2023年度
大学院理工学研究科【生命理学専攻】博士後期課程
一般選抜試験(第Ⅱ期)問題

英　語

開始時刻　午前10時00分
終了時刻　午前11時00分

【注意事項】

1．　解答用紙には受験番号、氏名を必ず記入してください。
Be sure to write your examination number and name on the answer sheet.

2．　試験終了後、答案用紙は必ず提出してください（問題用紙は提出しなくてよい）。
After the examination, the answer sheet must be submitted (question papers need not be submitted).

3．　問題番号が明記された答案用紙を使用し、解答してください。
Please use the answer sheet with the question number on it to answer the questions.

問題 1 以下の総説論文の文章を読んで、各問に答えなさい。Read the following text of review article and answer each question

Protein phosphorylation the selective addition of phosphate groups to proteins is a regulatory mechanism that is fundamental to life. Conversely, dysregulated phosphorylation has been implicated in conditions such as Alzheimer's disease, cancer and diabetes. The enzymes that catalyse phosphorylation, known as kinases, are major targets for drugs, so understanding their regulatory roles could provide new therapeutic opportunities. Advances in our ability to identify and quantify phosphorylation using mass spectrometry has led to a rapid rise in the number of known phosphorylation sites in human proteins (collectively known as the phosphoproteome), from hundreds at the turn of the century to more than 100,000 today. However, linking these sites with their associated kinases has been a laborious process. Writing in *Nature*, Johnson *et al.* take a major step towards resolving this problem, describing a comprehensive resource that defines the potential substrates for almost all members of one major class of human kinase. The phosphoproteome is highly complex, comprising tightly interconnected networks of hundreds of protein kinases and tens of thousands of their substrates. Together, they form cell-signalling networks that can function like microprocessors, by encoding, processing and integrating cellular information and regulating outputs in the form of myriad cellular processes, from gene expression to cell division. Such capabilities are possible only because different kinases have different specificities for the many possible protein substrates. The specificity of a kinase arises from many extrinsic and intrinsic factors. Extrinsic factors include whether the kinase and its substrate are expressed in the same cell type or in the same part of the cell, and interactions with other molecules, such as scaffolding proteins. Intrinsic factors arise from the biochemical and structural properties of the kinases and substrates. For example, the presence of electrically charged or bulky amino-acid residues in the vicinity of the phosphorylation site might promote or impede a kinase's ability to phosphorylate a given protein. Intrinsic specificity results in kinases having a preferred motif an ideal sequence of residues that surround the phosphorylation site. Johnson *et al.* use a cell-free technique called positional scanning peptide array analysis to determine the intrinsic substrate specificities of almost all kinases that target the amino acids serine and threonine representing roughly 99% of the phosphorylation sites in human cells. The approach involved screening a library of 303 human kinases to determine how capable each kinase is of transferring a phosphate group to the central serine or threonine residue of hundreds of different short strings of amino acids (Fig. 1) . Remarkably, the authors find that almost two-thirds of phosphorylation sites could be assigned to one of a small handful of kinases.

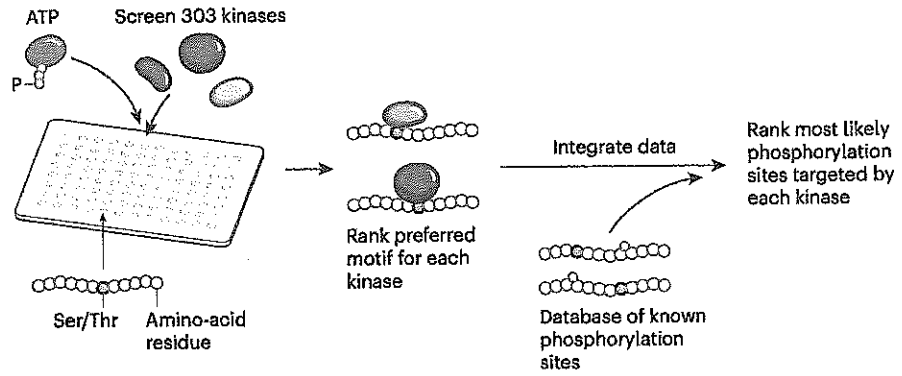

Fig. 1

Although intrinsic aspects alone can resolve potential substrates of the *kinome remarkably well, kinase specificity is also influenced by other factors. Ideally, these factors which include protein protein interactions, tissue and cell specific expression and cellular localization could be incorporated into topological models of cell signalling networks. However, this would require huge amounts of data on many cell types and biological contexts. Fortunately, mass spectrometry based proteomics is rising to meet this challenge. Continued improvements in how we map regulatory kinases will enhance our ability to interpret the language of cell signalling. [Nature **613**, 637–638 (2023)から引用]

*kinom: そのゲノムにおけるプロテインキナーゼ一式を意味する。 In molecular biology, biochemistry and cell signaling the kinome of an organism is the complete set of protein kinases encoded in its genome.

問 1　Question 1

この総説の内容に相応しい題目を日本語あるいは英語で書きなさい。State the title suitable for this review article in Japanese or English.

問 2　Question 2

質量分析は、どのようにこの研究に貢献したかを日本語あるいは英語で説明しなさい。Explain how mass spectrometry contributed to this research in Japanese or English.

問 3　Question 3

この研究の学術的意義と重要性を日本語あるいは英語で説明しなさい。Explain the academic significance and importance of this research in Japanese or English.

問 4　Question 4

Fig. 1 に相応しい説明文の題目と内容の説明を簡潔に日本語あるいは英語で書きなさい。Write the possible title and figure legend suitable for Fig. 1 in Japanese or English.

問 5　Question 5

この総説の要約を 5 行程度で日本語あるいは英語で簡潔にまとめなさい。 Summarize this article briefly in about 5 lines in Japanese or English

問題 2　下記の医学的技術に関連する説明の文章を読んで、各問に答えなさい。

Read the following article related to specific medical technology and answer each question.

A vaccine is a drug used to prevent infectious diseases. Vaccines can be produced either as non-toxic or attenuated antigens. These antigens can be made from the pathogens themselves, as designed gene vaccines (from chemically synthesized mRNA or DNA gene sequences) or as recombinant vaccines (proteins expressed by genetic recombination).. Vaccines are administered to stimulate the production of antibodies against pathogens in the body, thereby providing immunity against infectious diseases. Vaccination is practiced worldwide and is the most effective means in prevention of infectious diseases. Vaccines are particularly valuable against viral infections that do not respond to antibiotics and against the increased prevalence of drug-resistant bacterial infections. Because prevention is more cost-effective than treating infected individuals, it is desirable to prevent diseases with vaccines.

Smallpox is a highly lethal infectious disease. In Japan, smallpox pandemics used to occur every few decades, claiming many lives. The history of vaccine development dates to 1796, when Edward Jenner, an English physician, noticed that people who had cowpox (a disease similar to smallpox), did not get smallpox. Based on this observation, he developed a smallpox vaccine in which a small amount of cowpox virus was injected into a person to make them immune to smallpox. It was the first successful vaccine in history. The name "vaccine" comes from the Latin word *vacca* (= heifer/cows).

In the 1800s, French scientist Louis Pasteur discovered that infectious diseases can be caused by bacteria. He then expanded on Jenner's work and developed live attenuated vaccines, in which pathogens are artificially weakened by passing them through the bodies of animals. This led to the development of vaccines for rabies, anthrax, and fowl cholera. He also popularized "inoculation", in which a vaccine is administered in advance to create immunity and avoid contraction of contagious diseases.

In the 1940s, the World Health Organization (WHO) launched a global campaign to eradicate smallpox. With the widespread use of vaccination, the WHO declared smallpox eliminated in 1980, after the last smallpox outbreak in Somalia in 1977.

Max Tyler successfully attenuated the yellow fever virus by successively passaging mouse and chicken embryos, propagating the virus in these non-human cells, and introducing genetic changes into the cells to weaken the virus.

Later, safer inactivated vaccines were developed in England, rendering the pathogen non-toxic. In the 20th century, various vaccine production methods were developed, including the hatching hen egg culture, cell culture, and genetic modification.

Richard Mulligan and Paul Berg developed recombinant DNA technology. This technology allowed the use of yeast or baculovirus expression systems to produce vaccines against the hepatitis B virus (1986), human papillomavirus (2006), and influenza virus (2013).

In 2008, Kalikow-Katalin et al. in the United States developed a technology that used nucleosides to modify nucleic acids. In 2020, Pfizer-BioNTech and Moderna developed the first vaccine against COVID-19 (SARS-CoV-2) based on this technology, which was approved for emergency use by regulatory authorities in many countries worldwide.

Vaccine development is an ongoing process, and the history of vaccines includes other examples developed against various diseases. Vaccines consist of the whole pathogen or parts of the pathogen and are produced in several ways, including the following:

- Live attenuated vaccines are produced from live pathogens whose virulence has been weakened by suboptimal culture conditions or by a genetic modification that reduces virulence. Examples include vaccines against measles, mumps, rubella, and yellow fever.
- Inactivated vaccines are produced from pathogens that have been inactivated by chemicals or heat. Examples include polio and hepatitis A vaccines.
- Subunit, recombinant, or conjugate vaccines are produced from components of the pathogen, such as specific proteins, polysaccharides, or nucleic acids. These vaccines use parts of the virus or bacteria, such as proteins or sugars, to induce an immune response. Examples include human papillomavirus (HPV), Haemophilus influenza type b (Hib), and some pneumonia vaccines.
- Toxoid is used to induce an immune response. By treating the exotoxin produced by bacteria with formalin or other chemicals, the toxicity of the exotoxin is eliminated while it is still immunogenic. This is called toxoid. Examples include vaccines for tetanus, diphtheria, and pertussis.
- Messenger RNA (mRNA) vaccines, DNA vaccines, and viral vector vaccines deliver the genetic information for the proteins that make up the virus. Based on genetic information, the body manufactures the protein and produces antibodies against the protein, thereby acquiring immunity.

In addition to the antigen source solution, vaccines are prepared (mixed) with other liquids (such as water or saline solution), excipients, preservatives, and possibly adjuvants (immunization aids). Collectively, these ingredients are called additives and ensure that the quality and efficacy of the vaccine are maintained until the expiration date. Vaccines are always prepared in such a way that they are safe and immunizing when administered to humans.

attenuated :弱毒化した、cowpox :牛痘、smallpox :天然痘、heifer (cows): 雌牛、inoculation :(予防)接種

以下の単語は感染症の病名です。The words described below are names of infectious diseases.
rabies :狂犬病、anthrax : 炭疽菌、fowl cholera :家禽コレラ、measles :はしか、mumps :おたふく風邪、rubella:風疹、yellow fever :黄熱病、pneumonia :肺炎、tetanus :破傷風、pertussis :百日咳

問 1　Question 1

あなたがこの説明文のタイトルを付けるとしたら、どのようなタイトルをつけますか？ 日本語あるいは英語でタイトルを提案しなさい。

What would it be if you gave this article a title? Please suggest a title in Japanese or English.

問 2　Question 2

天然痘のワクチンはどのようなワクチンかを、簡単に日本語あるいは英語で説明しなさい。

What kind of vaccine is the smallpox vaccine?　Explain briefly in Japanese or English.

問 3　Question 3

SARS-CoV-2 に対するワクチンはどのような種類のものが現在の世界的主流（認可されているもの）となっているかを、日本語あるいは英語で簡単に説明しなさい。

Briefly explain in Japanese or English what vaccine against SARS-CoV-2 is the current worldwide mainstream (licensed) vaccine.

問 4　Question 4

ワクチン技術の医学的意義や重要性を日本語あるいは英語で簡単に説明しなさい。

Briefly explain the medical significance and importance of these vaccine technologies in Japanese or English.

問 5　Question 5

この説明文の要約を 5 (〜10)行程度で日本語あるいは英語で簡潔にまとめなさい。

Briefly summarize this article in about 5 (to 10) lines in Japanese or English.