※ 注意：請於試卷內之「非選擇題作答區」標明題號依序作答。

Part A. (30 pts) Read the following stories, (1) summarize their central theme precisely, and (2) provide at least 6 take-home messages for each.

[Topic of story and the source]

Lower Doses of Peanut Immunotherapy Could Make Allergy Treatment More Accessible

Learn more about peanut oral immunotherapy (OIT) and how lowering the treatment dose could help children with peanut allergies. (https://www.discovermagazine.com/lower-doses-of-peanut-immunotherapy-could-make-allergy-treatment-more-accessible-48487).

[Hint] You may include, but are not limited to

1. Immunotherapy

2. Allergies

What is Peanut Oral Immunotherapy?

According to the study, about 2 percent of children in Canada have peanut allergies. This is also similar to the U.S., where about 2 to 5 percent of children have allergic reactions to peanuts, according to University Hospitals.

However, peanut OIT may provide some benefit to children with peanut allergies. Peanut OIT involves feeding a patient a specified amount of peanut protein. Over time, the dose is gradually increased until the patient reaches a maintenance dose, which is then administered regularly after treatment to reduce the effects of peanut allergy. OIT can be a beneficial treatment for children. But the standard doses are rather large, and the treatment time can be lengthy. Treatments must be monitored by a medical professional as they can lead to anaphylaxis. Because of this, and because a child may dislike the taste of OIT, patients may discontinue the treatment.

As such, the researchers hope that by lowering the dose, they can help make treatments more accessible to patients.

For this study, the research team separated 51 children with peanut allergies into three distinct treatment groups:

A low-dose group with 30 mg as the maintenance dose

A standard-dose group with 300 mg as the maintenance dose

An avoidance group with no OIT administered

The results showed that each OIT group exhibited similar increases in allergic reaction tolerance, whereas those in the avoidance group showed little change.

"We were excited to find that peanut OIT maintenance doses can be much lower than previously thought and still contribute to positive outcomes," said Julia Upton, Head of the Division of Immunology & Allergy, Project Investigator in the SickKids Research Institute, Co-Director of the SickKids Food Allergy and Anaphylaxis Program, and co-first author of the study, in a press release. "The more options we have, the more we can support patients' experience and provide meaningful, tailored care."

The results also showed that patients in the low-dose treatment group experienced fewer severe reactions than those in the standard-dose group. The study authors also note that none of the children in the low-dose group discontinued treatment.

"This is a small enough dose that even children who do not like the taste can continue treatment," said co-senior study author Thomas Eiwegger, Adjunct Scientist in the Translational Medicine program, in a press release. "This is the first time we've compared standard doses to such a low dose, but the minimum maintenance dose to provide benefit may be even lower than 30mg."

The research team hopes that this additional treatment option could make OIT treatments more accessible to more children with peanut allergies, though ultimately, the treatment decision comes down to the patient and their parents or guardians. According to the study, some children may remain on the lower dose, while others may receive the higher dose; this depends on the patient's goals.

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"The study found that very small amounts of peanuts, that are associated with less reactions, could be used as effectively as large amounts for oral immunotherapy, making it safer and accessible to more Canadians, even those who are very sensitive to the allergen," concluded Moshe Ben-Shoshan, co-senior author of the study, a paediatric allergy and immunology specialist at the Montreal Children's Hospital and Scientist in the Infectious Diseases and Immunity in Global Health Program at the Research Institute of the McGill University Health Centre, in a press release.

(This article is not offering medical advice and should be used for informational purposes only)

[Topic of story and the source]

That Receipt in Your Wallet May Disrupt Hormones — A Safer Alternative Could Be Emerging

Learn how researchers are redesigning receipt paper to reduce everyday chemical exposure.

(https://www.discovermagazine.com/that-receipt-in-your-wallet-may-disrupt-hormones-a-safer-alternative-could-be-emerging-48485, accessed 1/2026).

If you have a receipt in your wallet right now, you're carrying more than proof of purchase. Thermal paper — the heat-sensitive material used in receipts, tickets, and shipping labels — is coated with chemicals known to interfere with hormones. These papers are handled daily, stored in pockets and bags, and touched repeatedly, making them one of the most common sources of routine chemical exposure most people never think about.

Most thermal paper depends on bisphenol chemicals to produce text when heated — compounds that have been linked to hormone disruption. Now, researchers report a way around that tradeoff. In a study published in Science Advances, a team describes thermal paper coatings made from plant-based molecules derived from wood and sugars that perform like conventional paper, without relying on bisphenols.

"We have developed thermal paper formulations — which are commonly found in daily products like cash receipts, package labels, airline tickets, etc. — made from plant-based molecules that have very low or no toxic signatures," said Jeremy Luterbacher, one of the study's authors, in a press release.

Instead of starting from scratch, the researchers looked to a material plants already make in abundance. Lignin — the polymer that gives wood its stiffness — contains chemical features capable of driving the color-changing reaction at the heart of thermal printing. It's also renewable, plentiful, and largely treated as waste, making it an appealing foundation for rethinking thermal paper chemistry.

The catch is that lignin isn't naturally printer-friendly. Standard extraction methods leave it dark, chemically inconsistent, and difficult to control — all problems for a material meant to produce crisp, readable text. To overcome that, the team used a refined extraction approach that yields lighter, more uniform lignin molecules. By stripping away many of the light-absorbing components, they created a version of lignin that could mix evenly into thermal coatings without dulling the printed image.

Heat adds another layer of complexity. Thermal paper only works if its components react at the right temperature. To make lignin respond under commercial printing conditions, the researchers added a heat-activated "sensitizer" — a compound that melts during printing and facilitates interaction between the dye and developer. Rather than relying on petroleum-based additives, they tested a sensitizer derived from plant sugars, using a molecule related to xylan, a common component of plant cell walls. The resulting coating could then be applied to paper and tested using real printers.

When heated, the plant-based coatings produced clear, readable text, reaching contrast levels needed for everyday thermal paper. The material also proved stable over time. Samples exposed to light resisted background darkening, and printed markings remained legible long after they were made.

Although the contrast does not yet exceed that of optimized commercial paper, the material met a practical standard: it printed as well as BPA-based products. That matters because even modest losses in image quality can make new materials unworkable at an industrial scale.

The biggest difference emerged in biological testing. The lignin-based developers triggered estrogen-like responses at levels hundreds to thousands of times lower than BPA, while the sugar-derived sensitizer showed no measurable estrogenic activity under the same conditions.

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The results suggest that thermal paper does not have to rely on bisphenols to work. By combining plant-derived molecules with relatively simple processing steps, the researchers outline a path toward receipts and labels that perform as expected — without inadvertently increasing everyday chemical exposure. While further refinement and large-scale testing remain ahead, the study points to a safer alternative for one of the most common materials people handle without thinking twice.

※ 注意：請於試卷內之「選擇題作答區」依序作答。

Part B. (20 pts) Choose the pair of words that best completes the analogy.

The relationship between the first pair should match the relationship between the pair you select.

1. Phagocyte : Pathogen ::
A. enzyme : cofactor
B. antibody : receptor
C. proteasome : ubiquitin
D. macrophage : bacteria
E. polymerase : ribosome

2. DNA : Nucleotide ::
A. lipid : hydrogen
B. protein : amino acid
C. starch : vitamin
D. pathogen : antibody
E. glucose : insulin

3. PCR : Amplification ::
A. centrifuge : separation
B. incubator : freezing
C. pipette : sterilization
D. microscope : digestion
E. buffer : dehydration

4. Ribosome : Protein ::
A. membrane : chromosome
B. lysosome : RNA
C. nucleus : glycolysis
D. chlorophyll : nucleus
E. mitochondrion : ATP

5. CRISPR : Gene Editing ::
A. antibody : metabolism
B. polymerase : mutation
C. vaccine : immune activation
D. catalyst : rust
E. neuron : digestion

6. Flow Cytometry : Cell Sorting ::
A. spectrophotometer : cell culture
B. mass spectrometry : ion detection
C. chromatography : protein purification
D. electrophoresis : antibody binding
E. SEM : metabolic activity

7. Plasmid : Bacteria ::
A. mRNA : ribosome
B. chromosome : animal

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C. antibody : antigen
D. lipid : membrane
E. ATP : mitochondria

8. Photosynthesis : Chloroplast ::
A. transcription : ribosome
B. glycolysis : cytoplasm
C. membrane transport : nucleus
D. respiration : vacuole
E. mitosis : mitochondria

9. Antigen : Immune Response ::
A. hormone : digestion
B. enzyme : contamination
C. pathogen : inflammation
D. glucose : photosynthesis
E. lipid : transcription

10. Oxidative Stress : Mitochondria ::
A. unfolded protein response : ER
B. phototransduction : nucleus
C. lipid oxidation : Golgi
D. glycosylation : lysosome
E. transcription : peroxisome

Part C. (12 pts) Read the following passage and answer the questions below. (2 pts for each question)

CRISPR-Cas9 is a groundbreaking genome-editing tool that has transformed biomedical research. Originally derived from a bacterial defense system, CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats) functions as an adaptive immune mechanism that protects bacteria from viral infections. Scientists have harnessed this mechanism to develop a powerful and versatile tool for targeted genome editing in various organisms, including humans, plants, and model organisms used in biomedical research.

The CRISPR-Cas9 system consists of two key components: a guide RNA (gRNA) and the Cas9 protein. The gRNA is designed to complement a specific DNA sequence, directing Cas9 to the target site. Upon binding, Cas9 induces a double-strand break (DSB) at the designated location. The cell then repairs the break through one of two major pathways: nonhomologous end joining (NHEJ), which often results in small insertions or deletions (indels) that can disrupt gene function, or homology-directed repair (HDR), which allows precise genetic modifications using a donor DNA template.

However, CRISPR-Cas9 approaches involve making cuts to the genetic code, which carries the risk of unintended changes that could lead to other health problems. To address this limitation, researchers have developed newer generations of gene editing tools. Base editing, for example, makes small changes to DNA without creating double-strand breaks. Prime editing uses a Cas9 nickase fused to a reverse transcriptase to introduce point mutations, insertions, or deletions without generating DSBs. The most recent advancement is epigenetic editing, which takes a completely different approach. Instead of cutting DNA strands to remove or edit faulty genes, this method targets chemical markers, known as methyl groups, attached to genes located in the nucleus of every cell.

Researchers have now demonstrated that removing these chemical tags can reactivate silenced genes, while adding methyl groups back can turn genes off again. This shows that DNA methylation is not merely a passive byproduct that accompanies gene repression but is a direct cause of it. Epigenetic editing could offer a potentially safer way to treat genetic diseases, such as Sickle Cell disease, by reactivating fetal hemoglobin genes without altering the DNA. This represents a significant breakthrough that could change the future of genetic disease treatment.

[Modified from Bell et al. (2025). Nature Communications]

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11. According to the passage, CRISPR was originally derived from:

A. A viral replication mechanism
B. A bacterial defense system against viruses
C. A human immune response pathway
D. A plant resistance mechanism

12. Which DNA repair pathway typically results in small insertions or deletions?

A. Homology-directed repair (HDR)
B. Nonhomologous end joining (NHEJ)
C. Base excision repair
D. Mismatch repair

13. What distinguishes base editing from traditional CRISPR-Cas9 editing?

A. Base editing creates larger deletions in the genome
B. Base editing does not require a guide RNA
C. Base editing makes changes without creating double-strand breaks
D. Base editing can only be used in bacterial cells

14. The word "versatile" in the first paragraph is closest in meaning to:

A. Expensive
B. Adaptable
C. Dangerous
D. Limited

15. What role do methyl groups play in gene regulation according to the passage

A. They are passive byproducts with no effect on gene expression
B. They directly cause gene silencing when attached to DNA
C. They activate gene expression by binding to promoters
D. They repair double-strand breaks in DNA

16. The passage suggests that epigenetic editing could treat Sickle Cell disease by:

A. Deleting the mutant hemoglobin gene entirely
B. Inserting a new functional hemoglobin gene
C. Increasing the expression of the mutant sickle cell gene
D. Reactivating fetal hemoglobin genes without cutting DNA

Part D. (12 pts) Read the following passage and answer the questions below. (2 pts for each question)

Organoids are three-dimensional (3D) cell cultures derived from human pluripotent stem cells or adult stem cells that recapitulate the cellular heterogeneity, structure, and function of human organs. These microstructures are invaluable for biomedical research due to their ability to closely mimic the complexity of native tissues while retaining human genetic material. Organoid research has experienced significant advancements in recent years, revolutionizing the fields of disease modeling, drug discovery, and regenerative medicine.

For many years, animal models and two-dimensional (2D) cell lines have played crucial roles in biomedical research, leading to significant breakthroughs in understanding developmental processes, disease mechanisms, and the effects of drugs. Despite their contributions, these models have notable limitations. Traditional 2D cell lines, while practical and cost-efficient, are inherently limited by their simplistic, single-layer structure. This approach fails to accurately mimic the complex three-dimensional environments and

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cell-cell interactions present in living organisms. Animal models, though more reflective of human physiology, face their own set of challenges due to species-specific differences.

A significant milestone in organoid development was achieved in 2009, when Sato et al. successfully established long-term, self-organizing intestinal organoids from adult stem cells. Since then, scientists have developed protocols for generating organoids that represent various tissues, including the brain, liver, kidney, stomach, lung, and pancreas. The integration of microfluidics and biomaterial scaffolds into organoid cultures has further enhanced the replication of organ-specific microenvironments. Additionally, the application of cutting-edge genomic tools, such as CRISPR/Cas9 gene editing and single-cell RNA sequencing, has enabled the generation of organoid models with precise genetic mutations.

Recent studies have demonstrated remarkable achievements in using organoids for therapeutic purposes. In a milestone study, Poling et al. demonstrated that intestinal organoids induced repair across all key layers of the intestine, including the musculature of the mesenchyme. The cellular product was much more than a surface patch over intestinal damage; it demonstrated extensive regenerative potential. In another breakthrough, clinical trials using pluripotent stem cell-derived islet cells showed that patients receiving treatment demonstrated evidence of islet cell engraftment, with the majority reducing or eliminating their need for exogenous insulin.

[Modified from Poling et al. (2024). Cell Stem Cell. Vertex Pharmaceuticals, 2024]

17. According to the passage, organoids are valuable for research primarily because they:

A. Can replicate the structure and function of human organs
B. Are cheaper to produce than traditional cell cultures
C. Are derived exclusively from embryonic stem cells
D. Can completely replace animal models in all experiments

18. What limitation of 2D cell lines is mentioned in the passage?

A. They are too expensive to maintain
B. They cannot survive long-term in culture
C. They fail to mimic complex 3D environments and cell-cell interactions
D. They cannot retain human genetic material

19. The word "recapitulate" in the first paragraph is closest in meaning to:

A. Destroy
B. Simplify
C. Reproduce
D. Analyze

20. According to the passage, which event marked a significant milestone in organoid development?

A. The discovery of human embryonic stem cells in 1998
B. The development of CRISPR-Cas9 technology
C. The first clinical trial of organoid transplantation
D. Sato et al.'s establishment of self-organizing intestinal organoids in 2009

21. Based on the statement, the study by Poling et al. demonstrated that:

A. Organoids induced repairs across multiple intestinal layers, including musculature
B. Organoids can only repair surface tissue damage
C. Intestinal organoids cannot survive transplantation
D. Animal models are superior to organoids for intestinal research

22. What outcome was observed in the clinical trial involving stem cell-derived islet cells?

A. All patients showed severe rejection of the transplanted cells

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B. The treatment had no effect on insulin requirements
C. Most patients reduced or eliminated their need for exogenous insulin
D. Patients required increased insulin doses after treatment

Part E. (12 pts) Read the following passage and answer the questions below. (2 pts for each question)

The 2024 Nobel Prize in Chemistry was awarded to Demis Hassabis and John Jumper from Google DeepMind for developing AlphaFold, and to David Baker from the University of Washington for his work on computational protein design. These innovations have revolutionized the understanding of protein structures by applying artificial intelligence. Proteins are composed of long chains of amino acids that fold into unique three-dimensional structures, which largely determine their function. Understanding these structures is critical for drug discovery and understanding disease mechanisms.

Before AlphaFold, determining 3D protein structures was complex and time-consuming, often requiring experimental methods like X-ray crystallography and cryo-electron microscopy (cryo-EM). Over the past 60 years, biologists have determined the structures of more than 190,000 proteins using these methods. However, determining the structure of just one protein can take several years and hundreds of thousands of dollars. AlphaFold solved this problem by predicting protein structures with remarkable accuracy in minutes.

AlphaFold is a neural network-based model powered by a deep learning algorithm that incorporates vast amounts of physical and biological data on protein structures. At the Critical Assessment of protein Structure Prediction (CASP14) competition in November 2020, AlphaFold2 predicted the structures of proteins based just on their amino acid sequences with astonishing accuracy. The system scored above 90 on CASP's global distance test (GDT) for approximately two-thirds of the proteins, a level of accuracy comparable to experimental methods. This achievement was widely hailed as a solution to the 50-year-old "protein folding problem."

In 2021, DeepMind partnered with the European Molecular Biology Laboratory (EMBL-EBI) to launch the AlphaFold Protein Structure Database, making these predictions freely and openly available. By July 2022, the team had uploaded predictions for around 200 million protein structures from over one million species, covering nearly every known protein on the planet. The freely available database has accelerated scientific research on a scale previously unimaginable. AlphaFold has been used by over 3 million researchers from more than 190 countries to inform their research.

AlphaFold3, announced in May 2024, extended beyond protein structure prediction to model interactions with nucleic acids (DNA and RNA), post-translational modifications, and selected ligands and ions. This has the potential to speed up new drug discoveries by modeling how chemicals bind to protein structures. Researchers continue to explore how to utilize AlphaFold's predictions to gain a deeper understanding of protein folding in living systems and its relationship to diseases such as cancer, Alzheimer's, and cystic fibrosis.

[Modified from Jumper et al. (2021). Nature; Abramson et al. (2024). Nature]

23. According to the message, the 2024 Nobel Prize in Chemistry was awarded for achievements in:
A. CRISPR gene editing and DNA sequencing
B. Protein structure prediction and computational protein design
C. Development of cryo-electron microscopy
D. Drug discovery and clinical trials

24. What experimental methods were traditionally used to determine protein structures?
A. X-ray crystallography and cryo-electron microscopy
B. Mass spectrometry and gel electrophoresis
C. PCR and DNA sequencing
D. Flow cytometry and Western blotting

25. The word "astonishing" in the third paragraph is closest in meaning to:
A. Disappointing

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B. Surprising
C. Moderate
D. Acceptable

26. How many protein structures had been determined experimentally over 60 years before AlphaFold?

A. About 20,000
B. Over 190,000
C. Around 200 million
D. Over 3 million

27. What was significant about AlphaFold2's performance at the CASP14 competition?

A. It failed to predict any protein structures accurately
B. It could only predict structures of bacterial proteins
C. It required several years to make each prediction
D. It achieved accuracy comparable to experimental methods

28. What new capabilities does AlphaFold3 offer compared to AlphaFold2?

A. It can model protein interactions with DNA, RNA, and ligands
B. It can only predict bacterial protein structures
C. It is limited to predicting amino acid sequences
D. It requires more time than experimental methods

Part F. (14 pts) Read the following experimental procedure and answer the questions below. (2 pts for each question)

Single-cell RNA sequencing (scRNA-seq) has become the state-of-the-art approach for unraveling the heterogeneity and complexity of RNA transcripts within individual cells, as well as revealing the composition of different cell types and functions within highly organized tissues, organs, and organisms. The technology enables researchers to see how different cells behave at single-cell resolution, providing new insights into cellular processes that were previously obscured by bulk sequencing methods which average gene expression across thousands of cells.

The first conceptual and technical breakthrough of single-cell RNA sequencing was made by Tang et al. in 2009, who sequenced the transcriptome of single blastomeres and oocytes. This pioneering study opened a new avenue for scaling up the number of cells and making high-throughput RNA sequencing possible at the single-cell level for the first time. Since then, an increasing number of modified and improved single-cell RNA sequencing technologies have been developed to introduce essential modifications and improvements in sample collection, single-cell capture, barcoded reverse transcription, cDNA amplification, library preparation, sequencing, and streamlined bioinformatics analysis. Most importantly, cost has been dramatically reduced, while automation and throughput have been significantly increased.

The initial stage of performing scRNA-seq involves extracting viable and individual cells from the specific tissue under investigation. Novel methodologies, such as the isolation of individual nuclei for RNA-seq (snRNA-seq), are used in conditions where tissue dissociation is challenging, or when samples are frozen or cells are fragile. After cell isolation, cells are captured individually using microfluidic devices or plate-based methods. Each cell is then lysed, and the released mRNA is reverse transcribed into complementary DNA (cDNA) using oligo-dT primers that bind to the poly(A) tail of mRNA molecules. Unique molecular identifiers (UMIs) are incorporated during this step to enable accurate quantification by distinguishing between original mRNA molecules and PCR amplification duplicates.

Following reverse transcription, the cDNA undergoes PCR amplification to generate sufficient material for sequencing. The amplified cDNA is then fragmented, and sequencing adapters are ligated to create the final library. After quality control assessment, libraries are subjected to high-throughput sequencing. The resulting raw sequencing data requires extensive computational analysis, including

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quality filtering, alignment to a reference genome, gene expression quantification, normalization to account for technical variations between samples, batch effect correction, dimensionality reduction (commonly using principal component analysis or UMAP), and clustering to identify distinct cell populations. Differential gene expression analysis between clusters enables the identification of cell-type-specific marker genes, revealing biological insights into cellular heterogeneity. *[Modified from Hwang et al. (2018). Experimental & Molecular Medicine; Mereu et al. (2020). Nature Biotechnology]*

29. According to the paragraph, when was the first single-cell RNA sequencing performed?

A. 2005
B. 2009
C. 2012
D. 2018

30. What is the main advantage of using snRNA-seq over standard scRNA-seq?

A. It provides higher sequencing depth
B. It is suitable for frozen samples or fragile cells
C. It requires less computational analysis
D. It eliminates the need for reverse transcription

31. In scRNA-seq, oligo-dT primers are used during reverse transcription because they:

A. Bind to the 5' cap structure of mRNA
B. Recognize specific gene sequences
C. Bind to the poly(A) tail of mRNA molecules
D. Amplify ribosomal RNA specifically

32. What is the primary purpose of incorporating unique molecular identifiers (UMIs)?

A. To distinguish original mRNA molecules from PCR duplicates
B. To identify different cell types
C. To increase sequencing speed
D. To label different tissue samples

33. According to the article, which step comes immediately after reverse transcription?

A. Cell lysis
B. High-throughput sequencing
C. Dimensionality reduction
D. PCR amplification of cDNA

34. The word "heterogeneity" in the passage is closest in meaning to:

A. Uniformity
B. Diversity
C. Simplicity
D. Stability

35. What is the purpose of normalization in scRNA-seq data analysis?

A. To identify rare cell populations
B. To amplify weak gene expression signals
C. To remove ribosomal RNA contamination
D. To account for technical variations between samples