

Potential and ethics

With the ongoing demand for assisted reproduction, the need and ability to study the fundamentals of human reproduction at a cellular level have never been greater. At this juncture, we join other Nature Research Journals in formalizing our ethical guidelines for papers in this growing field.

Later this month, the International Society for Stem Cell Research (ISSCR) will hold its annual meeting in Melbourne, Australia. Scientists will come together to discuss many important advances, from the utilization of induced pluripotent stem cell (iPSC)-derived preparations to model human disease pathogenesis to the development and clinical translation of stem cell-based therapies to treat human disease. Virtually all of this work seeks to harness, in one way or another, the insights gleaned from pluripotent embryonic stem cells (ESCs) for discovery or therapeutic purposes. It is this amazing intrinsic potential of ESCs themselves, as well as the germ cell and zygotic lineages from which they derive, that has enabled remarkable achievements in the field of reproductive medicine. These advances have not only furthered our understanding of the earliest phases of mammalian development, but also enabled groundbreaking advances in assisted reproductive technologies (ARTs) that have given hope to an increasing contingent of people struggling with fertility issues.

In addition to offering an annual forum for the presentation and discussion of exciting scientific work, the ISSCR assumes the task of setting and communicating internationally agreed-upon guidelines for the various forms of research that utilize stem cells, including the complicated ethical considerations that must be faced when studying, culturing, or manipulating human gametes and embryos. In a recent announcement published in *Nature* (*Nature* 557, 6, 2018), the Nature Research Journals family have agreed to formalize an internal policy that follows the most recent ISSCR recommendations (<http://www.isscr.org/membership/policy/2016-guidelines/guidelines-for-stem-cell-research-and-clinical-translation/>) for human embryo, gamete, or ESC research.

In accordance with this policy and in keeping with current community standards, Nature Research Journals, including *Nature Medicine*, will continue to refrain from considering studies that maintain human embryos or embryo-like organized structures in culture beyond the 14-day period that typically coincides with the emergence of the primitive streak, an early event that is thought to mark the acquisition of human organismal potential. Furthermore, our editorial team will continue to seek independent ethical evaluation alongside the traditional scientific peer review process for certain types of studies on a case-by-case basis, such as those that employ genomic engineering techniques in human embryos or oocytes. As part of our ongoing efforts to promote transparency in our research communications, we will also require that studies under consideration in these areas be accompanied by an Ethics Statement from the authors that identifies the committee(s) responsible for approving the research, reports the confirmation of informed consent from the relevant human donors or recipients, and describes the conditions under which donated material was obtained.

From a mechanistic perspective, research that employs human gametes or embryos is required to gain a better understanding of the processes that can give rise to pathological chromosomal abnormalities during gametogenesis or embryogenesis, which might be found in as many as 10% of oocytes. In this regard, it is important to consider that most of the research conducted in this area relies on egg cells and embryos that have been donated from in vitro fertilization (IVF) clinics. It remains unknown whether results from these donated cells and embryos, which typically come from couples with reproductive problems that prevent them from conceiving a child, are the most informative for an

understanding of normal human embryonic development. As a complementary approach, some investigators are turning toward the use of gametes or embryo-like structures derived or assembled from iPSCs.

Ethically responsible and transparent research will be necessary to address many unanswered questions and to fill the unmet clinical needs of both the general public and the reproductive biology research community. For example, improvements are needed to establish better, objective criteria for selecting embryos generated from IVF or intracytoplasmic sperm injection (ICSI) that have the highest likelihood for successful implantation. There is a growing need for these insights as more people turn to assistive reproductive technology (ART). For example, last year in the United States, the number of babies born as a result of ART surpassed 1 million. And relaxation of China's so-called one-child policy in 2013 has led to an increase in demand for ARTs that may be mirrored globally as populations age and couples wait until later in life to conceive.

We are just a few weeks away from celebrating the 40th birthday of the first individual successfully conceived by IVF. It is an appropriate time, therefore, to consider how to ensure that reproductive medicine research is conducted responsibly, as well as what the future holds for fundamental human embryonic development research and translational and clinical reproductive medicine. As a publisher of both translational and clinical research, *Nature Medicine* recognizes that standards are likely to evolve alongside technical and conceptual advances in the field, but is also committed to the responsibility that scientific progress must be accomplished in an ethical manner. □

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