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Integrating basic and applied researches of SARS-CoV-2 into the medical molecular biology teaching

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Abstract
Molecular biology is an important course for medical postgraduates to understand the practice of modern molecular medicine. At present, molecular biology has been widely used in the prevention, diagnosis, and treatment of clinical medicine. The COVID-19 pandemic forced all universities suspending academic activities and online teaching all over the world, which is a kind of crisis and has become people's memory of the times. The efforts from all sectors of society, include government, research institutions, and enterprises, have gave medical students a profound impact. The integration of memory of the times into molecular biology teaching will enhance students’ learning interest and understanding effect.

KEYWORDS
COVID-19, molecular biology education, undergraduate

Up to January 2021, COVID-19 epidemic continues in many countries in the global. For the memory of Harbin, a city in Northeast China, such an epidemic is no stranger. In the early 20th century, the pneumatic plague hit the Transbaikal region of Russia and spread fast to Manzhouli, a Chinese town, then to Harbin, causing many deaths. From 1910, Dr. Wu Lien-Teh who was called “plague fighter” later started to implement a series of measures, including burned corpses, isolated patients, proper mask wearing, and controlled the spread of disease successfully.1 In 1926, Harbin Medical College (which together with the Red Army Medical School later formed the predecessor of Harbin Medical University [HMU]) was founded and Dr. Wu Lien-Teh was the first president. Therefore, the staff and students of HMU have a sense of responsibility in the face of such an epidemic.

Undoubtedly, we are in this crisis and it will become the memory of the times in everyone’s heart.2 Many countries have made great efforts (Figure 1), such as China was the first country to report the epidemic situation, the first to complete virus isolation and nucleic acid sequencing, the government actively carried out measure: control the flow of personnel, wearing masks and other measures, until many countries around the world carried out nucleic acid testing, development of vaccines and
drugs. So far, all colleges and universities in mainland China have resumed classes. It can be said that the efforts of science and technology, education, and industry to cope with the COVID-19 pandemic are permeated with research and practice based on molecular biology. This deep memory into the teaching, can bring a surprise effect.

In the first term of 2020, Harbin Medical University, like many universities in China and the world, has experienced a variety of online teachings. Take our online-teaching in 2020 as an example, we taught three classes: medical undergraduates majoring in medical imaging and stomatology (Grade 2018, 143 students, named A class), forensic medicine (Grade 2019, 23 students, named B class) by Tencent software (QQ, a social software, and Tencent WenJuan, an online questionnaire and test software of China) and clinical medicine (Grade 2019, 182 students, named C class) by traditional classroom-teaching.

Firstly, we organized experienced professors to discuss the molecular biology course and the efforts in the pandemic. We sorted out the global efforts to deal with the COVID-19 pandemic situation, compares them with the main chapters of course (Figure 1), then interprets them in teaching process as cases. Here only three cases of them are taken as examples:

- Chapter: Preface

![Learning medical molecular biology from responding to COVID-19 pandemic](image)
Introduce the story of Dr. Wu Lien-Teh’s fight against the epidemic (pneumonic plague) in 1910s and the story of Harbin Medical University participating in the prevention and control of the epidemic. Introduce China’s cooperation with the world’s scientific and technological circles in COVID-19 pandemic, especially focus on molecular

| Table 1 Examples of basic and applied researches on SARS-CoV-2 |
|---|---|
| **Field and main findings** | **Ref.** |
| **Virologic characteristics of SARS-CoV-2** | |
| Direct RNA sequencing and early evolution of SARS-CoV-2. | SARS-CoV-2 sequencing DOI: 10.1101/2020.03.05.976167 |
| A new coronavirus associated with human respiratory disease in China. Nature. 2020, 579(7798): 265–269. | SARS-CoV-2 sequencing DOI: 10.1038/s41586-020-2008-3 |
| MINERVA: A Facile Strategy for SARS-CoV-2 Whole-Genome Deep Sequencing of Clinical Samples. Mol Cell. 2020, 80(6):1123–1134.e4. | SARS-CoV-2 sequencing DOI: 10.1016/j.molcel.2020.11.030 |
| Characteristics of SARS-CoV-2 and COVID-19. Nat Rev Microbiol. 2021, 19(3):141–154. | Review on characteristics of SARS-CoV-2 DOI: 10.1038/s41579-020-00459-7 |
| **ACE2 structure and function** | |
| Structural and functional basis of SARS-CoV-2 entry by using human ACE2. Cell. 2020,181(4): 894–904.e9. | Interaction of S protein and ACE2 DOI: 10.1016/j.cell.2020.03.045 |
| Structural basis of receptor recognition by SARS-CoV-2. Nature. 2020, 581(7807): 221–224. | S protein RBD structure DOI: 10.1038/s41586-020-2179-y |
| Mechanisms of SARS-CoV-2 Transmission and Pathogenesis. Trends Immunol. 2020. | Review on COVID-19 DOI: 10.1016/j.it.2020.10.004 |
| **Gene diagnosis** | |
| Detection of SARS-CoV-2 with SHERLOCK One-Pot Testing. N Engl J Med. 2020. 383(15):1492–1494. | Diagnosis based on CRISPR system DOI: 10.1056/NEJMc2026172 |
| Challenges in Laboratory Diagnosis of the Novel Coronavirus SARS-CoV-2. Viruses. 2020, 12(6):582. | Review on laboratory diagnosis of SARS-CoV-2 DOI: 10.3390/v12060582 |
| **Drug therapy** | |
| New Perspectives on Antimicrobial Agents: Remdesivir Treatment for COVID-19. Antimicrob Agents Chemother. 2020. 65(1): e01814–20. | Chemical drug application DOI: 10.1128/AAC.01814-20 |
| Studies in humanized mice and convalescent humans yield a SARS-CoV-2 antibody cocktail science. 2020, 369(6506): 1010–1014. | Neutralizing antibodies application DOI: 10.1126/science.abd0827 |
biological research and application in virus basic mechanism research, virus nucleic acid detection, and so forth.

- Chapter: Molecular biology techniques

Introduce the concept “domain,” the interaction of SARS-CoV-2 Spike protein (receptor binding domain, RBD) and ACE2 protein in human body and the detection technology.

- Chapter: Gene diagnosis and treatment

Introduce the technical principle of PCR and brief history of PCR technology (PCR, RT-PCR, real-time PCR and droplet digital PCR). Introduce the application of PCR technology in SARS-CoV-2 virus nucleic acid detection.

Introduce the discovery and application of COVID-19 neutralizing fully human antibody drug based on single B cell sequencing technology of convalescent patients and transgenic or transchromosomic mice.

Then, we actively feedback the results and experience of the epidemic in the classroom. The contents of the test questions were updated appropriately, such as “What are the molecular biological processes that may occur after the SARS-CoV-2 enters the human body? (interaction of S protein and ACE2 protein, virus RNA replication, translation according virus RNA using human body translational system).” Students can also study related knowledge from the articles (Table 1) use pushed by WeChat Official Account, another social software on cellphone or online. These have been impressive for students (Figures 2 and 3). The feedback results suggested that the students who have entered the clinical stage thought it (Figure 1) was more meaningful and helpful for them to understand molecular biology theory and application, and students would like to receive and promote it from NPS.

At present, China’s universities have resumed classroom teaching. The extensive online teaching in the first term of 2020 not only improves the teachers’ online

**Figure 2** Net promoter score (NPS) of students to “Learning medical molecular biology from responding to COVID-19 pandemic.”
(a) The ratios of scores (1–10). (b) The scores given by students who have (A class) or have not (B and C class) enter the clinical stage. NPS of A class is 64.71, NPS of B and C class is 39.41. (NPS = the ratio of promoters — the ratio of detractors, for example, NPS of total is 44.45 = 54.39–9.94)
teaching ability, but also provides reference for the follow-up offline-online mixed teaching, enriching teaching and improving teaching quality by using the first-class means. Meanwhile, we should respect science and scientific law, let science and technology serve health, and bear social responsibility.

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CONFLICT OF INTEREST
The authors declare no potential conflict of interest.

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