

※ 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。

一、選擇題 (3 分/題; 共 30 分)

- A pre-surgical patient has been tested to determine the blood group in case a transfusion is necessary during surgery. The results of the ABO grouping is as follows:

<i>Anti-A</i>	<i>Anti-B</i>	<i>Anti-A,B</i>	<i>A₁ cells</i>	<i>B cells</i>
3+	4+	4+	1+	0

What is the cause of this “discrepancy?”

 - B (A) phenomenon
 - hypogammaglobulinemia
 - Anti-A₁ in A₂ individual
 - sepsis resulting in acquired antigen
- If a mother is genetically AO and the father is genetically AA, the frequencies of phenotypes for potential offspring are:

 - all Group A
 - 50% Group A; 50% Group O
 - 75% Group A; 25% Group O
 - 25% Group A; 75% Group O
- The laboratory is very hot due to a malfunction in the heating system. How will this affect the ABO forward and reverse grouping?

 - no affect
 - both forward and reverse may have decreased reactions due to warm temperatures
 - both forward and reverse may have increased reactions due to warm temperatures
 - only reverse grouping may be affected but it is unclear how the temperature will impact the testing
- Which of the following phenotype is associated with Malaria?

 - Fy(a+ b+)
 - Fy(a+ b-)
 - Fy(a- b+)
 - Fy(a- b-)
- An anti-P is suspected when an immediate spin antibody screen is positive in one cell. The ideal temperature for identification is:

 - 17 °C

- B. 25 °C
- C. 37 °C
- D. 42 °C

6. The oligosaccharide molecule that creates the active A antigen is:

- A. Fucose
- B. Galactose
- C. *N*-acetylgalactosamine
- D. Paragloboside

7. Antigen systems that are associated with HDFN include

- 1. Lewis
- 2. Kell
- 3. P
- 4. Kidd
- 5. Duffy

- A. 1, 2, and 5 are correct
- B. 1, 3, and 4 are correct
- C. 2, 4, and 5 are correct
- D. 2, 3, and 5 are correct

8. The Weiner notation R_1R_2 translates to Fisher-Race as:

- A. CDe/cDE
- B. CDe/CDE
- C. CDE/cDE
- D. CDe/cDe

9. The antigen missing in the Rh negative individual is:

- A. C
- B. c
- C. D
- D. d

10. The cell surface charge of RBC is:

- A. Positive
- B. Negative
- C. Neutral
- D. Variable

二、問答題(共 50 分)

1. 請簡述 2018 年諾貝爾生理醫學獎得主美國學者艾利森 (James P. Allison) 跟日本學者本庶佑 (Tasuku Honjo) 對於癌症免疫療法之重大發現及其異同。(10%)
2. 隨時代演進，臨床微生物鑑定方法也日新月異。請以肺結核桿菌為例，闡述肺結核桿菌之特性 (5%) 及傳統鑑定方法及流程 (10%)，並舉三種新穎之鑑定方法學 (15%)。
3. 近年來許多報導指出腸道微生物菌相與人類健康息息相關，請舉出一例腸道菌相與疾病之相關性，並設計實驗說明之。(10%)

三、閱讀測驗(共 20 分)

Please read this abstract and answer the following questions:

Virus specific molecular assays such as real-time PCR (RT-PCR) are now considered the gold standard in the diagnosis of viral respiratory tract infections. They are rapid, relatively inexpensive and offer increased sensitivity and specificity over prior techniques such as virus culture and direct immunofluorescence. Assays can be developed quickly to detect novel/emerging pathogens and can be combined to identify multiple microbiological pathogens in a single test. Yet there is a limit to the number of targets, usually up to four, which can be included in an in-house test before compromising test sensitivity. As a result, diagnostic laboratories must develop a panel of multiplex tests in order to detect the whole range of pathogens. Also, as for all PCR based assays, detection is based on targeting conserved regions of the pathogen genome and mutations can lead to reduced sensitivity or false negative results. Furthermore, only the targeted pathogens included in the assay will be identified, therefore atypical or emerging pathogens will generally evade detection by PCR. Although commercial PCR based tests are available that overcome some of the pitfalls associated with in-house tests, they remain PCR based technologies and as a result suffer from the same sequence-based pitfalls outlined above.

Introducing NGS into a diagnostic setting may revolutionize the investigation of respiratory infections. Combining sequence independent amplification with NGS will potentially detect viral and non-viral pathogens within a clinical specimen without actively targeting them, while simultaneously analyzing the genetic sequence. NGS is established in virus discovery, whole genome studies and metagenome studies thus the simultaneous detection of multiple different pathogens with this technique is possible. However the efficacy and feasibility of employing such techniques in a diagnostic setting requires further study.

Reference:

Thorburn, F., Bennett, S., Modha, S., Murdoch, D., Gunson, R., and Murcia, P.R. (2015). The use of next generation sequencing in the diagnosis and typing of respiratory infections. *J Clin Virol* 69, 96-100.

1. Please explain what is real-time PCR (or quantitative PCR)? What the “real-time” means? (4 points)

2. After extracting nucleic acids from clinical samples, the quality of DNA/RNA samples usually determined by absorbance measurements made on a spectrophotometer. What kinds of substances will be measured at 260nm, 280nm and 230nm? What the 260/280 and 260/230 ratio are used for? (4 points)
3. What is NGS? Please briefly describe the basic principle of next generation sequencing technologies. (4 points)
4. What is metagenome? (4 points)
5. Based on this abstract, please describe the limitations of PCR and NGS in the diagnosis of viral infection. (4 points)