

## Science &amp; Society

## Synthetic gametes and the non-identity problem: the babies of tomorrow

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**Synthetic DNA technologies may eventually enable the creation of synthetic gametes, which would offer precise control over genetic inheritance. This possibility raises profound ethical questions about human identity, genetic selection, and evolutionary boundaries. While synthetic gametes sidestep person-affecting ethical concerns, they present challenges for balancing reproductive autonomy and minimizing heritable disease, prompting interdisciplinary reflection.**

**Engineering gametes *de novo***

Synthetic DNA (synDNA) refers to DNA sequences that are artificially designed and chemically synthesized rather than copied from natural templates. This method enables the creation of entirely novel genetic sequences, bypassing the need for a natural DNA template.

Since Craig Venter's team successfully synthesized and transplanted an artificial bacterial genome in 2007 [1], and later designed a computer-generated genome for *Mycoplasma mycoides* [2], the field has advanced rapidly. While synthesizing a full human genome remains technically unfeasible today, strides in synthesis efficiency suggest that it may not be far off. Gamete genomes are haploid, with about 3 billion base pairs – half the size of the diploid human genome's 6 billion base pairs – making their synthesis and assembly

simpler and more manageable. Additionally, successful engineering of haploid chromosomes has been demonstrated in species such as yeast, where fully synthetic chromosomes and haploid genomes have already been constructed and refined [3].

Rather than replicating the entire human genome, a more realistic short-term goal may be the creation of gamete genomes (Box 1). This opens the door to potentially engineering synthetic haploid genomes tailored for reproduction, without the immediate complexity of duplicating a full diploid genome. This concept involves first constructing a synthetic genome and introducing it into a suitable cellular environment where it can be expressed. In the context of reproduction, this would entail delivering a synthetic genome into an oocyte or modifying the genetic content of a sperm cell, thereby enabling the production of gametes with engineered or customized genetic information.

Bioethical discussions concerning reproduction have historically progressed from focusing on selection – such as choosing embryos based on genetic screening (prenatal genetic diagnosis, PGD) – to modification, where the genome of embryos or cells is actively altered: using, for example, clustered regularly interspaced short palindromic repeats (CRISPR) gene editing. We advance the discussion further, turning attention to creation: the *de novo* generation of designer gametes from scratch (Box 1), which introduces a fundamentally new paradigm for synthetic biology and reproductive genetics. However, the ability to design and synthesize genomes from scratch (re) raises profound ethical and societal questions [4]. Crucially, it raises the question of whether such actions directly affect a specific future individual, or whether they instead influence which individual comes into existence. Existing ethical frameworks, largely developed around interventions after fertilization, may not fully capture these subtleties or adequately address the

implications of shaping genetic identity at its inception.

Questions around identity, personhood, and the boundaries of human intervention in evolution will intensify as synDNA approaches clinical and reproductive frontiers. Whether these technologies are used to cure disease, enhance traits, or even create novel forms of life, they will challenge our moral frameworks. We ask whether engineering gametes for reproduction, which might result in a controlled genetic programming of the prospective embryo, is a person-affecting act or not: that is, whether genetic programming of the embryo harms or benefits a specific individual or whether it creates a whole new individual instead. In the context of engineered gametes, this distinction helps clarify whether genetic modifications are best understood as actions that directly affect the health or traits of a particular future child, or as factors that determine which child comes into existence in the first place. Recognizing this difference is essential for assessing the broader ethical and social responsibilities associated with applying genetic technologies to human reproduction.

**Non-identity problem and selecting the genes**

A central challenge in population ethics is the non-identity problem (Box 2), initially developed by Derek Parfit [5,6]. This dilemma arises when choices made before a person's existence determine which particular individual comes into existence. For instance, if prospective parents opt for *in vitro* fertilization (IVF) with donor gametes rather than conceiving naturally, the resulting child will be genetically different from the one they might have had otherwise (if conceived naturally). Since the child born from donor gametes would not have existed without the choice of using IVF, it cannot be said that the child is harmed by being brought into existence, even if having been brought into existence in suboptimal conditions: for example,

### Box 1. Creating gametes from scratch

Unlike current reproductive technologies, which rely on selection rather than design, synDNA offers the unprecedented possibility of engineering gametes from scratch [1,14] (Figure 1). Techniques such as PGD select among already fertilized embryos, limiting intervention to existing genomic combinations. *In vitro* gametogenesis, while promising, cannot predict the exact genome of resulting gametes due to the randomness of homologous recombination during meiosis. Even polar body sequencing in human oocytes provides only partial insight, predicting the genetic content of the oocyte post-fertilization but offering no information about the sperm's genome. By contrast, synDNA allows for the deliberate construction of haploid genomes with known, predefined sequences. This could enable the design of gametes with specific genetic traits, fundamentally transforming our decisions on genetic heritability.

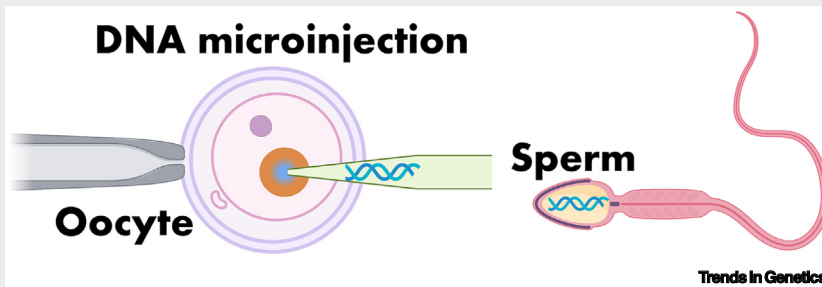


Figure 1. Gamete manufacturing through microinjection of synthetic DNA. Image created with BioRender.

having a genetic disorder such as cystic fibrosis; after all, the child's very existence depends on the decision to use IVF in the first place. Parents who use IVF and choose a specific embryo (or a set of embryos) to implant give that specific potential person (or potential persons) a chance to live, with the qualities – including potential diseases and disorders – that that individual (or individuals) happens to have [7]. The non-identity problem becomes

crucial when considering the ethics creation of synthetic gametes.

Unlike gene editing, which modifies an existing embryo, synthetic gamete production does not alter a pre-existing individual. Instead, it generates an entirely new genetic lineage, leading to the birth of a person who otherwise would not have existed. Because this act is not 'person-affecting' – meaning it does not change the circumstances of any

identifiable future individual, instead, it brings into existence a different individual – we can argue that it is morally permissible to design gametes this way. The resulting child's existence is contingent on the intervention itself, making traditional person-affecting harm-benefit assessments inapplicable.

However, critics might contend that this very feature weakens the moral justification for synthetic gamete production compared with other reproductive technologies. As other philosophers [8,9] point out, gene editing of embryos directly benefits a specific future person: for example, by correcting a disease-causing mutation, thereby sparing that individual from suffering. This person-affecting intervention carries clear moral weight because it improves the life of an identifiable being.

By contrast, manufacturing gametes to avoid a genetic condition does not benefit any particular individual; the child born from synthetic gametes would not exist without the procedure, meaning that no one is made better off in a person-affecting sense. This has led some to argue that synthetic gamete creation lacks the strong ethical justification of interventions like embryo editing [10].

Yet this critique overlooks an important distinction. While synthetic gamete production may not benefit a specific individual, it can still produce impersonal benefits: improvements judged not in relation to a particular person, but in terms of overall outcomes. As Hare [11] and Räsänen [12] argue, benefiting 'whoever is born' (e.g., 'the couple's future child') can sometimes be morally significant. If synthetic gametes result in the birth of a healthier child – albeit genetically a different one than would have been born without using such gametes – then the overall outcome is improved, even though no genetically specific individual has been directly benefited. In such cases, reproductive choices should aim for the best

### Box 2. The non-identity problem and the case of Lulu and Nana

The non-identity problem arises when actions affecting future individuals alter their identity, making traditional harm-based ethics insufficient. For instance, if a mother chooses to conceive a child with a genetic disorder now or delay conception for a genetically different, healthier child, the dilemma is that neither choice harms a specific child, as each child's identity is tied to the timing and manner of conception. In the case of Lulu and Nana, the first gene-edited babies, He Jiankui's use of CRISPR during IVF determined their unique genetic identities. Had their parents conceived naturally, the children born would have been entirely different individuals. Thus, potential harms from the editing (e.g., unintended mutations) cannot be framed as harming Lulu and Nana, since they would not have existed otherwise. However, Alonso and Savulescu point out that the harm in Lulu and Nana's case cannot be easily classified as a 'non-identity' problem [15]. Critics argue that the gene editing exposed the girls to person-affecting risks, such as an increased vulnerability to infections and other unknown health outcomes, since they could plausibly have existed without the CCR5 modification and its associated dangers. At the same time, if the editing had altered their psychological development or identity – for example, by causing significant intellectual disability – then the intervention could be seen as identity-altering, raising the stakes of the ethical debate. Complicating matters further, Lulu and Nana's existence depended on the specific context of IVF and He Jiankui's actions, without which different children may have been born. This ethical ambiguity highlights the limits of current frameworks and raises further concerns about consent, equity, and the risks of engineering the human genome.

possible future child [13], a morally relevant, if impersonal, consideration.

Thus, while the non-identity problem complicates traditional ethical assessments, it does not render synthetic gamete production morally neutral. Instead, it shifts the debate from person-affecting harms and benefits to broader considerations of impersonal wellbeing, reproductive autonomy, and the ethical weight of bringing a better-off child into existence.

### Natural selection becomes cherry picking

The ability to manufacture gametes using synthetic DNA offers a unique opportunity to avoid passing on harmful genetic variants without affecting the identity of any particular future person. In natural reproduction, genetic inheritance is a lottery: each gamete carries a random mix of parental variants. Synthetic gametes, by contrast, allow prospective parents to select which of their own variants to include, reducing the risk of transmitting conditions associated with serious diseases like cystic fibrosis or thalassemia.

This is not about choosing the ‘best’ possible genome, but about selecting among different possible combinations of one’s own genetic material to avoid foreseeable harm. Importantly, this does not harm or disadvantage anyone; if a person with a higher risk of suffering is not brought into existence, no one has been made worse off. Rather, the outcome is that a child with a lower likelihood of avoidable suffering comes into existence. The decision becomes ethically relevant without being person-affecting.

Additionally, when both reproductive partners manufacture gametes, they can coordinate their choices to avoid double inheritance of recessive disease-causing variants. Such collaborative planning enhances the potential to reduce risk without venturing into territory that seeks to create

‘perfect’ individuals. The goal remains modest and responsible: to minimize suffering where possible. In this light, synthetic gamete technology should be seen not as a tool for perfectionism or control, but as a cautious, rational, and ethical way to reduce preventable harm in future generations.

### Is it eugenics?

The development of synDNA to manufacture human gametes opens the door to unprecedented forms of reproductive autonomy. Yet this powerful technology has also prompted ethical concerns, particularly the fear that it could mark a return to eugenics.

Eugenics, historically, was marked by coercive policies aimed at controlling who could reproduce. By contrast, the use of synthetic gametes is grounded in individual reproductive liberty. No one is forced to use this technology; it is a tool available to those who choose to create genetically related children. The absence of coercion is ethically significant: reproductive freedom is a core value in modern bioethics, and synthetic gametes expand, rather than restrict, that freedom.

Furthermore, while critics of PGD raised concerns about selecting against certain disabilities, synthetic gamete technologies are not inherently discriminatory. They operate upstream of PGD, at the level of gamete creation, and are typically employed to prevent the inheritance of serious genetic conditions. The intention here is not to eliminate diversity, but to avoid predictable and often devastating harm.

### Concluding remarks

The development of synthetic DNA and engineered gametes marks a significant advance in reproductive technology, offering new possibilities for preventing heritable diseases and expanding reproductive options. Unlike traditional genetic interventions, creating synthetic gametes does not alter

existing individuals but enables the birth of individuals who would not have otherwise existed, shifting the ethical focus to broader questions of wellbeing and autonomy. Hence, its use raises important ethical considerations that require ongoing, careful discussion.

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### Declaration of interests

The authors declare no conflicts of interest.

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