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Non-viable embryos created with synthetic DNA

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It is plausible that in the future synthetic DNA (synDNA) technology could enable the creation of non-viable embryos for research, potentially bypassing ethical objections to embryo experimentation. This article explores how the technology might work, the ethical concerns it might mitigate, and the challenges that remain.

The moral status of the human embryo

Research on human embryos provides important insights into the processes of cellular differentiation, tissue formation, and organ development. These insights are fundamental not only for understanding congenital abnormalities and developmental diseases but also for enhancing regenerative medicine and improving fertility treatments [1]. However, the use of human embryos in research remains ethically contentious. The general objection is that embryo research is intrinsically illegitimate because human life is morally valuable from the moment of conception [2]. Even if embryos do not become fully-fledged persons, they are potential persons or pre-persons: unlike eggs and sperm, they contain all the genetic material that is needed to become a person and thus they should be protected in the same way as all other persons [3]. These concerns have motivated restrictions on embryo research the world over. It is these specific concerns that are addressed in creating embryos that lack some of the properties needed to become persons.

It must also be noted that it is almost universally agreed among those who do accept embryo research that legal restrictions are necessary. Currently, in jurisdictions where embryo research is permitted, the embryos used must be destroyed within 14 days of development [4,5]. This limit is significant because it is the point at which the primitive streak starts to form. This marks the beginning of individual development, beyond which there is no longer any possibility of twinning, and so represents the point at which we are dealing with a distinct human life [6]. This stage is also prior to the formation of the nervous system, which is an important consideration in ethical discussions on the basis that where there is no nervous system there cannot possibly be any sentience, a key consideration in utilitarian ethics [7]. However, the problem that this gives researchers is that there may be good scientific reasons to pursue research on embryos that are more than 14 days old and (at least assuming that there are moral reasons to pursue scientific research that promises to benefit humanity), therefore, moral reasons to do so as well – reasons that pull against the moral reasons for caution.

Avoiding the problem

In an attempt to circumvent the constraints of the 14-day rule, scientists have been working on alternatives, such as human stem cell-derived embryo models [8] (see Box 1).

However, these models often lack the cellular interactions and spatial organization seen in natural embryos, leading to less reliable experimental outcomes. Additionally, the efficiency of generating these stem cell-derived embryo models is currently low, further hindering their utility in large-scale and detailed studies. Ultimately, it seems unlikely that these models will ever perfectly match their 'natural' counterparts.

Another option involves modifying gametes so that the embryos they give rise to will lack the essential genes to develop further. This technique has been used for embryo research in The Netherlands, where an embryo is defined in law as a cell or group of cells with the capacity to develop into a human being and the creation of embryos for the purposes of scientific research is illegal [9]. However, this approach is extremely convoluted and demanding. It also involves a degree of uncertainty and risk, since it is not possible to control every aspect of the fertilization process, especially the imprinting of genes. Thus, the modified gametes might fail to produce an embryo-type organism at all.

In summary, the tools available at present may be of some use in advancing our knowledge, but they are limited both in terms of the technical challenges, the degree of resemblance to 'natural' embryos, and in regard to the supposed ethical advantages that they offer.

SynDNA

In light of these challenges, synDNA seems to offer a promising way forward. SynDNA technology involves the artificial synthesis of long DNA sequences by concatenating nucleotides, a method that has already proven successful in recreating the genomes of organisms such as bacteria and yeast [10,11]. Recently, this technology has been extended to replicate parts of the human genome, demonstrating its potential for more complex applications [12,13]. Because synDNA genomes are built from the ground up, nucleotide by nucleotide, this allows for the deliberate creation of a genome that lacks essential genes required for full embryonic development [10,11]. These synDNA-constructed genomes could then be introduced into eggs, which may undergo the early stages of development but will inherently lack the capacity to proceed to full-term development (Figure 1). Embryos created with synDNA techniques would thereby be

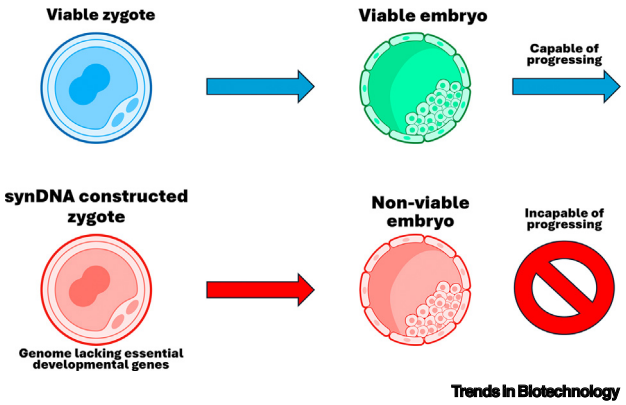

Figure 1. Comparison of viable and non-viable embryos lacking essential genes created with synthetic DNA (synDNA). Scheme comparing viable embryos (top) with non-viable ones (bottom) generated using synDNA. The non-viable embryos exhibit arrested development due to the lack of essential genes preventing full embryogenesis.

much less vulnerable to concerns about possible sentience, and the persisting worries about undermining their potential that beset altered nuclear transfer (ANT) (Box 1), since there would be no developmental potential at all.

Constructing synthetic embryos that lack the genes required for full development right from the outset could avoid some of the concerns related to both 'natural' and constructed embryos using existing techniques. This synthetic construction is a different kind of endeavor from the manipulation or alteration of an already existing genome. It requires no act of destruction, modification, or mutilation.

From a legal and regulatory perspective, it is not clear whether these creations would be treated as 'real' embryos. There have already been discussions as to whether embryo-like organisms created through parthenogenesis can be regarded as embryos in legal terms [14]. We do not attempt to answer that question here; but we note that if we are correct in suggesting that there is an ethically significant difference between synDNA and natural embryos, it would be possible to argue that these non-viable embryos would fall outside of the scope of extant regulation. It may be that the law could or should handle such embryos differently from 'natural' ones, because they lack any inherent capacity to develop beyond the embryonic stage. If so, the 14-day rule would not necessarily apply to them at all, opening new prospects for embryo research and paving the way for a legal system in which synDNA embryos may be regulated in one way, while the 14-day rule remains in place for 'natural' embryos. This in turn opens up new questions about where the cut-off point for synDNA embryos should be placed, or indeed, whether constraints would be required at all.

Concluding remarks

Non-viable embryos created with synDNA offer a way to circumvent some of the moral objections that have been raised against embryo research. Such technology avoids the deliberate alteration of existing genomes or embryos in a way that damages their potential. However, the moral question is not entirely resolved by the availability of synDNA embryos. To choose deliberately to create an organism that lacks certain capacities, especially those commonly deemed to be morally significant, is in itself a serious moral matter. Is it ethically preferable to create synDNA embryos rather than modifying existing ones? Perhaps not, if we recognize the creation and design of living organisms as being morally significant and regard scientists as having moral duties towards 'their' creations. The moral question may not hinge solely on the properties of the embryos. Insofar as opponents of research on human embryos object to the hubristic nature of embryo research as a whole, their concerns may be even greater when it comes to scientists intentionally designing embryos in such a way as to use them with even less regard for the life in their hands.

Box 1. Alternative methods for generating non-viable embryos

One option proposed to obtain embryo-like structures is known as altered nuclear transfer (ANT). ANT consists of removing specific genes from an adult cell and then using this modified cell to create embryos by nuclear transfer. The resulting embryos are incapable of progressing through full development.

ANT has generated significant ethical criticism, however [15]. The primary issue is that ANT involves starting with a complete, functional genome and then selectively removing essential genes. Therefore, the modification destroys aspects of the cell's potential, in order to render the research ethically acceptable. Yet if objections to embryo research are motivated by a concern about destroying the potential of an organism to become a fully-fledged human person, the deliberate manipulation of an otherwise normally-functioning genome in order to curtail its developmental potential offers no obvious ethical advantage.

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Declaration of interests

The authors have no interests to declare.

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