There are 6 essays in this test. Each essay contains a text followed by questions. **Please answer these questions BRIEFLY according to the text.**

Essay 1 (12%)

Genetic mutations that increase lifespan also seem to be particularly good at fighting tumours, a worm study suggests. The finding could shed light on why cancer risk increases as we get older, and may also suggest new targets for cancer therapeutics.

Cynthia Kenyon and colleagues from the University of California, San Francisco, studied the link in the tiny transparent worm *Caenorhabditis elegans*, a species that doesn't usually get cancer. Some genetic mutations in these worms are known to boost lifespan by affecting processes such as hormone signalling, food intake and respiration. Inactivating a gene called *daf-2*, for example, which is involved in regulating insulin, more than doubles the animals' lifespan from around 17 to 35 days.

When the researchers genetically altered the worms so that they were susceptible to cancer, inactivating *daf-2* still let the worms live to 35 days and restricted tumour growth to half the expected size. "These animals still live twice as long as normal even though they've got a tumour," says Kenyon. "It's really amazing."

To perform the study, the team first had to knock out a tumour suppressor gene called *gld-1* in the worms, causing cells in the animals' gonads to divide rapidly and form germ-line tumours. Left alone, these cancer cells break out of the gonad and fill the body, killing the worm at around 9 days old. They then investigated the effects of a handful of different 'longevity' genes in the tumour-ridden animals, to assess the effects on lifespan and tumour growth. All of the longevity mutations tested increased the worms' lifespans even though they had cancer, the team reports in *Science*.

In the *daf-2* example, the link isn't too mysterious. Researchers have long known that insulin boosts tumour growth in rats. And when tumour-bearing rats are made diabetic, decreasing insulin levels, tumour growth slows. In the worms, lowering insulin levels seems to slow cell division and increase apoptosis - the process by which some cells are able to commit suicide — with a particular impact on tumour cells. The results suggest that tumour cells are generally more susceptible to the effects of longevity-causing mutations than normal cells. So investigating these long-life mechanisms might provide better ways to target cancer. Drugs created this way might even have the side effect of prolonging life, beyond the usual limit for someone without cancer.

（背面仍有題目，請繼續作答）

Q1-1: What is the normal life span of *C. elegans*? (4%)
Q1-2: How does *daf-2* affect longevity and tumour growth? (8%)

Essay 2 (20 %)

Stimulating a protein on the surface of the brain's stem cells helps rats recover after a stroke, US researchers have found. Ronald McKay and his colleagues have now shown that one protein, called Notch, can boost the survival of three different types of stem cell. Notch sits on cell surfaces and is vital for the correct growth of embryos. The team studied rats afflicted with a stroke-like brain injury that normally dulls their movement. When they infused the animals' brains for one week with a molecule that stimulates Notch, the animals' movements improved. The rats also sprouted a collection of new cells in the brain.

Harnessing the body's own stem cells could offer an enticing alternative to attempts to harvest them from other sources, such as embryos. Many researchers are seeking chemicals or proteins that can coax stem cells into multiplying or generating particular cell types. But even when they are successful, the details are often unclear: exactly how does a particular protein, sprinkled on to the outside of a cell, end up causing changes inside?

McKay's team tried to figure this out for Notch. The team found that rousing Notch stops stem cells from dying within minutes. This rapid effect suggests that Notch has knock-on effects on signals being transmitted within the cell. Indeed, the team uncovered two chains of molecules triggered by Notch that have opposing effects on the cell and are fundamental in controlling growth of cancer cells. One promotes cell survival and division. A second seems to nudge stem cells into becoming other cell types instead. The team showed that triggering the survival pathway helps both human embryonic stem cells and cells from the developing mouse pancreas survive in a dish. This suggests that this same mechanism could be common in many, or even most, stem cells. The results also support the idea that cancer, in which cells divide uncontrollably, hijacks mechanisms normally used to schedule the orderly division of stem cells.

Q2-1: In this study, what improved the movements of stroke-suffering rats? (5%)
Q2-2: What is the major role of Notch in cells? What are the two downstream signaling pathways of Notch? (15%)

Essay 3 (16%)

Pharmaceutical fraudsters have had an easy ride for years — counterfeit drugs are notoriously difficult to detect through all the layers of packaging. But a new tweak to an old stalwart of

analytical chemistry could change all that.

Fake drugs are a major international concern, though estimates vary widely as to how bad the problem is. The US Food and Drug Administration suggests that 10% of all drugs are fake; other, unofficial estimates range up to 50%. The problem is worst in developing countries. But Internet sales are helping to push up the figures in the developed world too.

Now, chemists have enlisted a technique called Raman spectroscopy in the fight against fake drugs. By shooting a laser at the target, the technique probes molecular vibrations that are unique to certain chemical bonds — allowing researchers to identify specific molecules through their unique 'Raman' spectrum. The trouble is, the technique usually only works in a very small area, and on the surface. That's a problem when it comes to spotting fake drugs that are encased in capsules, blister packs, or bottles. Drug-testers need to be able to analyze a suspect drug quickly and without having to open the packet.

Pavel Matousek and colleagues at the Rutherford Appleton Laboratory in Didcot, UK, have tested their method on a range of over-the-counter drugs to show how to get around this packaging problem. They used a version known as spatially offset Raman spectroscopy (SORS), in which the detector is slightly offset from the point where the laser hits the sample. That allows the detector to detect photons that have spent time travelling through the actual drug, rather than ones simply bounced off the packaging. Matousek and colleague Charlotte Eliasson tested their stash of drugs, such as ibuprofen and paracetamol, without removing them from their blister packs or bottles. They then compared the resulting spectra with reference spectra for the drugs, and with conventional Raman spectra. Unlike conventional Raman, SORS could identify the drugs.

Darren Andrews from CLIK Knowledge Transfer Daresbury Laboratory in Didcot is setting up a company to develop SORS for commercial use in the new and growing anti-counterfeit industry. Adapting an existing handheld Raman spectrometer into a portable SORS detector should be relatively simple, he says — allowing it to be used in the field. Andrews also envisions other uses for drug companies, such as monitoring drugs as they go through the manufacturing process. The technique could save the industry substantial amounts of money, both from counterfeit drugs and in drug production.

Q3-1: What are counterfeit drugs? (5%)
Q3-2: How does Ramen spectroscopy work to identify a compound? (5%)
Q3-3: Where can SORS be used? (6%)

Essay 4 (16%)

（背面仍有題目，請繼續作答）

Cancer arises when cells rack up mutations in a number of their genes, and begin to divide uncontrollably. Researchers have already identified some of the genes involved in this process by cherry-picking promising candidates — but there are thought to be many, many more.

In the latest study, researchers searched for culprits by determining the genetic sequence of some 13,000 genes found in 11 breast tumours and 11 colorectal tumours that had been preserved for study. They then looked for differences in the genes between cancerous and normal tissues, and cross-checked the result with an additional bank of tumours from 24 breast or colorectal cancers.

The trawl unearthed a total of 189 genes that were mutated in the tumours and are suspected to be a cause of cancer; the majority of these had not been implicated in cancer before. The study confirms that cancer is a fiendishly fickle enemy. The team found that breast and colon tumours harbour almost completely different mutations — in fact, only two mutated genes were shared between them. Cancers in other tissues might also be driven by a different spectrum of mutations. In addition, the team found that no two tumours are exactly alike. All in all, the researchers estimate that a typical breast tumour carries mutations in more than 100 genes. Some 20 of these might be involved in causing the cancer, they say. Less than half of these are likely to be found in another breast tumour. The study is published in *Science*.

The results add weight to the idea that battling cancer is going to be a long and difficult task, as each person might need a different, tailored combination of drugs to combat the wayward cancer genes that are fuelling their disease. But there is some hope. One of the lead authors on the study, Victor Velculescu of the Sidney Kimmel Comprehensive Cancer Center in Baltimore, Maryland, points out that many of the mutated genes fall into groups with a common function, such as sending signals within a cell. So it is possible that drugs that interfere with these processes might work on many different cancers. "Simpler themes emerge within the complexity," he says.

Q4-1: What are the major findings of this study? (10%)
Q4-2: What is the best title for this article? (6%)

<u>Essay 5</u> (20%)

The 'miracle' malaria drug artemisinin is a step closer to being produced plentifully and cheaply. Synthetic chemists have put plant genes into yeast to make it churn out large amounts of the precursor artemisinic acid. The discovery brings hope to areas such as sub-Saharan Africa, where those who need the drug most can ill afford it. Researchers have praised the work and are excited that it may soon be possible to get artemisinin to the 300 million to 500 million people infected with

malaria each year. But many are also concerned that this will trigger the emergence of resistance to the drug, thus destroying our most effective weapon against the disease.

Artemisinin is extracted from the leaves of *Artemisia annua*, or sweet wormwood, and has been used for more than 2,000 years by the Chinese as a herbal medicine called *qinghaosu*. The parasite that causes malaria has become at least partly resistant to every other treatment tried so far. Artemisinin is still effective, but it is costly and scarce.

Jay Keasling at the University of California, Berkeley, and his colleagues tweaked a pathway and used three plant genes to persuade yeast (*Saccharomyces cerevisiae*) to produce and secrete large amounts of artemisinic acid, which is just a few chemical steps away from artemisinin. The researchers hope that once the process is scaled up it will allow artemisinin to be made industrially. A course of artemisinin currently costs US$2.40; cutting the cost to 10% of that should make it affordable for most sufferers.

The prospect of plentiful artemisinin is encouraging, but if the parasite becomes resistant, increased drug production will be worthless. There is no consensus on how likely resistance is, but some think the risk is high. Artemisinin works by disabling a calcium pump in the malaria parasite, and last year researchers reported that the mutation of a single amino acid was sufficient to confer resistance. When another team gave low doses of artemisinin to parasites taken from patients in French Guiana, some mutated, becoming highly resistant to the drug.

The main way to stop resistance arising is to always give the drug in combination with others. In January, the World Health Organization (WHO) made a plea to pharmaceutical companies to end the marketing and sale of single-drug artemisinin medicines. But as other malaria drugs grow increasingly ineffective, many feel that resistance to artemisinin is inevitable.

Q5-1: Which part of the world is the major area affected by malaria? (4%)
Q5-2: How was large scale production of artemisinin made possible? (6%)
Q5-3: Why is resistance to artemisinin a real concern? (10%)

Essay 6 (16%)

We are not the only animals to give ourselves names, says research on bottlenose dolphins. The dolphins' distinctive whistles may function as individual calling cards, allowing them to recognize each other and even refer to others by name.

The research reveals that bottlenose dolphins (*Tursiops truncatus*) each have their own personalized

（背面仍有題目，請繼續作答）

whistle, which is recognized by other dolphins even from a synthetic version played through a speaker. This suggests that the creatures recognize these as names in their own right, rather than identifying individuals based simply on the sound quality of their voice.

The dolphins have also been heard using each others' names in their 'conversation' — meaning that they may be able to call their comrades during social interactions. The calls may be used to bind groups together in the wild where individuals cannot always see each other, or to coordinate their delicately complex hunting manoeuvres.

The effect was revealed in bottlenose dolphins living at in Sarasota Bay, Florida. The individual whistles of these dolphins are well known, as they have been involved in capture and recording studies since 1975. Researchers created artificial versions of specific dolphins' signature calls and played them to other dolphins from the group. Dolphins were more likely to turn towards the speaker if it was playing the call of a close relative, rather than an unrelated dolphin, the team reports in *Proceedings of the National Academy of Sciences*.

The signature whistles are just a small part of a huge vocabulary of whistles, clicks and other calls. In the wild, name calls seem to make up around 50% of all communication. In a tank, where dolphins can all see each other, they drop out of the repertoire almost entirely, replaced by other whistles with meanings that remain enigmatic.

Dolphins are renowned for their communication skills — although the assumption that they possess fully formed language has never been proved. Nevertheless, they produce a bewildering range of different noises. Many animals, such as songbirds and monkeys, have distinctive calls. But these usually convey a message, such as a warning or a call for a mate, rather than a name. Among such animals, recognition of individuals is usually based on the quality of the voice, rather than the specific call. Dolphins are different, but we still know very little about dolphin communication. Some loud calls have been observed in contexts that suggest threats between rivals, or invitations to feast on a food source. For the most part, however, dolphins' whistles, and the constant snick-snick of their clicks, remain a fascinating puzzle.

Q6-1: What evidence suggests that bottlenose dolphins have names? (8%)
Q6-2: What indicates that dolphins possess extraordinary communication skills? (8%)