**Name:\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_**

**ID:\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_**

**Please return the midterm exam by 1:00 pm on 4/29. (send to peilin@gate.sinica.edu.tw)**

1. The central dogma of molecular biology describes the transcription from DNA to RNA and translation from RNA to proteins. All of these processes depend on the properties of chemical bonds. Please answer the following questions based on **chemical bonds**

(a) Why are DNA molecules used to store the genetic information (hint: stability) (2 pts)

(b) Why are mRNA molecules used to carry the message (2 pts)

(c) What is the difference between DNA and RNA molecules (2 pts)

(d) How does the sequence in mRNA molecule translate into protein sequence (4 pts)

1. (a) Please describe the original sequencing method. (Sanger sequencing) (10 pts)

(b) Please describe the principle of next-generation sequencing (sequencing by synthesis). (10 pts)

(c) Please describe working principles of the third generation sequencing techniques using zero-mode waveguide( 10 pts) and nanopore (10 pts)

(d) Please describe how to utilize sequencing techniques to trace the origin of our ancestors (both male and female ancestors) (10 pt).

(e)Please explain what is whole genome amplification and why it is needed for gene sequencing. (10pt)

1. In the recent outbreak of COVID-19, it is very important to isolate the infected patients.

(a) Please describe the standard method for identifying the SRAS-CoV-2 virus using RT-PCR (please explain the working principle of PCR and RT-PCR) (10 pts)

(b) Please propose a fast screening method using nanoparticles and a lateral flow microfluidic system (10 pts).

1. (a) What is protein corona? (2pts) How to avoid the formation of protein corona on nanocarriers? (3pts)

(b) Why is the average delivery efficiency of nanoparticles to the tumor sites less than 1% (5 pts)

(c) Could you design an efficient nanocarrier for gene therapy using CRISPR/Cas 9? Please describe the working principle of CRISPR/Cas 9. Please explain your design at the whole body, organ, and cellular level. (20 pts)

(d) What is immunotherapy? (10pts) Could you design a nanocarrier system for immunotherapy? (10pts)

1. (a) Please describe how to determine the sequence of proteins (from separation to detection) (10 pts)

(b)Please explain what is proteomic? (10pts)

(c)Please describe a system capable of performing single-cell proteomics and their working principle (20 pts)

(d)Please describe a system capable of performing spatially resolved transcriptomic and their working principle (20 pts)