Review Article

Ethical Perspective of The Usage of Genetic Editing For Cosmetic Purposes

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ABSTRACT

Gene editing is a new and upcoming technology used to alter the genetic makeup of organisms. Due to its popularity, gene editing technologies come with many ethical debates, social norms, and beliefs that analyze their importance and usage. This paper will explore the potential implementation of genetic engineering in the cosmetic industry by analyzing professional opinions and past implementations. The paper examines current cosmetic procedures like in vitro fertilization and plastic surgery, before delving into the ethical debates surrounding designer babies and germline editing for cosmetic-related traits. Some key risks identified and discussed include off-target effects, the complexity of the gene network, and the potential unintended consequences of altering pleiotropic genes. The paper also discusses recent advancements in prediction methods, such as in silico tools, aimed at reducing the risks associated with gene editing. Through a synthesis of numerous arguments, the use of this up-and-coming technology in cosmetics was deemed too risky in our current state but with more research and careful oversight, it could be a possibility in the future.

Keywords: Genetic editing; CRISPR; Designer baby; IVF; Plastic surgery

INTRODUCTION

The origin of gene editing technology dates back to the 1980s with the innovation of procedures utilizing zinc finger nucleases (ZFNs). ZFNs are gene-targeting tools that contain both a DNA-binding domain derived from zinc finger proteins and a DNA-cleavage domain. These two domains allow ZFNs to accurately bind to and cut specific DNA sequences. The development of ZFNs paved the way for more accurate and advanced genetic editing technologies such as Transcription Activator-like Effector Nucleases (TALENs) and, more recently, Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR) (Figure 1). Similar to ZFNs, TALENs use engineered proteins to induce double-stranded breaks in target DNA sequences. On the other hand, CRISPR-Cas9 utilizes a guide RNA (gRNA) to accurately find and bind to the target DNA sequence, and a Cas9 nuclease to cut the DNA.

Genetic editing allows us to modify unfavorable genetic sequences or replace them with favorable ones. While genetic editing has been used for a variety of different purposes, there are few that fall into the philosophically generally agreed upon ethical or "good" categories (2). One example of a good application is using

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genetic engineering to treat diseases. This is one of the most promising procedures and is commonly viewed as ethical (3). Procedures that edit genetic mutations have the potential to treat genetic diseases like cystic fibrosis, Huntington's disease, and many types of cancer. By editing these mutated sequences, genetic editing provides effective cures and the potential to transform our healthcare systems. In addition to various medical uses, genetic editing also plays a profound role in agriculture with the creation of genetically modified crops. Despite the controversy, Genetically Modified Organisms (GMOs) have been proven to be "as healthful and safe to eat as their non-GMO counterparts" (4). Since they were developed in the 1990s, GMO plants have increased nutritional value, allowed for fewer pesticides, and also reduced the cost of food.

Furthermore, GMOs increase food availability and allow for a stable supply of food throughout the year. As a result, overall they have been recognized as a solution to numerous global food challenges (4).

While biotechnology and genetic engineering have a promising future in many aspects of our lives, using these technologies for cosmetic purposes remains an ethical gray area. With the potential to change our physical appearance–our height, skin color, muscle mass, and more–genetic editing has emerged as a groundbreaking innovation with potential beyond medical and agricultural usage. Interest in choosing and changing physical appearances is evident in both current consumer industries, discussed below, and in various scientific surveys. Cincinnati psychologist Ann

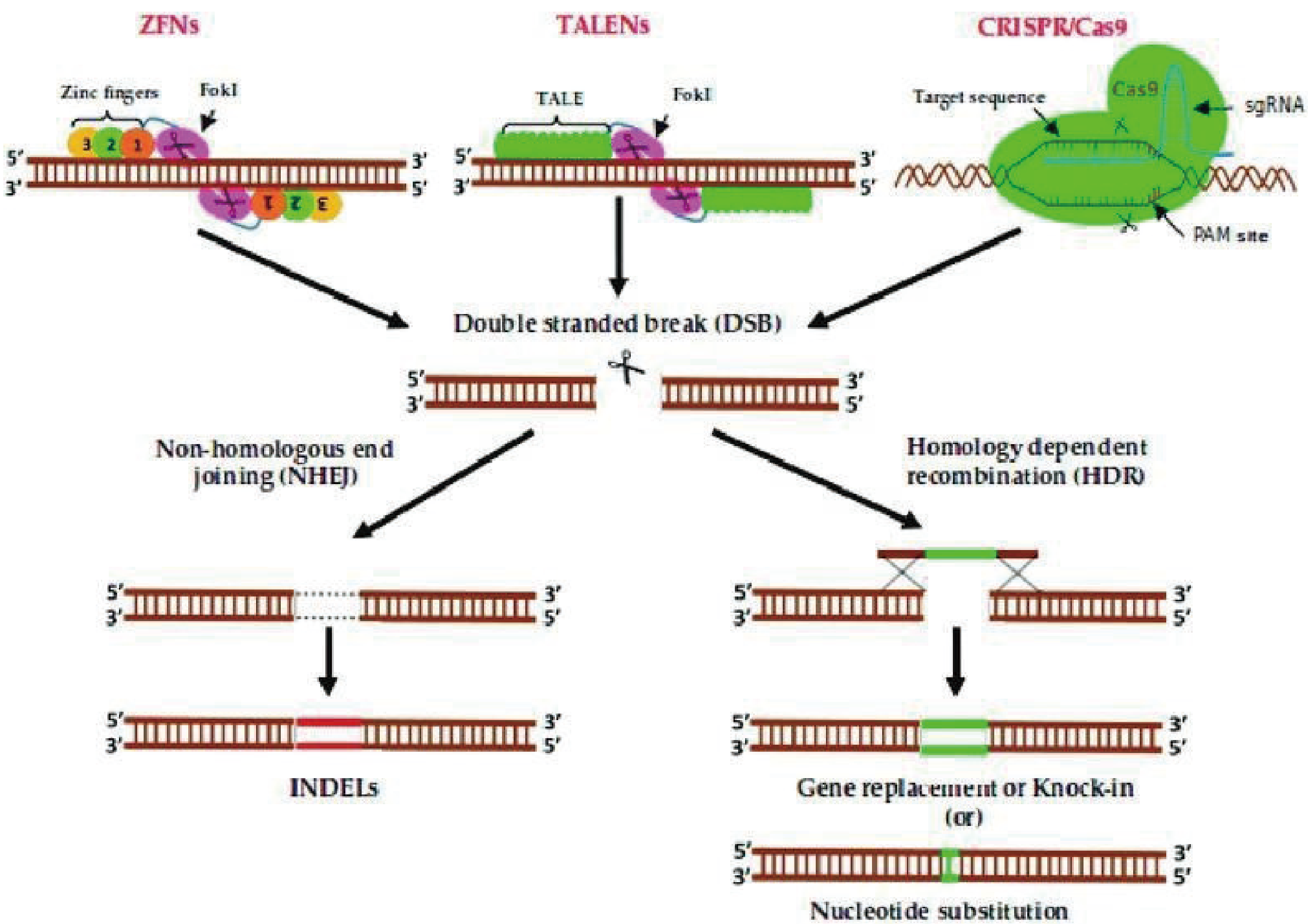

Figure 1. Differences between genetic editing methods. For ZFNs, a pair of ZFNs bind to the DNA and initiate a double-stranded break. TALENS uses a customizable DNA-binding region paired with a cutting enzyme to initiate a double-stranded break. CRISPR utilizes a 20-base guide sequence to direct the Cas9 enzyme to cut the DNA at a specific location (1).

Kearney surveyed about 45,000 participants and found that 56% of women and 43% of men were dissatisfied with their overall appearance, and the majority (89%) of women participants wished to change at least one part of their appearance (5). Furthermore, a cross-cultural study of almost 100,000 participants from various backgrounds revealed that both men and women spend an average of about four hours a day trying to enhance their physical appearance (6). These studies, among many more, reveal the human desire to be perfect and constantly change oneself to match societal standards.

As genetic editing technologies continue to advance, they provide opportunities to modify ourselves, especially our physical appearance. Thus, the rise in this technology also raises the question: To what extent should ethical considerations influence the usage of germline genetic editing technology for cosmetic purposes? We need to consider the risks and moral dilemmas that arise as we explore and develop groundbreaking innovations. This paper will first discuss current cosmetic procedures and then examine the various ethical concerns as well as risks and benefits associated with using genetic editing, especially for cosmetic purposes. Additionally, it is important to keep in mind that gene editing for cosmetics is not currently established in the United States.

CURRENT COSMETIC ALTERATIONS

In Vitro Fertilization

While CRISPR may allow for cosmetic alterations in the future, already existing procedures like in vitro fertilization (IVF) allow for a small selection of targeted features from the early development stage. IVF enables parents to test for abnormalities, potential genetic disorders, and even sex selection. The pre-implementation genetic diagnosis (PDG) and screening (PGS) for IVF allow parents to select embryos based on disease probability and gender (7). This procedure screens the embryo and identifies the probability of genetic diseases being passed down to the parents' baby. Furthermore, as reproductive technologies have advanced, parents can also use PGS to identify the gender of the embryo and have the option of gender selection if desired. One aspect of IVF that provides people with the most control over their baby's physical appearance is the ability to pick sperm donors. Many companies such as Cryobank America and FairFax FaceMatch allow people to search for their ideal sperm donor. Cryobank America allows you to narrow your search with filters on hair color, eye color, height, race, and even weight (8), while Fairfax allows you to input images to find a similar match (9). Many sperm donor companies provide the mother the opportunity to choose traits considered favorable to her and have the best chance at enhancing the physical appearance of her baby.

IVF is an expensive procedure–the cost of a single cycle ranges from $15,000 to $30,000–often requiring multiple cycles to be successful. Despite these costs, according to the U.S. Department of Health and Human Services, in 2021, 86,146 infants were born using assisted reproductive technology, with IVF accounting for 99% of these procedures (10). Although genetic editing for cosmetic purposes has not been legalized or fully established yet, procedures like IVF showcase the growing trend of wanting the power to influence the physical and medical outcomes of future generations.

Plastic Surgery

Another cosmetic alteration procedure is plastic surgery, which has become increasingly popular over the years with new procedures being developed. Plastic surgery can range from botox to breast reconstruction, liposuction, body lifts, rhinoplasty, and even other minimally invasive procedures that can essentially transform almost every part of a person. Around 1,600,000 cosmetic surgery procedures were performed by just members of the American Society of Plastic Surgeon Association (ASPS) and around 25,000,000 total minimally invasive cosmetic procedures were performed in 2023, totaling more than 25 million cosmetic procedures, making it a multi-billion-dollar industry (11). Table 1 indicates the surgeries performed by members of the ASPS, mentioning different categories of procedures performed throughout the year (11).

Limitations posed by these procedures: However, IVF and plastic surgery have their limitations. For IVF, the limitations and risks are endless. IVF can be extremely costly. This is because the procedure itself is expensive and also it increases the chances of having multiple babies.

Table 1. Statistical data of cosmetic procedures in 2023 (American Society of Plastic Surgery)

Type of procedures	Number of Procedures
Cosmetic Surgery - Breast	600,815
Cosmetic Surgery - Body	600,893
Cosmetic Surgery - Face	363,936
Cosmetic Minimally Invasive	25,442,640
Reconstructive	1,025,100

Furthermore, IVF raises the risk of having a premature delivery or a baby with low birth weight (12). Plastic surgery can only be used to modify physical appearances to a certain amount and involves significant risks as well as long recovery times. One of the biggest risks of plastic surgery is that "you might not achieve the result that you were expecting" (13), and in some cases, the results are not permanent.

Despite these limitations, the high demand for these procedures showcases the high demand for control over physical appearances and genetic outcomes in our current society.

GENETIC EDITING TO ENHANCE COSMETICS

Designer babies

Genetic editing has the potential to revolutionize the cosmetic industry and overcome the limitations of current cosmetic procedures. One of the most controversial applications of gene editing is the creation of "designer babies," in which parents can utilize germline editing to modify or "enhance" physical features such as height, hair color, eye color, skin tone, and muscle mass. Since the successful germline gene editing procedure performed in 2018 by biophysicist He Jiankui, there has been increasing interest in the possibilities associated with this technology.

Jiankui used CRISPR technology to prevent the babies from being able to be affected by HIV (14), claiming to have disabled the *CCR5* gene which enables HIV infection. Although Jiankui's treatment method was reported to be successful, it sparked many ethical debates, especially about where to draw the line between genetic enhancements and genetic treatments.

Treatment vs Enhancement

The distinction between enhancements and treatments is not always clear-cut. Obesity, for example, is one of many traits which fall into a moral gray area. Currently, a scientific team from the University of Barcelona and CIBERobn are working towards a solution for obesity that involves implanting modified cells. From a medical standpoint, obesity is a "chronic complex disease," which is associated with numerous health issues such as diabetes, heart disease, and even hypertension (15).

However, numerous studies have indicated that a low waist-to-hip ratio in women is favored by men and therefore desired by women (16), and thus seeking genetic editing for obesity can also be an enhancement or a modification to better appeal to societal views.

In addition to obesity, several other disorders or situations exist where the line between treatment and enhancement becomes blurred, such as muscle enhancements. Procedures and drugs aiming to enlarge muscles or overall athletic performance have sparked many ethical debates since they serve as both treatments and enhancements. Muscle enlargements can be used to treat disorders such as muscle dysmorphia and muscular dystrophy. In addition, muscle dysmorphia is a psychological disorder that is associated with "being preoccupied with worries that one's body is 'too small' or 'not muscular enough'" despite being normal and often leads to unhealthy or excessive exercise (17). Muscular enlargement procedures can become an alternative to steroid use because these procedures create the desired body or physical appearance. Muscular dystrophy, on the other hand, is a genetic disorder that causes progressive weakness and loss of muscle mass (18). This condition is caused by a mutation in genetic sequence which interferes with the production of proteins essential to forming healthy muscles. According to the International Journal of Medical Sciences, "Gene editing …can permanently correct DMD mutation" (19). However, muscle enlargements can also serve as cosmetic enhancements as they are used to give bodybuilders and everyday people a more desirable physical appearance.

The numerous situations blurring the line make it difficult to discuss the morality of this up-and-coming technology. Despite the potential of genetic editing to make cosmetic procedures more reliable, the long-term risks associated with these procedures are uncertain. Currently, the United States and many other developing countries, like China and the UK, have placed restrictions largely banning the usage of CRISPR in human embryos (20). Despite these bans, this new industry continues to evolve and the distinction between treatments and cosmetic enhancements needs to be addressed.

Risks

As with every great innovation, there are many risks and unknowns. One of the most significant concerns with genetic engineering in general is the potential for off-target effects. Off-target effects are the result of when genetic editing technology, such as CRISPR, binds and alters DNA sequences at an unintended site. Off-target effects occur when the Cas9 protein and gRNA bind to DNA sequences extremely similar to the target sequence. Despite the high specificity of the gRNA, it can still incorrectly bind and allow the Cas9 protein to modify DNA sequences that are similar to the target sequence (for example, those having only around 3 to 5 nucleotide differences) from the target sequence (Guo, 2023). Altering the wrong sequence can cause potentially dangerous mutations that can lead to unpredictable consequences, such as disruption of essential genes, potentially causing harmful genetic disorders, including cancer (21).

Another major risk of genetic editing is that altering sequences can backfire. Many genes serve more than one function within the body and altering a sequence can unintentionally disrupt other biological processes and cause detrimental issues. A non-cosmetic example is the genes that code for the PAX6 protein, as they are "involved in the development of a specialized group of brain cells that process smell," but they are also known to play a key role in eye development before birth (22). An appearance-related example, the *IGF-1* gene is known for making muscles grow but it also plays a huge role in the growth of prostate cancers. Small changes for those wanting to improve their physique can have unpredictable and potentially serious health complications (23). Thousands of genes like *PAX6* and *IGF-1* are involved in a variety of different functions, and disruptions to such genes could lead to harmful unforeseen issues.

Even the smallest of cosmetic changes made by genetic engineering technologies would require careful research and consideration. The vast gene network serves as a basis for the phenomena of gene pleiotropy, in which a single gene can influence multiple traits or biological processes. The interconnected gene network regulating genes makes it so that a single alteration can have a cascading effect throughout the genome (24). This makes it extremely difficult to anticipate and control genetic editing modifications, including those of a cosmetic nature.

Additionally, hundreds, even thousands, of genes are at play for any individual trait. According to Dr. Lea Witkowsky, a project and policy analyst at the Innovative Genomics Institute and the American Society of Microbiology organization, "The characteristics people tend to associate with designer babies–intelligence, height, and athletic ability–are not controlled by one or even a few genes" (20). Witkowsky gives the example of a 2009 study that estimated that 93,000 single nucleotide polymorphisms are required to explain 80% of the population variation in height (20). This highlights the complexity of the human body as well as the challenges associated with accurately predicting and altering genetic sequences to produce desired cosmetic changes.

Additionally, requests for changes to skin color and natural features in a healthy person lead to concerns about exacerbating racial or other prejudices. Rick Weiss, director of *SciLine*, a nonprofit science journal, emphasizes that genetic enhancements, especially cosmetic ones, may create a society where physical appearance becomes more standardized and promotes a culture where individuals conform to extremely specific standards of beauty (23). Although genetic editing has transformative potential, there are many risks and unknowns.

Benefits

As discussed earlier, a benefit of germline editing and other assistive reproductive technologies, like IVF, is the opportunity for the selection of the biological sex of offspring. This potential benefit can be helpful for several reasons, including medical, cultural, and personal preferences. For example, from a medical standpoint, families with a history of sex-linked genetic disorders may benefit from sex selection.

Being able to choose the sex of their child could prevent the spread of the disorder to their children and end up saving lives. Culturally, gender selection can address societal preferences. In some cultures, certain genders are viewed as more valuable or hold more authority than the other. For instance, according to the International Labour Organization, in Arab regions, men are viewed as masters of the house and hold much more authority while women are restricted to homemakers (25). As for personal preferences, gender selection allows parents to make decisions that reflect their desires and family history.

While gene editing for cosmetic procedures in humans needs further examination, researchers are making an effort to apply gene editing in lab-based procedures to improve sustainability in the cosmetic industry. With the increased demand for organic products came the shift towards organic cosmetics, and the natural ingredients market is expected to expand from $642 million in 2022 to a projected $1,095 million by 2030 (26). However, the downsides to organic cosmetics are the environmental impacts and the costs. Many ingredients commonly used in cosmetics are derived from animals and are not environmentally sustainable (27). Genetic engineering can overcome these issues by allowing us to create sustainable alternatives.

Evolva, a Swiss Biotechnology Company, has demonstrated the endless opportunities associated with biotechnology. Although this is not a cosmetic-related example it shows the potential for what genetic editing could do for cosmetics. Evolva uses genetic engineering in order to create yeast strands to produce artificial vanillin - the primary component of vanilla bean extract. Traditional vanilla extract creation requires intense labor and takes a toll on the amount of resources available, but Evolva's new approach allows for the production of vanillin in a controlled and stable environment. According to the U.S. Department of Agriculture, genetically engineered crops allow for the preservation of natural resources while also increasing year-round supply due to their resistant abilities, showing the potential for GMO agriculture biotechnology to solve environmental challenges (28). Labbiotech states, "CRISPR-Cas9 can be used to engineer microbes to make nature-based cosmetic ingredients using standard biotechnology facilities" (27).

Moreover, genetic engineering can significantly reduce the cosmetic industry's usage of animals for both ingredients and testing. More than 500,000 animals suffer and die for cosmetic purposes per year (29). By utilizing biotechnology, scientists can modify plants and microorganisms to allow for the production of high-quality ingredients that are usually obtained from animals. Furthermore, having control over the creation and production of these products means that scientists will also be able to manipulate the ingredients produced to better suit cosmetic needs. By adopting genetic engineering to produce organic products, the cosmetic industry can significantly improve its environmental impact and create a more sustainable future.

CONCLUSION

Based on our current state of knowledge, gene editing should not be used for germline cosmetic editing in humans. Due to the lack of sufficient research and unknowns, genetic editing for cosmetic purposes has yet to be safely executed. The main product of cosmetic gene editing is the development of designer babies. This allows parents to have some control over their baby's appearance. However, the lack of information makes it difficult to predict the outcomes of this gene editing. In contrast, advancements in forensics technology, especially in forensic DNA phenotyping (FDP), have enabled us to predict a variety of traits such as eyebrow color, freckles, hair structure, height, and hair loss from DNA (30). In the future, when combined with FDP, germline editing can potentially be used to accurately modify and determine a baby's features before birth. Thus, efforts to minimize any risks associated with gene editing are vital to prepare for a possible future of germline editing for cosmetic purposes.

As previously discussed, a significant risk of genetic editing is off-target effects, and in an attempt to mitigate this risk, researchers have developed numerous prediction methods to prevent this from happening. One of the most popular methods for this is in silico tools. In silico tools are computational models that analyze hypotheses and are used as data analysis models. These prediction tools can "minimize off-target effects through algorithmically designed software" (31). In silico predictions rely on a variety of approaches and algorithms such as sequence alignment, machine learning, homology models, and databases. Cas-OFFinder, for example, is a tool to detect off-target sites by evaluating the guide RNA and target sequence (32). This algorithm-based technology scans the genome to find potential off-target locations by comparing it with the target sequence. Another popular in silico tool is CRISPRoff which utilizes machine learning to predict off-target effects by analyzing patterns in previous experiments (33). These advancements in prediction methods are making genetic editing procedures safer and more reliable. As researchers gather more information, this technology will continue to evolve and resolve many of the risks associated with it.

Even with new technology and advancements, concerns remain about the distinction between enhancements and treatment. While some cosmetic procedures may be ethical and performed for treatment purposes, the same procedures, when used for enhancements raise many ethical concerns or may not even be worth the safety risk. A huge challenge lies in drawing the line between where treatment ends and enhancement begins.

There is already a growing demand for cosmetic alteration, as previously evidenced by the popularity of current non-genetic editing cosmetic procedures such as plastic surgery. These procedures allow individuals to modify their appearance to adhere to their preference of societal values. On the extreme end of enhancement vs treatment, there are designer babies created for enhancement. Designer babies raise many significant social ethical concerns, particularly since it involves making changes before the baby is born. As opposed to plastic surgery or other cosmetic changes to adults, the creation of designer babies doesn't take into account the child's opinions. Although this could allow the baby to have socially approved appearances and mental capabilities, it takes away the baby's freedom and increases social inequality while also increasing the chances of unintended genetic consequences. Furthermore, unlike non-genetic editing cosmetic procedures, germline editing permanently alters the baby's genome, making changes to future generations' genetic outcomes as well. On the other end, designer babies for treatment, babies could be genetically modified for medical purposes. Germline genetic editing can be used to prevent future genetic disorders or medical concerns. While this is more justifiable, there are still many concerns about where the line should be drawn between necessary treatment and enhancement.

Despite future mitigation of these risks, there are still many concerns surrounding this technology. Genetic enhancements like muscle enhancements may “undercut the Olympic spirit of earning rewards through hard work and training” (23). This raises important concerns about the value of effort and hard work in the future when one can simply pay for artificially engineered advantages and traits, essentially questioning the authenticity of future achievements. These concerns raise many ethical questions we must grapple with. For instance, should there be cosmetic germline genetic editing, or should this technology be limited to the development of cosmetic ingredients and products? This is a difficult question and we can look to organizations such as the World Health Organization and the Health Ethics & Governance division to oversee and regulate these advancements.

DECLARATION OF CONFLICT OF INTERESTS

The author declares that there are no conflicts of interest regarding the publication of this article.

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