Recognition of, interest in, and understanding of induced pluripotent stem cells and regenerative medicine in Japanese students

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A B S T R A C T

We studied the recognition of, interest in, and understanding of induced pluripotent stem (iPS) cells and regenerative medicine in a total of 2659 junior high school, senior high school, and university students. The number of valid responses received was 2396 (90.1%). We report the following seven observations [1]. More than 80% of students reported recognition of iPS cells and regenerative medicine, and Professor Shinya Yamanaka, and a similar number were interested in and supportive of regenerative medicine [2]. Regenerative medicine was viewed as a medical treatment option. However, females were more cautious regarding use of regenerative medicine as a treatment compared with males [3]. Approximately 90% of students were interested in the latest medical care. Among the new treatment methods, they more frequently selected those that they were more familiar with and perceived less invasive to be ideal [4]. Regarding organ or tissue donation in regenerative medicine, students focused more on the characteristics of the donors [5]. Approximately 90% were supportive of storing their own cells. However, approximately 50% of students supported storing iPS cells for use in regenerative medicine [6]. Most students were anxious regarding the side effects, safety, and treatment costs of regenerative medicine, but supported the need of education regarding regenerative medicine [7]. More than 70% of students thought that education of regenerative medicine was necessary for the public. These findings suggest the importance of social approach, in addition to medical approach such as research and development, to improve QOL in community by developing the public understanding of regenerative medicine through science communication and school education, for the establishment of systems to promote this field.

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1 Int Introduction

Induced pluripotent stem (iPS) cells were first reported after the reprogramming of mouse fibroblasts in 2006, and human fibroblasts in 2007 [1–3]. The cells were originally generated by introduction of the OCT3/4, SOX2, KLF4, and c-MYC genes by a retrovirus [1]. More effective experimental procedures have since been developed to obtain iPS cells from somatic cells by expression of various combinations of transcription factors or by addition of chemical compounds [3–12]. Professor Shinya Yamanaka, director of the Center for iPS Cell Research and Application (CiRA) in Kyoto University, won the Nobel Prize in Physiology or Medicine in 2012, by his series of such studies.

Stem cells, which include somatic stem cells such as hematopoietic cells, embryonic stem (ES) cells, and iPS cells, have both self-renewal capability and ability to give rise to differentiated cell lines [13,14]. Tissue homeostasis is maintained via the self-renewal and differentiation of somatic stem cells. Especially, hematopoietic stem cells can enter the cell cycle and either self-renew or differentiate into multipotent progenitors that provide diverse mature blood cells [15]. On the other hand, ES cells that obtain from inner cell mass of mammalian embryos in blastocyst stage, have been reported to be established in mouse in 1981 [16,17] and human in 1998 [18]. The capacity for unlimited growth and potential to
develop into all cell types in the adult organism of ES cells has suggested the possibility for cell transplantation therapy, drug screening or toxicity by using patient-specific differentiated cells. However, as for organ transplants, tissue rejection remains a significant concern for ES cell transplantation. Another concern is the use of human embryos [19]. Therefore, establishment of iPS cells in human in 2007 promoted regenerative medicine due to the resolve of the ethical problems of ES cells. The great efforts of the researchers have found possibility of the transplantation therapy with stem cells. QOL of patients is about to improvement by these medical approach.

iPS cells theoretically possess the ability to differentiate into any type of cell allowing construction of various tissues and organs, and have the advantage of being able to be prepared using somatic cells collected directly from the patient. iPS cells provide the opportunity for widespread application, not only limited to cell transplantation therapy, but also for disease modeling in vitro for investigation of pathogenesis and drug screening for novel medications [19–21]. Therefore, multilateral studies, including preparation of tissues and organs, construction of iPS cell stocks for transplantation, as well as basic studies of the reprogramming mechanism for iPS cells from somatic cells, were started all over the world. In Japan, the Ministry of Education, Culture, Sports, Science and Technology-Japan (MEXT) has started various projects for the realization of regenerative medicine using iPS cells from 2007 [22,23]. In 2014, clinical research on age-related macular degeneration using patient iPS cell-derived retinal pigment epithelial cells was started by Dr. Masayo Takahashi’s team [24,25]. Although fibroblasts were originally used the somatic cells for the preparation of iPS cells [1–3], modified methods utilizing while blood cells [11] and a feeder-free culture system [12] have been established for use in medical treatment. The construction of medical iPS cells stocks was discussed among the Ministry of Health, Labour and Welfare (MHLW) [26], CiRA, and the Japanese Red Cross Society, and these organizations have begun to cooperate in its construction. For transplantation of an organ or tissue, it is necessary to at least partially match the human leukocyte antigen (HLA) between the donor and recipient to reduce the incidence of graft rejection; three loci, HLA- A, -B, and DR, are important for this process [27,28]. Okita et al. estimated that the establishment of 140 HLA-homozygous lines for iPS cells selected from 160,000 individuals would provide a match for 90% of the Japanese population [10]. Therefore, the understanding and cooperation of the Japanese public for the construction of such an iPS cell stock is essential.

Recently, importance of science communication is pointed out. After nuclear power disaster in Fukushima, communication gap among scientists, media, and the public was indicated [29,30], and then Horiguchi suggested that training for the skill improvement is essential in the risk communication among them [30]. Concerning iPS cells and regenerative medicine, on the other hand, the area of interest about iPS cells differs among scientists, media, and the public [31], and Hatta has mentioned there is a gap in ability of the regenerative medicine and social expectation [32]. It seems to be insufficient that our public has an individual opinion through science communication and education, although 10 years are going to pass since the establishment of iPS cells. The knowledge about the regenerative medicine of the public was based on information obtained from the media particularly TV [33,34]. Although, the public thought to be familiar with the terms iPS cells and regenerative medicine, they decided to adopt a “wait and see” approach [34]. In this survey [34], the number of responders younger than 20 years old who are essentially the stakeholders of such a technology when regenerative medicine is realized, was remarkably low, because it was targeted to members of a particular company as well as newspaper readers. Therefore, it is remained to be elucidated how the Japanese students feel about iPS cells and regenerative medicine. By medical approach, which is effort of researchers in research and development such as establishment of ES cells and iPS cells, and laboratory to clinical research, regenerative medicine might realize as one of the medical cares in future. Therefore, social approach, which is the public understanding of regenerative medicine through science communication and school education to construct better medical care with medical approach, plays critical roles for the realization. Thus, they are important for us to understand science knowledge and technical terms for regenerative medicine through them, and then to construct better medical care with medical approach, or to be able to understand the medical care when we receive it. Such social approach to improve consciousness of the public might be necessary for realization of regenerative medicine together with medical approach.

Therefore, in the present study, we investigated the recognition of, interest in, and understanding of iPS cells and regenerative medicine in junior high school, senior high school, and university students.

2. Methods

2.1. Participants

Participants were 2659 students at five junior high schools, two high schools, and five universities. The number of valid responses received was 2396 (male: n = 967, female: n = 1429) (junior high school: n = 724, high school n = 866, university n = 806) with a valid response rate of 90.1%. This study applies judgmental sampling design. We asked principal and faculty to perform questionnaire by mail. The school and faculty which obtained its consent were qualified in the sex ratio of pupils, a scale of the class, and achievement level of pupils. Students in schools that obtained consent from principal and faculty, filled out a questionnaire. Numbers of participants in each school depended on the circumstance. Because numbers of participants among kind of schools adjusted almost same, numbers of schools in kind of schools has been different. The survey was conducted between October and November 2013 under the supervision of classroom teachers in each school.

2.2. Questionnaire

The questionnaire contained 19 questions covering the following 5 categories: (1) background of responder, (2) recognition of iPS cells and regenerative medicine, (3) future medical development, (4) relationship between the public and regenerative medicine, and (5) education for regenerative medicine (Table 1).

2.3. Statistical analysis

SPSS statistics version 20 (IBM Japan, Tokyo) was used for statistical analysis. Pearson’s chi-square test was used to compare differences with respect to sex and kind of school.

2.4. Ethical consideration

We explained the purpose of this research to the principal and faculty of each junior high school, high school, and university. Teachers supervising the questionnaire verbally explained to the students that participation was anonymous and voluntary, and that the data would be used only for the purpose of this research.
3. Results

3.1. Recognition of iPS cells, regenerative medicine, and the winning of the Nobel Prize by Professor Shinya Yamanaka

When students in the junior high schools, high schools, and universities were asked regarding their recognition of iPS cells, 50.7% of the participants answered “I know the word and subject matter”, 32.0% answered “I know the word but not the subject matter”, and 12.2% answered “I know the word and subject matter well” (Table 2). Therefore, 94.9% of the participants knew the word, and 62.9% knew both word and subject. Recognition of iPS cells significantly differed among the kinds of schools (p < 0.001). Recognition of iPS cells in males was also significantly higher than in females (p < 0.001). Concerning recognition of regenerative medicine, “I know the word and subject matter well”, “I know the word and subject matter”, and “I know the word but not the subject matter” received 8.2%, 42.9%, and 32.3% of total responses, respectively (Table 2). Therefore, 83.4% knew the word, and 51.1% of the participants recognized both word and subject. The proportion of those reporting recognition of regenerative medicine was similar to the proportion of those reporting recognition of iPS cells. Total proportion of those reporting recognition of Professor Shinya Yamanaka’s winning of the Nobel Prize in Physiology or Medicine in 2012 was 88.9% (Table 2).

These findings demonstrated that more than 80% of students have recognition of iPS cells, regenerative medicine, and Professor Shinya Yamanaka. Report of detailed recognition was higher in males than females, and increased in an age-dependent manner.

3.2. Interest in regenerative medicine and its realization

When the participants were asked regarding their interest in regenerative medicine, 55.3% of participants answered “I am interested in regenerative medicine” and 21.2% as “I am very interested in regenerative medicine” (Fig. 1). Taken together, 76.5% of participants reported interest in regenerative medicine. The

Table 1
List of questions.

| Q1 | What is your occupation?  |
| Q2 | What is your sex?         |
| Q3 | Do you know about iPS cells, regenerative medicine, and the winning of the Nobel Prize by Professor Shinya Yamanaka? |
| Q4 | Are you interested in medicine that transplant tissue and organ prepared from someone's cells? |
| Q5 | Do you believe there is a need for realization of medicine that transplant tissue and organ prepared from someone's cells? |
| Q6 | How would you feel if you were informed by a medical doctor that it was necessary for you to receive a transplant of someone's organ or tissue to save your life? |
| Q7 | What treatment would you want to receive, if you suffered from an incurable disease? |
| Q8 | Are you interested in the development of new medical technologies for incurable diseases? |
| Q9 | What is your ideal treatment, if you suffered from an incurable disease? |
| Q10 | What is your occupation? |
| Q11 | Whose cells would you want to receive for treatment if you receive a transplant of organ or tissue prepared from someone else’s cells? |
| Q12 | To what recipient(s) would you agree to provide your cell-derived organ or tissue to? |
| Q13 | Do you want to cryopreserve your own cells to use the cells for disease or accident? |
| Q14 | What do you want to know about iPS cells and regenerative medicine? |
| Q15 | What are your anxieties concerning iPS cells and regenerative medicine? |
| Q16 | Do you expect the establishment of iPS cell and regenerative medicine usage? |
| Q17 | Do you think you will be involved in work with iPS cells or regenerative medicine in the future? |
| Q18 | Do you think that education for the understanding of iPS cells and regenerative medicine is necessary for the public? |
| Q19 | Do you want to undergo education for improving your understanding of iPS cells and regenerative medicine? |

Table 2
Recognition of iPS cells, regenerative medicine and the winning of the Nobel Prize by Professor Shinya Yamanaka [%].

| Sex (n) | Junior high school | University | Total (2396) |
|---------|--------------------|------------|--------------|
| Male (374) | Female (350) | Total (724) | Male (311) | Female (555) | Total (866) | Male (280) | Female (526) | Total (806) | Male (967) | Female (1429) |
| **I know the word and subject matter well.** | 15.0 | 4.3 | 9.8 | 14.5 | 8.3 | 10.5 | 25.0 | 11.6 | 16.3 | 17.7 | 8.5 | 12.2 |
| Male (302) | Female (513) | Total (815) | Male (280) | Female (526) | Total (806) | Male (967) | Female (1429) |
| **I know the word and subject matter.** | 46.3 | 36.0 | 41.3 | 49.5 | 54.6 | 52.8 | 51.8 | 59.7 | 56.9 | 48.9 | 51.9 | 50.7 |
| Male (302) | Female (513) | Total (815) | Male (280) | Female (526) | Total (806) | Male (967) | Female (1429) |
| **I know the word but not the subject matter.** | 30.2 | 53.1 | 41.3 | 28.6 | 32.4 | 31.1 | 20.7 | 26.8 | 24.7 | 27.0 | 35.4 | 32.0 |
| Male (302) | Female (513) | Total (815) | Male (280) | Female (526) | Total (806) | Male (967) | Female (1429) |
| **I don’t know it well.** | 11.8 | 4.6 | 8.3 | 6.8 | 5.9 | 6.2 | 19.3 | 5.5 | 10.3 | 12.3 | 5.5 | 8.2 |
| Male (302) | Female (513) | Total (815) | Male (280) | Female (526) | Total (806) | Male (967) | Female (1429) |
| **I know the word and subject matter.** | 11.8 | 4.6 | 8.3 | 6.8 | 5.9 | 6.2 | 19.3 | 5.5 | 10.3 | 12.3 | 5.5 | 8.2 |
| Male (302) | Female (513) | Total (815) | Male (280) | Female (526) | Total (806) | Male (967) | Female (1429) |
| **I don’t know it.** | 14.4 | 16.9 | 15.6 | 12.2 | 14.1 | 13.4 | 8.9 | 8.7 | 8.8 | 12.1 | 12.8 | 12.5 |
| Male (302) | Female (513) | Total (815) | Male (280) | Female (526) | Total (806) | Male (967) | Female (1429) |
| **Winning of the Nobel Prize by Prof. Yamanaka.** | 46.3 | 28.9 | 37.8 | 43.7 | 35.9 | 38.7 | 47.5 | 33.1 | 38.1 | 45.8 | 33.1 | 38.2 |
| Male (302) | Female (513) | Total (815) | Male (280) | Female (526) | Total (806) | Male (967) | Female (1429) |
| **I know it well.** | 40.1 | 54.6 | 47.1 | 46.3 | 55.5 | 52.2 | 45.0 | 56.3 | 52.4 | 43.5 | 55.6 | 50.7 |
| Male (302) | Female (513) | Total (815) | Male (280) | Female (526) | Total (806) | Male (967) | Female (1429) |
| **I don’t know it very well.** | 5.6 | 8.6 | 7.0 | 4.2 | 4.7 | 4.5 | 2.9 | 5.9 | 4.8 | 4.3 | 6.1 | 5.4 |
| Male (302) | Female (513) | Total (815) | Male (280) | Female (526) | Total (806) | Male (967) | Female (1429) |
| **I don’t know it.** | 8.0 | 8.0 | 8.0 | 5.8 | 4.0 | 4.6 | 4.6 | 4.8 | 4.7 | 6.3 | 5.2 | 5.7 |

Statistical significance: ###p < 0.001; ***p < 0.01; **p < 0.05 vs. sex.
interest was higher in males than females (p < 0.001), and increased in an age-dependent manner (p < 0.001). Concerning the need of regenerative medicine realization, “Strongly agree” and “Agree” were answered by 36.5% and 50.9% of all participants, respectively (Fig. 2). On the other hand, “Strongly disagree” was answered by 1.3% of all participants. The need of its realization was higher in males than females (p < 0.001), and increased in an age-dependent manner (p < 0.001). Therefore, approximately 80% of students reported interest in regenerative medicine, and affirmed the need of regenerative medicine.

3.3. Opinions on treatment by regenerative medicine

We asked the participants their opinion on receiving regenerative medicine if they suffered from a deadly or inconvenient medical condition. As shown in Fig. 3, participants reported that they would positively receive an explanation from a medical doctor in the case of a deadly disease (32.1%, A) or to improve an inconvenient medical condition (32.0%, B). Treatment with an organ (tissue) prepared from everyone’s cells, including their own, was 27.0% and 25.7%, respectively. However, less than 1% of the participants answered that they would accept an organ (tissue) prepared from cells from others, in contrast with use of their own cells (approximately 20%). Total responses to the use of regenerative medicine for treatment were similar between life-threatening and inconvenient medical conditions (p = 0.863, data not shown). On the other hand, there was significant difference between males and females in each case (p < 0.001). Regenerative medicine with an organ (tissue) prepared from cells of everyone was higher in males than females. Females reported
a higher preference of “explanation from a medical doctor” and “my cells” than males ($p < 0.001$). These findings suggest that regenerative medicine may be regarded as an accepted medical treatment for life-threatening and inconvenient medical conditions. However, females were more cautious in the use of regenerative medicine as a treatment than males.

### 3.4. Interest in the latest medical treatment

Participants reported interest in the development of new medical technology for untreatable diseases as follows: “I am very interested in it” (42.8%), “I am interested in it” (46.7%), “I am not very interested in it” (8.4%), and “I am not interested in it at all” (2.1%) (data not shown). These findings reveal that approximately 90% of students are interested in the latest medical treatments.

### 3.5. Regarding ideal and receivable treatments for incurable diseases

We asked the participants their ideal treatments for incurable diseases, allowing multiple answers. Treatment with “internal medicine” and “advanced operation with few burdens” was selected by 58.0% and 47.8% of participants, respectively (Table 3). “Medical patches” and “ointments” were selected by approximately 40% of participants. Females preferred these treatments more than males ($p < 0.001$). The most infrequently chosen option (2.6%) was treatment with animal organ (tissue). In contrast, frequently chosen receivable treatments included “internal medicine” (63.6%), “ointments” (55.6%) and “medical patches” (55.5%). Females also preferred these treatments more frequently than males ($p < 0.001$). Treatment with animal organ (tissue) was selected by 4% of participants. Furthermore, more than 80% of the participants who...
selected internal medicine, medical patches, and ointments as ideal treatments, regarded them as receivable treatments. In contrast, the proportions of those selecting treatment with animal organ (tissue) and by genome editing as receivable treatments were 32.3% and 36.9%, respectively. Although 9.8% of the participants selected treatment with human organ (tissue) as ideal, 49.4% of participants selecting this treatment as ideal also selected it as receivable. This proportion was higher than those of treatment with animal organ (tissue) or by genome editing. These findings suggest that among new treatment methods, students, especially females, consider those that are more familiar and less invasive to be ideal.

### 3.6. Regarding the subject's role as a recipient or donor in regenerative medicine

When asked whose cells the participants wanted to receive as a recipient of regenerative medicine, allowing multiple answers, approximately 60% of participants responded wanting their own recipient of regenerative medicine, allowing multiple answers, regarding organ or tissue donation for regenerative medicine, age-dependent manner (p < 0.001). In contrast, the proportion of males answering “for me” was 34.0%. Females preferred “for me” (p < 0.001). The proportion of participants who selected “person whom the hospital and specialized agency chose” was 38.6%. As a donor, “for family”, “for anyone”, and “for me” were selected by 48.0%, 45.7%, and 43.2% of participants, respectively (Table 4). The proportions of females who answered “for me” and “for family” were higher than that of males (p < 0.001). There was no significant difference in those who answered “for anyone” between males and females. Participants who answered “person whom the hospital and specialized agency chose” increased in an age-dependent manner (p < 0.001). These findings suggest that regarding organ or tissue donation for regenerative medicine, students focused more on the characteristics of the donors.

### 3.7. Cell stocking

We asked the participants their opinion on the cryopreservation of their own cells, allowing multiple answers. As a result, 46.6% wanted to stock their cells “for family”, and a similar proportion selected “for me” (46.0%) (Fig. 4). The proportion of participants who answered “for everyone” was 34.0%. Females preferred “for me (p < 0.05)” and “for family (p < 0.001)” more than males. The

### Table 3

Ideal treatments willing to be received for incurable diseases (%).

| Gender (n)   | Ideal treatment | Receivable treatment | Percent receivable treatment of ideal treatment (% | Percent receivable treatment of non-ideal treatment (%) |
|--------------|-----------------|----------------------|---------------------------------------------------|-------------------------------------------------------|
| Male (967)   | 53.8            | 38.9                 | 81.4                                              | 38.9                                                  |
| Female (1429)| 60.9            |                      |                                                   |                                                       |
| **Total (2396)** | ***58.0   | **63.6**             | **81.4**                                          | **38.9**                                              |
| Male (967)   | 32.4            | 55.5                 |                                                   |                                                       |
| Female (1429)| 43.9            |                      |                                                   |                                                       |
| **Total (2396)** | ***39.2   | **55.5**             | **81.9**                                          | **55.5**                                              |
| Male (967)   | 31.1            | 82.1                 |                                                   |                                                       |
| Female (1429)| 43.9            |                      |                                                   |                                                       |
| **Total (2396)** | ***38.7   | **55.6**             | **82.1**                                          | **55.6**                                              |
| Male (967)   | 20.7            | 31.2                 |                                                   |                                                       |
| Female (1429)| 27.8            |                      |                                                   |                                                       |
| **Total (2396)** | ***24.9   | **42.7**             | **77.2**                                          | **31.2**                                              |
| Male (967)   | 14.3            | 25.6                 |                                                   |                                                       |
| Female (1429)| 20.6            |                      |                                                   |                                                       |
| **Total (2396)** | ***18.0   | **33.7**             | **70.6**                                          | **25.6**                                              |
| Male (967)   | 38.9            | 29.3                 |                                                   |                                                       |
| Female (1429)| 53.9            |                      |                                                   |                                                       |
| **Total (2396)** | ***47.8   | **48.8**             | **70.2**                                          | **29.3**                                              |
| Male (967)   | 11.4            | 6.0                  |                                                   |                                                       |
| Female (1429)| 7.3             |                      |                                                   |                                                       |
| **Total (2396)** | **8.9**   | **8.8**               | **36.9**                                          | **6.0**                                               |
| Male (967)   | 9.2             | 9.5                  |                                                   |                                                       |
| Female (1429)| 10.2            |                      |                                                   |                                                       |
| **Total (2396)** | **9.8**   | **13.4**              | **49.4**                                          | **9.5**                                               |
| Male (967)   | 3.4             | 3.3                  |                                                   |                                                       |
| Female (1429)| 2.0             |                      |                                                   |                                                       |
| **Total (2396)** | **2.6**   | **13.4**              | **49.4**                                          | **9.5**                                               |
| Male (967)   | 27.4            | 18.1                 |                                                   |                                                       |
| Female (1429)| 24.0            |                      |                                                   |                                                       |
| **Total (2396)** | **25.4** | **23.9**              | **58.1**                                          | **18.1**                                              |
| Male (967)   | 2.3             | 1.6                  |                                                   |                                                       |
| Female (1429)| 2.9             |                      |                                                   |                                                       |
| **Total (2396)** | **2.6**   | **2.4**               | **33.3**                                          | **1.6**                                               |

Statistical significance: *p < 0.05, **p < 0.01, ***p < 0.001 vs. kinds of schools; #p < 0.05, ##p < 0.001 vs. sex.

### Table 4

Role as a recipient and donor in regenerative medicine (%).

| Sex (n) | Junior high school | High school | University | Sex | Total p |
|---------|---------------------|-------------|------------|-----|---------|
| Male (374) | 54.8 | 48.4 | 43.8 | 50.8 | 45.1 *** |
| Female (350) | 70.0 | 67.4 | 61.2 | 69.0 | 65.9 *** |
| Total (724) | 62.0 | 64.7 | 64.3 | 66.0 | 66.0 *** |
| Male (311) | 59.6 | 56.2 | 43.8 | 55.8 | 56.0 *** |
| Female (555) | 67.2 | 64.7 | 43.8 | 66.5 | 66.5 *** |
| Total (866) | 62.9 | 64.7 | 43.8 | 66.5 | 66.5 *** |
| Male (280) | 46.4 | 45.7 | 43.8 | 45.3 | 45.3 *** |
| Female (526) | 68.8 | 66.5 | 43.8 | 43.2 | 43.2 *** |
| Total (806) | 61.0 | 66.5 | 43.8 | 43.2 | 43.2 *** |
| Male (967) | 59.3 | 54.3 | 43.8 | 43.2 | 43.2 *** |
| Female (1429) | 65.0 | 60.2 | 43.8 | 43.2 | 43.2 *** |

Statistical significance: *p < 0.05, **p < 0.01, ***p < 0.001 vs. kinds of schools; #p < 0.05, ##p < 0.001 vs. sex.
proportion of participants who disagreed with cryopreservation of their own cells was 11.6%. The proportion of participants who wanted to stock cells for people whom the hospital and specialized agencies chose significantly increased in an age-dependent manner \((p < 0.001)\). Furthermore, regarding use of cryopreserved cells as a medical resource, the proportions of participants who answered “I want to stock my cells for the people the hospital and specialized agencies choose” and “I want to stock my cells for everyone” were 19.3% \((n = 463)\) and 34.0% \((n = 814)\), respectively. Because 148 participants answered “yes” to both cases, the total number of participants answering “yes” to either option was 1129 \((47.1\%)\). These results reveal that approximately 90% of students had a positive view on the storage of their own cells. Students who had a positive view on the storage of iPS cells for use in a medical iPS cell stock was approximately 50%.

3.8. Interests and anxieties regarding iPS cells and regenerative medicine

We asked the participants regarding their interests and anxieties of iPS cells and regenerative medicine, allowing multiple answers. As shown in Tables 5 and 6, most participants selected side effects, safety of the organ or tissue transplanted, method of transplantation, and treatment cost, as both points of interest and anxiety. Interest and anxiety of these factors were significantly higher in females than in males (Tables 5 and 6). Thus, most students were interested and anxious regarding the side effects, safety, and treatment costs of regenerative medicine.

3.9. Expectation of the establishment of iPS cell and regenerative medicine usage

Expectations of the establishment of iPS cell and regenerative medicine usage was as follows: “I highly expect it” \((55.9\%)\), “I expect it” \((38.1\%)\), “I don’t really expect it” \((4.0\%)\), and “I don’t expect it at all” \((1.0\%)\) (data not shown). These findings reveal that 95.0% of the participants expected the establishment of iPS cell and regenerative medicine usage.

3.10. Involvement in work with iPS cells or regenerative medicine in the future

We asked whether participants foresaw involvement in work with iPS cells and regenerative medicine in the future. Responses
were as follows: “Extremely likely” (6.6%), “Likely” (29.1%), “Unlikely” (46.3%), and “Extremely unlikely” (18.0%) (Fig. 5). There was significant difference among kinds of schools (p < 0.001), and between males and females (p < 0.001). These findings suggest varied interests in career paths among the students.

3.11. Need of education on iPS cells and regenerative medicine

We asked the participants whether they thought education for the public increased in an age-dependent manner (p < 0.001), and it increased in an age-dependent manner (p < 0.001). Thus, more than 70% of students supported education for the understanding of iPS cells and regenerative medicine.

4. Discussion

In this study, we showed that more than 80% of students had recognition of iPS cells and regenerative medicine, and approximately the same number of students reported interest in and support of regenerative medicine. Ninety-five percent expected the establishment of iPS cell and regenerative medicine usage. However, many students reported having concerns of the side effects, safety, and treatment costs of regenerative medicine, and supported education for improving the understanding of iPS cells and regenerative medicine.
and regenerative medicine. In addition, approximately 50% of students supported storing iPS cells for use in regenerative medicine.

Shineha et al. reported in 2010 that recognition of iPS cells and regenerative medicine by Japanese public was 73.7% and 87.3%, respectively [34]. In this study, we showed 94.9% and 83.4% of students recognized iPS cells and regenerative medicine, respectively (Table 2), suggesting recognition of iPS cells was increased compared with report by Shineha et al. The increase in the recognition of iPS cells in students might result from winning Nobel Prize of Professor Yamanaka. Concerning the need of regenerative medicine realization, the proportion of need of the realization (Fig. 2) was similar to the proportion of reported by Shineha et al. [34]. Furthermore, 21.6% said that they would like to cooperate by offering cells and/or blood, and 69.4% would like to wait and see the results of further research [34]. In contrast, our study indicated that students who had a positive view on the storage of iPS cells for use in a medical iPS cell stock was approximately 50%, suggesting that cooperative people increased. More than 70% of students thought that education was necessary and wanted to receive education for improving their understanding of iPS cells and regenerative medicine (Fig. 6), whereas approximately 20% would like to search for information through internet, books or seminars [34]. Therefore, our study suggests that students are positive to realize regenerative medicine.

It is suggested that thinking patterns differ between males and females [35,36]. In the present study, significant sex differences were observed. Males reported better understanding of iPS cells and regenerative medicine (Table 2), and were highly interested in them (Fig. 1). More males reported support of regenerative medicine (Fig. 2) compared with females. Furthermore, males have interests and anxieties about sciences such as “progress of research” and “research institutes and universities” than females (Tables 5 and 6), and preferred “organ (tissue) prepared from cells of everyone” in regenerative medicine to save or improve own life (Fig. 3). On the other hand, more females reported to be interested in and anxious regarding the “side effects”, “safety”, and “treatment costs” (Tables 5 and 6), wanted to undergo the education for iPS cells and regenerative medicine (Fig. 6B), and considered more familiar and less invasive treatments (Table 3). Furthermore, females would make a decision in consultation with a medical doctor (Fig. 3). Our data suggests that there are sex differences in regenerative medicine. Males might view iPS cells and regenerative medicine as one of the new technologies than females. However, females might think them as one of the realistic medical treatments than males.

Some textbooks of junior high schools or high schools describe regarding iPS cells and regenerative medicine. However, there are in topic and development sections, and the words such as regenerative medicine and iPS cells are not listed in a course of study in Japan. Therefore, it depends on the publishing company whether contents about regenerative medicine and iPS cells are listed in textbooks. However, in this study, we showed that more than 80% of the students recognized iPS cells and regenerative medicine, and approximately 50–60% knew both words and subjects, and the recognition increased in an age-dependent manner (Table 2). Although, the knowledge about the regenerative medicine of the public was based on information obtained from the media particularly TV [33,34], education in schools might also contribute the knowledge. According to a course of study in Japan, students learn some words to understand regenerative medicine and iPS cells, for example, “cell” in the science of seventh grader and “gene” in the science of ninth grader. Students who answered “person whom the hospital and specialized agency chose” as both recipient and donor, increased in an age-dependent manner (p < 0.001, Table 4), and “for the people the hospital and specialized agencies choose” in cell stock (p < 0.001, Fig. 4) increased an age-dependent manner. This tendency might result from learning “organ transplantation” in the health of eleventh grader and the basic biology in high school. Therefore, it is thought that students deepen the knowledge of regenerative medicine through the learning various subjects in schools.

In the present study, we reported that many students support development of regenerative medicine, and those with negative opinions were few (Figs. 1–3 and Table 4), suggesting that students may consider the use of regenerative medicine as a possible medical treatment if needed in the future. When organs or tissues prepared from iPS cells are transplanted to the recipient, it is important to match at least partially the HLA type, such as HLA-A, B, and DR, between the donor and recipient to prevent graft rejection. Okita et al. estimated

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**Fig. 5.** Involvement in work with iPS cells or regenerative medicine in the future. Extremely likely (closed), likely (hatched), unlikely (dotted), and extremely unlikely (open). Statistical significance: p < 0.05 vs. kinds of schools; p < 0.001 vs. sex.
that establishment of 140 HLA-homozygous iPS cell lines would provide a match for 90% of the Japanese population, but would require 160,000 individuals for construction [10]. We reported that approximately 50% of students supported medical storage of iPS cells for use in regenerative medicine. The present results also suggest that the establishment of the 140 HLA-homozygous lines may be performed smoothly in Japan. However, as a donor, it should be noted that support of iPS cell storage for use in regenerative medicine was only approximately 50%, whereas opposition was approximately 10% (Fig. 4). In contrast, as shown in Table 4, many students reported a preference of receiving regenerative medicine treatment using their own cells (60.9%), or cells collected from their family (57.7%) or someone chosen by the hospital and specialized agency (38.6%), suggesting that these students preferred an organ or tissue from a source perceived as being highly reliable. Possible ethical problems and the future direction of stem cell therapy, such as iPS cells therapy, have been described by Kanemura [37]. Regarding cell transfer for regenerative medicine, improvement of understanding of as both donors and recipients may promote recognition and satisfaction of this therapy.

QOL of the public including patients might be improved by both medical approach and social approach. Both approaches are important for the public including patients to improve the QOL in community through understanding of regenerative medicine. As shown in Table 6, anxieties of possible side effects and safety may be a result of the students’ exposure to reports of gene misinsertion and tumor generation [4,38,39] by the mass media following the establishment of iPS cells. Therefore, transmission of information on the scientific and medical progress in technology is important for improvement of student’s understanding. Because target diseases (56.9%) and treatment cost (51.3%) were frequently selected as points of interest (Table 5), as well as students’ general opinion as shown in Fig. 2, it is thought that students recognize the importance of regenerative medicine as a medical care. Regarding education, more than 70% of students supported its need (Fig. 6). Some students reported having concerns of possible prejudice and bullying in the community (Table 6). The public most likely obtains information regarding iPS cells and regenerative medicine via media including TV [33,34]. However, students reported the desire

Fig. 6. Need of education of iPS cells and regenerative medicine. (A). Q18. Do you think that education for the understanding of iPS cells and regenerative medicine is necessary for the public? Statistical significance: p < 0.001 vs. kinds of schools; p < 0.001 vs. sex. (B) Q19: Do you want to undergo education for improving your understanding of iPS cells and regenerative medicine? Statistical significance: p < 0.001 vs. kinds of schools; p < 0.001 vs. sex. Strongly agree (closed), agree (hatched), disagree (dotted), and strongly disagree (open).
to learn more of those topics (Fig. 6), suggesting that students prefer the acquisition of comprehensive knowledge compared with fragmentary information provided by TV. Furthermore, it is important for students to participate in programs for science communication at university and museum. The organization such as the California Institute for Regenerative Medicine (CIRM) is also one of the participation. Now that clinical studies have been started, it may be time to promote educational programs for the students to facilitate individual, educated consideration of regenerative medicine as an alternative in medical care, together with understanding of the road map for iPSC cells and regenerative medicine presented by MEXT.

In this study, we applied the judgmental sampling. Our sampling was depended on a judgment of principal in each school. Therefore, there might be included a selection bias. Further investigation is necessary for the public understanding of regenerative medicine through social approach with medical approach.

In conclusion, we described the recognition of, interest in, and involvement by students to facilitate individual, educated consideration of regenerative medicine by students, by supporting spread of information and education.

Conflict of interest

All authors declare no conflict of interest.

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