The ethics of synthetic DNA

Adrian Villalba,[1,2] Anna Smajdor ,[3] Iain Brassington ,[4] Daniela Cutas[5]

[1]Université Paris Cité, Paris, France
[2]University of Granada, Granada, Spain
[3]IFIKK, University of Oslo, Oslo, Norway
[4]CSEP/ Dept of Law, University of Manchester, Manchester, UK
[5]Clinical Sciences, Lund University, Lund, Sweden

Correspondence to
Dr Adrian Villalba;
adri.vife@gmail.com

Received 5 May 2024
Accepted 13 October 2024

To cite: Villalba A, Smajdor A, Brassington I, *et al*. *J Med Ethics* Epub ahead of print: [please include Day Month Year]. doi:10.1136/jme-2024-110124

ABSTRACT

In this paper, we discuss the ethical concerns that may arise from the synthesis of human DNA. To date, only small stretches of DNA have been constructed, but the prospect of generating human genomes is becoming feasible. At the same time, the significance of genes for identity, health and reproduction is coming under increased scrutiny. We examine the implications of DNA synthesis and its impact on debates over the relationship with our DNA and the ownership of our genes, its potential to disrupt common understandings of reproduction and privacy, and the way in which synthetic DNA challenges traditional associations between genes and identity. We explore the degree to which synthetic DNA may further undermine overgeneticised accounts of identity, health, reproduction, parenthood and privacy that are prevalent in the public domain and in some areas of policy-making. While avoiding making normative claims of our own, we conclude that there is a need for reflection on the ethical implications of these developing technologies before they are on us.

INTRODUCTION

DNA has occupied a special place in the popular imagination as 'the building block of life' since its structure was first published.[1] As well as being what makes us human, it is widely assumed that DNA also makes us the unique individuals that we are.[2] When we reproduce, it is DNA that links us with our offspring.[3] Moreover, DNA is revealing. It tells us things about ourselves and about each other.[4] It enables us to identify who has been at a particular place,[5] who is related to whom[6] and what diseases an individual may be predisposed to.[7] It can give us information about a person's background, their ethnicity and where their ancestors were from.[8]

Ordinarily, we may expect this information to be securely stored in our cells, only to be known to others if we wish to share it. But the possibility of synthesising DNA from scratch calls all this into question. Synthetic DNA (hereafter 'synDNA') is the latest in a series of advances in biology that pose challenges to the ways in which biotechnological development is regulated.[9] SynDNA can be seen as another aspect of synthetic biology, a field that has already garnered a significant degree of bioethical attention over the past decade.[10] Our purpose with this paper is to discuss the ways in which synDNA calls into question understandings of genetic relatedness, identity, privacy and control. In particular, the development of synDNA offers an opportunity to re-evaluate the significance we place on genes. Ongoing work in areas such as research into in vitro-derived gametes tends to re-enforce a genetic-essentialist account of reproduction and parenthood.[11] But synDNA—by challenging assumptions about the rights and interests we have over our genes—may have the opposite effect. If we cannot maintain the idea that genes are the essence of identity or reproduction, or that we should have the right to control who has access to those genes, it becomes less tenable to regard genes themselves as holding the answers to questions about identity, reproduction or privacy.

SynDNA is created through the systematic joining together (concatenation) of single nucleotides (A, T, G, C). To date, only genomes from bacteria and small eukaryotic organisms have been constructed in this way. However, with further improvements, it is expected that the synthesised portions could be much longer. Ultimately, it is feasible that scientists will have the ability to concatenate full mammalian chromosomes and even genomes. This possibility, though still some way off, raises some challenging questions about the relationship between individuals and their genetic code, and about what it means to produce such genes in the laboratory. It is important to start thinking about the ethical, legal and regulatory implications of this technology well before it becomes an actuality.

Until recently, it has been widely accepted that genetic information is profoundly important and requires special protection under the law. Before the human genome was sequenced, and indeed, afterwards, people feared that whoever had access to a person's genetic makeup had almost unlimited knowledge, and hence power, over that individual and their future. Underpinning these beliefs was the fundamental conviction that we are our genes.[12]

A belief in the special status of genes, referred to in the academic literature as genetic exceptionalism,[13–15] was cemented by the idea that their secrets were deeply embedded in our cells and could not be accessed without specialist equipment. The mystique of DNA could be maintained fairly easily while very few people had the ability or resources to 'reveal' let alone construct genes. But this is no longer the case. Even those who know little about genetics are familiar with the spiral ladder-like structure (double helix) of DNA, with 'base pairs at every rung'. DIY CRISPR kits are sold to people to experiment with at home. 'Garage biology' and biohacking communities have known for many years that biological research, including access to, and manipulation of genetic material, is not solely the province of multimillion dollar laboratories.[16–18] Nevertheless, our legal systems, common intuitions and much of our ethical analysis still tend to treat genes as being somehow exceptional both in terms of their significance and in respect of their need for special regulatory and legal attention.

When the DNA molecule can be assembled and manipulated in the laboratory, this exceptionalism comes under pressure. Some of the assumptions that underpin existing frameworks and beliefs

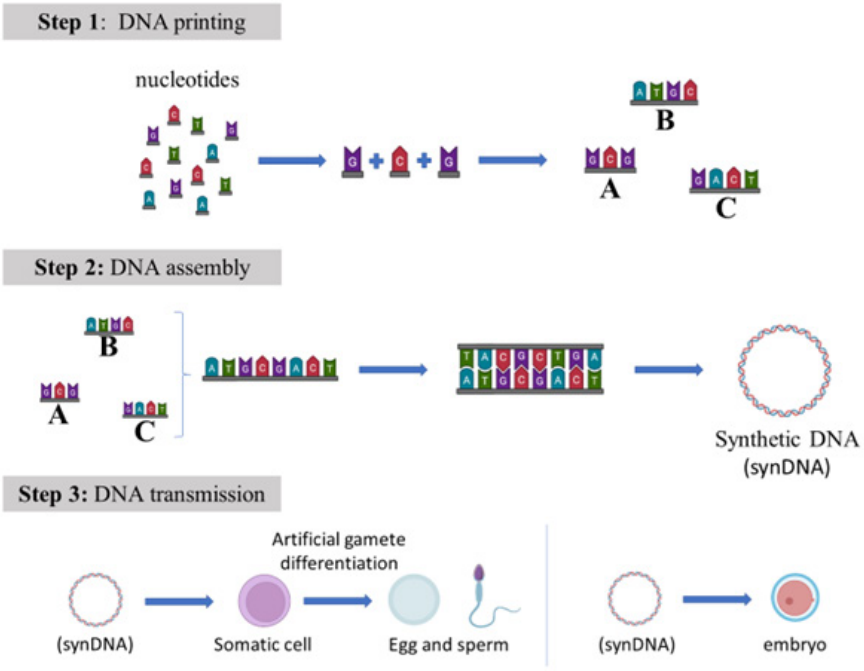

Figure 1 Schematic representation of the artificial DNA synthesis process. The first step—known as DNA printing—involves the addition of nucleotides in a string, allowing the manufacturing of sequences up to 150–200 nucleotides. The second step—known as DNA assembly—involves the concatenation of different strings of DNA and their hybridisation to a complementary strand. Finally, the third step consists of transferring this synDNA to a living cell. For reproduction purposes, synDNA could be transferred either to a somatic cell and then differentiated into artificial gametes, or transferred directly to a human embryo.

concerning genes may likewise appear questionable in an era where our powers of DNA manipulation extend beyond modification or selection, to enable us to create genomes from scratch.

We begin with a brief account of how synDNA is created, and of potential developments. We then review some potential therapeutic applications for synDNA, before setting out to explore a number of concerns that may be raised by its use. We focus on issues of ownership, reproduction (and parenthood), privacy, and identity. Throughout the paper, we compare and contrast the potential of synDNA with that of other (prospective) technologies and the degree to which the ethical concerns that it may give rise to are, or are not, unprecedented. Finally, we raise some questions for future discussion.

It is worth noting here that the biological information of an organism is not exclusively encoded in its DNA (genetics). It also depends on how the cell interprets this information by switching on and off the genes by adding or removing chemical compounds to the DNA, compressing and relaxing the double helix or allowing a specific contact between distant genomic regions (epigenetics). In this article, we focus only on aspects that relate exclusively to the information encoded in the DNA, which can be freely manufactured by synDNA techniques.

How synDNA is created

DNA synthesis is the process of generating DNA molecules by producing chains of the four nucleotides, adenine (A), thymine (T), guanine (G) and cytosine (C). In the laboratory, DNA synthesis involves stacking nucleotides together in the desired order.[19] Artificial gene synthesis involves two steps: (1) DNA printing of small sequences of around 200 nucleotides and (2) DNA assembly, which consists of the concatenation of the previous DNA printed sequences (figure 1). In recent years, the efficiency of DNA synthesis methods has increased considerably.

While further improvements in the technical aspects of DNA synthesis are required before the creation of human genomes can be achieved, progress has been steady since 2007, when a research group headed by Craig Venter built and transplanted an entire artificial bacterial genome.[20] Three years later, the same group redesigned the entire genome of *Mycoplasma mycoides*.[19] Their previous experiment had recreated the sequence of an already existing organism; now they were synthesising the first sequence that was entirely designed on a computer.[21] Further successes have been reported since these initial developments.[22]

The synthesis of human DNA will of course be extremely challenging. A yeast chromosome contains far fewer nucleotides (around 250 000) than a human one (c. 200 million). Yet human DNA synthesis is feasible: genetics progresses very quickly. It took 5 years to sequence the first human genome,[23 24] but at the time of writing an individual's genome can be sequenced in less than 24 hours. Given that it is already possible to manufacture human genes, it seems plausible to think that further progress in human DNA synthesis is on the horizon. If we want to avoid being taken by surprise when it becomes a reality, we should be starting to think now about its implications.

Possible benefits of synDNA

There are many potential benefits to be achieved through the synthesis of DNA. In this paper, we do not give an exhaustive account of what these benefits might be but provide a brief outline. One of the most obvious clinical applications of synDNA would be single-chromosome synthesis undertaken to help people with chromosomal abnormalities. For example,

this might be beneficial in patients who have acute leukaemia caused by the Philadelphia chromosome.[25] These patients suffer from a translocation of chromosomes 9 and 22, resulting in an uncontrolled proliferation of haematopoietic stem cells. Somatic replacement of synthesised new chromosomes or even genomes in haematopoietic stem cells obtained from these individuals might help them recover from leukaemia.

There are other chromosomal aneuploidies that might benefit from synDNA. For instance, Wolf-Hirschhorn[26] and Cri du chat[27] syndromes are diseases arising from the partial deletion of chromosomes 4 or 5, respectively. Another example is Turner syndrome: women affected by this syndrome carry only one copy of the X chromosome and therefore cannot produce eggs. The synthesis of an extra X chromosome could theoretically help them to produce 'their own' eggs.

Another therapeutic aspect that could be addressed is the regeneration of telomeres. These are repetitive DNA sequences located at the extremes of chromosomes that are progressively lost during ageing. Studies in laboratory animals in which telomere length is restored showed an increased lifespan and reduced symptoms of ageing.[28] SynDNA could perhaps be employed to restore telomere length in somatic cells to counteract ageing.

On the reproductive side, synDNA could be employed in cases where prospective parents know they have a genetic mutation that they wish to avoid transmitting to offspring. Similarly, it could offer an alternative to the need for donated gametes. SynDNA could also offer an alternative mode of treatment for patients who risk transmitting mitochondrial disease to their offspring. Currently, such patients rely on donated enucleated eggs containing the healthy mitochondria of the donor. With the advent of synDNA, mitochondria designed and constructed in the laboratory could be used, thus avoiding the invasive business of egg-harvesting and the inclusion of third-party DNA in the resulting offspring.[29] We discuss reproductive possibilities in more detail in a later section.

It is worth noting that any therapeutic application of synDNA would involve considerable research in addition to the creation of the required DNA sequence itself. The synDNA would need to be packaged and delivered within the cell in ways that enable it to be taken up by the body. We do not suggest here that it would be easy to use synDNA in these therapeutic ways; our point is that the prospect of such use generates a clear reason to pursue synDNA research for the creation of human DNA sequences. In the following sections, we consider how synDNA might be used in ways that call into question our understanding of what makes our genes 'ours', and the ways in which losing control over 'our' DNA might challenge prevailing assumptions about the role of DNA in relation to reproduction, identity and privacy.

Creating synthetic persons?

Among the possibilities that synDNA opens up is the prospect of synthesising an entire human genome. If transferred into an enucleated egg cell, this would be a similar process to nuclear transfer ('cloning') techniques,[30] but the resulting offspring would not necessarily be identical to any other human being. Similarly, synDNA could be transferred to somatic enucleated cells that could then be manipulated to undergo differentiation into gametes or even directly transferred to enucleated egg cells, for example, to employ them for reproductive purposes (as stated in figure 1).

Would a person created from synDNA somehow also be 'synthetic'? This may seem like a peculiar question, but some scholars have suggested that babies born following human cloning or the use of in vitro-derived gametes would indeed be 'synthetic' in some sense.[31 32] The argument seems to be that when an embryo does not arise from conception (the union of naturally occurring gametes), then neither cloning nor in vitro-derived gametes constitutes reproduction.[33] Likewise, synDNA may be perceived as more productive than reproductive because it also does not involve conception. If human cloning, in vitro gametes and synDNA are not reproduction, then arguably they do not give rise to a (natural) person. While these arguments may seem unpersuasive, they do reveal the complexities that arise when embryos can be created outside the natural or normal ways. Even if we agree that what matters morally is the fact that such embryos have all the usual features of a human being, they may have a different legal status in jurisdictions where the law is premised on how an embryo is created.

Ownership and DNA replication

The possibility of creating synDNA also raises some entirely new questions. For one thing, it would be possible to replicate the DNA of living people without having any direct contact with the 'replicated' person or any of their biological material. There is already a body of literature on the question of ownership of genetic material, and some scholars have suggested that it is not obvious that we should think of ourselves as owning 'our' genes to begin with. Montgomery, for example, argues that in contexts where genetic material has been taken and is being used for biomedical purposes, it might better be understood as being owned by the medical institution, rather than the individual from whom the material was originally obtained.[34] This is the legal position reflected in cases such as *Moore*.[i]

In the case of synDNA, there would be no individual from whom the material was originally obtained, suggesting perhaps that ownership rests more squarely with the 'creator'. If so, we would have no moral or legal cause for complaint if a scientist replicated some of 'our' DNA in a laboratory. (Indeed, it is not clear what it would even mean for a person to claim DNA as 'theirs' in such circumstances. And we might want to know whether it matters how much of an individual's DNA is synthesised. A mere gene might be insignificant, but what about a chromosome, or my entire genome? In principle, the concatenation technique allows for all of these possibilities.) Since the cells produced in this way could include gametes as well as somatic cells, this would clearly pose serious challenges to systems that rely on DNA evidence for the ascription of paternity. Likewise, for forensic purposes, it would no longer be possible to infer, solely on the basis of DNA evidence, that a particular individual had been present at a crime scene.

In many jurisdictions, the existence of certain genetic similarities between a baby and an adult is regarded as sufficient to assign legal parental (and more specifically paternal) responsibility. This opens the possibility of legal difficulty when sperm is obtained by nefarious means—so-called 'sperm theft'. These possibilities have been discussed in relation to *in vitro* gametes.[35] Being able to recreate someone's genome or gametes using synDNA would take this a step further; it would not even require biological material to be 'stolen' from the victim. The 'theft' in such a case would be informational only, but the consequence, the creation of a child genetically related to someone to a certain degree, would be similar.

[i]Case court reference: Moore v. Regents of University of California, 51 Cal.3d 120.

Deliberate replication of a known person's DNA could perhaps be banned or closely regulated. It might even make sense to insist that researchers use the 'reference genome'—an agglomerate of genetic information that is specific to no particular individual, but which is taken to be a standard human genome. As such, replication of, or use of the reference genome for scientific and medical purposes might seem less problematic than the replication of gene sequences that 'belong' to real people. However, there are some limitations associated with this possibility: the reference genome is fixed.[36] It does not allow for the full exploitation of the kind of flexibility and experimentation that synDNA would offer.

Another interesting challenge here is the possibility that scientists might inadvertently replicate someone's genome. Unless we were to sequence every single individual and match them against the DNA strands being concatenated in laboratories to make sure that 'new' genomes are unique, there would be a risk that specific people could find 'themselves' partially or entirely replicated. Would a person be wronged if their genome were wholly or partially synthetically replicated in a laboratory? The answer might depend on whether the resemblance arose by chance or was intentional; and if it was intentional, whether it might foreseeably harm the person whose gene was replicated or was designed to derive profits from 'their' genetic material.

Historically, most legal systems have rejected claims of ownership in relation to human beings, their bodies and biological tissues.[37] However, my genetic code is not biological tissue per se, nor is it part of the body. In the contexts we are discussing, the creation of 'my' code in a laboratory need have nothing whatsoever to do with me as a person. This opens the way to a separation between the rights we have over our bodies and the rights we have over our genomes and the information therein. Even framing this without begging the question is difficult since people talk so naturally of their genomes being theirs.

There are three primary angles to examine here. The first has to do with one's reproductive legacy. Genetic information is commonly assumed to be one of the most, if not the most, significant aspect of reproduction, even if bioethicists have largely come to dispute this view.[38 39] As noted above, if scientists can create 'my' genes in the laboratory and insert them into cells, I could become a genetic parent without my knowledge or consent, and without there being any biological trajectory from me to the child. It would be of 'my' genes, but not of my body. A second angle has to do with the common assumption that genomes are in some sense private. That is, although we may not necessarily own them, we have rights concerning them, and this imposes constraints on what others may do with them or the access that they may have to them. The third issue is that of identity. Again, it is commonly assumed that genes are a crucial part of our identity. This links in with concerns about privacy and reproduction. Genes concern identity in a way that bodily tissues themselves do not. People donate blood or lose limbs without thinking that this undermines their identity. However, the loss or replication of one's genome is another matter.

Reproduction

As noted above, the prospect of one's genes being used reproductively without one's knowledge or consent may seem particularly disturbing. We usually feel we should have some control over our reproductive legacy. Writing in 1985, Jansen argued that—whatever our relationship with other cells—we have a special claim for ownership over our gametes. According to Jansen, the donation of gametes is motivated by very different intentions from the donation of other bodily tissues, and the 'dispossession' of gametes or embryos is far more psychologically significant than the idea of what happens to one's other bodily tissues, especially after death.[37]

Jansen's claim rests on the assumption that there are clear differences between gametes and other cells. Yet, on reflection, these distinctions do not hold. Since in vitro-derived gametes and cloning became (theoretical) possibilities, it has become clear that the boundary between gametes and somatic cells is more fluid than was previously understood. With the possibility of creating synDNA, the barrier between somatic and germ cells completely disappears. If it is possible to engineer both somatic cells and gametes, any individual's genome can be wholly or partially used in the creation of new people. To echo a question raised above, whether we term this 'reproduction' in the absence of a biological trajectory from the individual whose DNA is synthesised to the new, genetically similar individual becomes an open question. But it is a question worth asking.

If any cell can become a gamete, there is no essential moral difference between the creation of a gamete and a somatic cell. Indeed, there is a sense in which the creation of a cell with 'my' genome in a laboratory is in itself reproductive whether or not it is used to create an embryo or gamete. Here, not only does the boundary between somatic and germ cells become blurred, but the boundary between creation and reproduction does as well. If reproduction is the reproduction of my DNA, then the creation of that DNA in a laboratory could also be viewed as reproductive even if there is no child involved. In some sense, the re-production of DNA is more 'reproductive' than the creation of children with another person's DNA. But the creation of a specific strand of DNA makes no-one a genetic parent. In contrast, when a baby comes into the world, it is taken by some to change the ontological status of those who stand in a specific genetic relationship to that child in a profound way.[40]

As discussed earlier, in most jurisdictions, if a man, M, has the right kind of genetic resemblance to a child, C, this is sufficient to ascribe paternity, and whatever obligations flow from it under the prevailing law. The question of whether M consented to the use of his sperm in the creation of C need not have any bearing on M's paternal status—at most, it speaks to questions of who has what obligations granted that he is the father, and the existence of C provides a moral foundation for whatever decisions we make about M's obligations, even if his sperm was stolen or acquired duplicitously.[35] The emergence of synDNA will call into question the justice of relying on genetic testing as a basis for assigning parenthood. In the synDNA era, we will not be able to make inferences of bodily contact, nor intent, on the basis of mere facts about genetic resemblance.

It might nevertheless be argued that adults whose DNA has been used in reproductive projects without their knowledge or consent are still parents. That is, if we accept a purely genetic account of parenthood, the absence of intent or direct involvement in the conception of a child are simply irrelevant. The harms of unwanted reproduction can be separated into physical, economic and psychological.[41] Physical and economic harms are fairly straightforward. A man who undergoes a procedure to which he didn't consent, to harvest sperm, may be physically harmed. If not harmed, he may nevertheless be wronged because his bodily integrity would have been violated. And a man who is forced to pay money for the support of a child to whose existence he contributed is clearly disadvantaged by that, even if we don't regard him as having been wronged.[35] Learning that one has a genetic child about whom one was unaware may generate a number of responses from great happiness to shock; but a man who learns that he has fathered a child generally knows how this

happened. He would have to accept it as a consequence of his own choices and decisions. By contrast, it is unlikely that many people would welcome the prospect of having no control over who creates 'their' children.

A more general point about the implications of synDNA for reproductive purposes is that it may enable prospective parents to choose between the genes they wish to transmit, and to create gametes accordingly. Reproduction would no longer be a matter of chance in this respect: some aspects of the genome could be designed from scratch, rather than chosen from among the genes available in the cells of the prospective parents. Thus, if there were known deleterious genes, these could be replaced in the synDNA process with entirely new, specially constructed genetic sequences. It seems reasonable that for at least some prospective parents, this would be preferable to reproduction by means of donated gametes or to embryo testing and selection. Indeed, the use of donated gametes could become a thing of the past, which might be welcome to people who prefer not to complicate their family with the legal, moral and possibly emotional ties to external parties, that supervene on genetic links.

The prospect of genetic enhancement—the manipulation of genetic material in reproduction for non-therapeutic purposes, such as to ensure desirable characteristics in the offspring—has animated debates in bioethics for many years and has generated resistance to some potential developments. For example, the European Convention on Bioethics forbids the use of interventions on the human genome that are not 'for preventive, diagnostic or therapeutic purposes' or that aim 'to introduce any modification in the genome of any descendants'[ii] (Article 13). It seems reasonable to expect that the use of synDNA for the purposes described above would be seen as legally problematic in many, if not most, jurisdictions. However, many years have passed since the convention was drafted, and more recent analyses of the permissibility of genetic enhancement are more nuanced. For example, in 2018, the UK's Nuffield Council of Bioethics noted that appeals to the inviolability of human nature have often formed the basis for strong objections to intervening on the human genome. It adds that these objections rely on an essentialist approach that is itself problematic.[iii]

It is an open question as to whether the use of synDNA to construct desirable genes constitutes 'enhancement' per se. In contrast to using technology to add or remove genes in an organism that already exists, synDNA would involve making choices between nucleotides when building an organism. There is no pre-existing entity on which the intervention is undertaken: no 'modification', in the language of the Convention on Bioethics. There is no organism that is enhanced, even if the resulting individual may be better off, in some respects, in relation to the rest of the population. If a particular genetic variant already exists in the population (say, a rare variant for the *EPO* gene being used in the hope to create a child with superior potential for athletic performance), a choice could be made between these genes or others.

With synDNA scientists may also be able to design genetic variants that do not already exist. Again, nothing would be 'modified' or enhanced, so much as built from scratch: only this time a new genetic variant is introduced in the population. While this may pose risks to the individual that is created, the focus of ethical concerns in such cases might be on effects on others and the general population—or more abstractly, on the human genome.

The prospect of using synDNA to design embryos also calls into question the degree of genetic alteration that would be consistent with regarding oneself as the parent of the resulting offspring. Suppose that specially constructed genes derived from no specific individual are used in the creation of an embryo in order to avoid genetic disease, or to introduce desirable characteristics. Would this insertion undermine the claim of the gamete-providers to be the parents? It might be argued that they are partial parents; or that there is no parent to be associated with the inserted gene, or perhaps conversely, that the designer of the DNA (which would be highly likely to be a computer programme) would be the parent, at least in respect of this particular gene.[42] Thus, synDNA seems to offer new reproductive possibilities as a fertility treatment, but at the same time, to cast some doubt on how to define genetic parenthood, or even reproduction itself.

Another intriguing possibility that arises with regard to synDNA for reproduction is that it would no longer entail the need for a second party for reproductive purposes. The ethical issues associated with reproductive cloning have been widely discussed.[43] The possibility of solo reproduction facilitated via in vitro-derived gametes has also been explored.[33] In both these cases, it is clear that there would be significant risks and uncertainties involved as a result of genetic anomalies. However, the case of synDNA is significantly different, in that there need be no such risks. Rather than the replication of a genome, or the derivation of complementary gametes from one person's cells, a gamete could be produced and synDNA used to generate the complement without any other person's DNA being involved. Since the complementary gametes could be designed in theory to any specification, this could be considerably less risky than cloning, or reproduction with in vitro-derived gametes, and might indeed be safer than 'natural' reproduction.

And finally, one could design gametes that are not derived from any specific individual's genetic make-up. This would indeed be an innovation in human reproduction and could allow, for the first time, a determination of parenthood in the absence of immediate genetic filiation. Although there are multiple, competing accounts of how parenthood should be established (eg, biological, functional, intentional or solely by appeal to children's interests), genetic ties have long been seen as the paramount indicator of parent–child and family relationships, not only morally but also legally.[44 45] SynDNA would undermine this view.

Privacy and confidentiality

Concerns about the impact of genetic technologies on privacy and confidentiality are nothing new. A naïve view would be that our genomes are by their nature private because the information they contain is inaccessible without sophisticated technology. A little consideration shows that this was never the case for some genes: if one knows which genes control (say) eye colour, one can derive information about a person's genome from a quick glance at their face. Beyond that, deriving genetic information is a little harder—but the relative cheapness and ready availability of genetic testing, whether it be medical or direct-to-consumer, means that it is still fairly straightforward. However, as long as it remains true that most people rely on experts to acquire and interpret genetic information, it still makes sense to think that we can raise questions about privacy and its potential violation.

[ii]European Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine, Convention on Human Rights and Biomedicine, Oviedo, 1997, European Treaty Series - No. 164.

[iii]Nuffield Council. Genome editing and human reproduction. 2018. Available at nuffieldbioethics.org/wp

It is worth spending a little time to consider what privacy is, at least in a genetic context. On one account, 'the private' is described as that which is not ordinarily in the interpersonal realm.[4] So, for example, if one leaves one's home, information about what one is wearing cannot be private; but because genetic information does require the input of some effort in order to obtain it, it can be thought of as private. 'Privacy' is not quite the same as 'the private'; Véliz[46] offers another account of privacy as something that an agent has in respect of personal information or personal space when that information or space has not been accessed by another. One slight point of difference between these two accounts is that the latter holds that privacy may be maintained if information is accessible but not accessed, whereas according to the former account, something's being accessible because it is by its nature in the interpersonal realm is sufficient to show that no claim about its being private can succeed.

We should also take care here in respect of what it means for something to be accessible: in one sense, genetic information is accessible insofar as it is possible to access it quickly and easily; but in a more everyday sense, it is inaccessible, because one has to 'do something' to access it. Even if one knows about, say, the relationship between eye colour and a particular gene, one still has to make a deduction in order to discover the information about a person's genome; but when it comes to learning about that person's predisposition to, say, heart disease, one has to do that much more. By contrast, how someone is dressed when they go to the shop is neither personal information, nor is noticing it anything that would require further 'work' to bring it into the interpersonal realm.

One way or the other, though, any situation in which one person accesses genetic information about another is likely to mean a diminution of privacy; and it is not implausible to think that when it comes to privacy—at least in respect of genomes—it is information, and control over access to information, that is at the core of what concerns people. Part of the reason for this relates to autonomy and agents' ability to grant or withhold access to information about themselves as they see fit. And the obverse of this concern allows us to say that one of the reasons why privacy matters rests on an appeal to the moral value of resisting heteronomy—of others having a kind of control over our lives or some aspect of them. This account of the wrong of a violation of privacy also hints at the harm it represents. The fact that certain information is known may leave a person vulnerable to risks that exacerbate the wrongness of a loss of control of personal information.

What is crucial when we are thinking about the potential harms of genetic information's accessibility is that things can be done with that information that may have an impact on the lives of either the referent, or of those around them. And it is the fact that things are done with it that is relevant to potential concerns surrounding synDNA.

Suppose that Alice's genome is sequenced, and that sequence is stored on a computer somewhere. For the sake of the argument, allow that this is with her knowledge and approval. But now suppose that Bob, who has access to both the genetic information derived from Alice's cells, and the right kind of technology to do something with it, is able to take that genetic information and use it to build a replica of those cells. Genes are, after all, only sequences of molecules; and the technology we are considering here is one in which, having learnt the sequence of molecules in a gene or in a chromosome or in a cell, we are able to recreate it. What might (or ought) Alice to think? She has consented to have her information stored on the computer, but not for Bob to use it in order to replicate her DNA.

In one sense, Alice's privacy would plainly have been violated simply by virtue of Bob's having accessed information about her if she did not authorise his doing so, and she would have a reason to think she had been wronged. This wrong may be compounded by a further wrong committed in replicating the information that he has obtained to build a new version of her genome. It would not matter whether Bob's reasons for building it are defensible. Yet even here, it seems that the moral attention would have shifted from the creation of the cell to the reasons for creating it. Furthermore, it would still not be clear that any wrong would be specific to the use of synDNA: if the same concerns would arise because a scientist reverse-engineered a cell to become pluripotent, then the fact that our example concerns synDNA and a gene built from chemical raw materials seems not to add anything much to the moral debate. And in the end, even if as a matter of fact there is no motivation that would satisfy us as having been sufficient to justify creating this new cell in all particular cases we consider, we cannot infer from that that there could be no good-enough reason in principle. And that being the case, the onus would be on the critic to show what it might be. Moreover, it would also have to be shown that the concerns related to privacy rather than to something else.

That 'something else' may be confidentiality. Privacy and confidentiality are different, despite their often being conflated. A person may permit another to have access to certain information; this does not imply any permit to share it with a third. Doing so would not violate privacy, since the information was already in the interpersonal domain and the third would have done nothing to make it accessible to himself; but it would breach confidentiality. Since synDNA technology revolves around the possibility of genes or genomes being recreated in a laboratory from their bare chemical 'recipe', breaches of confidentiality may be relevant in a way that they would not be in respect of brute biomaterials. Securing our genomes is that bit more difficult when the information they contain and from which they are built can be duplicated with no more difficulty than it takes to copy a file from one computer to another. And though privacy and confidentiality are different things, privacy may also be implicated in cases like this. Hence we might imagine that a hacker accesses the computer on which a person's genomic information is stored and downloads it. Yet, morally, this looks to be not all that different from any other situation in which a 'black hat' may access sensitive information, be it biomedical, financial or anything else. Much the same would be said in the event that a person authorised to access information breaches confidentiality by sharing it without permission: synDNA does not really add anything to the story in either case, save as a possible explanation about how it is that the information came to be held by a person to begin with.

When push comes to shove, it looks as though any intuitive qualms that we might have about synDNA *qua* synDNA cannot be easily grounded by appeals to privacy and confidentiality. SynDNA does not look to be all that special in these regards except insofar as it further reduces the degree of control we have over 'our' genes and opens new pathways for transforming genetic data into actual genes.

Identity

One other possible candidate explanation for the wrong done to Alice when Bob synthesises her genome would have to do with identity. If Alice's genome is synthesised, it opens the possibility that a genetically identical individual could be born without her knowledge or consent. How would she feel about meeting her duplicate unexpectedly (and what ought we to think about this

possibility)? If the material is held in storage for many years, Alice might be genetically duplicated many years after her own demise. Thus, if genes really are identity, it seems that with the development of synDNA, Alice has no assurance that she will rest in peace. She may be called back into existence at any time, on the whim of some future individual.

The link between genes and identity has been an ongoing subject of debate in bioethics for many years. Again, while in the past there was a greater endorsement of a broadly genetic essentialist conception of identity, this has come under pressure more recently.[47 48] This literature questions the degree to which we can claim to be our genes, and accordingly, renders it more complex to account for identity-based concerns relating to genetic identity in the context of synDNA.

A difficulty right from the start is that the word identity has several senses. If we take identity to mean simply 'sameness', then concerns about the way that synDNA might affect identity can be easily rebutted. At the most obvious level, it is already the case that some people share a genome, and so cells formed from the same genetic recipe: these are identical twins. This does not undermine the identity or uniqueness of either twin in any morally meaningful way. Working the other way, even having the same genome does not mean that individuals would be phenotypically identical. A nice illustration of this point is demonstrated by the case of a man who had his beloved pet cat, Garlic, cloned. Having paid a large sum of money for the procedure, the man was shocked to discover that the new cat's markings were noticeably different from those of the 'original'.[iv] And so we can see that sharing a genome with a physically identical entity is not sufficient to undermine 'identity' claims in a morally important sense; but neither is sharing a genome with a phenotypically different one. It is increasingly clear that even if one does endorse a wholly or partially genetic account of identity, it is not simply a question of genes themselves, but also of epigenetics that is likely to matter.

The degree to which genes still play a significant role in our understanding of identity is reflected in the influence that Derek Parfit's 'non-identity problem' has had in the bioethics literature.[49] While we do not have scope to embark on a detailed analysis here, it is clear that Parfit's account has been taken by many commentators to indicate a genetic view of identity, whereby the identity of an embryo is fixed, genetically, at the moment of conception.[50] Accordingly, interventions that alter the genetic makeup of a fetus or the circumstances of conception, are regarded as being 'identity-changing', while interventions that do not change genes may be harmful or beneficial but not change who is affected.[51 52] An interesting aspect of synDNA is that there is no prefixed identity that a genome has when it is being designed and constructed in the laboratory. Therefore, the distinction between identity-changing and beneficial/harmful alterations appears unclear.

Perhaps we should not be surprised that a genetic essence of identity starts to look less plausible on closer inspection. Humans have only around 20 000 genes in total. It does not take a talented mathematician to work out, on the basis of this fact, that for any particular gene we care to identify, there are millions, or possibly billions, of people (and a good many nonhumans) who share it. But this being the case, the idea that there are specific genes that are 'mine' or that can be tied to my identity seems misguided. Accordingly, it is hard to see what grounds I have to complain that I am wronged if a scientist chooses to create one of 'my' genes through recreating a particular sequence of nucleotides in a laboratory. And if we respond by saying that it is not the presence of a gene, but the presence of the particular sequence of genes that constitutes someone's genome that matters, we are brought right back to the identical-twin objection.

However, another sense of the word identity speaks not so much about sameness, as about a person's sense of who they are as a unique moral being. Might the possibility of one's genome being recreated from its bare chemical recipe threaten that in some way? It is not obvious that anyone ought to feel their identity threatened even if a version of their genome were created in a laboratory. Of course, they might have invested a lot of their self-understanding in their understanding of their own particular genome and feel that it is threatened by the possibility of its recreation elsewhere; but it is not implausible to think that this is only really a meaningful likelihood if a person has overestimated the importance of genomes, or even particular genes, in moral identity to begin with.

Many of the concerns raised by synDNA in the context of identity reflect those associated with cloning. SynDNA could facilitate the creation of a genetic twin years after the 'original'. But there are differences between cloning and synDNA in this regard. To make a clone, one needs access to biomaterials from the progenitor; synDNA would require only that we have a readout of the chemical components of a gene or genome. As we have seen, this means that there are potential requirements in respect of information security that arise in respect of synDNA that would not arise, at least not arise so easily, in respect of genetic 'reproduction' that required the physical presence of a person's biomaterials. But these differences are fairly superficial, too. In all, it is not obvious that synDNA poses any real threat to 'identity', whatever theoretical commitments we have concerning the nature of identity. What synDNA does do is call into question the degree to which identity is connected with genes, and indeed what is meant by 'identity'.

CONCLUSION

We have discussed the ethical concerns that arise as the frontiers of DNA synthesis advance to a point where it becomes possible to generate partial or complete human genomes. We considered the implications for ownership, reproduction, parenthood, privacy and identity. We suggest that the development of synDNA further undermines the grounds for genetic essentialism. Not only does it illustrate the problems inherent in the idea that we own 'our' genetic information, but it gives us grounds for doubting that such information is ownable at all as a matter of conceptual possibility as well as legal fact. One of the most significant impacts of artificial DNA synthesis is the breakdown of the traditional distinction between somatic and germ-line cells. This has far-reaching implications for reproduction, as we have discussed. Furthermore, the potential for partially or fully engineering a human genome opens up entirely new avenues of genetic parenthood and this represents a significant shift in our understanding of reproduction. This technology presents a new era of reproduction that disrupts traditional notions of passing on a part of one's own genome to one's offspring. Additionally, we have looked at the impact that synDNA technologies are

[iv]Røsjø, B, Haakstad E. Pointless to clone a pretty cat. Titan.uio.no Forskningsnyheter om realfag og teknologi. Jan. 12, 2016. Available at: https://www.titan.uio.no/english/2016/pointless-clone-pretty-cat.htm

likely to have on concerns about the control and use of genetic data.

Finally, it is important to acknowledge that numerous pertinent questions remain unanswered regarding synDNA. What would the consequences be if someone were to reproduce only a portion of another individual's genome, such as specific genes or even an entire set of chromosomes? What are the implications of creating a genome entirely from scratch? What possibilities for human enhancement might synDNA open up—and would it even be 'enhancement', or would it be something else, something new? These are all important questions that should be tackled—preferably before the technology is upon us.

X Adrian Villalba @villalbaciencia, Anna Smajdor @acsmajdor and Iain Brassington @ibrasso

Acknowledgements The authors are grateful to the five anonymous reviewers for their helpful comments.

Contributors AV and AS wrote the first draft. IB and DC expanded it. All authors contributed substantially to all parts of the paper, approved the final submission, and take responsibility for the content.

Funding Work towards this publication has benefitted from funding from the Víctor Grífols i Lucas Foundation (BEC-2024-007) and the Marcus and Amalia Wallenberg Foundation (MAW2020.0074).

Competing interests None declared.

Patient consent for publication Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement No data are available.

ORCID iDs
Anna Smajdor http://orcid.org/0000-0002-9752-6302
Iain Brassington http://orcid.org/0000-0002-1097-0567

REFERENCES

1 Rudolph FB. *Biotechnology: Science, Engineering, and Ethical Challenges for the Twenty-First Century*. The National Academies Press, 1996.
2 Kass LR. The wisdom of repugnance: why we should ban the cloning of humans. *Valparaiso Univ Law Rev* 1998;32:679–705.
3 Chadwick RF. Ethics, reproduction, and genetic control. 1992.200.
4 Brassington I. Private life of the genome: genetic information and the right to privacy. Available: https://books.google.com/books/about/The_Private_Life_of_the_Genome.html?hl=fr&id=0mO1EAAAQBAJ [Accessed 5 May 2024].
5 Cho MK, Sankar P. Forensic genetics and ethical, legal and social implications beyond the clinic. *Nat Genet* 2004;36:S8–12.
6 Kaebnick GE. The natural father: genetic paternity testing, marriage, and fatherhood. *Camb Q Healthc Ethics* 2004;13:49–60.
7 Saunders CJ, Miller NA, Soden SE, *et al*. Rapid whole-genome sequencing for genetic disease diagnosis in neonatal intensive care units. *Sci Transl Med* 2012;4:154ra135.
8 Lewis ACF, Molina SJ, Appelbaum PS, *et al*. Getting genetic ancestry right for science and society. *Science* 2022;376:250–2.
9 Murray T. What Synthetic Genomes Mean for Our Future: Technology, Ethics, and Law, Interests and Identities. Valparaiso Univ Law Rev 2011.
10 Thompson PB. Synthetic Biology Needs A Synthetic Bioethics. *Ethics Policy Environ* 2012;15:1–20.
11 Scott R. New Reproductive Technologies and Genetic Relatedness. *Mod Law Rev* 2024;87:280–316.
12 Brock DW. Human cloning and our sense of self. *Science* 2002;296:314–6.
13 Garrison NA, Brothers KB, Goldenberg AJ, *et al*. Genomic Contextualism: Shifting the Rhetoric of Genetic Exceptionalism. *Am J Bioeth* 2019;19:51–63.
14 Condit CM. Public understandings of genetics and health. *Clin Genet* 2010;77:1–9.
15 Evans JP, exceptionalism BWG. Too much of a good thing. *Genet Med* 2008;10:500–1.
16 Rogers WA, Dalziell J. What Feminist Bioethics Can Bring to Synthetic Biology. *IJFAB: Int J Feminist Approaches Bioethics* 2023;16:46–63.
17 Keulartz J, van den Belt H. DIY-Bio - economic, epistemological and ethical implications and ambivalences. *Life Sci Soc Policy* 2016;12:7.
18 Heavey P. Consequentialism and the Synthetic Biology Problem. *Camb Q Healthc Ethics* 2017;26:206–29.
19 Hutchison CA 3rd, Chuang R-Y, Noskov VN, *et al*. Design and synthesis of a minimal bacterial genome. *Science* 2016;351:aad6253.
20 Lartigue C, Glass JI, Alperovich N, *et al*. Genome transplantation in bacteria: changing one species to another. *Science* 2007;317:632–8.
21 Annaluru N, Muller H, Mitchell LA, *et al*. Total synthesis of a functional designer eukaryotic chromosome. *Science* 2014;344:55–8.
22 Zhao Y, Coelho C, Hughes AL, *et al*. Debugging and consolidating multiple synthetic chromosomes reveals combinatorial genetic interactions. *Cell* 2023;186:5220–36.
23 Venter JC, Adams MD, Myers EW, *et al*. The Sequence of the Human Genome. *Science* 2001;291:1304–51.
24 Lander ES, Linton LM, Birren B, *et al*. Initial sequencing and analysis of the human genome. *Nature New Biol* 2001;409:860–921.
25 Foà R, Chiaretti S. Philadelphia Chromosome-Positive Acute Lymphoblastic Leukemia. *N Engl J Med* 2022;386:2399–411.
26 Battaglia A, Carey JC, South ST. Wolf-Hirschhorn syndrome: A review and update. *Am J Med Genet C Semin Med Genet* 2015;169:216–23.
27 Cornish K, Bramble D. Cri du chat syndrome: genotype-phenotype correlations and recommendations for clinical management. *Dev Med Child Neurol* 2002;44:494–7.
28 Mojiri A, Walther BK, Jiang C, *et al*. Telomerase therapy reverses vascular senescence and extends lifespan in progeria mice. *Eur Heart J* 2021;42:4352–69.
29 Dimond R. Ethics of mitochondrial gene replacement therapy. Clin Ethics Crossroads Genet Reprod Technol 2018;31–53.
30 Matoba S, Zhang Y. Somatic Cell Nuclear Transfer Reprogramming: Mechanisms and Applications. *Cell Stem Cell* 2018;23:471–85.
31 Baertschi B. The Moral Status of Artificial Life. *Environ Values* 2012;21:5–18.
32 Lippman A, Newman SA, Testa G, *et al*. The Ethics of Deriving Gametes from ES Cells. *Science* 2005;307:515c–7c.
33 Cutas D, Smajdor A. 'I am Your Mother and Your Father!' In Vitro Derived Gametes and the Ethics of Solo Reproduction. *H C Anal* 2017;25:354–69.
34 Montgomery J. Data Sharing and the Idea of Ownership. *New Bioeth* 2017;23:81–6.
35 Smajdor A, Cutas D. Artificial gametes and the ethics of unwitting parenthood. *J Med Ethics* 2014;40:748–51.
36 Miga KH, Wang T. The Need for a Human Pangenome Reference Sequence. *Annu Rev Genomics Hum Genet* 2021;22:81–102.
37 Jansen RP. Sperm and ova as property. *J Med Ethics* 1985;11:123–6.
38 Mertes H. Gamete derivation from stem cells: revisiting the concept of genetic parenthood. *J Med Ethics* 2014;40:744–7.
39 Sparrow R. Reproductive technologies, risk, enhancement and the value of genetic relatedness. *J Med Ethics* 2014;40:741–3.
40 Smajdor A. Why bother the public? A critique of Leslie Cannold's empirical research on ectogenesis. *Theor Med Bioeth* 2021;42:155–68.
41 Smajdor A. The Moral Imperative for Ectogenesis. *Cambridge Q Healthcare Ethics* 2007;16:336–45.
42 Palacios-González C, Harris J, Testa G. Multiplex parenting: IVG and the generations to come. *J Med Ethics* 2014;40:752–8.
43 Brassington I, Oultram S. The Topsy-Turvy Cloning Law. *Monash Bioeth Rev* 2011;29:1–18.
44 Cutas D, Smajdor A. Duped Fathers', 'Cuckoo Children', and the Problem of Basing Fatherhood on Biology: A Philosophical Analysis. *Assist Reprod mit Hilfe Dritter* 2020;171–82.
45 Helander D. *Bordering through Genetics: Dna Testing, Family Reunification and Swedish Migration Control*. Umea University, 2003. Available: https://www.dissertations.se/dissertation/62c0e54a2f/
46 VélizC. The ethics of privacy and surveillance. 2024. Available: https://global.oup.com/academic/product/the-ethics-of-privacy-and-surveillance-9780198870173 [Accessed 5 May 2024].
47 Boniolo G. Is an account of identity necessary for bioethics? What post-genomic biomedicine can teach us. *Stud Hist Philos Biol Biomed Sci* 2013;44:401–11.
48 Liaw YQ. An analysis of different concepts of 'identity' in the heritable genome editing debate. *Med Health Care Philos* 2024;27:121–31.
49 Parfit D. Future People, the Non-Identity Problem, and Person-Affecting Principles. *Philosophy & Public Affairs* 2017;45:118–57.
50 Wrigley A. Harm to Future Persons: Non-Identity Problems and Counterpart Solutions. *Ethical Theory Moral Pract* 2012;15:175–90.
51 Räsänen J, Smajdor A. Epigenetics, Harm, and Identity. *Am J Bioeth* 2022;22:40–2.
52 Sparrow R. Human Germline Genome Editing: On the Nature of Our Reasons to Genome Edit. *Am J Bioeth* 2022;22:4–15.