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Changing the public perception of human embryology

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Human embryology is flourishing thanks to an impetus provided by embryo models formed from stem cells. These scientific advances require meticulous experimental work and a refined ethical framework, but also sensible public communication. Securing public support is essential to achieve societal impact.

A human embryo is the origin of a new individual. It carries important emotional and ethical significance, and its study demands thoughtful and careful consideration. In recent years, models of embryos have been formed 'in a dish' from animal and human stem cells to help illuminate the fundamental principles of development and contribute to medical advances. Inaccurate presentation or discussion of these models runs the risk of distorting the nature of the underlying research and misinforming the public, which could feed into other trends that undermine scientific endeavour and erode trust in science and medicine. As scientists and professionals in stem cell ethics and policy, we must strive for a sensible public perception of human embryology.

Past public misperceptions hindering progress

Distrust in the ways and means of human embryology is not new, and it has its roots in ancient collective beliefs. The possibility of humans creating humans from scratch has long been fantasized, from Sumerian legends about genesis from clay and blood and mediaeval alchemists allegedly creating homunculi, to the modern myths of human cloning, ectogenesis and transhumanism[1]. Such 'fabricated humans' are often depicted as less or more than humans and have long fuelled fears of the moral degradation of our species, or its disappearance. These dystopias, which recur in popular culture and science fiction, can be useful to some extent in thinking about the ethical limits of human embryology. But unfortunately, nowadays, ideas about such dystopias impede genuine scientific and medical advances that aim to produce positive impacts for society.

A pertinent example of misperception that could have impeded medical progress is the severe criticism faced by the scientists who pioneered in vitro fertilization (IVF). These researchers were under intense pressure from most of society, including other scientists, to abandon their attempts to make 'test-tube babies'[2]. Strong political and religious views held back this research for nearly 10 years and included misrepresentations of, or derogatory comments about, the research and researchers. Moreover, peer scientists feared that babies would be abnormal, and either did not consider infertility a significant issue—with emphasis mainly lying on birth control – or did not believe that IVF could alleviate it. Nevertheless, the scientists pursued their research, and in 1978 the first IVF baby was born. IVF now accounts for approximately 4% of all births in Europe and is widely accepted by society. Clearly, the intended and unintended consequences of scientific and medical progress must be discussed at an early stage, but it is important to bear in mind that our views on ethics today are not necessarily the same as those of tomorrow.

Human stem cell biologists and embryologists have demonstrated from the onset their commitment to carving out an ethical path toward advancing our knowledge of how we come to be and solving ethical and medical conundrums, from regenerative medicine and ageing to reproductive health[3,4]. Nevertheless, concerted efforts are constantly needed to maintain high scientific and ethical standards and to disseminate a realistic picture of human embryology: one that conveys potential benefits to society and conforms to ethical processes at all levels.

A new chapter in human embryo research

High scientific and ethical standards have become even more important recently given forays into modelling the early stages of development with stem cells. This endeavour began with mouse and human stem cells that, under certain conditions, could spontaneously organize into structures with rudimentary resemblance to early embryos. Different models, obtained with different methods, emerged and exhibited different levels of completeness when compared to embryos. However, even the embryo models that most closely resemble embryos, in mouse for example, fail to form a viable organism. In their current state, therefore, these models should not be scientifically or legally equated with embryos.

Knowledge about early human embryogenesis has largely been gained from surplus IVF embryos donated by generous individuals who have completed their parental journey. Research can then be conducted with these IVF embryos in highly specialized laboratories to answer defined questions, provided specific approval has been obtained, and under the supervision of ethics committees and, typically, with some degree of national oversight. However, for ethical reasons, this research must cease at an early stage, usually within 14 days of fertilization, or earlier in some countries. Although research with human embryos is still very much needed, stem cell-based embryo models can be conveniently formed and studied without the need to use actual embryos. As such, embryo models may, in some situations, provide an alternative to the use of surplus IVF embryos for research, especially in countries where research on donated embryos is not permitted. The utility of these models is thus based on their ability to

facilitate research made possible by their practicality and by the fact that they are not embryos.

We believe that embryo models can help fill an important knowledge gap in our understanding of how we form and of the basis of abnormal developmental events or miscarriages. We do not yet know how well these models mimic actual embryogenesis, but if they are sufficiently accurate and predictive, they might reveal the genes, molecules and cells at play. This knowledge will be especially useful in studies that are currently impracticable or not permitted with human embryos, including modelling the later stages of the implantation process to better understand development, developing medicines to combat infertility and early pregnancy loss, and possibly revealing the origins of congenital birth defects, health and disease. Although the field is still in its infancy, it is already yielding previously unachievable insights into science and medicine, for example to improve IVF procedures[5].

Defining embryo models for scientists and the public

But the approach also raises questions. What exactly is being replicated? What realistic contribution can these models make to science and medicine? What is their legal status? Will they ever be used for reproduction? Society needs to be reassured that biologists, ethicists, philosophers and legal scholars recognized and discussed these moral concerns early on and formulated answers to these questions, albeit incomplete and requiring revisiting as science advances[6–11]. Scientists have proactively initiated these discussions, and included experts in the field of stem cell ethics and policy, as well as representatives of the general public, which resulted in international guidelines[3,4]. Propositions were made that human embryo models, especially the most complete ones, should be used with caution, that research may be conducted only out after ethical approval is obtained and that these models should not be transferred into a uterus[4]. From the ensuing discussions, it emerged that the use of more complete models of human embryos is not always justified from a scientific and ethical perspective, especially when less ethically loaded alternatives (such as gastruloids, assembloids and organoids) can provide equivalent or better insights into specific developmental processes[9,12]. These propositions serve as a blueprint for ongoing discussions by national ethics committees in several countries, including in Europe[13] and Japan, to maintain high ethical standards consistent with societal values. This roadmap is thus overseen by national ethics committees, national and international funding agencies, and international scientific societies, including the International Society for Stem Cell Research (ISSCR) and the European Society for Human Reproduction and Embryology (ESHRE).

In the second half of the twentieth century, basic ethical principles were crafted to supervise science and medicine (summarized in ref. 9) and were applied to the specific case of human embryology. Despite this, in the 2000s, politically and religiously motivated fears led the Bush administration in the USA to ban federal funding for human embryonic stem cell research because human embryos were destroyed in the process of obtaining the stem cells. This decision was reversed by the Obama administration, but the discussions had dented public perceptions of this type of research in pervasive and enduring ways, particularly in the USA and the European Union. For example, in Germany, the use of surplus IVF embryos for any research remains forbidden in 2023 and, although most German citizens have a favourable view of such research, a significant proportion still firmly oppose it. To fully restore public confidence and avoid repeating decisions that curtail scientific and medical advances, we need to shape a realistic portrait of human stem cell biology in the context of embryology, one that is based on fact while avoiding sensationalism.

Importantly, dissemination of a realistic image of human embryo research requires appropriate communication of scientific results to the public. As outlined in the ISSCR Fundamental Principles, scientists have a duty to communicate their results in a manner that is trustworthy, accessible and timely in order to maintain public confidence[4]. We believe that communication with the public is extremely important and that it is only possible if data are publicly available, and thus verifiable. Preprints accelerate the pace of scientific discovery, but their hastened use can come at the expense of scientific quality, independent scrutiny and adequate public communication. Reanalysis of public results and attempts to reproduce the work of others are essential to assess whether protocols are reproducible and whether the statements made stand the test of time. This course of collective authentication is necessarily slow, but it limits and corrects mistakes or misinterpretations, thereby achieving thoughtful public presentation. We, as a community, should fully embrace these facts, because they ensure that science is meticulously done and adequately communicated.

Setting standards for research dissemination

The importance of the scientific and popular press in this context cannot be overstated. Scientists and academic press offices must disseminate findings (for example, through press releases and press interviews) in a measured and accurate manner. For an appropriate coverage of scientific advances, journalists should also engage with scientists with a critical attitude toward the publications and seek the opinion of several independent researchers on the findings and their realistic societal implications. International scientific societies such as the ISSCR and ESHRE, local committees such as the Cambridge Reproduction Initiative, and media hubs such as the Science Media Centres in the UK, Spain and Germany aim to provide diverse and measured opinions. A vivid example of this is that these stem cell–based embryo models have often been referred to in the media as 'synthetic embryos', a term that can evoke science fiction imagery and convey the idea that these are embryos created from scratch for reproduction[9,14]. The philosopher Albert Camus once said that "to misname an object is to add to the misfortune of this world." Proper naming of these entities using a consistent nomenclature is critical to ensure coherent, responsible and accurate science communication and to maintain clarity for the public. The ISSCR, for example, recommends the use of the umbrella term 'stem cell-based embryo models', to reflect our current understanding and avoid misunderstandings[15].

Will stem cell-based embryo models one day be considered embryos? Will they remain rudimentary but contribute to advancing medicine? We do not yet know the answers to these questions, but by entering this uncharted territory, we are treading a path that promises to expand our knowledge of the earliest stages of human embryogenesis in the hope of improving human health. With these goals in mind, research does not run untethered, but is accompanied by numerous public and institutional discussions on the ethical aspects of the work being done. However, to ensure an sensible and accurate public perception of human embryology, progress must be made without haste and reported without hype. And when new discoveries are made, it is essential that we collectively evaluate their scientific validity and regularly revisit the ethical questions and governance policies of the day, to ensure that researchers work within acceptable societal limits, which may change over time. In addition, scientists at all career levels should feel entitled and be encouraged to become more engaged in

communicating with the public to help convey accurate information to lay communities. We believe that such conscientious science and communication will lay a stronger and more resilient foundation for human embryology that is critical to achieving societal impact.

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Competing interests

N.C.R. is an inventor on the patents "Blastoid, cell line based artificial blastocyst" (EP2986711) and "Blastocyst-like cell aggregate and methods" (EP21151455.9), which are both licensed to dawn-bio, a company he co-founded. A.M.A. and N.M. are inventors on the patents "Polarised three-dimensional cellular aggregates" (PCT/GB2019/052668) and "Human polarised three-dimensional cellular" (PCT/GB2019/052670), maintained by Cambridge Enterprise.