

Annotated Bibliography:

Sources for the Scientific Controversial Research Paper

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Tachibana, Masahito, Amato, Paula, Sparman, Michelle, Gutierrez, Nuria marti, Tippner-Hedges, Rebecca, Ma, Hong, . . . Mitalipov, Shoukhrat. (2013). Human Embryonic Stem Cells Derived by Somatic Cell Nuclear Transfer. *Cell*, 153(6), 1228-1238.

In this research journal, the researchers reprogrammed somatic cells, or body cells, into embryonic stem cells (ESCs) via SCNT or somatic cell nuclear transfer. Their intention was to study disease mechanisms and develop different therapies. After past failure to develop NT-ESCs or nuclear transferred ESCs, they optimized their approach in the SCNTs and was able to design premium quality human oocytes. The NT-ESCs were able successfully display diploid karyotypes, which are commonly found in human cells, while inheriting the genomic material exclusively from parent somatic cells.

Masahito Tachibana is a researcher in the Division of Reproductive & Development Sciences at the Oregon Health & Science University. He along with his team conducted a research on developing human embryonic stem cells from somatic or regular body cells by inducing pluripotency via introducing different transcription factors. The paper was published in Cell Press (cell.com), a well-established publisher of scientific journals and research papers, in 2013. It is a well-constructed research which established via extensive background research as well as proper results evaluation. The result data was properly visualized and analyzed further through cross referencing with multiple similar researches.

This research laid the technological breakthrough for developing embryonic stem cells in vitro without difficulties in acquiring the starting pluripotent cells as they can be produced from regular somatic cells. Furthermore, the development of SNCTs

enabled current researchers to grow an embryo in vitro up to 14 days. If the 14-day cap was not present, this development could have been progressed further. After this breakthrough, the question was raised, whether or not should an embryo developed from somatic cell be considered a living being, and if the 14-day cap should be removed to develop our understanding further in human embryonic stage developments.

Chan, Sarah. "How and Why to Replace the 14-Day Rule." *Current Stem Cell Reports* 4, no. 3 (September 1, 2018): 228–34. <https://doi.org/10.1007/s40778-018-0135-7>.

In this article Sarah Chan, a Chancellor's Fellow in Ethics and Science Communication at The Usher Institute at the University of Edinburgh, focuses on the "14-Day Rule", which limits the growth of fertilized human embryo within 14 day and asks the question whether or not this rule should be replaced. The author addresses two findings that prompted this question, firstly, the new technological advancement that enabled growth of human embryo for 14 days at minimum. Secondly, the successful pluripotent somatic cell growth that formed structures that resembled the early stages of embryonic development. As a result, the author argued that this rule must be prompted to change after proper evaluation of this issue among publics from all sides of the spectrum.

The article was published by Springer International Publishing and funded by Wellcome Trust. The author constructed the article with a well-developed flow of information, starting from introduction, to ethical policies, definitions and following through the necessity to change the 14-day rule as well as how to change it without

causing any moral concerns. The issue with the 14-day rule was properly constructed with definitions and histories. The author also evaluates the current guidelines provided for stem cell research and correlates with embryonic stem cell research.

This article underlines the key necessities for revoking the 14-day rule while bringing ethical concerns in view. As the author correlates all aspects that concerns the 14-day rule including the current policies, benefits of the change, moral concerns, boundaries for embryonic development and how to address a new rule in the place of the 14-day rule. This article resembled my intended pattern for the controversial research paper, as a result, it can not only be used as a guideline but also to check if all ethical concerns were addressed during the discussion of whether or not change the 14-day rule.

Jonlin, E. (2018). Perspectives on the New ISSCR Guidelines for Stem Cell Research and Clinical Translation. *Current Stem Cell Reports*, 4(3), 240-247.

In this article, Eric Jonlin, a researcher at the Institute for Stem Cell and Regenerative Medicine, University of Washington, revised the New guidelines set by ISSCR (International Society of Stem Cell Research) on the maintenance and standards of stem cell research at a clinical level. It is pointed that the guidelines put forth well-grounded regulations which not only ensures that the standards meet up with the Society's believes and faiths, but also, a professional and public educational system which formulates a basic understanding on the new findings via research. These, as author finds out, will provide the proper instruments to individuals to help them understand the steps of the clinical application of stem cell research while avoiding ambiguous words and description of the processes. This article shows our

current regulations on Stem Cell Research in a simpler form.

The paper was published in *Current Stem Cell Reports* 2018 and was modeled around as a review paper for the ISSCR guidelines. The author highlighted key element of the guidelines while addressing the new findings. Rather than providing arguments, the author concentrated on portraying the capacity and success of the guidelines as it gave the latest forms of recommendations and guidance especially for clinical trials.

The ISSCR provided guidelines is well established guidelines for stem cell research and clinical trials and accepted throughout the scientific communities. Though this rule is not regulated by a government body and not enforced by regulations of a country, it acts as guideline for all the researches while ensuring that researchers that do not follow these does not receive funding, research materials or support from other researchers. The guideline is the backbone for regulations when researching stem cells and reestablishes the 14-day rule. However, it did not define any method of embryonic developing procedure nor a proper definition for the embryo. This evaluation of the guidelines by Jonlin (2018) helped me to portray the current lacking in our regulations when considering the embryonic stem cell development.

Piciocchi, Cinzia & Martinelli, Lucia. "The change of definitions in a multidisciplinary landscape: the case of human embryo and pre-embryo identification." *Croatian Medical Journal*, vol. 57, no. 5, 2016, p. 510+. Gale Health and Wellness, https://link-gale-com.ccny-proxy1.libr.ccny.cuny.edu/apps/doc/A488820663/HWRC?u=cuny_ccny&sid=HWRC&xid

=540ac430. Accessed 28 Oct. 2019.

The authors Cinzia Piciocchi is a faculty of law at the University of Trento and Lucia Martinelli, a researcher at the MUSE – Science Museum of Trento, in this article emphasize on the importance of words used in the field of human embryo research. Acknowledging the importance of words and its meaning on particular context, the authors point that the definition of the words are to be accurately adjusted correspondent to laws and regulations. Considering these facts, the authors argue that there are differences in the word “embryo” when used in stem cell research, Assisted Reproduction Technologies (ARTs), compared to it when used in abortion laws. The understanding of this difference is crucial because it can direct the ethical understanding of public regarding the human embryonic research. The necessity of terminology when updating the regulations when changing the 14-day rule, to ensure there is no misunderstanding at an ethical level. Furthermore, the authors discuss the ISSCR guidelines and how it defined the 14-day rule including the correlation of this rule with the term “pre-embryo”. The authors believe that, through understanding the complex nature of these rules and regulations, different interdisciplinary approach is possible

The article was published in Croatian Medical Journal in 2016, which is an international peer reviewed journal and can be accessed by scientists from all over the world. The authors provided significance of definitions of words by giving many examples with contexts from different fields. They also portrayed several cases concerning the definition of embryo when those cases led to the establishment of laws. They also correlated with the ISSCR guidelines and discussed thoroughly how ISSCR provided the guideline for the 14-day rule.

This article provided the importance of definitions, especially when it concerns ethical standards in public community. Where we draw the line between “embryo” and “pre-embryo” and what these words signify, is very important to understand before proposing a different rule in the place of 14-day cap. In the controversy paper, definitions or the meaning of words play key role when establishing an argument and showing evidences. Thus, the article of Piciocchi & Martinelli (2016) provided significant insight and examples when the 14-day rule is addressed.

Hyun, I., Wilkerson, A., & Johnston, J. (2016). Revisit the 14-day rule. *Nature*, 533(7602), 169-171.

The author and his colleagues discuss why there is a requirement for changing the 14-day rule in human embryonic stem cell research. They described that the rule was established partly on the fact that the early researches were unable to grow the human embryo in vitro successfully for a period of that many days. However, current technologies and different developing methods had made the 14-day rule more as a constraint to further and important researches. The application of this rule needs to be addressed depending on the differences of the embryonic research and concerns of the society must be reflected upon while evaluating the effects on both sides by the change of this rule. This article is comparable to the previous article, but it goes deeply into the roots of the problem that has brought us here in front of the 14-day rule as it discusses the importance of the accommodation of moral concerns and accepting the ISSCR guidelines as well-established practical pathway for adopting and developing the 14-day rule for future research.

Insoo Hyun is a Professor of Bioethics and Philosophy at Case Western Reserve

University in Cleveland, Amy Wilkerson is the associate vice-president for research support at Rockefeller University and Josephine Johnston is the director of research at the Hasting Center. These researchers collaborated to address the 14-day rule and published the article “Embryology Policy: Revisit the 14-day rule” in the *Nature* in 2016, which is a well-established peer reviewed publisher. In the paper, the authors analyzed the 14-day rule by revisiting its history, current similar regulations placed based on different parts of the globe and the importance of ISSCR guidelines when regulating stem cell research.

The article provides an extensive understanding of the global standing on the 14-day rule, and the importance of addressing both the researchers and public morality before suggesting removing and adopting a new rule. This helps to establish a foundation to avoid controversial approach when regulation embryonic stem cell research especially when we consider based on the specific rules of different countries.

Shahbazi, Marta N., et al. “Corrigendum: Self-Organization of the Human Embryo in the Absence of Maternal Tissues.” *Nature Cell Biology*, vol. 18, no. 6, 2016, pp. 700–708.

In this article, the researchers remodeled the human embryo implantation since it had remained a mystery because of the experimental difficulties. They successfully established an *in vitro* system to develop a human embryo through the stages of implantation without the need of maternal tissues. Their results provided an effective way of progressing through those stages via cellular polarization which led to cavity formation. This provided evidence that the critical remodeling events that happen

during the human embryonic development are autonomous and independent of the requirement for maternal tissues. This experiment showcased the self-organizing capabilities of human embryos in vitro.

The leading authors Marta N. Shahbazi, Agnieszka Jerdusik and Sanna Vuoristo are researchers from the Department of Physiology at the Mammalian Embryo and Stem Cell Group of University of Cambridge. They equally contributed towards the paper which was published in Nature in 2016. This is well-conducted research on the development of monkey embryos in vitro, as model for human embryo, outside of maternal tissue. Afterwards, the experiment was replicated for human embryos and they established an in vitro culture system specific for that purpose. The results were shown both with data and imaging, providing an extensive showcase of the experiment. In this experiment, since they dealt with human embryos, they went through throughout discussions over ethical concerns while providing the proper licensing from the Human Fertilization and Embryology Authority (HFEA).

This experiment's success can act as catalyst for future development of human embryos in vitro towards further stages. This act as a dilemma, if the 14-day rule is changed, it is only a matter of time before researchers are successfully able to develop artificial humans from embryonic stem cells. If in the future this experiment is linked to the development of ESCs from SNTCs then our capability to develop artificial humans or organs will be only decades away from realization.