

Human Embryos Genetically Modified: A Review

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Abstract

The modification of an organism, "genetically" is been a fascinating field of research for researcher for long time. Much of research is done in terms of Gene Editing and Genetic Modification. Tools such as chemicals and radiation to cause mutations are now outdated as it used to cost a lot of time and money. The efficiency was also not to the level to which it was desired as researchers were unable to target the specific position that they wanted in the genome. For Gene editing it's a new era known as Regularly Interspaced, Short Palindromic Repeat (CRISPR) Technology. This is a much efficient technology in comparison to all others which existed before. This article is a review on the whole process of the development and efficiency of the technology and also on the till date future perspective of it.

Keywords: Cas9, CRISPR, DNA; Embryo; Genome editing genetics; Genetic engineering, Genes

Introduction

Human embryo

The human embryo can be defined as the collection of entities which are produced in the fertilization process of a human oocyte by a human sperm. Different recent technologies are all capable of creating these entities called embryos by other means, for example somatic cell nuclear transfer (SCNT) and induced parthenogenesis [1].

Genetic engineering

The genetic code of organisms along with human beings is complicated, with almost 3 billion base pairs. The ones three billion base pairs are arranged in unique sequences, yielding approximately 25,000 genes, every of that's responsible for a few trait or aspect of each of us. While combined with environmental factors, versions inside the coding of those genes outline our specific identities. No longer is each trait cosmetic. Whilst genes deliver records approximately features consisting of hair and eye colour, top, and so forth [2-8]. They also bring facts approximately essential organic features. Mistakes in the sequencing of some genes can produce genetic disorders. There are extra than four thousand known genetic problems [9-15]. Those conditions and diseases can be persistent or degenerative or maybe latent and undiscovered for a while, but are ultimately harmful to the organism. In some instances, genetic issues are the result of mistakes which creep into germline cells because of environmental factors; a few mistakes creep into the genome as a result of copying mistakes during replication. In other times, defective genes can be handed on thru generations of mother and father in which the trait has no longer been deadly. In many instances, genetic sicknesses remain as dormant, recessive traits ready to be exceeded on to offspring of mother and father who both manifest to have the recessive feature. Over the years, all of those means of genetic trade have resulted in the modern-day form of people [16-21]. The process of mutation, chargeable for the emergence of genetic sicknesses, is also the underlying mechanism of evolution. Evolution is the system of genetic alternate over the years, as some of those adjustments bring about a more healthy model of the species greater apt to live on than others, and these effective traits are then exceeded on to succeeding generations. In some cases, the mistakes conferred a survival benefit in some environments even as sooner or later conferring a condition classified as an ailment in other environments, as with the hemoglobin-s gene, chargeable for the sickle-mobile trait, which confers a few immunity to malaria however additionally results in anemia [22]. Most errors in DNA replication

result in mistakes within the production of proteins. Somatic cellular DNA is largely a protein-making code that directs cellular metabolism at some stage in an organism by way of controlling the production of important proteins that direct the ongoing survival and functioning of discrete cells in each organ of the body. Due to tissue differentiation mechanisms, also a part of the guidance set of DNA; different types of cells inside the body produce extraordinary types of proteins. Genetic diseases commonly involve errors in an organism's DNA collection that bring about disruption in the regular production of a sure protein [23]. Cancers, however, commonly involve harm to somatic mobile DNA that disrupts cell replica itself, now not simply metabolism or protein manufacturing. While the actual mechanisms of genetic diseases are complicated, scientists are learning more about their reasons and how to locate them [24-29]. some of the relevant DNA modifications arise inside the gene inflicting the disorder; other modifications, at the same time as now not gift inside the at once applicable gene, adjust the functioning of that gene; a 3rd kind of exchange, even as now not causing a selected sickness, suggests that the individual with that specific collection is extra at risk of developing the sickness. Many of those changes can now be detected and scientists keep discovering correlations between among particular DNA sequences and genetic diseases [30-33]. By way of understanding these correlations, scientists may want to take a look at for the presence of a particular disease, or the susceptibility to that sickness, and possibly devise treatment plans primarily based upon the understanding of these correlations [23]. Besides the promise of treating or curing genetic sicknesses, manipulating DNA can permit scientists to develop new strains of organisms, which includes mice that function models of human illnesses beneficial for pharmaceutical testing, or sheep that secrete drugs in their milk [34]. New traces of agricultural crops had been engineered, through putting genes from animals or different plant life, making them proof against cold, sickness, or insecticides [35]. In sum, as we find out about the specific functioning of genes in numerous species, we are able to expand new, beneficial life forms; manufacture new medicines; and

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enhance human existence, health and the environment. However those drugs, cures, and different products of genetic engineering gift moral challenges. For purposes of know-how these demanding situations, it's far beneficial to distinguish unique categories of genetic intervention [36]. They are: somatic gene remedy, which ambitions on the treatment or prevention of sickness without affecting future generations, and is the least morally objectionable; somatic genetic enhancement, which objectives to improve the functioning of the individual; germline gene therapy, which objectives at preventing ailment, but includes heritable genes; and germline genetic enhancement, which goals to enhance the functioning of destiny generations. Germline genetic enhancement is, now not suddenly, the most debatable shape of genetic intervention. Bioethicist Ronald inexperienced makes the factor forcefully: "improvements are continually greater controversial than healing procedures or preventions, much less in all likelihood to be funded with the aid of society and much more likely to be morally and legally prohibited if the risks to people or society are more than the benefits [37].

Genetically Modified (GM) Organisms and GM Foods

The genetically modified food product targets lower price and greater benefit (in terms of durability or nutritional value) or both. GM organism's increases\improve crop protection from insects or viruses or through increased tolerance towards herbicides. The resistance against insects is produced by the incorporation of gene of toxin production from the bacterium *Bacillus thuringiensis* (Bt) to the food plant. This technique makes the plants less susceptible to the diseases caused by such viruses, resulting in higher crop yields [38-42]. Genetically modified organisms (GMOs) can be characterized as organisms (i.e. plants, animals or microorganisms) in which the hereditary material (DNA) has been changed in a way that does not happen normally by mating and/or by characteristic recombination. The technology is all about exchanging selected genes from one organism to another even between unrelated species [43].

Gene Editing vs. Genetic Modification

Genetic modification is a vast term referring to hereditary alterations in general which also includes mixing genes from different species. That end of the genetic modifications is transgenetics. Genetic editing is done by changing or altering an animal by turning off a gene [44-50]. The genes of mice, monkeys and zebra fish are altered by using this technology and for human diseases such as HIV also it is applied [50-58]. As for cows to be hornless; DNA from different species is not required but just the DNA from the different breed of cattle [59].

Gene Editing Tools

Genome editing has experienced a rapid growth in the technology and it has become a standard technique which is being utilized by many biological researchers. Geneticists utilized chemicals or radiation to cause mutations. In any case, they had no chance to get of controlling where in the genome the transformation would happen. For quite a while researchers have been utilizing 'gene targeting' to present changes in particular spots in the genome, by evacuating or including either entire genes or single bases [60-69]. Traditional it has been exceptionally profitable for examining qualities and hereditary qualities; in any case it requires a long investment to make a mutation and is genuinely costly. The CRISPR-Cas9 system at present emerges as the quickest, least expensive and most solid technique for 'editing' genes. This rapid growth can be credited to the rise of clustered, regularly interspaced, short palindromic repeat (CRISPR) technology. This technology easily and efficiently modifies endogenous genes. Another version of CRISPR-

Cas9 system can select heterologous domains which can further regulate endogenous gene expression or label particular genomic loci in living cells [70].

Working of Regularly Interspaced, Short Palindromic Repeat (CRISPR) Technology

In CRISPR-Cas9 system there are two main parts a Cas9 enzyme and small RNA molecule. The Cas9 enzyme cuts through the DNA like a pair of molecular scissors and RNA molecule targets the specific position of the DNA to make the cut. This cut can be repaired by the cell's DNA repair machinery but often it makes mistakes. This mistake can be vitally used by the scientists [71-80]. During repair a small error can produce a total different protein with totally different sequence. This repair process can also be controlled by providing a template. The template gives the liberty to the scientists to edit the genome with almost any sequence they want at about any site of their choosing [81].

Epigenome

Epigenome is the cluster of chemical compounds present in histones. These chemicals decides the access to the DNA, they can either open or close it for the proteins which will further lead to gene expression. Much of money and time was invested in this field but CRISPR-Cas9 has made it simpler by adding acetyl groups [81].

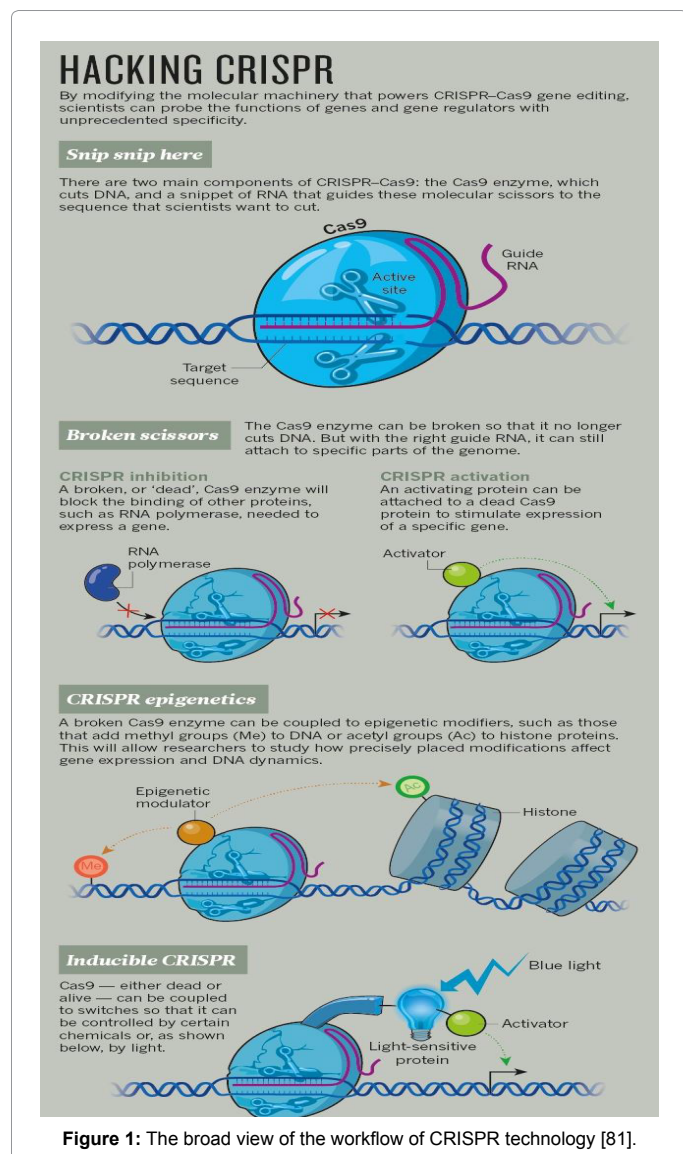
Control

The Cas9 acts as the scissors which can activate genes. Some proteins were added to it that is activated by blue light. The gene expression was triggered when cells are exposed to the light, and stops it when the light is taken off [82-85].

CRISPR Studies

There is a series of studies that took place in the development of the CRISPR technology (Figure 1).

In 2012, CRISPR RNAs (crRNAs) was used for silencing the invading nucleic acids in the bacteria and archaea. This silencing produced adaptive immunity against viruses and plasmids [86]. In 2013, CRISPR was applied in Mice [87] with specific target to correct genetic diseases [88] and for the first time CRISPR-cas9 was used in the human genome [89]. In 2014 Gene of a primate was edited for the first time using CRISPR-cas9 [90] later it was also applied to enhance pest resistance in wheat [91]; in removal of virus from the host genome in human cell lines [92]; in reproduction of carcinogenic effects of specific chromosome translocations in mouse [93]; it also created a line of model mice that naturally express Cas9 [94]. The broad and rapid increase in the use of the CRISPR raised the issue to get the technology patented, so it was patented based on the methods in a seminal 2013 paper [95]. In 2015, CRISPR was used in the conversion of heterozygous to homozygous mutations [96]; gene editing in human triprenuclear zygotes was also performed [97]. The use of Pig organ in human transplant is possible because CRISPR is used to inactivate PERVs in pig genes [98], mosquitoes are engineered with anti-malaria gene that can be passed on to most of their offspring [99]. Duchenne muscular dystrophy was treated in mouse model using CRISPR [100-103]. Histone was altered at distant gene enhancers by CRISPR which controlled gene expression [103]. The great achievement of CRISPR can be considered the genetically modification of human embryos by Chinese scientists [104,105]. But the off-target effects were also observed in CRISPR-mediated gene editing in human zygotes [106]. Further research found protein which could improve the accuracy of gene-



editing technique and three more proteins were identified which could serve in place of Cas9 [107,108]. Further research on modulation of gene expression was done using cells from a child with Duchenne muscular dystrophy [109,110] and in short pieces of DNA [111].

As it's heavily discussed that much of the human genome is of noncoding element so CRISPR/Cas9 was used to screen these elements in the human genome [112]. Recently another Chinese team reported gene editing in human embryos. This study introduced HIV-resistance mutation into embryos using CRISPR technology [113].

Conclusion

As per the discussion related to the ethical and religious beliefs, Ronald Cole-Turner who teaches theology and ethics at Pittsburgh Theological Seminary shares his views saying it is needed to have a combined discussion with the different religious believes [114-120]. He suggests in Christianity and Judaism is surprisingly positive in their assessment of this possibility. Dr. Paul Knoepfler who is a biomedical scientist suggests that human resistant HIV infection is capable of invoking creation of genetically modified person [121-126]. In this

particular research field the two major issues haunting the researchers are ethical and scientific [126].

CRISPR code cracking

Epigenetic marks on DNA are by all account not the only genomic code that is yet to be broken. More than 98% of the human genome is of noncoding sequence i.e. it does not code for proteins. Yet, analysts surmise that a reasonable lump of this DNA is accomplishing something critical, and they are receiving CRISPR-Cas9 to work out what that is. Some of it codes for RNA molecules, for example, microRNAs and long non-coding RNAs that are thought to have different works than making proteins. Enhancers are other sequences that increase the expression of the genes. The vast majority of the DNA sequences connected to the danger of common diseases lie in regions of the genome that contain non-coding RNA and enhancers [127-135]. In any case, before CRISPR-Cas9, it was troublesome for scientists to work out what those sequences do. CRISPR-Cas9 has made research more advance and sophisticated (Figure 1) [81]. After much of waiting UK scientists receive license to edit genes in human embryos. It remains illegal to alter the genomes of embryos used to conceive a child in the UK, but according to researchers this license could resolve the debate over deploying gene-editing in embryos for therapeutic uses in the clinic. This study may find the genetic modifications could help researchers to develop treatments for infertility [136- 140]. Further federal biosafety and ethics panel approved the genome-editing technology's first ever study in patients. An experiment that would use CRISPR to create immune system that will attack three kinds of cancer [141-148].

Thus it is evident that much of ethical and scientific issues have to be resolved. But the future perspective of the research field looks bountiful.

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