Chapter 1
Introduction

Joachim Huarte and Antoine Suarez

Abstract The search for principles allowing us to decide whether a particular cell entity is a human being or not, is the main motivation of this book. Even if the different contributors don't always reach a consensus in their proposals, the arguments they provide represent a significant step towards a consistent answer to the query.

Keywords Altered nuclear transfer • Human embryo • Moral status • Parthenogenesis • Reprogramming of somatic cells

The central question to which this book offers a series of answers is whether or not particular cell entities of human origin ought to be considered a human being. Answering this question is important insofar as one believes that there is some kind of intrinsic relationship between *human* species membership and the rational foundation of rights. On this view, the identification of a cell entity as an animal of the species *Homo sapiens* is relevant for making moral decisions vis-à-vis research and experimentation.

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This question of identification became especially relevant in 2004 when many prominent research scientists proposed methods for deriving embryonic-like pluripotent stem cells without destroying human embryos. Such a solution had certain scientific and political advantages. On the one hand, such techniques only required human ova, not human embryos. This meant that researchers would not be restricted to solely using human embryos leftover from fertility clinics. On the other hand, such techniques, in theory, would not require the destruction of human embryos and would therefore bypass the political impasse over the subject of embryo experimentation.

The two main proposed methods were Altered Nuclear Transfer (ANT) and parthenotes. In ANT, one genetically alters the nucleus of a somatic cell (a skin cell, for example) before transferring it into an enucleated oocyte. In fact one inactivates a gene crucial for trophectoderm (TE) development. The inactivation eliminates the potential to form the fetal–maternal interface, but spares the inner cell mass (ICM) lineage. The resulting entity does not develop a healthy TE and is therefore incapable of uterine implantation. Researchers then would use the ICM of this entity to produce pluripotent stem cells sharing the self-renewal and differentiation potential of embryonic stem cells (ESCs). A parthenogenetic blastocyst, on the other hand, results from the development of an egg that only possesses a maternal genome, whose resultant ICM can also be used to derive pluripotent stem cells. Given these proposals, it was important from an ethical point of view, but was also interesting from a scientific point of view, to ascertain whether these alternative techniques produce cell entities that would be more properly classified as disabled human beings or if, indeed, they are not human beings at all. The ensuing debate raised interesting ethical and scientific questions, but also proved to be a profound cultural moment in which scientists and moral philosophers collaborated extensively with one another in order to get to the heart of the matter.

Four years later, however, the interest prompted by this discussion wavered due to the arrival of induced pluripotent stem cells (iPSCs) obtained through the reprogramming of adult somatic cells. Also this method made it possible to produce embryonic-like pluripotent stem cells without the necessity of destroying embryos and the prevailing consensus was that iPSCs were not human beings. However, recent research casts doubts about whether the reprogramming of adult cells could become a new sort of cloning. Indeed, it is already possible to create a mouse fully derived from iPSCs. What this suggests is the possibility that iPSCs could be considered equivalent to the ICM of a developing human embryo. Suppose that by improving the reprogramming methods one obtains “better” iPSCs. Suppose that one injects these “better” iPSCs into a TE vesicle from which the ICM cells have been removed. Suppose that this reconstituted blastocyst in which the ICM has been replaced by the iPSCs is capable of developing to birth. If this is the case, then we need to ask whether or not the destruction of a cluster of such “better” iPSCs could be equivalent to the destruction of a human embryo.

In order to answer this question, one is required to think about the necessary epigenetic components and functionality required for scientists to consider a certain cell entity to be a human being. Attempting to identify those components requires

scientific knowledge and philosophical precision since one will be required to identify which components are directly or *essentially* related to the identity of a human person and which components are indirectly or *accidentally* related to this identity.

Additionally, iPSCs open up the possibility of generating gametes in vitro which could then be used to mass-produce human embryos for research and experimentation. The achievement of deriving full-grown mice from ESCs or iPSCs is being used as an argument in favor of such a possible utilization of iPSCs. The argument goes something like this: if one states that the ICM of embryos produced in vitro are to be considered equivalent to the ESCs and iPSCs used to make mice through tetraploid complementation, then embryos before implantation can be considered equivalent to a clump of stem cells.

Recent research also shows that it is possible to directly convert adult somatic cells of a nonneural lineage into neuronal cells without the necessity of going through an undifferentiated stage of iPSCs. One can conjecture that if the technique further improves, the cells obtained this way may supersede iPSCs for use in disease modeling and regenerative medicine, and dream of reprogramming adult cells without having to worry about whether one is making human beings. Nonetheless, direct reprogramming itself also heralds how rapidly these techniques are progressing and that soon it may be possible to obtain iPSCs capable of developing to birth when injected into a blastocyst without ICM.

In light of all these recent achievements, the question of whether or not a cell entity is a human being reaches again an unexpected importance even in the context of reprogramming adult cells.

Alas, this is not the end of the story. Ethical analysis of recent proposals to develop human–animal hybrids for research will also require us to make scientific-philosophical distinctions regarding a certain cell entity's moral status. For if one wishes to perform experimentation on a hybrid entity, it is necessary to identify, insofar as it is possible, what kind of entity is being experimented on. Answering this question is important for ensuring ethical modes of experimentation on hybrid organisms, but also for ensuring those experiments properly comply with legal requirements for scientific research. Indeed, if one believes that no experimentation should be done on human embryos, it becomes especially important that one be able to distinguish whether or not a hybrid composed of genetic material of a monkey and human being ought to be considered a human or a monkey. Again, we are led to the question: when should a cell entity of human origin be considered a human organism? And even assuming that the production of such hybrids would not entail the destruction of human beings (e.g., if they were brought to gestation and birth), we would need to at least ask the question of whether hybridization is ever ethically objectionable?

This book aims to present contributions exploring the status of the different cell entities produced by the recent technologies and especially embryos in vitro, stem cells, and human–animal hybrids. The work was initiated by a group of researchers convened by the Social Trends Institute to study this topic. While some of the chapters here are papers that were delivered during this consultation

sponsored by the Social Trends Institute (STI), others were commissioned and added later.

In Chap. 2, *Boris Greber and Hans Schöler* present a general scientific overview and outlook of the reprogramming of somatic cells to both pluripotent stem cells and cells of a different lineage. This chapter hopes to introduce the reader to the relevant scientific data needed to adequately engage with essays introduced later in the volume.

In Chap. 3, *Maureen Condic* discusses the biological and moral status of the embryo in vitro, offering her own account about the moral and organismic status of pluripotent stem cells derived from embryos, direct reprogramming, and Altered Nuclear Transfer (ANT). Drawing on the importance of *organization* as a principle of life – a view advocated by a number of scientists, philosophers, and theologians– she argues that the recent embryological studies indicate molecular criteria present within the single-celled zygote that allow us to delineate between a single-cell entity with a per se developmental trajectory towards adult human organismic functioning and a cell entity, like those produced from research methods like ANT, which lack such organismic status.

In Chap. 4, *Nicanor Austriaco* presents a proposal for determining the organismic status of parthenotes and complete hydatidiform moles. In so doing, he draws upon two important distinctions: that between an active and passive potentiality and that between a whole and a part. Austriaco argues that those cell entities with an *active* potentiality (i.e., a potential actualized wholly from within the entity itself) to develop into a *whole* tumor ought to be considered nonorganisms, whereas those cell entities with a *passive* potentiality (i.e., a potential actualized from without) to develop into a *partial* tumor ought to be considered disabled human organisms. He also argues that a separated Inner cell mass (ICM) of a blastocyst should be considered equivalent to a clump of isolated pluripotent stem cells.

In Chap. 5, *Joachim Huarte and Antoine Suarez* present criteria for distinguishing between embryos and nonembryos that is grounded in the *proper* biological potential for developing the neural activity responsible for controlling spontaneous motility. They argue that the presence of any cellular or genetic deficiency that directly inhibits the appearance of neural activity (DIANA deficiency) is indicative that said cell entity is not, properly speaking, a human being (i.e., a human animal organism). They further argue that their criteria make better sense of the clinical definition of brain death thereby establishing an important relationship between the identification of the presence of life and death in a cell entity of human origin.

In Chap. 6, *Patrick Lee* tackles the question of how can one determine that a product of a reproductive technique is a human embryo or not. Lee proposes a criterion: does the entity produced have the genetic–epigenetic state, and overall organization, such that it will develop itself to the mature stage of a human organism (an organism with a brain that can provide experience suitable to be the substrate of conceptual thought), provided a suitable environment and nutrition? The chapter briefly defends that criterion and applies it to various types of biological entities.

In Chap. 7, *Pablo Requena* shows that the problem of the epistemological status of bioethics has yet to be resolved. He analyzes the category "person" and the various meanings it has acquired in philosophy over the centuries. He presents the catholic view on this theme and on some recent proposals for obtaining ESCs (like in ANT), relying primarily on the Vatican bioethical instruction *Dignitas Personae*. At the same time, Requena stresses the importance of discovering a valid criterion for distinguishing between an embryo and what is an embryo-like entity also in other contexts. So he argues that many of the products of fertilization that perish are probably not human embryos and therefore are not persons, because these cell entities contain genetic aberrations which are incompatible with life.

In Chap. 8, *Manfred Spieker* discusses whether a human being has a right to life, and analyzes the political, philosophical, and social conflict between two undeniable goods: "freedom of research" and "embryonic protection." The frame of reference for Spieker's discussion is the contemporary debate over embryonic experimentation in Germany. Spieker identifies the relevant historical and legal particularities of the German debate, but also attempts to highlight how the issue has been framed by different parties to that debate. The result is an interesting study in how the particularities of a country's social and political history can help to frame the debate over the moral status of human embryos and the limits of science in interesting and complex ways.

In Chap. 9, *Neville Cobbe* discusses the claim that interspecies mixing undermines the uniqueness of being human and discusses various features of human life that allegedly mark it off from nonhuman life. By surveying a host of literature on the subject, Cobbe's contribution gives the reader a comprehensive survey and introduction to the scientific and ethical discussion surrounding hybridization. In the end, he concludes that there is no "smoking gun" to which we can attribute human uniqueness, but rather that one ought to consider Man's uniqueness in a holistic way by viewing the various dimensions held together in humans. He advocates this view as opposed to the view that there might be only one distinctive feature that sets humans apart from nonhumans.

In Chap. 10, *William Hurlbut* discusses recent proposals for human–animal hybridization/experimentation, reflecting on what kind of moral controversies they are bound to bring into focus. Hurlbut formulates a list of specific public policy proposals for guiding such research as well as articulating some general moral principles from which these proposals derive. In all, his reflection aims to promote a deeper understanding and appreciation of what defines the human creature.

In Chap. 11, *Antoine Suarez* argues that reprogramming adult cells can in principle produce a human being and discusses when this may be the case. He shows that to ultimately settle this question a new experiment is required, which is of scientific relevance as well. He goes on to answer various objections raised to the DIANA criteria (proposed in chapter 5) and shows that according to Aristotelian-Thomistic hylemorphism it is possible to have organisms that, in spite of sharing human origin and features of animal life, are not animated by a spiritual soul. This oddity can be avoided by pairing hylemorphism with the principle that the proper

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