※ 注意：全部題目均請作答於試卷內之「非選擇題作答區」，請標明題號依序作答。

Part A. (32 pts, 8 pts for each) Read the following stories, and summarize precisely their center theme and provide at least 4 take-home messages per story to the readers.

1. **Why Does Pain Hurt? Scientists Find the Neurons That Cause Our Aches. Pain can light up all regions of the body, making us feel bad. Scientists have now found the brain cells behind that agony (http://blogs.discovermagazine.com/d-brief/2019/01/18/neurons-that-cause-pain-feel-bad/#.XEQ_z1wzY2w, accessed 1/2019).**

A group of researchers have found the brain cells responsible for the emotional unpleasantness of pain — well, they've at least found them in mice. But the results, published in *Science*, could help scientists develop new treatments for chronic pain if that same cluster of cells exits in humans.

"While painful stimuli are detected by nerves," says Gregory Scherrer, one of the study's authors, in a press release, "this information doesn't mean anything emotionally until it reaches the brain. So we set out to find the cells in the brain that are behind the unpleasantness of pain."

Scherrer and his team, based at Stanford University, started by zeroing in on the amygdala, a part of the brain that's long been known to be key in regulating emotions. While exposing mice to a quick, painful stimulus — a drop of hot (but not scalding) water on one of their paws — the group, with the help of brain imaging, spotted some neurons that were more active than when the mice weren't dealing with any painful stimuli.

"But that really only tells you that those neurons were active at some point, and it's not specific enough," says Scherrer. "What we wanted was to look at the neurons of freely moving animals."

So they mounted a so-called miniscope, about the length of a paperclip, onto the rodents' heads. With these mobile microscopes tracking brain activity, the mice were free to wander their cages and encounter painful stimuli on their own. These stimuli included both uncomfortably hot and cold drops of water, neither of which were extreme enough in temperature to actually hurt the mice. When the critters came into contact with the drops, they withdrew. And the neurons the researchers had flagged earlier? They lit up again — a more concrete clue that pointed to these brain cells as the ones responsible for the unpleasantness the brain associates with pain.

To make sure this brain activity was actually linked to the negative emotions of pain and not just emotions in general, Scherrer and his team drilled down even more. This time, they gave the mice a sweet treat: sugar water. If those same neurons that lit up when the mice touched the hot and cold drops also lit up while the rodents were slurping away, then the team would know they were off-track. But the miniscopes showed nothing.

"After all of that, we concluded that this ensemble of neurons selectively responds during pain" Scherrer says. "But it still didn't fully demonstrate that they underpinned the emotional response."

One last test would help him and his team tie that emotional response to the neurons. They set up a surface divvied up into three invisible sections for the mice. One was uncomfortably hot, another uncomfortably cold and the last was a normal temperature. They let two different groups of mice explore this surface. One group was just a regular control group, but in the second group of mice, the scientists had muted the response of the amygdala neurons they'd flagged in previous portions of the study.

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The control mice quickly realized which lane was a comfortable temperature and stuck to it. But the mice with the altered amygdalae, though they still reacted to the hot and cold lanes by pulling their paws away, quickly adjusted and walked about all of the lanes without preference. "Pain was just no longer unpleasant for them," Scherrer says.

And this distinction is an important one. If researchers can find this same cluster of cells in humans, it could help unlock new treatments for people suffering from chronic pain. "There's really no good treatment for chronic pain in humans," Scherrer says. "And that's a major driver of the opioid epidemic. But you'll notice, patients who take opioids for pain report that they can still feel the sensation of pain but say it's less bothersome. The emotions of pain are different."

2. Gut Bacteria Protects Against Food Allergies (http://blogs.discovermagazine.com/d-brief/2019/01/18/gut-bacteria-food-allergies-microbiome/#.XERCN1wzY2w, accessed 1/2019).

In the study, Nagler and a team of researchers found that healthy infants have gut bacteria that prevents the development of food allergies. The researchers also pinpointed a species of gut bacteria that offers a protective effect against allergic reactions to food.

The finding came after the team transplanted gut microbes from babies — four with a cow's milk allergy, and four without — into mice via fecal samples. Mice that received microbes from babies without a cow's milk allergy didn't have an allergic reaction when exposed to the milk. But mice that received microbes from allergic babies experienced life-threatening anaphylaxis when exposed to cow's milk.

The mice included in the study were raised in a sterile, germ-free environment and were fed the same formula as the infants to ensure bacteria colonized properly. Because the mice had no bacteria of their own, they offered a "blank slate" that allowed researchers to study how microbiome composition can affect allergic responses.

The results of the experiment were clear: The microbiome plays a role in determining whether someone develops an allergic reaction to food, Nagler said.

"We showed that the microbiome alone can determine whether or not you get an allergic response," Nagler said.

The researchers identified a single bacteria species that protects a person from having an allergic reaction to food: *Anaerostipes caccae*, which belongs to a common class of bacteria known as *Clostridia*. In a previous study, Nagler and the research team observed that the presence of *Clostridia* in the gut prevented allergic reactions triggered by nuts. Nagler said the researchers were "overjoyed" to again observe *Clostridia*'s role in allergy protection — this time to an entirely different food allergen.

The microbiome's defense mechanisms against food allergens are rooted in butyrate, a short-chain fatty acid produced by the bacteria. Butyrate, which is critical to a healthy microbial community, is currently the focus of new microbiome-based therapies that could treat many common food allergies.

"When you have this disordered microbiome … you're susceptible to allergic responses to all the food allergens," she said. "The drugs we're making should treat all the food allergies."

A treatment for food allergies perhaps can't come soon enough. Food allergies, once considered rare, now affect 15 million Americans, including 5.9 million children. That's 1 in 13 children, or roughly two in every classroom.

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Because there is currently no treatment for food allergies, sufferers must strictly avoid the allergen, which can be difficult. Common food allergens – like milk, nuts, or soy — are everywhere. Exposure to food allergens can cause digestive problems, hives, and swollen airways. In severe cases, life-threatening anaphylaxis can strike. Once anaphylaxis has started, the sufferers' only hope may only be an epinephrine injection and timely medical intervention. Allergic reactions to food can be unpredictable — a food that triggered mild symptoms on one occasion may cause more severe symptoms in the future.

About 90 percent of allergic reactions come from just eight foods: Milk, eggs, peanuts, tree nuts, soy, wheat, fish, and shellfish. Although researchers don't know for sure why the world is becoming more allergic to food, they believe modern lifestyles have altered our internal bacterial communities. The paper says the "misuse of antibiotics, dietary changes, and higher rates of Caesarean birth and formula feeding" are some of the culprits that may be changing our microbiomes and fueling what could be considered a food allergy epidemic.

"The microbiome is the new frontier in science and medicine. We have at least as many microbes living in our bodies as we do cells, if not more. They control every aspect of our physiology and control our response to drugs. Understanding how they interact with us are going to be key to the medicines of the future," Nagler said.

3. **Light-activated, Nano-sized Protein Factories Show Promise For Drug Delivery (http://blogs.discovermagazine.com/80beats/2012/08/13/light-activated-nano-sized-protein-factories-show-promise-for-drug-delivery/#.XERFBlwzY2w, accessed 1/2019)**

Some of the most exciting medical research these days involves light. Light therapy for cancer, in which a tumor-seeking dye becomes toxic as soon as a light is switched on, manages to avoid slaughtering nearby healthy cells. Optogenetics—using light to turn on or off the expression of neurons—has advanced researchers' understanding of neurological diseases.

Light might someday be used for exquisitely tailored drug delivery: tiny packages bearing all the molecular machinery to build a protein are idle when injected into mice, but spring into action when exposed to UV light.

The nanoparticles are little envelopes of cellular membrane, wrapped around a basic set of protein-building machinery and the gene for whatever you'd like manufactured—the researchers used a glowing fluorescent protein for their test. The gene can't be accessed by the machinery because it is sealed into a loop by a piece of molecular adhesive, but shine a UV light on it, and the adhesive unsticks. Then the machinery transcribes the gene, and the protein is expressed. The researchers found that when they injected the particles into mice and turned on the UV light, the injection site glowed.

Though we're far from swapping drugs or medically helpful proteins into these remote-control nano-factories just yet, showing that they can function in a live animal is an exciting advance.

4. **Nanotech Breathalyzer Detects Telltale Signs of Lung Cancer (http://blogs.discovermagazine.com/80beats/2009/08/31/nanotech-breathalyzer-detects-telltale-signs-of-lung-cancer/, accessed 1/2019)**

In a doctor's office in the near future, part of a smoker's routine checkup could involve blowing into a tube connected to a small sensor. The doctor will look at the sensor's display and know immediately whether she has to deliver the grim diagnosis: lung cancer. Researchers in Israel have invented a new "breathalyzer" that can detect chemical compounds produced by lung cancer

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cells. The finished device should be portable and inexpensive and provide a faster, easier, and more sensitive way to screen for tumors than X-rays or blood tests. Such screening should help doctors detect cancer early, when it's most treatable.

The new device, described in *Nature Nanotechnology*, is not the first to find evidence of cancer on a person's breath. Other attempts to do this have yielded promising results, but those devices require a higher concentration of the telltale biomarker chemicals than the Israeli device. The chemicals, called volatile organic compounds (VOCs), are metabolic products present in the vapors that we breathe out, but they occur in such small amounts that researchers have had to find ways to increase their concentrations before testing. But the new sensor has such sensitivity that it can detect traces of the compound in their natural concentrations in human breath, and it can therefore give results immediately, without processing and analyzing the sample in a lab.

The sensor relies on a film of gold nanoparticles, which conducts electricity, layered over a carbon-based substrate. When a patient breathes into the device, particulates in the breath accumulate on the carbon layer and the sensor swells pushing the gold nanoparticles further apart, which, in turn, alters the resistance of the film. Each type of particulate has a unique effect on the resistance which can be measured by having a current flow through the sensor. "The user gets a figure on the device's display panel that indicates whether the person is healthy or has cancer", says lead researcher Hossam Haick.

Lung cancer kills 1.3 million people a year and is the leading cause of cancer death across the world. Only 15 percent of patients live more than 5 years, in part because the disease is usually diagnosed so late. The new sensor was able to clearly differentiate between healthy people and patients with stage-3 or stage-4 lung cancer, meaning that the disease had already progressed significantly. The researchers note that the sensor would be of even greater medical value if it can pick out people in the earlier stages of the disease.

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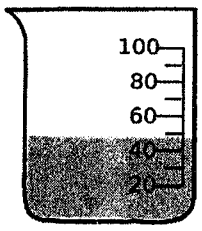
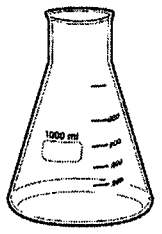
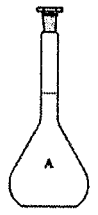
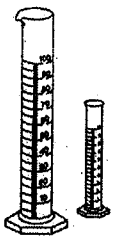
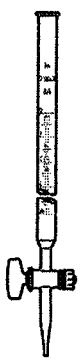
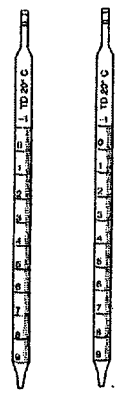
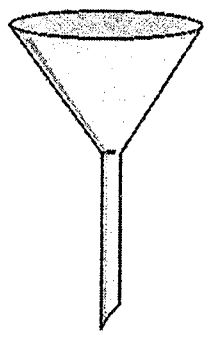
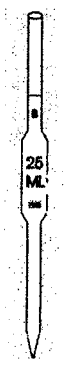
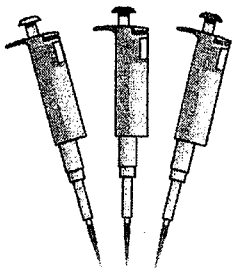
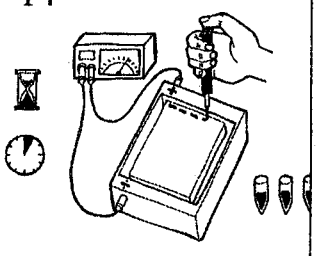
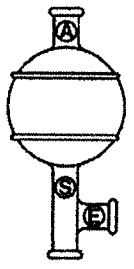
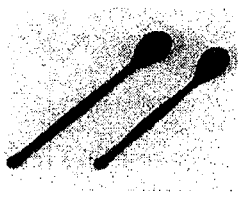
Part B. (18 pts, 1.5 pt for each) Match the following drawings with the Chemical Lab Equipment in the below list (A to L). Write the letter for the drawing that matches in the blank.

5 	6 	7 	8 
9 	10 	11 	12 
13 	14 	15 	16 

(A) Micropipettes
(B) Volumetric flask
(C) Graduated cylinder
(D) Buret
(E) Graduated pipet
(F) Volumetric pipet
(G) Funnel
(H) Spatula
(I) Pipet filler
(J) Erlenmeyer flask
(K) Beaker
(L) Gel electrophoresis

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Part C. Please read the following article and answer the questions [source: Neuron. 100(5):1209-1223 (2018)].

Drugs of abuse, like alcohol, modulate gene expression in reward circuits and consequently alter behavior. However, the *in vivo* cellular mechanisms through which alcohol induces lasting transcriptional changes are unclear. We show that Drosophila Notch/Su(H) signaling and the secreted fibrinogen-related protein Scabrous in mushroom body (MB) memory circuitry are important for the enduring preference of cues associated with alcohol's rewarding properties. Alcohol exposure affects Notch responsivity in the adult MB and alters Su(H) targeting at the dopamine-2-like receptor (Dop2R). Alcohol cue training also caused lasting changes to the MB nuclear transcriptome, including changes in the alternative splicing of Dop2R and newly implicated transcripts like Stat92E. Together, our data suggest that alcohol-induced activation of the highly conserved Notch pathway and accompanying transcriptional responses in memory circuitry contribute to addiction. Ultimately, this provides mechanistic insight into the etiology and pathophysiology of alcohol use disorder.

17. What aspects are irrelevant to this text? (4%)

(A) alcohol consumption (B) molecular signaling (C) drug development (D) brain memory

18. What is the main message conveyed in this paragraph? (4%)

(A) the molecular mechanism for alcohol induced addiction

(B) Dop2R dysfunction is the major cause toward the brain disease

(C) Notch pathway will be altered during disease treatment

(D) alcohol provides an alternative cure for brain malfunctioning

Part D. Please read the following article and answer the questions

[source: https://www.sciencedaily.com/releases/2018/12/181213101308.htm; Nature, 564 (7735): 249 (2018)].

The researchers developed a new method for assessing the climate impact from land-use, and used this, along with other methods, to compare organic and conventional food production. The results show that organic food can result in much greater emissions. "Our study shows that organic peas, farmed in Sweden, have around a 50 percent bigger climate impact than conventionally farmed peas. For some foodstuffs, there is an even bigger difference -- for example, with organic Swedish winter wheat the difference is closer to 70 percent," says Stefan Wirsenius, an associate professor from Chalmers, and one of those responsible for the study. The reason why organic food is so much worse for the climate is that the yields per hectare are much lower, primarily because fertilisers are not used. To produce the same amount of organic food, you therefore need a much bigger area of land. The ground-breaking aspect of the new study is the conclusion that this difference in land usage results in organic food causing a much larger climate impact.

"The greater land-use in organic farming leads indirectly to higher carbon dioxide emissions, thanks to deforestation," explains Stefan Wirsenius. "The world's food production is governed by international trade, so how we farm in Sweden influences deforestation in the tropics. If we use more land for the same amount of food, we contribute indirectly to bigger deforestation elsewhere in the world." Even organic meat and dairy products are -- from a climate point of view -- worse than their conventionally produced equivalents, claims Stefan Wirsenius. "Because organic meat and milk production uses organic feed-stock, it also requires more land than conventional production. This means that the findings on organic wheat and peas in principle also apply to meat and milk products. We have not done any specific calculations on meat and milk, however, and have no concrete examples of this in the article," he explains.

More on: The consumer perspective

Stefan Wirsenius notes that the findings do not mean that conscientious consumers should simply switch to buying non-organic food. "The type of food is often much more important. For example, eating organic beans or organic chicken is much better for the climate than to eat conventionally produced beef," he says. "Organic food does have several advantages compared with food produced by conventional methods," he continues. "For example, it is better for farm animal welfare. But when it comes to the climate impact, our study shows that organic food is a much worse alternative, in general."

For consumers who want to contribute to the positive aspects of organic food production, without increasing their climate impact,

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an effective way is to focus instead on the different impacts of different types of meat and vegetables in our diet. Replacing beef and lamb, as well as hard cheeses, with vegetable proteins such as beans, has the biggest effect. Pork, chicken, fish and eggs also have a substantially lower climate impact than beef and lamb.

19. What is the topic of this research? (4%)

(A) a novel methodology that has been established to reduce the carbon footprint of farming

(B) deforestation can reduce the farming efficiency

(C) a new viewpoint that favors conventional food production in terms of climate impact

(D) all of above

20. How can you help to minimize carbon dioxide emission according to the authors? (4%)

(A) purchase organic beef as the protein source

(B) replace lamb with beef

(C) buy organic food

(D) eat fish and chicken

21. What does "deforestation" mean? (4%)

(A) desertification (B) carbon fixation (C) cultivation (C) eutrophication

Part E. Please read the following article and answer the questions

[source: https://www.technologyreview.com/s/612465/crispr-inventor-feng-zhang-calls-for-moratorium-on-baby-making/].

Feng Zhang, one of the inventors of the gene-editing technique CRISPR, has called for a global moratorium on using the technology to create gene-edited babies. The call from Zhang, a member of the Broad Institute of MIT and Harvard, comes a day after a Chinese researcher, Jiankui He, claims to have created twin girls with modified genes to make them resistant to HIV. "Given the current state of the technology, I am in favor of a moratorium on implantation of edited embryos," Zhang said in a statement provided to MIT Technology Review.

The researchers in the Chinese trial edited human embryos to remove a gene called CCR5, which they said would make the children resistant to HIV. The study was carried out in secrecy, however, and medical experts question whether it was necessary or safe. Zhang said the risks of the experiment outweigh the benefits and said he was "deeply concerned" that the Chinese project was undertaken in secrecy. Previously, academic bodies including the US National Academy of Sciences have said genetically modified children should be made only under strict conditions of safety and oversight. Feng's call for a complete moratorium comes the day before a major genome-editing summit being held in Hong Kong. The Broad Institute said Zhang was on a flight heading to the conference and was unable to comment further. In 2013, Zhang was first to show how the CRISPR tool could be used to edit DNA in human cells, a step that allowed its eventual use to modify human embryos.

22. What are the synonyms for "moratorium" ? (4%)

(A) suspension (B) encouragement (C) development (D) excitement

23. What is the experimental subject in the article? (4%)

(A) mice (B) cancer cells (C) monkey (D) human

24. Which statement is correct according to the text? (4%)

(A) Jiankui He invented CRIPSR technology

(B) Feng Zhang conducted the gene editing on human embryos

(C) there remain safety and ethical concerns of the CRISPR-human trials

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(D) all of above

Part F. Please read the following article and answer the questions

[source: Nature. (2019). DOI: 10.1038/s41586-018-0858-8].

The increasing prevalence of diabetes has resulted in a global epidemic. Diabetes is a major cause of blindness, kidney failure, heart attacks, stroke and amputation of lower limbs. These are often caused by changes in blood vessels, such as the expansion of the basement membrane and a loss of vascular cells. Diabetes also impairs the functions of endothelial cells and disturbs the communication between endothelial cells and pericytes. How dysfunction of endothelial cells and/or pericytes leads to diabetic vasculopathy remains largely unknown. Here the authors report the development of self-organizing three-dimensional human blood vessel organoids from pluripotent stem cells. These human blood vessel organoids contain endothelial cells and pericytes that self-assemble into capillary networks that are enveloped by a basement membrane. Human blood vessel organoids transplanted into mice form a stable, perfused vascular tree, including arteries, arterioles and venules. Exposure of blood vessel organoids to hyperglycaemia and inflammatory cytokines *in vitro* induces thickening of the vascular basement membrane. Human blood vessels, exposed *in vivo* to a diabetic milieu in mice, also mimic the microvascular changes found in patients with diabetes. DLL4 and NOTCH3 were identified as key drivers of diabetic vasculopathy in human blood vessels. Therefore, organoids derived from human stem cells faithfully recapitulate the structure and function of human blood vessels and are amenable systems for modelling and identifying the regulators of diabetic vasculopathy, a disease that affects hundreds of millions of patients worldwide.

25. What is "NOT" the typical symptom of diabetic patients? (4%)

(A) changes in the structure of blood vessels

(B) heart failure

(C) removal of lower limbs

(D) lung infection

26. Which biological hierarchy does "organoid" belong to in the context? (4%)

(A) organelle (B) cell (C) organ (D) organism

27. What title will be most appropriate to the article? (4%)

(A) diabetes and molecular mechanisms

(B) engineering biological scaffolds for replacing diabetic vessels

(C) human blood vessel organoids as a model of diabetic vasculopathy

(D) cell therapies of diabetic disease

Part G. Please read the following article and answer the questions

[source: Science Translational Medicine. 10 (428), eaar7534. (2018); Nature Biomedical Engineering 2: 27–37 (2018)]

Chemoprevention—the use of medication to prevent cancer—can be augmented by the consumption of produce enriched with natural metabolites. However, chemopreventive metabolites are typically inactive and have low bioavailability and poor host absorption. Here, the authors show that engineered commensal microbes can prevent carcinogenesis and promote the regression of colorectal cancer through a cruciferous vegetable diet. The cruciferous family of vegetables, which includes broccoli, brussels sprouts, cabbage, and kale, are unique in their near-ubiquitous prevalence of glucosinolates. These sulfur-rich organic compounds lend these vegetables their notoriously bitter taste but also happen to be useful chemical precursors. The authors engineered probiotic *E. coli* Nissle 1917 to constitutively produce and secrete myrosinase, a type of self-defense enzyme naturally present in plants that hydrolyze glucosinolates into isothiocyanates, which have anticancer activity. In the model, the authors show that murine models of colorectal carcinoma fed with the engineered microbes and the cruciferous vegetable diet displayed significant

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tumour regression and reduced tumour occurrence.

28. What is main active chemical that possesses chemopreventative ability in the text? (4%)

(A) myrosinase

(B) glucosinolates

(C) isothiocyanates

(D) Nissle 1917

29. What would you suggest after reading this article? (2%)

(A) eating vegetables is beneficial for health

(B) do not keep a vegetable diet

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