

## Ordinary Citizens' Expectations for Regenerative Medicine and Induced Pluripotent Stem Cells Researches in Japan

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### Abstract

**Objective:** In order to examine people's expectations for regenerative medicine and iPS cells researches in Japan, we conducted an attitude survey not only among ordinary citizens but also among patients with age-related macular degeneration.

**Methods:** 2,656 ordinary citizens, 445 age-related macular degeneration patients, and families of 210 age-related macular degeneration patients answered 5 question items.

**Results:** Knowledge of iPS cell research, expectations for treatment using iPS cells, and Information acquisition of studies using iPS cells were significantly higher among patients and their families, in comparison with citizens. Regarding iPS cells researches, the ordinary citizens were favor of promoting development of therapeutic drugs for intractable diseases rather than "organ regeneration, including the liver and kidney" and "creation of sperm and ova for assisted reproductive technology".

**Conclusions:** Expectations for regenerative medicine, using iPS cells, were greater both among individuals involved in the disease and ordinary citizens. Especially, they count on development of therapeutic drugs for intractable diseases.

**Keywords:** Regenerative medicine; iPS cells researches; Bioethics; Attitude survey; Ordinary citizens; ELSI

### Introduction

Currently, regenerative medicine is among the medical fields that have attracted the greatest attention in Japan. Since Professor Yamanaka won a Nobel Prize for his research on induced pluripotent stem (iPS) cells, ordinary citizens have paid attention to regenerative medicine in Japan [1]. In addition, large-scale projects sponsored by the Japanese Government, such as the Research Center Network for Realization of Regenerative Medicine, have actually advanced [2].

Various ethical, legal, and social issues (ELSI) have been reported for regenerative medicine using iPS cells [3]. Therefore, for the advancement of this medical field, social consensus building among ordinary citizens is essential, as is the participation of patients and their families [4]. In this study, we decided to conduct an attitude survey on knowledge of and expectations for regenerative medicine, and whether its promotion is right or wrong. The attitude survey was also conducted among patients with age-related macular degeneration, a representative disease for which regenerative medicine has been promoted. Their families were concurrently surveyed, and the awareness of ordinary citizens was compared with that of patients with intractable diseases, as primary stakeholders in research on regenerative medicine.

### Methods

This survey aimed to obtain responses from 2,400 ordinary citizens, 400 age-related macular degeneration patients, and families of 200 age-related macular degeneration patients. These were extracted from a group (approximately 1,200,000 people) monitored by a major research company, between March 18 and March 24, 2014. For ordinary citizens, an online survey was conducted by adjustment for the population ratio of all 47 prefectures in Japan × sex ratio × single and married people, based on the 2005 Population Census in Japan. This survey was conducted after obtaining the approval of the ethical review board of the Faculty of Medicine, The University of Tokyo (Review number: 10437). Informed consent was obtained from all individual participants included in the study. In the beginning of this survey, studies using iPS cells were illustrated in a form that was as easily understood as possible by nonspecialists, on a four page online screen. The subjects were then asked to answer five questions regarding the level of subjective understanding of studies using iPS cells, information acquisition about such studies, whether promotion of each technology using iPS cells was right or wrong, and expectations for these studies (Table 1). SPSS supplied by IBM was used for statistical analysis. For questions (1), (2), and (4), responses were provided on a four-point scale and defined by an ordinal number. The data were analyzed using the Mann-Whitney and Kruskal-Wallis tests, and adjusted for multiplicity using Bonferroni's correction. In addition, for question (4), McNemar's test was used to assess the percentage of ordinary citizens who support the studies, and adjusted for multiplicity using Bonferroni's correction. For question (5), the data were analyzed

using the chi square test, and adjusted for multiplicity using Bonferroni's correction.

1	<b>How much do you know about intractable disease studies using iPS cells?</b>
	1. Know very much
	2. Know
	3. Not know very much
2	<b>To what extent do you actively acquire information on iPS cells?</b>
	1. Strongly active
	2. Active a little
	3. Inactive a little
3	<b>What is your source of information about iPS cells?</b>
	1. Television
	2. Magazine
	3. Internet
	4. Newspaper
	5. Academic journal
	6. Book
	7. Lecture meeting
8. Other	
4	<b>Do you think how should studies be promoted among the following studies using iPS cells?</b>
	A. Organ regeneration (e.g., liver and kidney)
	B. Development of therapeutic drugs for intractable diseases
	C. Creation of sperm and ova for assisted reproductive technology
5	<b>How effective do you think the use of iPS cells for treatment of age-related macular degeneration will be?</b>
	1. Strongly improve
	2. Partly improve
	3. Improve a little
	4. Inhibit deterioration
	5. No payback

Table 1: Question items.

## Results

Of 10,472 subjects who were asked to participate, a total of 3,311 valid responses were obtained, with a return rate of 31.6% (2,656 ordinary citizens (80.2%), 445 age-related macular degeneration patients (13.4%), 210 families of age-related macular degeneration patients (6.3%); 1,723 men (52.0%), 1,588 women (48.0%).

### Knowledge of iPS cell research and expectations for treatment using iPS cells

For the subjective question: "How much do you know about intractable disease studies using iPS cells", the mean score of the

citizens was  $2.18 \pm 0.59$  (n=2656). The mean scores of the patients and their families were  $2.38 \pm 0.61$  (n=445) and  $2.30 \pm 0.56$  (n=210), respectively (Table 2). The mean score of the citizens was significantly lower than that of the patients and families ( $p < .001$ ,  $p = .002$ , respectively). In addition, a five-point scale was used to determine the degree of expectations for regenerative medicine using iPS cells ("How effective do you think the use of iPS cells for treatment of age-related macular degeneration may be?"). Responses indicating some expectation for improvement in visual acuity ("Visual acuity may be greatly improved", "may be improved to some extent", and "may be improved a little") were obtained from 76.8%, 88.8%, and 90.0% of citizens, patients, and families, respectively. Thus, the expectations for treatment were significantly higher among patients and their families, in comparison with citizens ( $p < .0001$ ).

	Amount of knowledge	Degree of information acquisition
<b>Ordinary citizens</b>	a, b $2.18 \pm 0.59$ 95%CI: 2.16-2.20 n=2656	c, d $1.66 \pm 0.66$ 95%CI: 1.63-1.68 n=2420
<b>Age-related macular degeneration patients</b>	a $2.38 \pm 0.61$ 95%CI: 2.32-2.43 n=445	c $1.92 \pm 0.68$ 95%CI: 1.85-1.98 n=420
<b>Families of age-related macular degeneration patients</b>	b $2.30 \pm 0.56$ 95%CI: 2.22-2.38 n=210	d $1.89 \pm 0.69$ 95%CI: 1.79-1.98 n=200
There was a significant difference in a, b, c, and d ( $p < 0.017$ )		

Table 2: Subjective decision for the amount of knowledge and degree of information acquisition on intractable disease studies using iPS cells.

### Information acquisition of studies using iPS cells

For the question: "To what extent do you actively acquire information", the mean scores of the citizens, patients, and families were  $1.66 \pm 0.67$  (n=2420),  $1.92 \pm 0.68$  (n=420), and  $1.89 \pm 0.69$  (n=200), respectively. Thus, the mean score of the citizens was significantly lower than that of the patients and families ( $p < .001$ ). Regarding the source of information for iPS cell research (multiple answers allowed), television was first (n=1521), followed by newspapers (n=853), the Internet (n=791), weekly and monthly general magazines (n=199), books (n=67), academic journals (n=55), lectures or symposia (n=24), and others (n=16).

### Use of iPS cells for organ regeneration, development of therapeutic drugs for intractable diseases, and assisted reproductive technology

The ordinary citizens were asked whether the following studies using iPS cells should be promoted: "organ regeneration, including the liver and kidney"; "development of therapeutic drugs for intractable diseases"; and "creation of sperm and ova for assisted reproductive technology". The mean respective response scores were  $3.36 \pm 0.72$  (n=2656),  $3.67 \pm 0.59$  (n=2656), and  $2.80 \pm 0.87$  (n=2656). For "organ regeneration, including the liver and kidney", and "development of therapeutic drugs for intractable diseases", there was a significant difference between the responses of citizens and patients, and between responses of the citizens and families (Figure 1). Among the citizens,

the percentages of those who greatly supported promotion, or promotion to some degree, of "organ regeneration, including the liver and kidney", "development of therapeutic drugs for intractable diseases", or "creation of sperm and ova for assisted reproductive

technology", were 96.0%, 98.7%, and 61.4%, respectively. Thus, there was a significant difference in the percentages of supporters and non-supporters of promotion ( $p < 0.001$ ). There was a significant difference in a, b, c, and d ( $p < 0.001$ ).

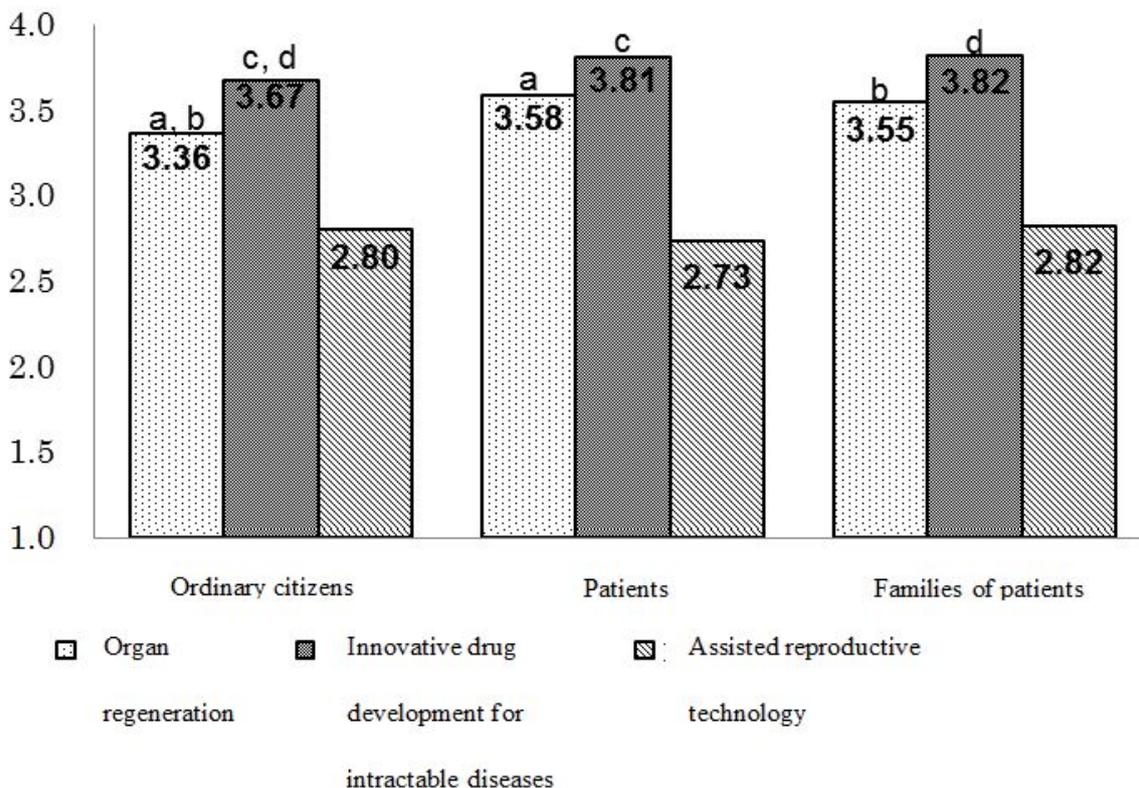


Figure 1: Degree of support of promotion by type of study using iPS cells.

## Discussion

This is the first report comparing awareness of regenerative medicine research, using iPS cells for intractable disease, between ordinary citizens and individuals involved in the disease.

For the effect of regenerative medicine on age-related macular degeneration, the number of responses indicating that the subjects thought visual acuity may be improved was greater among individuals involved in the disease, than among ordinary citizens. However, although iPS cell-derived retinal pigment epithelium (RPE) cell sheets under clinical study may inhibit progression of the disease, they are not expected to improve visual acuity substantially [5]. These results suggest that individuals involved in the disease have excessive expectations. This may reflect their desires, or a lack of accurate knowledge. On the other hand, the amount of knowledge regarding regenerative medicine using iPS cells tended to be greater among individuals involved in the disease than among ordinary citizens. Furthermore, active information acquisition also tended to be greater among individuals involved in the disease, compared with ordinary citizens. For the source of knowledge, television was identified more often than the Internet or books, both by ordinary citizens and

individuals involved in the disease, indicating that information was primarily acquired passively. Individuals involved in the disease have excessive expectations for the effect of regenerative medicine on age-related macular degeneration; therefore, current television-centered information acquisition may be insufficient. With the example of issues related to Stimulus-Triggered Acquisition of Pluripotency (STAP) cells [6], scientific news reporting *via* television tends to prioritize sensationalism over accurate scientific information. A previous study reported that there is no association between information acquisition *via* television and scientific knowledge, although information acquisition *via* the Internet is associated with scientific knowledge [7].

There are many aspects to regenerative medicine research using iPS cells, which have now spread through many fields. In this study, we surveyed individual awareness of three items (organ regeneration, including the liver and kidney; development of therapeutic drugs for intractable diseases; creation of sperm and ova for assisted reproductive technology). Results showed that both ordinary citizens and individuals involved in the disease strongly felt that studies for innovative drug development should be promoted, although organ regenerative medicine tends to be focused on by the news. This result may be associated with resistance to incorporation of tissue derived

from iPS cells directly into the body. There is a reported sense of crisis that incorporation of foreign material may eliminate one's sense of self, which is a fundamental argument against the field of enhancement [8]. The belief that regenerative medicine should be promoted for assisted reproductive technology was lower among both ordinary citizens and involved individuals, as compared with that for organ regeneration and innovative drug development. As the primary reason for this result, subjects may think that assisted reproductive technology has a low priority, because it is not treatment for a disease [9]. As a secondary reason, creation of ova and sperm may produce a sense of psychological resistance, through association with cloning techniques [10].

This study has some limitations. First, the question of knowledge was limited to subjective issues. Second, responses may not be generalizable because individuals involved in a disease were limited to patients with age-related macular degeneration. Third, bias may occur among respondents, depending on the degree of informatization, because an online survey was conducted. Despite these limitations, this is the first survey comparing awareness of regenerative medicine research using iPS cells between ordinary citizens and individuals involved in the disease. The study also revealed that expectations for regenerative medicine research were generally high, especially among individuals involved in the disease.

## Conclusion

This survey revealed that expectations for regenerative medicine, using iPS cells, were greater both among individuals involved in the disease and ordinary citizens. However, there are various ELSI in studies using iPS cells. To promote regenerative medicine research using iPS cells in the future, it will be necessary to build social consensus regarding regenerative medicine. To that end, it is essential to provide information on regenerative medicine as quickly and accurately as possible.

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## Compliance with Ethical Standards

Yoshiyuki Takimoto, Eisuke Nakazawa, Atsushi Tsuchiya, Kazuhiro Yoshiuchi and Akabayashi Akira declare that they have no conflict of interest.

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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