REVIEW ARTICLE

Genomic Editing, Human Enhancement, and Transhumanism: A Brief Overview

Kresimir Pavelic[1], Sandra Kraljevic Pavelic[2]

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Abstract

A scientific debate on genetic engineering, human enhancement (HE), and transhumanism has been largely pursued in scientific literature, but so far, the public opinion on this issue has not been properly surveyed or heard. In this article, we accordingly join the debate through presentation and discussion of chosen scientific facts and opinions on genomic editing (GE) along with perspectives and concerns, HE, designing of baby with genetic engineering, transhumanism, and the culture of life.

Finally, we are questioning the idea of an indefinitely long lifetime. While significant scientific advancements in the area of genetic engineering and HE are expected in the future, a reasonable approach and caution in the new knowledge and technologies usage and implementation may be strongly advised. Indeed, legal, ethical, and social issues need to be discussed and evaluated in light of novel possibilities to avoid an eventual critical era of human existence.

Keywords: Designing a baby, Genetical engineering, Genomic editing, Human enhancement, Transhumanism.

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Recent discussions on preimplantation or intrauterine interventions and prenatal diagnosis on fetuses and babies have opened up serious questions about the purpose and consequences of genetic editing, HE, and designing of babies by means of gene editing. All these questions, especially from the methodological and socio-humanistic point of view, are reflected under the common topic known as transhumanism. In this chapter, we, therefore, present and discuss the fundamentals of GE and HE within the topic of transhumanism.

Genomic Editing

Science is nowadays facing an essential issue of how to manage unprecedented scientific and technological achievements and progress within sociocultural evolution. It can indeed be foreseen that, soon, our survival and well-being are going to depend on the new wisdom that may be attained only through interdisciplinary thinking and interdisciplinary approaches in science, comprising natural, social, and humanistic fields. The so-called "bio-optimists" predict a bright future for humanity if we become able to use our technology to enhance our sense of morality and our capacity for social responsibility. Still, we cannot evaluate the consequences of future major scientific or technological advancements. Instead, the current focus remains limited mainly to research and technologies that are meant to enhance human health or substantially prolong the human life span. These are GE and HE approaches that encompass current biomedical technologies and their possible development into enhancement technologies in general.[2]

Genomic editing is a genetic engineering procedure whereby the genetic material, the DNA, is intentionally inserted, cut, modified, or replaced in the genome of any living organism. The purpose of GE is to modify the DNA sequence or genotype of a cell or organism for the purpose

[1]Faculty of Medicine, Juraj Dobrila University of Pula, Pula, Croatia

[2]Department of Biotechnology, Center for High-throughput Technologies, University of Rijeka, Rijeka, Croatia

Corresponding Author: Kresimir Pavelic, Faculty of Medicine, Juraj Dobrila University of Pula, Pula, Croatia, Phone: +385 52 377 000, e-mail: pavelic@unipu.hr

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of modification. The method is mostly based on the use of "molecular scissors" or enzymes known as nucleases, which create specific double-strand DNA breaks at certain sites in the genome. The created breaks are repaired with nonhomologous end joining (NHEJ) or homologous recombination (HR) mechanisms, which results in editing or target mutations.[3] GE also appears in natural processes, without artificial genetic engineering. For example, viruses or subvirus RNA agents[4] are capable of editing the genetic code. Genetic engineering methods used thus far include different approaches; for example, forward genetics methods include different approaches to the study of the genetic basis of phenotype, including mutations induction or insertional mutagenesis methods, where a new phenotype is first observed and then the underlying genetic base is explored.[5] Also, the study of the gene function through analyses of phenotypic effects can be done through modifications of the DNA in the reverse genetics process in a target organism by means of site-directed mutagenesis, that is, using a phage or polymerase chain reaction-mediated method and short DNA-oligonucleotide sequences containing desired mutations.[3] Another way of studying genes is through recombination-based methods, which use the natural ability of cells to alternate their own and exogenous DNA. Still, these approaches are not completely adequate with regard to efficiency. The engineered nucleases used in GE seem to be a promising approach that enhances the efficiency and increases the accuracy of the reverse genetic procedures.

Genomic editing is possible due to accumulated knowledge on DNA repair mechanisms. The main mechanisms on which GE is based are the NHEJ, which is based on multiple enzymes that directly affect double-strand breaks (DSB) in the DNA and HR, whereby the homology-directed homologous sequence repair in DSB is performed by using a template for repair at the break site. The problem of creating specific DSB-restriction enzymes is that certain restriction endonucleases recognize several pairs of DNA bases as their targets, so it is certain that such base pairs will be present in many locations along the genome and not only at the wanted site of intervention during the eventual GE. This problem was solved with the development of a site-specific DSB procedure through distinct classes of nucleases. Indeed, this method of GE was proclaimed the method of the year in 2011 by the journal *Nature*,[6] and, since then, the following types of nucleases have been continuously developed: meganucleases (MAGE), zinc-finger nucleases (ZFN), transcription activates-like effector-based nucleases (TALEN), and the clustered regularly interspaced short palindromic repeats (CRISPR/Cas) nuclease system.

Meganucleases are a family of endonucleases enzymes that can induce HR and are characterized by the ability to recognize and cut off large DNA sequences (12–40 pairs of bases).[5,7] MAGE-based GE methods are considerably less toxic to cells in comparison to ZFN-based GE methods, probably due to a stricter recognition of DNA sequences. The MAGE can be engineered to replace or modify almost any wanted DNA sequence in a highly targeted way. MAGE applications are in multiple target sites, individual genetic mutations or one-target site, and multiple genetic mutations or multiple-target sites.[8,9]

Zinc-finger nucleases engineering involves unspecific cuttings of DNA where ZFN contains a zinc finger DNA-binding domain and a DNA-cleavage domain. The zinc ion found in 8% of all human proteins plays an important role in organizing the ZFN three-dimensional structure. In transcription factors, they are usually located on the protein-DNA interaction side where stabilizing the motif. The C-terminal part of each "finger" is responsible for the specific recognition of the DNA sequence. ZFN is used for genetic engineering of stem cells and for the modification of immune cells for therapeutic purposes.[10,11] For example, ZFN-modified T lymphocytes have been tested within clinical studies for the treatment of glioblastoma and the treatment of AIDS patients.[12]

Transcription activator-like effector nucleases or TALEN are artificially created restriction enzymes obtained through the fusion of specific TAL effector DNA-binding domains with a DNA-cleavage domain. DNA-binding domains can be designed to bind almost any desired DNA sequence.[11,13] A study *in vitro*, for example,[14] successfully studied TALEN-induced mutations of 15 genes in cultured somatic cells and human pluripotent stem cells. The authors were able to demonstrate cell-autonomous phenotypes that point to a number of diseases including insulin resistance, lipodystrophy, or motor-neuron death. Moreover, the first clinical use of TALEN genetically engineered cells was based on the treatment of CD19+ lymphoblastic leukemia cells in an 11-year-old child. TALEN-modified T-cell carriers were designed to "attack" leukemia cells to be resistant to alemtuzumab and to avoid the host immune system after application. The patient's condition improved several weeks after receiving therapy. One year after the treatment, the patient is still in remission.[15] The same approach was further developed[16] and several more similar examples of HIV and hematological malignancies therapy through T-cell GE have been documented so far.[17] Therapeutic examples of ZFN or TALEN GE-based approaches also include GE of X-linked severe combined immunodeficiency (X-SCID) through *ex vivo* correction of the DNA gene *IL2RG* in SCID-X1 patient, HSCs and progenitor cells using ZFNs or a correction of mature lymphoid cells *in vitro* in induced pluripotent stem cells derived from SCID-X1.[18] Similarly, a correction of *Xeroderma pigmentosum* cells *in vitro* with TALEN has been successfully performed.[19]

Further on, CRISPRs are genetic elements, specifically the viral genome DNA sequences, which have been incorporated into the bacterial genome upon bacteria viral infections. Therefore, this system is an important adaptive immunity system of bacteria toward bacteriophage infections. CRISPR-associated proteins Cas are involved in the processing of these sequences and they ultimately cut the corresponding homologous viral DNA sequences. CRISPR/Cas (hereinafter CRISPR) system used for GE is based on the use of a piece of RNA called guide RNA, which guides the Cas9 nuclease to a specific position on the DNA sequence.[20] Induced cleavage is subject to the cell's DNA repair mechanisms when wanted corrections of the DNA sequences can be induced in the targeted DNA position.[21] Such CRISPR system has been widely used in diverse genetic studies and is being rapidly developed towards *in vivo* therapeutic models. Recently, it has also been tested in clinical trials, that is, therapeutic GE of malignancies[22] or HIV,[23] which has opened up a number of regulatory questions, especially those related to the safety of such a GE approach. Some issues for CRISPR technology at the moment include the delivery and precision of the CRISPR system. Particularly, researchers have been intensively evaluating the "off-target" toxicity, that is, the alternation of the genome or off-target mutations at the nontarget loci. Solutions including augmentation of the CRISPR system specificity or a limitation of the Cas nuclease action have been tested so far to circumvent the "off-target" issue.[24]

An extremely wide range of genome-engineered applications documented in the scientific literature so far by means of using engineered nucleases includes the research of gene function in plants, animals, and humans as well therapeutic application *in vivo* with promising results. In particular, a major GE outcome of relevance to human health and longevity is gene therapy. Its main purpose is to replace defective genes with normal alleles at their natural site or to control the symptoms of the disease by modifying genes involved in pathological processes. The delivery of genes within gene therapy does not usually require the delivery of the entire gene sequence given that only a small sequence of the gene has to be altered in order to cure or control the disease. The first GE clinical trial for Europe was announced in 2018 for the biotech company CRISPR Therapeutics, which aims to treat patients with sickle cell disease and β thalassemia[25]; however, this has been challenged in a recent paper that proved that CRISPR/Cas technology may induce dangerous and unwanted DNA changes that may initiate malignant processes in cells.[26] There is still much to learn before coming to a conclusive approach for safe GE in humans.

Another application of GE methods may be also envisaged in the field of synthetic biology, which aims to build artificial biological systems either for the purpose of research, medical purposes, or even biosensors and medical devices. The ability of the engineered nuclease to add or remove genomic elements and thus create complex systems are central to this field.[27] Within this field, GE methods can be used, for example, for the creation of artificial cells and organs with new functions. This may be envisaged in current research of the human microbiome, which is increasingly correlated with systemic human disorders, including bone disease, cancer, or neurodegenerative pathologies. GE in synthetic biology approaches might foster the development of effective microbiota-based therapeutics.[28] However, risks that synthetically engineered DNA from microbes may compromise the wider microbiota environment.

Perspectives and Concerns

What are the perspectives and implications of GE for the future of our civilization? Despite some tangible successes of genetic engineering technologies and GE, specificity and certainty of nuclease procedures are still not adequate for major genome interventions. Detection and understanding of the unwanted, "off-target" events are essential elements for further GE applications in humans. Besides the accuracy of GE processes, a better understanding of the basic recombination and DNA damage-repair mechanisms are also required. The CRISPR and TALEN methods are precise and efficient, cheap, and will probably remain the methods of choice for large-scale GE procedures in the future. In particular, the CRISPR method can help to bridge the current gap between GE studies in animals and humans. This is especially important as mice or other animal model studies failed to be translated into humans[29] and genotype-phenotype relationships have been found not to be reliably inferred by studying a single genetic background of the inbred model animals.[30] The use of CRISPR opens up new opportunities as it is used to produce a mutant in nearly any genetic background.[31] Indeed, CRISPR has been extensively used in animal models, mainly mouse models, including the modification of the fertilized zygote using CRISPR to achieve the desired modifications.[32] It is also possible to apply CRISPR in xenotransplantation. In a recent study, for example, it was shown that the replacement of pig genes with human genes with CRISPR precision may be seriously evaluated in the production of donor pigs for xenotransplantation.[33] In addition, CRISPR was used to target and eliminate endogenous retroviruses from the pig genome, which reduces the risk of disease transmission and reduces immune barriers.[34] Eliminating these problems may improve the possibility to use pigs as organ donor animals for humans, and the application of this method brings the idea of pig xenotransplantation closer to reality. Still, one might speculate on the real risk of pig retrovirus infection and the necessity to heavily edit the pig genome for the purpose of xenotransplantation as the GE might add to the complexity of a xenotransplant in a still undefined dimension.

Genome editing techniques are so appealing and work very well in the experimental set-up that many socio-humanist scientists believe that GE will potentially contribute to improving the human race or HE (a term which is explained in greater detail in the continuation of the text). In this connection, the problem of designing a baby has also been elaborated by a number of ethical commissions or research institutions.[35,36] It seems that the majority of participants involved in this debate agree that a moratorium on GE research is counterproductive and that other solutions found within a wide social dialogue might generate appropriate guidelines. One suggested approach was a clear distinction between somatic cells and germ cells in GE research. Still, research was already conducted on human embryos, providing relevant information on the CRISPR method efficiency at this developmental stage. For example, it was shown that gene targeting and editing have to be done in a certain cell cycle phase as it is associated with DNA synthesis.[37] In its 2017 report, the American National Academy of Sciences and the National Academy of Medicine published a comprehensive GE report recommending clinical testing as GE was identified as a procedure that might one day solve serious health problems assuming that it is undertaken in strict and controlled conditions and under assumptions that issues on efficiency and safety have been adequately resolved.[38] This was an important release as any new, thus potentially dangerous, technology raises abuse concerns, such as for the first serious critics towards research results on infected mice with a modified pox virus that caused their infertility.[39] A potential mass bioterrorist usage of this publicly available research has been the subject of debates as the results may be used to create a vaccine resistant to other pox viruses, such as smallpox, that can infect people.[40] There is also the ecological fear of the release of an artificially engineered gene into the environment and "wild" populations. This danger is very difficult to evaluate appropriately as it cannot be readily transferred to a laboratory environment. Concerns are present due to the simplicity and low cost of CRISPR technology that can be used for the production of massive weapons of mass destruction, which is especially applicable to nations without strict regulation and ethical standards in the genetic manipulation area. For example, CRISPR and similar GE technologies might be used for the mass production of killer mosquitoes.[41] The fears are also related to the risks but also the potential benefits of modification of the human genome and the transfer of these modifications to future generations. This requires some urgent ethical scrutiny. Such modifications could have unwanted and unexpected consequences that could damage not only children but their future offspring, as an alteration of their genes will be contained in their germ cells permanently.[42,43]

Human Enhancement

Human enhancement is generally understood as a term describing any attempt to temporarily or permanently alter the existing limitations or disadvantages of the human body, either by natural or artificial means. This also implies technological means of selection or change of human traits and capacities regardless of whether this change results in characteristics that represent the existing human limits.[44]

Human enhancement technologies are not just those intended to treat patients with certain diseases or injuries but also those designed to improve human traits and capacities.[45] Often, HE is used as a synonym for human genetic engineering using nanotechnology, biotechnology, information technology, and cognitive science with the aim of improving human characteristics (memory enhancement, communication skills, senses, multidimensional thinking, psychical, and physical improvement, acceleration of mental and general thinking abilities solving problems).[46] The innovativeness in such an interdisciplinary area is envisaged to be self-catalyzing towards an improvement of human performance. Numerous socio-humanistic issues arise in connection with the application of HE. Particularly, HE has been increasingly identified with the term transhumanism as a controversial ideology and movement that has developed to support the recognition and protection of the rights of citizens to maintain or modify their own intellect and body and to allow them freedom of choice and informed consent to use HE technology for themselves and their children freely. Transhumanism, as defined by More, pursues the acceleration of the evolution of intelligent life beyond its currently "human form" and "human limitations" by means of science and technology, guided by life-promoting principles and values.[47] The most frequent criticism is that these technologies will be usually practiced with uncontrolled and short-term selfish perspectives ignoring long-lasting consequences on individuals and the rest of society. For example, it may be envisaged that some so-called enhancements, which will create unequal physical and mental benefits, are given to those who can afford this technology or that an unequal approach to such enhancement will arise, which will deepen the difference between those who may or may not have it.[48,49] Unfair competition of those who can apply such technology for the purpose of trading has also been mentioned. It is possible that this technology will disrupt the dynamics of relationships within families and close relationships. Socio-humanist thinkers also often point to the problem of inequality and social disruption. Enhancement of the human body can cause significant changes in everyday situations. For example, the sport will change dramatically if enhanced people are allowed to take part in competitions, whereby they will have a tremendous advantage over people who will not have access to such enhancement.[50] Also, no one can exactly know at this point whether enhancements will really be satisfactory for individuals and society in the long term. Still, it should be noted that biological or pharmacological enhancements, such as those potentially envisaged by GE and aimed to promote human health, capacities or dramatically extend the lifespan, are different from technological enhancements, that is, the development of nanotechnology or further advancements in artificial intelligence (AI). While nanotechnology potentially poses serious and immediate risks to humanity itself, AI may accelerate the creation of superintelligence that, on one hand, holds great promises to solving many humanity issues including implementation of nanotechnology but, on the other, may lead human evolution into another direction. Philosopher Nick Bostrom, for example, emphasizes that artificial intellects need not have humanlike motives or psyches, which makes their goals potentially radically different or opposite to those of humans. In Bostrom's opinion, the risks of developing superintelligence include the risk of failure to give it a philanthropic goal.[51] Such debates will require a deeper discussion and re-evaluation of humanity goals and understanding of humans in general.

When evaluating the potential HE impact on the economy, it should be mentioned that HE might significantly extend the life span, and adaptive measures for the legal and economic implications of retirement will be necessary in order to compensate for longer retirement or to postpone retirement for several years. If these adaptations are not made and longevity is not taken into account, this could negatively affect resources such as energy or available food. Resources are inevitably something that will have to be re-evaluated as well. In addition, if AI leaves enough room for human jobs, then candidates with neural enhancements, that is, those in the form of transplants aimed to increase their abilities will easily surpass other candidates. Such social injustice is already exaggerated in our society and maybe, therefore, a real scenario in the future that is further exacerbated with enhancement opportunities.[52] Accordingly, it is clear that the availability of these methods may be achievable only for certain groups of individuals depending on the socioeconomic situation[53] even in a very optimistic scenario. Also, HE will heavily influence human identity by acting on self-conception. Taking into account the fact that at this point many do not seriously evaluate these questions, often focusing instead on everyday problems and existence, an enormous area of discussion may be opened up before fostering and implementing HE. Extreme personality changes can affect relationships between individuals, and people will probably have problems with relying or interacting with newly formed individuals who have been subjected to enhancement. Ultimately, risk is inherently present in these enhancement technologies as well, as a certain level of robustness should be achieved to prevent theft and influence (interfere with) human augmentation.[54]

While we have to acknowledge that new and radical technologies are already here and more are to come, it is difficult to envisage that these will necessarily provide all solutions to our problems and morality. It is more likely that they will reflect the state of their creators, “us-humans,” and with this knowledge further developments should be carefully guided.

Designing a Baby with GE

The concept of a designed baby (DB) implies a human embryo that is genetically modified, usually following the instructions of a parent or a scientist to obtain the desired properties. This can be achieved with various methods, such as embryonic cell engineering or preimplantation genetic diagnosis. These technologies are the subject of ethical debate, as they imply a concept of genetically modified “superhumans” who will eventually replace the present population.

Modifications of germ cells have been carried out since the 1980s, mainly on animals.[55] A successful embryonic modification requires the knowledge of the exact gene insertion procedure so that the new property can be successfully transmitted to the next generation and maintained in the offspring.[56] GE of the germline DNA will be passed onto further generations if the changes are present through the development of germ cells. Manipulation of the germline genome for the purpose of achieving the desired properties is technically already possible and depends on the medical procedure. For example, the cloning process can be used to create genetically identical organisms. In addition, scientists may use gene therapy vectors to modify target DNA, including the DNA of DBs. This can be easily envisaged in an *in vitro* fertilization (IVF) environment where the creation of a genetically engineered baby may occur.

Even though these effects can be positive, that is, the correction of inherited disorders, an inherent risk of possible amplification of negative properties is still a plausible risk at this stage of scientific knowledge. Since the results of such germline genetic manipulations are a complex matter and long-term effects are difficultly observable, it is not easy to evaluate the eventual benefits or enhanced negative effects. It is thus rather questionable whether to allow parents to design their children and to select desired qualities given that the means for human germline GE would be soon available.

Ethical implications and the risks associated with baby designing are already a matter of debate. It is emphasized that DB may be generated through genetic engineering without the exact knowledge on the far-reaching effects on the overall human genes.[57] On the contrary, it is argued that DB can play an important role in counteracting the dysgenic trend. The main ethical issue on DB is that these types of treatment will create changes that can be passed on to future generations so that any mistakes, known and unknown, will be transmitted to their descendants.[56] Therefore, theoretically, a sudden emergence of new diseases and their transfer onto offspring could appear.[58,59] It is therefore not surprising that GE and the transmission of donor mitochondria are the subjects of intense controversy and concerns. If a patient is subjected to germline modification, the offspring will be monitored for a long period of time for any adverse consequences. This period may induce very harmful psychological consequences for these persons and the problems can occur at a significantly later moment in life.[60] On a larger scale, genetic modification can strongly impact the gene pool of the entire human race, both in a positive and negative way.[55] GE modifications are, however, ethically and morally more easily acceptable when the patient or a future baby is seriously ill and the treatment may improve the genotype but also the safety of future generations. Used for these purposes, such treatment can fill the gaps that other technologies are unable to solve.[55]

Of course, experimentations with embryonic cells or embryos are ethically overwhelmingly questionable. Some countries allow these experimentations with fertilized egg cells available in excess after IVF.[60] It should be remembered, of course, that the embryo cannot give consent and that these procedures give way to long-lasting and potentially harmful implications. Human embryo editing is currently illegal in many countries. The American National Academy for Science, Engineering and Medicine recently supported the research and interventions into human embryos but only in cases of the prevention of serious illness and conditions as a "last option" when others had failed. Embryonal editing can prevent large numbers of medical problems in the future and it is worth noting that about 10,000 medical conditions are associated with specific mutations, including Huntington's disease, cancer caused by *BRCA* gene mutations, Tay-Sachs disease, cystic fibrosis, sickle cell anemia, and some cases of early Alzheimer's disease. Replacing a mutation on responsible genes could theoretically eradicate these inherited diseases and prevent the transmission on to next generations, so that future family members would not have similar problems.

Some of the dilemmas and fears about human embryo GE can be compared with similar fears and dilemmas present at the very beginning of the application of IVF. These dilemmas are present even today after more than 5 million IVF babies have been born using this wide human reproduction experiment. Some researchers warn about IVF consequences and call for a serious follow-up of IVF conceived babies as longer-term health outcomes for these children may include cardiometabolic problems[61] or even a shorter life span as suggested by the evolutionist Pascal Gagneux from University of California.[62] Gagneux emphasized that assisted reproduction might lead to biological and social consequences that have not been evaluated enough. Therefore, the embryo GE dilemma on creating a world where children would be considered superior to the other, unedited ones, may be observed from a different angle—is it possible that designed babies may have poorer chances for long-term survival? Both the scientists and ethics share concerns about the accessibility of this procedure. A premise is that any clinical intervention should be available to everyone and society should not create inequality, but should firstly solve issues of safety and long-term outcomes. We must reconcile the fact that new fears arise with each new technology and that these fears may be justifiable or not. Often, these are replaced by some other objective problems during the implementation process that turns the societal outcomes into new, previously unknown directions.

While human embryo GE is prohibited by law in most countries, there are recommendations or guidelines in China for the ban or restrictions in clinical use, but not a statutory prohibition. Indeed, in a very recent paper, by Chinese scientists on a multiple CRISPR, GE of human embryos showed an efficient correction of the Marfan syndrome pathogenic mutation in the *FBN1* gene, which provides instructions for making a large protein called fibrillin-1, with efficacy up to 89% and without detected "off-target" mutations. This research opens the door for GE in genetic correction at the embryonal stage.[63] This procedure was conducted as proof of the concept on 18 embryos, but in two embryos unintentional editing occurred as well. It is still unclear whether such procedures might be considered safe for further IVF procedures and human reproduction.

Transhumanism and "The Culture of Life"

Major cultural changes have been elaborated in the socio-humanistic literature; for example, the culture of perfection of society has been viewed as dominant. It implies human ideals of rationality, freedom, equality, and justice. It also includes belief in science. On the contrary, "the culture of life," which is, according to Knorr Cetina,[64] a radically distinct mentality based on the promises of individual enhancement and life extension. Humanity and humanism are accordingly replaced by, what Knorr Cetina denotes, the "notion of individual life" where individuals feel a need for enhancement of life in general, often fed by biological sciences and promises of life extension and antiaging approaches, which have major social and economic implications as well.[64] Biological sciences may be identified as the major driving force that inspires ideas on human individual enhancements based on GE, biotechnology, and biology. These ideas are then dependent on knowledge and technologies available for their implementation, such as, for example, preimplantation genetic diagnosis, screening, germline engineering, GE, pharmacological interventions, and human cloning. Furthermore, bioengineering ought to combine nanotechnology, information science, and cognitive research (NBIC) with the aim of developing devices that enhance and augment biological human nature, often in the direction of prolongation of life span. When assessing NBIC goals, a major question may arise on how to define a sharp distinction between humans and machines/technology and whether this approach will bring true "enhancement" to a human or just partial enhancements with unknown consequences to other human structures. One can speculate that NBIC may lead to performance enhancements, especially in the elderly population, such as expanded memory capacity, faster thinking speed, or even enable novel sensor capabilities, that is, infrared and ultraviolet wavelengths "sight".[65] It may also repair genetic damage and prevent illnesses. Knorr Cetina thinks that moving to a "culture of life" implies deep societal changes beyond ethical questions of certain scientific disciplines (Table 1).

The main purpose of transhumanism is a substantial improvement of human intellectual and physiological abilities, and the so-called "transhumanist parties" have been established in several countries so far. For example, the U.S. transhumanist party supports activities or means to improve the human condition for "as many people as possible, with as much beneficial impact as possible–and without regard for scoring political points or defeating the other side."[66] Even the European Union has acknowledged transhumanism as a new exponential future thinking that has a political aim.[67] It is, therefore, obvious that tremendous changes are going to happen in the next era of our civilization, which will require new, constructive solutions to the challenges of societal transformation. Scientists and thinkers, therefore, increasingly consider the benefits and dangers of newly created technologies and knowledge

Table 1: Questions about the rights of transhumans and the ethics expected from them

Question	*Possible implications of HE*
Will those with a higher percentage of prosthetic/techno body parts have fewer rights than biological persons?	Increased capabilities, on one hand, along with decreased human characteristics, on the other, may lead to unknown social relations.
Why should a biological cell structure be an adequate criterion for establishing a distinction between human and techno-human alike beings?	Erasing a clear line between human and techno-human beings alike may lead to unknown or unpredictable ethical or moral consequences.
What will it mean if life-extending technologies together with reduction of birth rates increase the population of the elderly?	Unknown consequences on the human reproduction and population status, especially health status and evolutionary important premises may arise.
How will the political area and social institutions have to change under HE-induced circumstances?	Current systems fail to follow novel societal challenges and novel solutions may fail to protect civilization achievements or philanthropic values.
What are the implications for families when relatives—such as siblings, aunts, and uncles—are replaced by the simultaneous existence of four or five generations of parents and children?	Unknown implications for development of the human being in early developmental stages (childhood and adolescence) may be due to the loss of current biologically rooted development.

that can overcome human limitations but also current ethical barriers to their use.[68] Among transhumanists, for example, the fundamental and most common position is finding avenues to transform humans into beings with abilities that visibly outgrow the original state (posthuman beings).[69] Still, the similarity of the transhumanist vision of changing the future seems influenced by science fiction and is encouraged by numerous supporters or opposed by a wide range of professions, including philosophers and theologians.[70]

One of the aspects of transhumanism, but also scientific advancements in general, is the development of AI tools or AI *per se*. In its infancy, AI is understood as a prerequisite for the creation of superintelligent devices that can significantly outperform all human intellectual activities. The assumption is that such devices will design novel AI more intelligently. Some argue that the invention of the first superintelligent device will possibly be the last human invention and that the development of this field should, therefore, be carefully evaluated.[71] Even though transhumanism shares many elements of humanism, including the respect for science, the commitment to progress, and the appreciation of transhuman existence, it differs from humanism in its commitment to improve attributes that humanists often consider unique to humanity (i.e., intelligence and autonomy) but through technology.[72] Currently, the main purpose of transhumanism is to eliminate aging as well as to "repair" and "improve" intellectual, physiological and psychological capacities. From a philosophical point, transhumanism is concerned with human race development or even evolution by new and innovative pharmacological and/or technological means into a new, enhanced species. This includes ideas on creating highly intelligent animals or humans with cognitive enhancement.[70,73]

Many transhumanist theorists advocate immediate and often radical implementation of scientific and technological achievements to reduce the severity of an illness, physical inability, and malnutrition throughout the world.[72] The urge for immediate implementation of scientific and technological achievements is often driven by the fear of not living long enough to benefit from improvements. Since transhumanism deals with the enhancement of the human body on an individual level, many transhumanists actively assess the potential of future technologies and innovative social systems to improve the quality of life in general. Interestingly, transhumanist philosophers claim that no obligatory ethical basis can be found to prevent humans to choose and use human condition improvement programs. In their view, it is possible and desirable for people to engage in the transhuman phase of existence where individual decisions will drive their own personal enhancements. Transhumanists also strongly support the development of methods of "improvement" of the human nervous system, including the peripheral nervous system or brain as a primary target of transhumanist ambition.[74] In particular, the idea is to "merge" or "connect" the human mind and the computer, going in the direction of "mind uploading" human consciousness to an alternative medium.[75] Transhumanists advocate technologies such as sex-cell screening, nanotechnology, information technology, and cognitive science as well as hypothetical future technologies, such as simulated reality, AI, superintelligence, 3D bioprinting, mind uploading, and cryonic. They believe that people need and must apply these technologies if they are to have better properties than existing human characteristics.[75] Therefore, they encourage the recognition and/or protection of cognitive freedom, morphological freedom, and deceitful liberty as civil liberties in order to allow for a free application of HE technology to themselves and their children.[76] Some distinctive currents of transhumanism are listed in Table 2.

Many of these transhumanist ideas have been critically evaluated by a number of philosophers and sociologists[89,90] whereby serious questions beyond the scope of this overview have been raised, including those on ethical issues, societal changes, political context, and future perspectives of our civilization. Indeed, the concept and likelihood of HE and similar issues provoke public controversy, even suggesting that transhumanism is the

Table 2: Term explanation

Term	*Explanation*	*Literature*
Democratic transhumanism	A political ideology synthesizing liberal democracy, social democracy, radical democracy, and transhumanism.	74,77
Extropianism	An early school of transhumanism that promotes critical and creative thinking on emerging technologies as well as management and risks to maximize the benefits and opportunities arising from emerging technologies.	78,79
Immortalism	A moral ideology based on radical life extension and technological immortality goals, advocating research and development to ensure such a scenario.	80–82
Libertarian transhumanism	A political ideology synthesizing libertarianism and transhumanism.	83,84
Postgenderism	A social philosophy which seeks for a society without genders through the use of advanced biotechnology and assisted reproductive technologies.	85,86
Singularitarianism	A philosophy based on the acknowledgment of an approaching moment in human evolution beyond which technological progress will become incomprehensively rapid and complicated.	86,87
Technogaianism	An ecological ideology that aims to use technology to counteract eco crisis.	74,88

"latest site for the struggle" of the progressive ideologies of liberalism and socialism.[90] Critics and opponents often see transhumanist goals as a threat to humanistic values. Some authors believe that humanity is already becoming transhuman as a consequence of continuous advances in the medical sector that has changed our species significantly. Some prominent transhumanists also remain skeptical on the technical feasibility in the near future. They speculate that even if it were possible to predict a deep integration of individuals into the machine system, people would remain "biologized" and essential changes to their own form and character would not arise as a consequence of information technology but rather from direct manipulation of their genetics, metabolism or biochemistry.[91]

A current hot topic in the area of HE is the intervention on embryo development, especially in the phase of early embryogenesis. This means correction of diseases or unwanted traits that interfere with normal development and life, including corrections of basic properties of the embryo to enhance the human being in the later developmental and life phases. The most common unexpected risks of these processes that can disrupt embryonic development are a subject of debate. Experiments directed towards permanent biological consequences on a person have been acknowledged as a violation of the accepted principles of the Helsinki Declaration, that is, that biomedical research involving human subjects cannot legitimately be carried out unless the importance of the objective is in proportion to the inherent risk to the subject or concern for the interests of the subject must always prevail over the interests of science and society.[92]

In addition, experimental "enhancement" or GE outputs in a specific species, that is, rats or mice do not mean automatic transmission of results to a new species, that is, humans, without further experimentation. It is thus considered that at this point, when the knowledge on "enhancement" procedures, including GE, is still vague, genetic manipulation of people at an early stage of development is not justified.[93] Moreover, some scientists and thinkers believe that advances in science and technology can lead to greater catastrophe than progress. At the same time, they are techno-progressive with caution, and demand for greater security and new ways on traditional availability approach and distribution of scientific data and knowledge.[94] Some emphasize the importance of careful, slow progress and discontinuation of research in potentially dangerous areas, such as HE and GE. Some cautious scientists and thinkers find that articulate intelligence and robotics represent the possibility of alternative forms of knowledge that can endanger human life.[95] Contrary to that, GE perceived as anything more than a "natural" progression is viewed by some scholars as an expression of our humanity, rather than a "dehumanizing" concept.[2] Ultimately, enhancement may be good for us as current physiological limitations, which we consider to be normal, are only "natural" or "normal" in the context of one human generation and its culture. Many scientists believe that this topic should be, therefore, discussed within a specific socio-historical context of our current civilization. In particular, they think that biological limitations will soon be replaced with new biological, artificial, and mixed carbon/silicon-based technologies. Also, biology is not the only field where perceptive beings with the ability to react and adapt can evolve; computer-based entities and their software may even become sentient in the future and new forms of life may emerge.[2]

Living Indefinitely Long

Since its dawn, human civilization has been fascinated by overcoming death. Therefore, it is not surprising that immortality, eternal youth, or at least the perspectives of biblical life have always been a powerful topic of religion and art. Life and death or eternal life are central elements of all religions. Only recently, intensive efforts have been made in modern science to understand and prevent aging and prolong life. An effective antiaging therapy might, indeed, dramatically change modern society and a number of debates are ongoing in this field. Although this problem has not been solved today, scientific discoveries provide some intriguing promises for substantial prolongation of the life span. Some promises include pharmacotherapy, actions directed towards senescent cells, or use of stem cells. An extension of the average lifespan and maximum age has an immense social and political impact and, as expected, opinions on this subject vary. Some models suggest the possibility of extending life to 120 years[96]; others think that such a prolongation of human life is impossible since the human lifetime has already reached the biological limit.[97] Westendorp argues that medical advances during the past century and reduced childhood mortality, which remove the pressure of having to produce progeny, are not only increasing the average but also pushing the maximal life expectancy, as our bodies adapt to a new environment by investing resources into maintenance and longevity, which had not been previously possible.[98]

Prevention or delaying of aging seems to be more problematic. Still, a possible scenario may be that human life will be extended to about 120 years and that man will live for 90 years as healthy and active as 50-year-olds today.[99] A most radical scenario has envisaged the necessity to rely on the continuous repair of damage caused by basic metabolic processes and environmental factors. This might result in permanent maintenance of physiological functions and prevention of aging, enabling people to live for thousands of years.[100]

In conclusion, a number of high-quality scientific debates on GE, HE, and transhumanism are available to a wider audience but so far, no public opinion on this issue has been heard.[101] This, in turn, gives ambitious groups and individuals the chance to pursue their own visions of the future and the society will be split between those pushing enhancements without limitations and those who will choose a sustainable approach to technology-aided evolution. It also seems that the public will have a tremendous interest in the technologies for the extension of biological life, mostly because of the fear of death, the fear of aging, and the desire to maintain a healthy life. However, it appears that the desire for a longer life depends on the health status and quality of life, which again raises the question of the social context and rethinking of society. Steps noticeable in this area are not often related to science but are instead exploited for marketing, sales, or beauty treatments and interventions that claim to overcome the effect of aging and prolong life.

While significant scientific advancements in the area of GE and HE are expected in the near future, a reasonable approach and caution in the new knowledge and technologies usage and implementation may be advised. In particular, safety issues, short- or long-term consequences of the human germline GE, a re-evaluated understanding of the concept of humanity and a person on the individual level with all facets should be explored and studied in more detail prior to GE and HE consideration in medical applications. Legal, ethical, and societal issues need to be scrupulously discussed and evaluated in light of novel evidence and information to avoid critical dangers in this delicate, yet exciting era of human existence.

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