempt to curb smoking rates, the Australian government has voted to standardize the content on cigarette packets.

Cigarette packets will be almost identical. The only variation will be the vivid image — a sickly child on a respirator, say, or a gangrenous foot — which, combined with large text health warnings, will take up over 75% of the surface of the packet. The rest of the pack will be a brown paper background. The company and cigarette brand name will be small and in a prescribed position and font. There will be no logos, no promotional text, no glossy paper and no colour variation.

Tobacco advertising was completely outlawed in Australia by 1992, after bans on radio and television in 1976. This means that cigarette packets are one of very few ways that tobacco companies can use to entice potential customers. Australian public-health experts hope that taking away this means of promotion and making the packets highly unattractive will deter non-smokers, especially young people, from taking up the habit, and make existing smokers feel uncomfortable when they pull out a packet, prompting them to smoke less or even quit.

In its *Report on the Global Tobacco Epidemic, 2011*, the World Health Organization provides statistics from multiple countries showing that packet warnings, particularly pictorial labels, boost the number of people who intend to quit, quit, remain abstinent and do not start smoking.

In Australia, the proportion of 12–17 year olds who smoke every day is only 2.5%. These children have never seen a cigarette advertisement in their everyday environment. The adult smoking rate is 15.1%.

Smoking-related diseases kill around 15,000 Australians a year, and a 2009 report by the Western Australian Cancer Council estimated that tobacco use cost Australia more than $31 billion in 2004–05. This greatly outweighs the $5.6 billion or so the country receives in annual tax revenue from tobacco sales. The predicted health and economic benefits of plain packaging have garnered all-party support for the plan in the Australian parliament, although this took more than two years of debate in the face of strong resistance from tobacco companies and retail associations.

Q3-1: What did Australian government do previously to reduce cigarette smoking population? Did their policy work? (10%)

Q3-2: What's the strategy of the new rule which takes effect in December, 2012? (5%)

(背面仍有題目,請繼續作答)

Q3-3: What's the major driving force for Australian government to pass this new rule? (5%)

Essay 4: Pituitary gland in a dish' makes up for lost hormones

A pituitary gland made from stem cells may some day treat diseases in which people produce little or none of the sex, growth or stress hormones that the organ normally churns out.

Japanese scientists have coaxed mouse embryonic stem cells into forming a working anterior pituitary gland, made of several different kinds of hormone-producing cells. When transplanted into mice, the engineered organ produces a stress hormone called corticotrophin.

The results, from Yoshiki Sasai's team at RIKEN Center for Developmental Biology in Kobe, Japan, are published in *Nature*. The same team created a retina from mouse stem cells, then the most complex tissue yet made from stem cells.

Sasai's team engineered both tissues in three-dimensional cell culture structures that provide support and needed growth factors. To develop properly, the pituitary gland was grown nestled up to stem cells that developed into neurons. This contact mimics the situation in normal pituitary development in which the anterior pituitary gland (which releases growth, sex and stress hormones) develops from the same tissue that makes the oral cavity, while the posterior pituitary (which is involved in regulating fluid balance) forms from neural tissue.

To simulate this in the laboratory, Sasai's team transformed mouse stem cells into both kinds of tissues, side by side. After three weeks, the cells at the intersection had formed an anterior pituitary gland made up of several kinds of hormone-releasing cells. When stimulated with another hormone, the engineered cells produced the stress hormone corticotrophin. Transplanted beside the kidneys of mice lacking pituitary glands (transplanting it where the pituitary normally resides would have destroyed too many blood vessels), the engineered organs produced the same hormone. These mice also were more active and lived longer than mice that didn't receive a transplant.

Professor Mehul Dattani of Paediatric Endocrinology at University College London says pituitary glands made from human stem cells could form a treatment for hypopituitarism, a suite of endocrine disorders caused by low levels of sex, growth and stress hormones. Current treatments involve a lifelong course of potent replacement hormones, and an engineered pituitary gland could rid patients of this burden.

Before this happens, scientists will need to figure out how to transform human embryonic stem cells (and perhaps reprogrammed pluripotent stem cells made from adult tissue) into pituitary glands.

A bigger hurdle to engineering human pituitary glands (besides the safety caveats that come with stem-cell treatments) could be wiring them up properly, Dattani says. The hypothalamus controls the release of many pituitary hormones, and it could prove difficult getting lab-made pituitary glands to talk to the hypothalamus.

Q4-1: Which types of hormone does anterior pituitary gland produce? (5%)

Q4-2: How did the researchers induce pituitary gland formation in cell culture? Is the induced pituitary functional *in vivo*? (10%)

Q4-3: What are 1) the potential therapeutic use for the induced pituitary gland and 2) the difficulties to overcome? (10%)

Essay 5 Sickle-cell mystery solved

It has been a medical mystery for 67 years, ever since the British geneticist Anthony Allison established that carriers of one mutated copy of the gene that causes sickle-cell anaemia are protected from malaria. The finding wasn't trivial: in equatorial Africa, where Allison did his work, up to 40% of people are carriers of this mutated gene. Since then, scientific sleuths have wondered how exactly the gene protects them.

With a paper published in *Science,* the answer — or a large part of it — seems to be at hand.

Sickle cells infected with *Plasmodium falciparum* collapse and prevent the parasite from interfering with the cell's actin proteins, protecting the host against malaria.

Michael Lanzer and his colleagues used powerful electron microscopy techniques to compare healthy red blood cells both with 'normal' cells infected with the malaria parasite *Plasmodium falciparum* and with infected cells from people carrying the mutated "S" gene that causes sickle-cell disease, as well as another mutation, dubbed "C," which occurs at the same spot. Both mutations lead to the substitution of a single amino acid in the hemoglobin molecule, causing the haemoglobin to aggregate abnormally inside the cell. In people with two copies of the S mutation, they deform into a half-moon shape - the 'sickle cells' that give the disease its name.

The researchers saw that in healthy red cells, very short pieces of actin filament — threads of protein crucial to maintaining the pliable internal 'skeleton' that lets the red blood cell squeeze through tiny blood vessels — are clustered just under the cell's outer membrane. But in infected cells, they observed that the malaria parasite steals this actin and uses it to construct an intracellular bridge to transport a parasite-made protein to the cell surface. This protein, called adhesin, makes the infected red blood cells 'sticky', causing them to adhere to each other and to the vessel wall to cause the widespread microvascular inflammation characteristic of malaria.

The parasite doesn't get everything its own way, however. Enter the sickle-cell factor. In red blood cells containing the aberrant sickle-cell haemoglobin, Lanzer and his team observed that the hijacking of actin filaments by the parasite was hobbled. The actin bridge was cut off from the intracellular depot of adhesin, and the vesicles that would normally transport the adhesin to the cell surface were floating free in the cytoplasm.

Further experiments led the team to hypothesize that ferryl haemoglobin, produced when the mutant haemoglobin reacts with oxygen, subverts the parasites' efforts to reorganize their host cells' actin by preventing the actin proteins polymerizing to form long filaments.

The take-home message, says Lanzer, "is that the parasite, in order to survive within the red blood cell, has to remodel the host actin — and that evolutionary pressure has resulted in mutations in human haemoglobin that prevent this remodelling." People who carry just one mutated copy of the sickle-cell gene still make enough normal haemoglobin and so are largely asymptomatic. So being a carrier confers a survival advantage in countries where malaria is endemic.

Q5-1: What's the "sickle cell mystery"? Why is it an important scientific issue? (10%)

Q5-2: What are the major differences in responding to malaria infection between normal RBCs and sickle cells? (10%)

Q5-3: What's the advantage to carry one copy of sickle-cell mutatant gene? (5%)