

Note S1 Questionnaires

S1-1 Questionnaire for the researchers

Survey of Attitudes in Researchers About Stem Cell or Embryo-Related Research

Request for responses to our web-based survey

In May 2021, the International Society for Stem Cell Research (ISSCR) published new guidelines. The guidelines specify what research is acceptable and what is not acceptable in stem cell- and embryo-related research.

The purpose of this survey is to gather the opinions of researchers conducting research on stem cells and regenerative medicine in order to consider the future of Japanese laws, regulations, and guidelines for related research. In this survey, we ask for your opinions on several research activities (e.g., research in which human embryos are cultured beyond 14 days, research to create embryo models, etc.) in light of the ISSCR guidelines and Japanese laws, regulations, and guidelines.

We invite you this survey through the Japan Society for Regenerative Medicine (JSRM) and Japan Agency for Medical Research and Development (AMED). Therefore, some respondents may have received duplicate invitations to this survey. The survey can be accessed via the QR code on the mail from JSRM or the URL on the e-mail sent by JSRM or AMED. You may access the survey from any location, but we ask you to answer the survey only once per person.

1. The purpose of the web-based survey

We ask for the researches' thoughts on ethical and social issues regarding regenerative medicine and stem cell research.

2. Target audience for web-based survey

Members of JSRM. Researchers conducting research related to stem cells or embryos supported by AMED.

3. Use of results, protection of personal information

Your answers will be compiled into a statistical number, such as "XXX is the percentage of respondents who answered 'XXX'". Your name and personal information will not be disclosed. Your personal information will not be handled by the University of Tokyo, University of Yamanashi, Tokyo Metropolitan Geriatric Hospital and Institute of Gerontology which are the survey administrators. The results will never be used for any purpose other than research purposes.

Please read the above text carefully and select whether you are willing to participate in this survey or not.

1. Yes
2. No

[F] What is your age? [select one]

1. 0–19 years
2. 20–29 years
3. 30–39 years
4. 40–49 years
5. 50–59 years
6. 60–69 years
7. 70 years and above

[F] What is your sex? [select one]

1. Female
2. Male

[F] Did you access this survey screen via email or mail from JSRM or email from AMED?

1. Email or mail from JSRM
2. Email from AMED

[F] For those who accessed via email from AMED, are you a member of JSRM?

1. Yes
2. No

[Q] Research activities on human embryo models created from stem cells are allowed in both ISSCR guidelines and Japanese rules. Would you consider conducting research on embryo models in the future, or if you are currently conducting such research, would you consider continuing to do so?

1. Would consider conducting
2. Don't know
3. No plan to conduct.

(Branching question)

[Q] For those who answered “No plan to conduct.” Do you think Japanese rules should be changed to prohibit such research?

1. No change; should remain allowed
2. Change; should be prohibited
3. Cannot judge

[Q] According to the ISSCR guidelines, while this research activity is subject to the specialized scientific and ethics oversight process. In Japan, research on human embryo models created from iPSCs should be conducted in accordance with the “Ethical Guidelines for Medical and Biological Research Involving Human Subjects,” but there are no regulations specific to this type of research. Do you think that the rules for research on embryo models should be clarified in Japan?

1. Clarification of the rules is necessary
2. Clarification of rules is not necessary
3. Cannot judge

S1-2 Questionnaire for the public

Survey of Public Attitudes About Stem Cell or Embryo-Related Research

[SC] What is your sex? [select one]

1. Female
2. Male

[SC] What is your age? [select one]

1. 0 – 19 years
2. 20 – 24 years
3. 25 – 29 years
4. 30 – 34 years
5. 35 – 39 years
6. 40 – 44 years
7. 45 – 49 years
8. 50 – 54 years
9. 55 – 59 years
10. 60 – 64 years
11. 65 – 69 years
12. 70 years and above

Request for responses to our web-based survey

In recent years, the state of medical research involving human subjects has been changing rapidly, with particularly remarkable progress in regenerative medicine and stem cell research.

Regenerative medicine" is a medical treatment that aims to artificially manipulate the regenerative ability of tissues to restore impaired tissues and organs to their normal state. Experiments are being conducted to process human cells and fertilized ovum (embryo) in order to realize regenerative medicine. However, because of various bioethical concerns, there is an ongoing effort to promote international alignment on what types of experiments are acceptable. In addition to researchers, the opinions of patients, their families, and the general public are also important. This survey asks about the public's awareness of the state of

regulation of research on human stem cells and fertilized eggs (embryos). We apologize for the inconvenience this may cause you, but we appreciate your cooperation.

1. The purpose of the web-based survey

We ask for the public's thoughts on ethical and social issues regarding regenerative medicine and stem cell research.

2. Target audience for web-based survey

Registered survey panel members

3. Use of results, protection of personal information

Your answers will be compiled into a statistical number, such as "XXX is the percentage of respondents who answered 'XXX'". Your name and personal information will not be disclosed. Your personal information will not be handled by the University of Yamanashi, which is the survey administrator. The results will never be used for any purpose other than research purposes.

Please read the above text carefully and select whether you are willing to participate in this survey or not.

1. Yes
2. No

[Q] We will now ask you about experiments in which an embryo model is made from human stem cells and the embryo model is cultivated for a time outside the body (the embryo model is subsequently discarded).

[Video: Descriptions about research creating an embryo model]

An “embryo model” is not a fertilized ovum (embryo), but rather is a model that functions as a fertilized ovum (embryo). The use of embryo models allows us to understand the growth process of fertilized ova (embryos) without having to use actual fertilized ova (embryos).

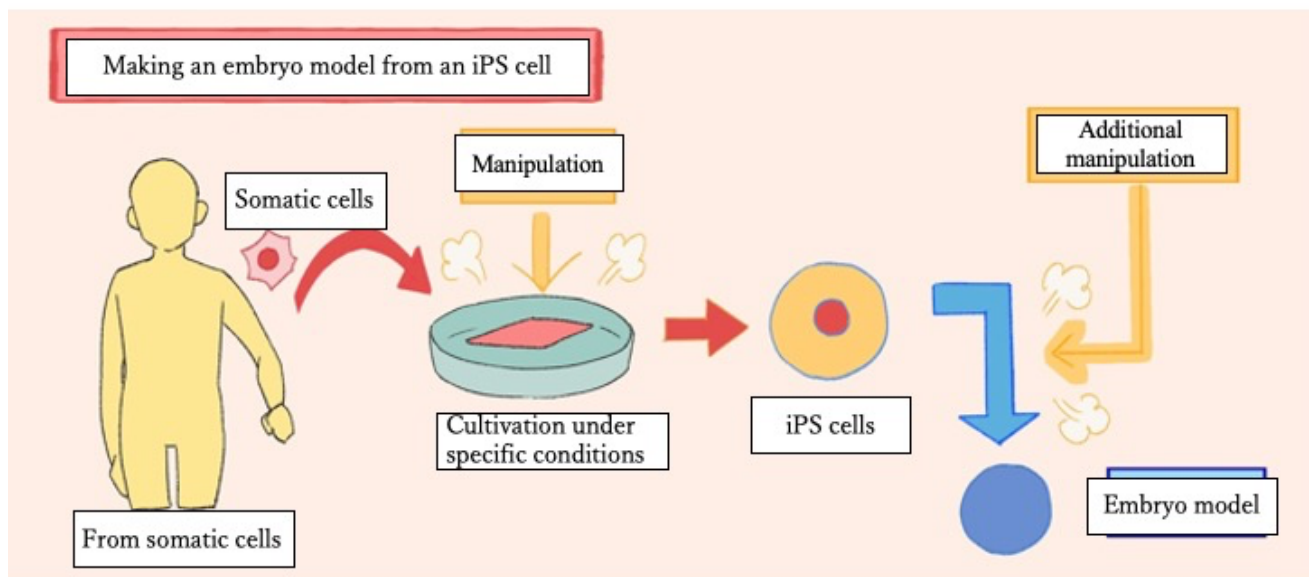
Do you think that these kinds of experiments should be allowed under rules in your country? [select one]

*These kinds of experiments are not prohibited under current Japanese rules, but no determination has yet

been made regarding the conditions under which they could be conducted.

*Anticipated outcome: Obtaining knowledge that would be useful in matters such as the development of infertility treatments, the prevention of miscarriages, and the prevention of congenital diseases.

*Bioethics issue: Although not an actual fertilized ovum (embryo), an object that could become the germ of life is artificially created and then discarded.



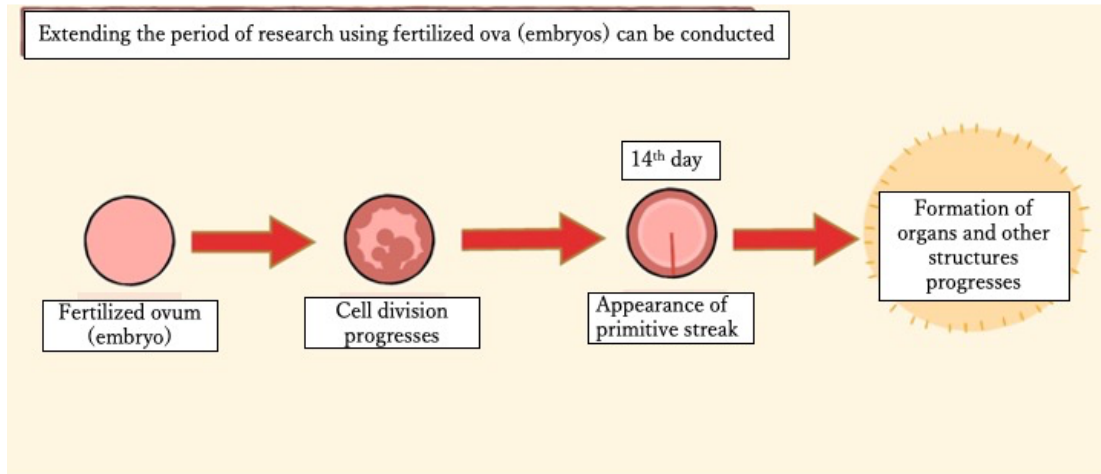
1. Should be allowed
2. Should be prohibited
3. Cannot not judge

[Q] In this question we will ask you about “research in which a human fertilized ovum (embryo) is cultivated outside the body beyond 14 days.”

[Video: Descriptions about research involving the culturing of human embryos in vitro beyond 14 days.]

Once a human fertilized ovum (embryo) passes the 14-day mark, the so-called “primitive streak” — which is a line that eventually becomes nerves — appears. Then, the organs and other structures subsequently form. Currently, the formation of the primitive streak is considered the point at which the fertilized ovum begins developing into a unique human being. After a cultivation experiment using such an ovum is

completed, the fertilized ovum (embryo) is discarded; it is not transplanted into a human uterus.



Do you think that research using fertilized ova (embryos) that are cultivated beyond 14 days should be allowed in your country? [select one]

*Under current Japanese rules, human fertilized ova (embryos) can only be cultivated outside the body for a period of 14 days. However, in recent years there has been international debate over whether to abolish this rule.

*Anticipated outcome: Knowledge can be obtained that will be useful in the development of infertility treatments, the prevention of miscarriages, and the prevention of congenital diseases.

*Bioethical problem: Research using fertilized ova will be conducted for longer periods of time than currently allowed, and the fertilized ova used in this research will then be discarded.

1. Should be allowed
2. Should be prohibited
3. Cannot not judge

(Branching question)

【The following question is for those who selected No. 2 (“Should be prohibited”)】

[Q] This question is for those who selected “It should be prohibited” in response to “cultivation for a period of more than 14 days.”

Do you think that the cultivation of human fertilized ova (embryos) for 14 days or less should be allowed? [select one]

1. Should be allowed
2. Should be prohibited
3. Cannot not judge