

國立中山大學 104 學年度碩士暨碩士專班招生考試試題

科目名稱：普通生物學【海科系碩士班甲組】

題號：458002

※本科目依簡章規定「不可以」使用計算機(問答申論題)

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A. 解釋名詞 (每題 4 分)

1. Prokaryotes
2. Biosphere
3. Isotope
4. Autotrophs
5. Homeostasis
6. Clone
7. Cell respiration
8. Commensalism
9. Reproductive isolation
10. Niche

B. 問答題(每題 20 分)

1. Please explain the structural differences between terrestrial and aquatic animals?
2. Please explain the energy flow in an ecosystem?
3. What is the true definition of evolution?

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科目名稱：科學英文【海科系碩士班乙組、丙組】

題號：458001

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A. Vocabulary: translate the following words into Chinese (10 points; 1 point each).

- (1) significance, (2) reliable, (3) establish, (4) mechanism, (5) imply,
(6) probably, (7) interpret, (8) negative, (9) frequently, (10) gradient.

B. Vocabulary: translate the following words into English according to the category specified in the parentheses (10 points, 1 point each).

- (1) 量化 (verb), (2) 交換 (noun), (3) 結論 (noun), (4) 直接地 (adverb),
(5) 溶解 (verb), (6) 強烈地 (adverb), (7) 正確的 (adjective), (8) 範圍 (noun),
(9) 混合的 (adverb), (10) 分離 (verb).

C. Reading: Read the following report and answer the questions according to the text. For each multiple-choice question, there might be MORE THAN ONE correct or best answer (50 points; 2 points per choice).

STAP Cells Succumb to Pressure

Dennis Normile & Gretchen Vogel (from *Science* 344, 1215–1216, June 2014)

(專有名詞中文: stem cell, 幹細胞; pluripotency, 超多能分化性; embryos, 胚胎; placentas, 胎盤)

Two papers that electrified—and confused—the stem cell field just 6 months ago appear to have lost their last defenders. Last week, lead author Haruko Obokata (小保方晴子) of the RIKEN Center for Developmental Biology (CDB) in Kobe, Japan, agreed to retract a *Nature* paper that described a startlingly easy way to produce stem cells; she had agreed to the retraction of a related paper a week earlier. Obokata's Japanese co-authors had previously called for the moves, and it has been widely reported that another key author, Charles Vacanti, a tissue engineering specialist at Brigham and Women's Hospital in Boston, has agreed to the retractions as well. (He declined to speak with *Science*.)

Last week's developments, which also included new technical challenges to the claims, only add to the puzzlement of many in the field about how the papers were published in the first place. They described a method, called stimulus-triggered acquisition of pluripotency, or STAP, which involves briefly bathing blood cells from newborn mice in a mildly acidic solution and then carefully culturing them. The authors claimed such stimuli generated pluripotent stem cells that could produce mouse embryos and placentas.

But soon after the papers were published, questions emerged about manipulated images. RIKEN, the home institution of several authors, conducted an investigation that found Obokata guilty of research misconduct. Since then, no independent lab has been able to replicate the production of STAP cells. The saga has raised anew perennial questions about the responsibility of senior authors on a paper and the efficacy of the peer-review process—although *Science* has learned that an initial STAP cell paper was rejected by three journals, including *Nature*. Still, the work was ultimately published, leaving open a major question: How did leading stem cell scientists who were co-authors fail to detect the myriad apparent problems with the work?

Hans Schöler, a stem cell scientist at the Max Planck Institute for Molecular Biomedicine in Münster, Germany, offers one lesson from the affair: “Repeat [the experiment] right away.

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Other people in the lab have to do it before it goes out.”

Obokata still says, through her lawyer, that despite the problems in the papers, the procedure works as she claimed. A group at RIKEN, led by co-author Hitoshi Niwa, is trying to determine if she is right. But more problems with the papers have come to light. Last week, Japanese media reported that genetic analysis of cell lines provided by co-author Teruhiko Wakayama of the University of Yamanashi to a third party for testing suggests that what were thought to be STAP cell lines were not derived from the mouse strains supposedly used to create the cells.

Japanese media also reported that Takaho Endo, a researcher at the RIKEN Center for Integrative Medical Sciences in Yokohama, looked at RNA sequences the authors had deposited in databases for a particular type of stem cells derived from STAP cells. He, too, concluded that the sequences came from mouse strains different from those identified in the paper. Moreover, Endo said, the RNAs, which reflect a cell's gene activity, suggested the cells were derived from a mix of embryonic stem cells and trophoblast stem cells—precursors of the placenta.

Many are wondering how the papers got through the peer-review process to begin with. On 4 February, just 6 days after the papers appeared online, an anonymous contributor to PubPeer, a website where published papers are discussed, pointed out that in one article, an image of an electrophoresis gel showing a genetic analysis, Figure 1i, appeared to have been spliced together contrary to normal practice. At about the same time, allegations of plagiarism in the methods section of the article were circulating on Twitter. A RIKEN investigating committee in a 13 March report confirmed those and several other problems with the papers. The committee later concluded that the gel image manipulation constituted research misconduct.

Sources in the scientific community confirm that early versions of the STAP work were rejected by *Science*, *Cell*, and *Nature*. For the *Cell* submission, there were concerns about methodology and the lack of supporting evidence for the extraordinary claims, says Schöler, who reviewed the paper and, as is standard practice at *Cell*, saw the comments of other reviewers for the journal. At *Science*, according to the 8 May RIKEN investigative committee's report, one reviewer spotted the problem with lanes being improperly spliced into gel images. “This figure has been reconstructed,” the RIKEN report quotes from the feedback provided by a *Science* reviewer. The committee writes that the “lane 3” mentioned by the *Science* reviewer is probably the lane 3 shown in Figure 1i in the *Nature* article. The investigative committee report says Obokata told the committee that she did not carefully consider the comments of the *Science* reviewer.

Schöler says it is possible that the *Nature* reviewers placed too much trust in some of the authors on the papers. Asked if other reviewers should have noticed the spliced gel image, he said, “I wouldn't have even thought to look for it because Hitoshi [Niwa], Teruhiko [Wakayama], and Yoshiki [Sasai] were on the paper; there are some people you 100% trust.” Niwa and Sasai are respected stem cell researchers at RIKEN CDB. All three are co-authors of the *Nature* papers, but it is not clear at what point they joined the STAP cell team or which ones were coauthors on the previous submissions.

Both *Science* and *Nature* declined to comment on any particular submission, review, or retraction. “The science of the two papers was rigorously, robustly peer-reviewed as part of our usual editorial procedures. Any inaccuracies in the presentation of data that may have come to light since the peer review are being investigated,” a *Nature* representative wrote in

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an e-mail. "We are currently conducting our own evaluation and we hope that we are close to reaching a conclusion and taking action."

It remains to be seen if the STAP cell debacle touches off the kind of broader soul-searching that followed the unraveling of the Woo Suk Hwang scandal. Hwang, then of Seoul National University, and colleagues made several breakthrough announcements in cloning and stem cell work in *Science* and *Nature* in 2004 and 2005, only for much of it to be revealed as fraudulent in spring 2006.

"Everyone's awareness of the potential for image manipulation has increased significantly since 2006," writes *Science* Executive Editor Monica Bradford in an e-mail. And partly in response to the Hwang scandal, "*Science* and *Nature* and their associated journals are now collaborating to develop standards that promote the reproducibility of research publications," another *Nature* representative wrote in an e-mail.

Many in the field are still waiting expectantly for the results of Niwa's attempts to reproduce the results, hoping they will shed some light on how so many top labs were apparently misled. Schöler says he won't pass final judgment until those results are made public. "I'm going to wait for Hitoshi's final word."

Questions:

- (1) Who is/are the coauthor(s) in Obokata's *Nature* paper?
(A) Hitoshi Niwa (B) Hans Schöler (C) Woo Suk Hwang
(D) Yoshiki Sasai (E) Charles Vacanti
- (2) Based on the method of production, which of the following food would be the best analog of Obokata's STAP cells?
(A) Steam rice (B) Beefsteak
(C) Soda water (D) Pickled cucumber
(E) Hamburger
- (3) Which of the following(s) was/were inferred to be misconduct in the work of Obokata and coauthors?
(A) They reconstructed the electrophoresis gel image.
(B) There was plagiarism in the methods section of the article.
(C) They agreed to retract the paper from *Nature*.
(D) They bathed the blood cells from newborn mice in a mildly acidic solution.
(E) The RNA sequences deposited by the authors in open databases were not consistent with what they claimed to be.
- (4) According to the article, which of the following statement(s) is/are true?
(A) The Obokata case was the first academic scandal related to stem cells since 2000.
(B) The journal *Science* was the first journal to which Obokata and coauthors submitted their article.
(C) The efficacy of peer-review process in academics has been questioned before.
(D) Obokata admitted her misconduct, but still believed her method to be workable.
(E) Obokata had two papers on STAP cells.
- (5) According to the article, what is the best way to avoid research dishonesty and controversy like the Obokata case? Provide your answer in a minimum of 50 words. (10

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points)

D. Writing

“My expectations of graduate school education”

Write a short essay describing your expectations of graduate school education. Try to provide two to three points to elaborate the topic, and use examples to support your argument. The text should have at least 200 words. (30 points)