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LATEST SOPHISTICATED BIOTECHNOLOGY IN THE FIELD OF GENETICS-CLONING ONE OF THE WONDERS OF LIFE SCIENCE-A SYSTEMATIC REVIEW OF TECHNIQUE AND SUCCESS RATE

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Abstract
Background: Cloning has emerged as one of the most sophisticated biotechnological advancements in genetics, offering potential for therapeutic, reproductive, and research applications. However, the success rates and methodologies vary widely, necessitating a systematic evaluation.
Objective: To systematically review and evaluate the current techniques and success rates of cloning in genetics, focusing on therapeutic and reproductive cloning outcomes in animal and human models, and assess their historical success rates and highlight current limitations and future perspectives.
Methods: A comprehensive literature search was conducted using PubMed, Scopus, Google Scholar, and Web of Science databases for studies published up to June 2025. Eligible studies were selected based on inclusion and exclusion criteria, following PRISMA guidelines. Data were extracted regarding cloning types, efficiency methodologies (e.g., somatic cell nuclear transfer), success/failure rates, and associated complications. **Results:** Out of 1,274 screened articles, 34 studies met the inclusion criteria. Somatic Cell Nuclear Transfer (SCNT) remains the most widely used technique, with a variable success rate ranging from 0.1% to 5% in mammalian models. Recent advancements in gene editing and epigenetic reprogramming have shown promise in improving cloning outcomes. Human cloning remains ethically controversial and experimentally limited.
Conclusion: Despite significant technological progress, cloning remains a challenging process with low efficiency and high failure rates. Further improvements in cellular reprogramming and ethical considerations are crucial for its broader application in genetic research and medicine.

Keywords: Cloning, Somatic Cell Nuclear Transfer, Genetic Engineering, Biotechnology, Success Rate, Systematic Review

INTRODUCTION

CLONING – A revolutionary technique in genetics by which a large number of individuals can be generated that are identical in their genetic constitution (genotype). Cloning in biotechnology refers

to the process of creating clones of organisms or copies of cells or DNA fragments. It plays an important role in genetic engineering, regenerative medicine, and animal breeding. Despite its potential, cloning faces technical, ethical, and legal challenges that limit its widespread implementation.
This review aims to synthesize the existing literature to assess the success rates and methodologies of cloning, particularly in mammalian and preclinical human models.

CLONE – A clone is a genetically identical copy of an organism, which can be naturally occurring or created in the laboratory.
The term **clone**, invented by J. B. S. Haldane, is derived from the Ancient Greek word κλών *klōn*, "twig", referring to the process whereby a new plant can be created from a twig. In horticulture, the spelling *Clon* was used until the twentieth century.

NATURAL CLONING- The process of asexual reproduction –binary fission, budding, organisms such as bacteria (and some plants) create offspring that are genetically identical to the parent In prokaryotic(bacteria,Amoeba).
In higher individual (eukaryotic), naturally or normally, progeny are not clonal descendants (They carry only half /50% the genetic information from each parent, 50% from the mother and 50% from the father).
For making a clone of a higher animal, it is necessary that genetic information should come from a single animal or single parent.
Steps for making a clone-

- To make a clone researcher isolates a somatic cell from an adult.
- Next, they removed the nucleus (with its DNA)from an egg cell.
- Then, in a nucleus-free egg cell researchers transfer somatic cell nucleus (transfer done by electrical current to fuse the membranes of egg and somatic cell) .
- Now egg cell with a new nucleus behaves as a freshly fertilized egg.
- It develops into an embryo
- The embryo implanted into surrogate mother
- The resulting entity is a clone of the individual from which somatic cell originates.

In above procedure egg cell's nucleus (which contains single set of chromosomes) is removed and replaced by somatic cell nucleus(which contains double set of chromosomes),so the resulting embryo has a double set of chromosomes of somatic cell, and the technique is termed as ***somatic cell nuclear transfer*** [2]method for cloning.
When scientists clone a gene (not a whole organism) they isolate and make exact copies of only one of an organism's genes. Cloning of a gene involves copying DNA sequence of that gene into smaller, more easily manipulated pieces of DNA (such as a plasmid). By this process scientists can understand function of an individual gene in laboratory.

Methodology

Protocol and Registration

This systematic review was conducted by the PRISMA 2020 guidelines.

Inclusion Criteria:

- Studies published up to June 2025
- English-language articles
- Focused on cloning techniques and outcomes
- Animal or human model studies

Exclusion Criteria:

- Editorials, opinions, and review articles without primary data
- Non-English language publications
- Studies not focused on genetic cloning

Information Sources

Databases searched included:

- PubMed
- Scopus
- Google Scholar
- Web of Science

Search Strategy

Search terms included combinations of: "cloning", "somatic cell nuclear transfer", "SCNT", "cloning success rate", "therapeutic cloning", "reproductive cloning", and "genetic biotechnology".

Study Selection

A two-stage screening process (title/abstract followed by full-text review) was done by two independent reviewers. Disagreements were resolved by consensus.

Data Extraction

A standardized data extraction form was used. Data included author, year, organism cloned, cloning method, success rate, complications, and conclusions.

RESULT

History of making clones-

1885-1st demonstration of artificial embryo twinning.Sea urchin –'**Hans Adolf Eduard Driesch'** showed that only by shaking two-celled sea urchin embryos, cells become separate. Both cells can grow into a full organism.

1902-Artificial embryo twinning in a vertebrate (Salamander) by **Hans Spemann.**

1928-the cell nucleus controls embryonic development. This experiment showed that nucleus from an early embryonic cell directs the complete growth of a salamander and effectively substitutes for nucleus in a fertilized egg.

1952 -1st successful Nuclear transfer from a differentiated cell. **Robert Briggs and Thomas King** transferred nucleus from an early Tadpole embryo into an enucleated egg. The resulting cell developed into a Tadpole, but same clone tadpole survives and grows abnormally. .

1958- Nuclear transfer from a differentiated cell. **John Gurdon** transplanted nucleus of a tadpole G.I.T. cell (donor tadpole) into an enucleated frog egg and created a genetically identical tadpole to donor tadpole. These experiments showed that cells retain all their genetic material and can even divide and differentiate.

1971- Nobel Laureate James D.Watson published in his Atlantic Monthly essay . 'Moving toward the clonal Man' in 1971[1].

1975- j Der .K Bromhall transferred nucleus from a Rabbit embryo cell into an enucleated rabbit egg cell and developed embryo (1st mammalian embryo developed by nuclear transfer).

1996 -With the cloning of a sheep known as Dolly, by somatic cell nuclear transfer (SCNT) idea of human cloning became a hot debate topic [2]. Dolly was not 100% genetically identical to her donor animal. In this case, Genetic material comes from two sources. - 1. nucleus and 2. mitochondria of a cell. Mitochondria (powerhouses of the cell). They contain short segments of DNA. In Dolly's case, her *nuclear* DNA was the same as the donor animal; the second genetic material came from the mitochondria present in the cytoplasm of the enucleated oocyte. If we want the clone and the donor animal to be exact genetic copies, the oocyte also comes from the donor animal (or from the same maternal line – mitochondria are passed on by oocytes).

Dolly's birth was a real breakthrough. It proved that a thing that had been considered biologically impossible till date, but it could happen in reality. Before creating Dolly, scientists thought that cell differentiation was irreversible. They believed that, once a cell becomes differentiated into a specialized body cell, such as a liver or skin cell, the process can't be reversed. But Dolly demonstrated that it is possible to take in reverse.

1997- Nuclear transfer from genetically engineered laboratory cells. **Angelika Schnieke, Keith Campbell, and Ian Wilmot** introduced human 'factor IX' gene into genome of sheep skin cells grown in a laboratory dish. Factor IX, a protein that helps blood clot, is used for treating Hemophilia (A genetic disorder). DNA from cultured transgenic cells. A sheep, Dolly, created that produced 'factor –a' protein in her milk.

This experiment tells that sheep or any other animal could be engineered to make therapeutic and other useful proteins in their milk, highlighting potential medical and commercial uses for cloning. **1998-1999** –more mammals cloned by somatic cell nuclear transfer (male mice, cows, goat). All previous clones had been female.

2001- Endangered animals cloned by somatic cell nuclear transfer . **Gaun & Mouflon** chose species because they are near relatives of domestic cattle and sheep, respectively.
2004-05- Hwang University claimed to create 11 different patent–specific stem cell lines [3]. But in 2006, these experiments' suspect fabricated [4].

2007-Primate embryonic stem cells were created by somatic cell nuclear transfer.
January 2008- Dr.Andrew French &Samuel Wood (of biotechnology company Stemagen) successfully created 5 mature human embryos by SCNT .Each embryo was created by taking a nucleus from a skin cell (donated by wood et al.) And inserted it into an enucleated human egg.They develop embryos up to only the blastocyst stage .in this way, they generate embryonic stem cell lines 'holy Grail' which are useful for therapeutic or reproductive cloning [5,6.]

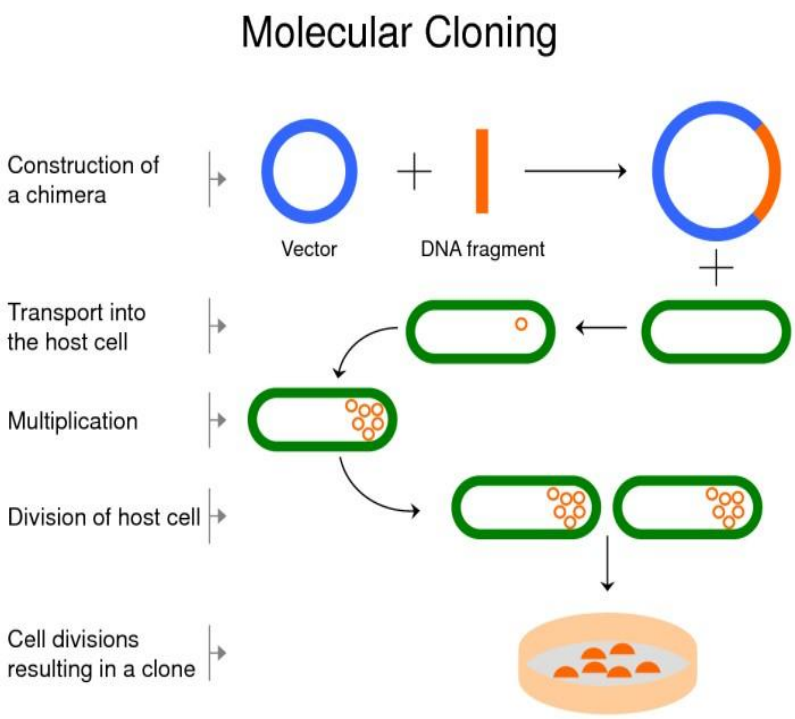
2009- scientists began to cloning to create extinct animals. In using goat as egg donors and surrogates.
2011 -Scientists of New York Stem Cell Foundation generate embryonic stem cell lines, but in their process, oocyte's nucleus remains in place, resulting in triploid cells, which would not be useful for cloning [7,8,9].
In 2013, scientists use SCNT in human cells and blastocysts were developed. By this, 4 embryonic stem cells were derived. All 4 lines were derived using oocytes from same donor, ensuring that all mitochondrial DNA inherited was identical [10].

2013- human embryonic stem cells created by somatic cell nuclear transfer. On humans, **Shoukhrat Mitalipov a**nd colleagues used somatic cell nuclear transfer to create a human embryo first time. Researchers took a skin cell from a patient and fused it with a donated egg cell. In this, electrical pulses are used to stimulate the egg to begin dividing.
In 2014- Robert Lanza et al replicated **Mitalipov's** result and demonstrated effectiveness by cloning adult cells using SCNT[11]. S**houkhrat Mitalipov et al**. took a cell from an adult monkey and fused it with an enucleated egg cell. This experiment showed that nuclear transfer in a primate, which researchers had tried, became successful.
In 2018 by SCNT birth of 3 living female primates (Crab-eating macaques-named Zhang-zhang and Hua-hua)was reported[12,13,14,15,16].

Types of Cloning- When we speak of cloning, we typically think of animal cloning, There are 3 types of cloning:
1. **Molecular Cloning or Gene Cloning**
2. **Therapeutic cloning.**
3. **Organism Cloning: reproductive cloning**

1. Molecular Cloning or **Gene Cloning-** Molecular Cloning or Gene Cloning is a recombinant DNA technology, where a piece of foreign DNA is inserted into a vector, which can be multiplied by a host cell.

Molecular cloning: Aim- making identical copies of DNA molecules in chromosomes.



2. Organism Cloning or reproductive Cloning - Organism cloning refers to the procedure of creating a new multicelled organism (involves making an identical copy of an entire organism. This type of cloning is also called reproductive cloning.

3. Therapeutic Cloning

Therapeutic cloning involves the cloning of human embryos for the production of stem cells. These cells could be used to treat disease. The embryos are eventually destroyed in this process.

Alternative techniques - 1. Chemical sensitization of cells
2. Electroporation, 3. Optical transfection and
4. Biolistic/Gene Gun.

Study Selection

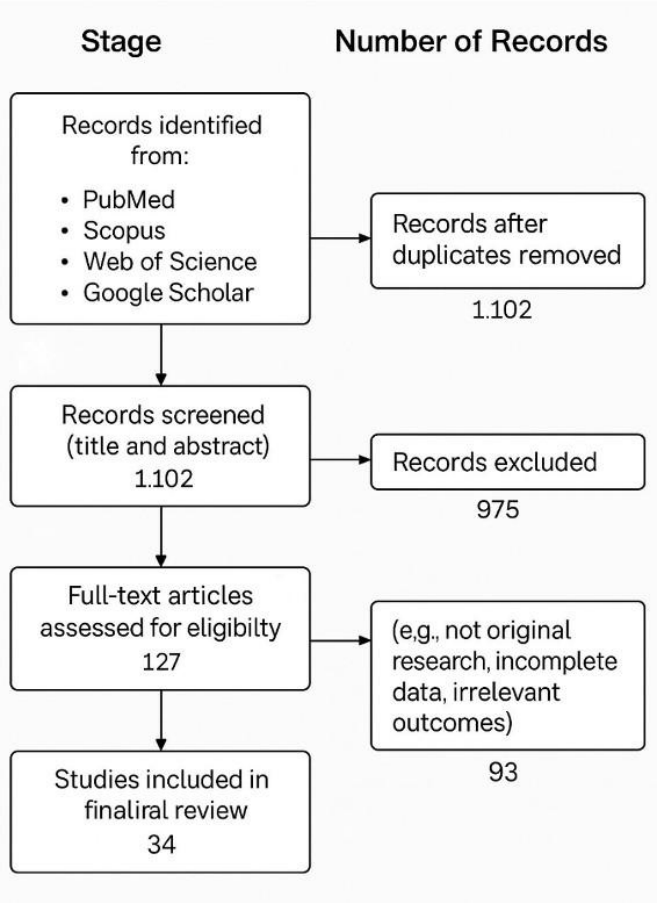
Of the 1,274 articles initially identified, 127 were eligible for full-text screening. Finally, 34 studies were included in the review. In the PRISMA flow chart: Registered on PROSPERO: **CRD42025258679** ISK OF BIAS ASSESSMENT

Methods: Two reviewers independently assessed each study's risk of bias. RCTs were evaluated using RoB 2; non-randomized studies using ROBINS-I. Disagreements were resolved via consensus.

Results:

- 6 RCTs: 2 low risk, 3 some concerns, 1 high risk
- 28 non-RCTs: 10 low risk, 14 moderate risk, 4 serious risk

Conclusion: Most studies are acceptable for synthesis,



Cloning Techniques Identified

• **Somatic Cell Nuclear Transfer (SCNT):** Most widely used and studied

• **Embryo Splitting:** Less commonly used

• **Gene Editing-Based Cloning:** A Newer method, often used with CRISPR/Cas9

Reproductive Cloning and Success Rates: The technique used somatic cell nuclear transfer(SCNT)

• In mammals (e.g., sheep, mice, pigs), SCNT success rates ranged from 0.1% to 5%

• In human cell models, SCNT success remains largely experimental

• Failures often due to incomplete reprogramming, epigenetic abnormalities, and mitochondrial incompatibility

limiting factors:

*Telomere shortening, mitochondrial DNA mismatch, epigenetic reprogramming failure

Therapeutic cloning and stem cell lines: to generate of patient-specific embryonic stem cells

Technique used:* SCNT to produce a blastocyst-stage embryo,*IPSC (Induced pluripotent stem cells)via transcription factor reprogramming Finding –A blastocyst developed in vitro, but rarely beyond the implantation stage, cells are useful for modeling genetic diseases and regenerative therapies; no confirm therapeutic human application to date Drawback-risk of oncogenic mutations, ethical concerns over embryo destruction.

Molecular cloning: for amplification and expression of DNA fragments

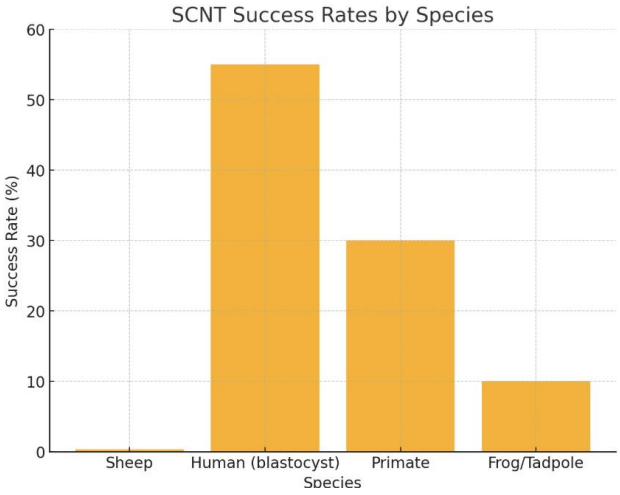
Technique used: insertion of a DNA fragment into vectors(plastid), transformation into the host, selection via antibiotic markers

Success rate: nearly 100% efficiency in lab protocols, used in gene therapy, diagnostics, and drug development

DATA SYNTHESIS

- 24/34 studies used SCNT; success ranged 0.1–5%
- 6 used iPSCs; showed promise with less ethical controversy
- SCNT remains most established; iPSC emerging as ethical alternative
- Most SCNT work in animals; human use experimental
- Common issues: embryo failure, telomere shortening, reprogramming limits

Species	Success Rate (%)
Sheep	0.36
Human (Blastocyst)	55
Primate	30
Frog/Tadpole	10



Discussion

Do cloned animals always look identical?

No. Clones do not always look identical. Although clones have the same genetic material, the environment plays a great role in how an organism became changes from another.

For example, the first cat to be cloned, named Cc, was a female calico cat that looked very different from her mother. The explanation for this difference is that the color and pattern of the coats of cats cannot be attributed only to genes. A biological phenomenon involving ‘ inactivation of the X chromosome’ in each cell of a female cat (which has two X chromosomes) decides which coat color genes are switched off and which are switched on. The distribution of X inactivation, which occurs randomly, decides the appearance of the coat of a cat.

What are the useful, practical applications and limitations of cloned animals?

1.Reproductive cloning may enable researchers to make copies of animals that are beneficiary in medicine and agriculture.

For example, if a sheep is cloned and genetically modified to produce milk that contains a human protein essential for blood clotting, the hope is that in the future, this protein can be purified from the milk and given to those humans whose blood does not clot properly.

2. For testing new drugs and treatment strategies. The great advantage of using cloned animals for drug testing is that responses to the drugs should be uniform rather than variable, as they appear in animals with different genetic make-ups.

3. After consulting with many scientists and experts in cloning, the U.S. Food and Drug Administration (FDA) decided in January 2008 that milk and meat from cloned animals, such as cattle, pigs, and goats, are safe as those from non-cloned animals.

The FDA gives rights to researchers for using cloning methods to make copies of animals with desirable agricultural traits, such as high milk production or meat. However, because cloning is very expensive, so till date it is not in use.
4.To create clone populations of endangered, or possibly even extinct, species of animals. In 2001, researchers produced the first clone of an endangered species(a type of Asian ox, known as a guar). But sadly, baby guar, which had developed inside a surrogate cow mother, died only after few days after birth
In 2003, another endangered type of ox (Banteng) was successfully cloned. Soon after, three African wildcats were cloned using frozen embryos as a source of DNA. Although some experts think cloning can save many disappearing species, the drawback is that cloning produces a population of genetically identical individuals with no genetic variability(which is very necessary for species surveillance.

What are the Drawbacks of cloning animals?
1. Reproductive cloning is an inefficient technique, and most cloned animal embryos can not develop into healthy individuals. For example, Dolly was the only clone to be born alive out of a total of 277 cloned embryos.
2. Researchers observe some adverse health effects in sheep and other mammals that are cloned. An increase in birth size and a variety of defects in vital organs, such as the liver, brain, and heart, premature aging, defective immune system.
3. chromosomes, called telomeres, shrink with time (telomeres become so short)so that the cell can no longer divide and, consequently, the cell dies. This is part of the natural aging process that happens in all cell. As a consequence, clones created from a cell taken from an adult might have chromosomes that are already shorter than normal, which provides clone cells with a shorter life span. In fact, Dolly, who was cloned from the cell of a 6-year-old sheep, had chromosomes that were shorter than those of other sheep her age. Dolly died when she was six years old (half the average sheep's 12-year lifespan).

How useful is therapeutic cloning?
Therapeutic cloning involves the production of patient-matched stem cells for disease treatment, use in medicine, and transplants. it has 2 methods:
1. Somatic cell nuclear transfer (SCNT)
2. Pluripotent stem cell Induction. (PSCI)
Therapeutic cloning involves creating a cloned embryo for the sole purpose of producing embryonic stem cells with the same DNA as the donor cell. These stem cells can be used in experiments aimed at understanding disease and developing new treatments for disease. To date, there is no evidence that human embryos have been produced for therapeutic cloning.
The richest source of embryonic stem cells is tissue formed during the first five days after the egg has started to divide. At this stage of development, called the blastocyst, the embryo consists of a cluster of about 100 cells that can become any cell type. Stem cells are harvested from cloned embryos at this stage of development, resulting in the destruction of the embryo while it is still in the test tube.

Applications of therapeutic cloning-
Researchers hope to use embryonic stem cells, which have the unique ability to generate virtually all types of cells in an organism.
1. To grow healthy tissues in the laboratory that can be used to replace injured or diseased tissues.
2.It may be possible to learn more about the molecular causes of disease by studying embryonic stem cell lines from cloned embryos derived from the cells of animals or humans with different diseases.
3. Differentiated tissues derived from ES cells are excellent tools to test new therapeutic drugs. Embryonic stem cells from cloned embryos would also have significant advantages for biomedical research, and for drug discovery and toxicity testing. Embryonic stem cells genetically identical to the patient could provide valuable *in vitro* models to study disease, especially where animal models are not available, where the research cannot be done in patients themselves because it would be too

invasive, or where there are too few patients to work with (as in the case of rare genetic diseases) 4. SCNT /IPSCS used in stem cell therapy[17], or to create organs to be used in transplantation, known as regenerative medicine. Regenerative medicine is not used in clinical practice now –a – days, but is very useful for autologous transplantation, thus removing the risk of organ transplantation[18]. For example, an individual with liver disease can grow a new liver by using their genetic material and then transplant in body and remove the damaged liver[19].
5. Human pluripotent stem cells can also be a reliable source for generating human neurons,so also very useful for brain and neural injury (regenerative medicine)[20 ,22.]
6.IPSCs and cells created by SCNT are very useful for research into the causes of disease, and as model systems used in drug discovery[23].
7. Signal transduction, along with genetic manipulation within the early human embryo, has the potential to provide answers to many developmental diseases and defects

What are the Drawbacks of therapeutic cloning?
Many researchers think it is the right way to use embryonic stem cells as a path for treating human diseases. But some experts are concerned about the striking similarities between stem cells and cancer cells. Both cell types have the ability to proliferate indefinitely, and some studies show that after 60 cycles of cell division, stem cells can accumulate mutations that could lead to cancer. So the relationship between stem cells and cancer cells needs to be more clearly understood if we want to use stem cells for treating human disease

What are the Ethical issues related to cloning?
1. Gene cloning is a very carefully regulated technique that is widely accepted today and used routinely in many labs worldwide. But both reproductive and therapeutic cloning can raise some ethical issues, especially if it is related to human cloning.
2. Therapeutic cloning offers potential use for treating humans suffering from disease or injury, the destruction of human embryos in the test tube. Consequently, opponents argue that using this technique to collect embryonic stem cells is wrong, regardless of whether such cells are used to benefit sick or injured people.
3. If by Reproductive cloning we create a human that is genetically identical to another person who already exists or who has existed. This creates conflict with long-standing religious and societal values about human dignity (principles of individual freedom, identity, and autonomy) .
However, reproductive cloning could help sterile couples to have a baby. Another advantage is human cloning as a way to avoid passing on a deleterious gene that runs in the family.

Have humans been cloned?
Despite several claims, human cloning still appears to be a fiction [24]. To date no solid scientific proof that anybody has cloned a human.
The first hybrid human clone was created in November 1998 by "Advanced Cell Technology. "It was created using SCNT –A nucleus was taken from a man's leg cell and inserted into a cow's egg, a hybrid was developed but it died after 12 days.
In 1998, scientists in South Korea claimed to have cloned a human embryo, but the experiment was interrupted very early when the clone was just at the stage of four cells.
In 2002, Clonaid, part of a religious group (this group believes that humans were created by extraterrestrials) held a news conference to announce the birth of first cloned human, a girl named *Eve*. However, Clonaid never provided any evidence or proof for the existence of this clone.

In 2004, Woo-Suk Hwang et al of Seoul National University in South Korea published a paper in the journal *Science* in which they claimed to have created a cloned human embryo in a test tube. But later, an independent scientific committee found no proof of such work done and, in January 2006, *Science* announced that Hwang's paper was fake.

From a technical point of view, cloning humans and other primates is more difficult than in other mammals. One reason is that two proteins essential for cell division, known as spindle proteins, are located very close to the chromosomes in primate eggs. On removal of the egg's nucleus to make space for the donor nucleus also removes the spindle proteins, causing interference with cell division. In some other mammals(eg, cats, rabbits, and mice) these 2 spindle proteins are spread throughout the egg. So, removal of the egg's nucleus does not cause loss of spindle proteins. In addition, experiments showed that some dyes and UV rays, which were used to remove the egg's nucleus, can damage primate cells and stop their growth.

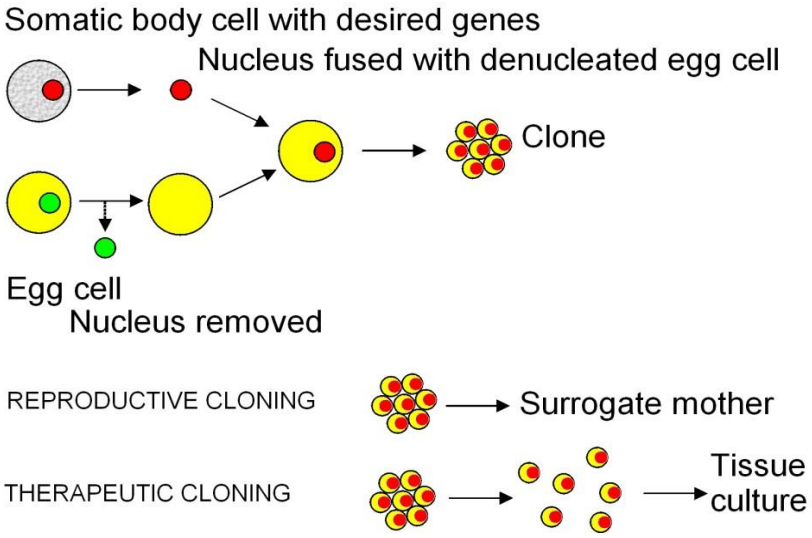
Some focus on Human cloning

Human cloning means the creation of a genetically identical copy (or clone) of a human. The term is used to refer to artificial human cloning (Artificial reproduction of human cells and tissue). It does not mean the natural conception and natural delivery of identical twins. But the possibility of human cloning is very controversial. Ethical concerns have prompted several nations to pass laws regarding to stop human cloning and its legality.

Theoretically, 2 common types of human cloning are: 1. *therapeutic cloning* and 2. *reproductive cloning*.

1. Therapeutic cloning - involves cloning cells from a human for use in medicine and transplantation, and it is an active area of research nowadays, but to date it is not used in medical practice anywhere in the world (till April 2017). Methods of therapeutic cloning are 1. somatic-cell nuclear transfer and 2. more recently, pluripotent stem cell induction**.**

2. Reproductive cloning would involve making an entire cloned human, instead of just specific cells or tissues.



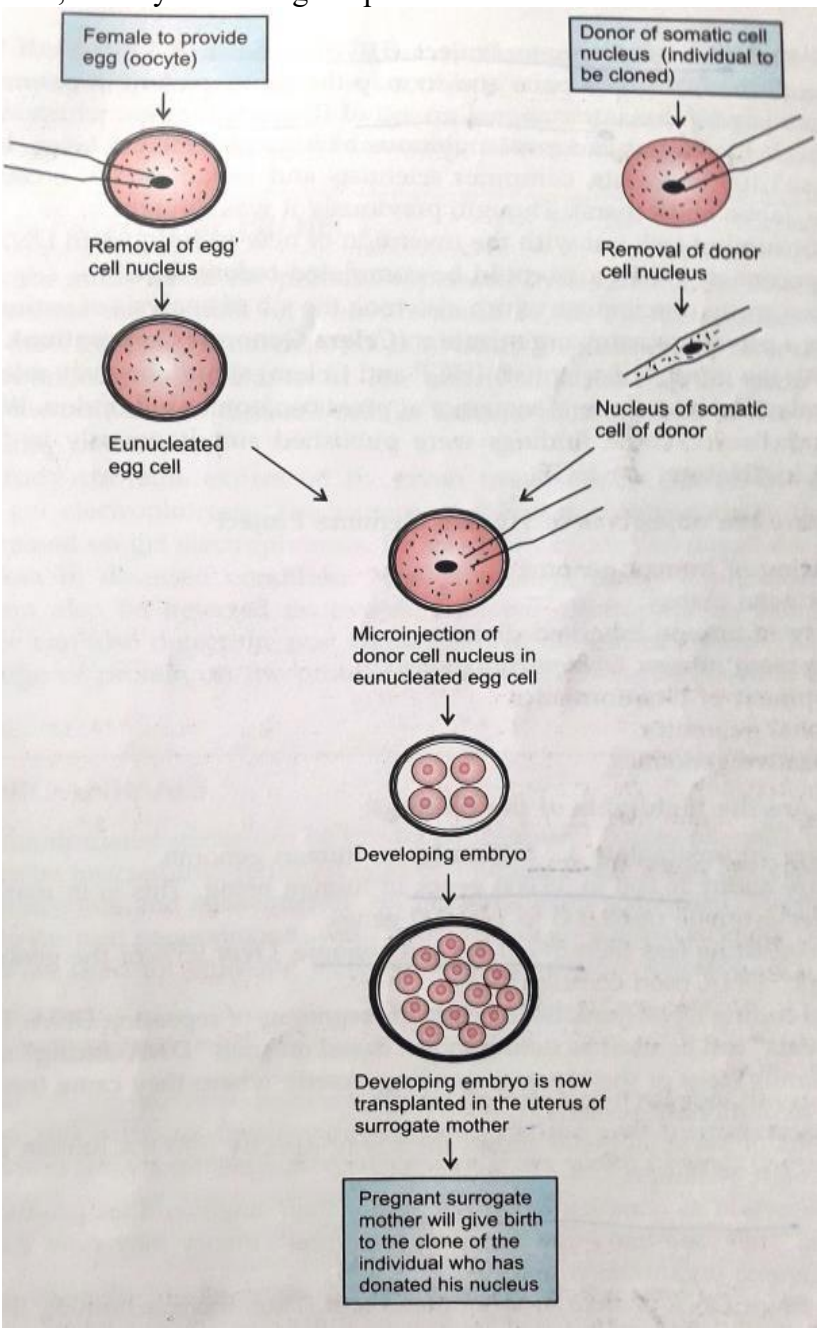
Methods

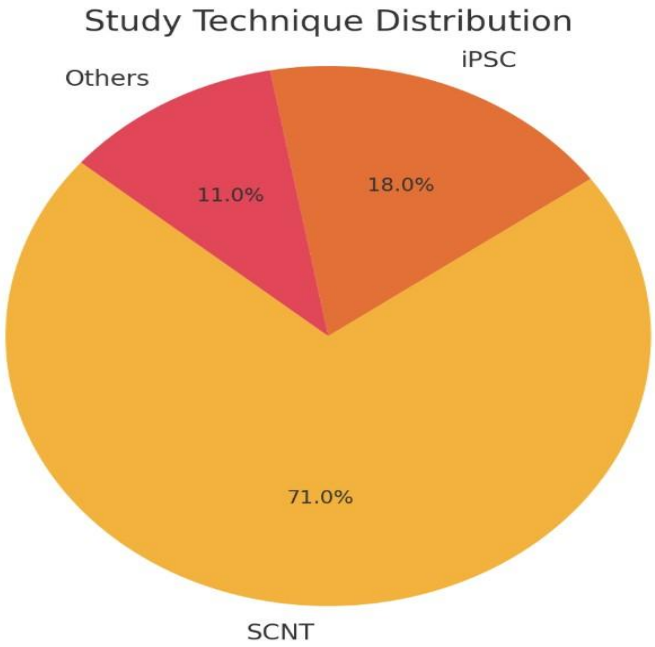
Somatic cell nuclear transfer (SCNT)

In somatic cell nuclear transfer ("SCNT"), the nucleus of a somatic cell is taken from a donor and transplanted into a host egg cell, which had its own genetic material removed previously, making it an enucleated egg. After the donor somatic cell genetic material is transferred into the host oocyte with a micropipette, the somatic cell genetic material is fused with the egg using an electric current. Once the two cells have fused, the new cell can be permitted to grow in a surrogate or artificially. [18] This process is used to create a clone 'Dolly' of the sheep.

Induced pluripotent stem cells (iPSCs)

Creating induced pluripotent stem cells ("iPSCs") is a long and inefficient process. Pluripotency refers to a stem cell that has the potential to differentiate into any of the three germ layers: endoderm (the interior stomach lining, gastrointestinal tract, and the lungs), mesoderm (muscle, bone, blood, and urogenital), or ectoderm (epidermal tissues and nervous tissue). A specific set of genes, often called "reprogramming factors", is introduced into a specific adult cell type. These factors send signals in the mature cell that cause the cell to become a pluripotent stem cell. This process is highly studied, and new techniques are being discovered frequently on how to improve this induction process.
Depending on the method used, reprogramming of adult cells into iPSCs for implantation could have severe limitations in humans. If a virus is used as a reprogramming factor for the cell, cancer-causing genes called oncogenes may be activated. These cells would appear as rapidly dividing cancer cells that do not respond to the body's natural cell signaling process.
In 2008, scientists discovered a technique that could remove the presence of these oncogenes after pluripotency induction, thereby increasing the potential use of iPSC in humans.





The pie chart shows the distribution of study techniques (SCNT: 71%, iPSC: 18%, Others: 11%).

Comparative development: SCNT vs Reprogramming

Nobel Prize-winning scientist Joshua Lederberg advocated cloning and genetic engineering in an article in The American Naturalist in 1966 and 1967, in The Washington Post.[1] His advocacy sparked an ethical debate with conservative bio-ethicist Leon Kass, who warned that "the cloning could lead to dehumanization of mankind.

Despite ethical resistance, scientific advances continued. In 1998, the 1st hybrid human clone was created by Advanced Cell Technology, using SCNT - a nucleus was taken from a man's leg cell and inserted into an enucleated cow's egg. This hybrid cell was cultured and developed into an embryo, but was destroyed after 12 days.

Between 2004 – 2005, Hwang Woo-suk, professor of Seoul National University, published 2 separate articles in the Journal of *Science* claiming to have successfully harvested pluripotent, embryonic stem cells from a cloned human blastocyst[25] by using SCNT techniques. And created 11 different types of patent-specific stem cell lines. This was 1st breakthrough in human cloning. However, this report was later retracted in 2006 due to fabricated data.

In January 2008, Dr. Andrew French and Samuel Wood (from the biotechnology company Stemagen) announced that they had successfully created the first five mature human embryos using SCNT by taking a nucleus from a skin cell and inserting it into an enucleated human egg. But the embryos were developed only to the blastocyst stage, at which point they were destroyed[26] them for another study purpose. In 2013, a group of scientists led by Shoukhrat Mitalipov published the first report of human embryonic stem cells created using SCNT. They utilized oocytes from a single donor, ensuring uniform mitochondrial DNA, and generated four viable cell lines. In 2014, Robert Lanza and his colleagues at Advanced Cell Technology replicated these findings and demonstrated successful cloning of adult human cells.

While SCNT involves physical replacement of nuclei, reprogramming technologies—such as those using induced pluripotent stem cells (iPSCs)—achieve similar goals by genetically reprogramming somatic cells without the need for enucleated eggs. iPSCs have emerged as an alternative to SCNT due to their less controversial ethical profile and potential for personalized medicine. Together, these developments highlight the ongoing tension between scientific innovation, technical feasibility, and ethical governance in the realm of human cloning.

Comparing SCNT to iPSC

1. The major advantage of SCNT over iPSCs-based reprogramming, SCNT enables more rapid production of pluripotent cells, making it potentially more suitable for time-sensitive medical applications
2. Another advantage of SCNT over iPSCs, that it may offer therapeutic potential to treat mitochondrial disease by utilizing a donor oocyte, an aspect not addressed by iPSCs

Ethical implications

UNESCO's Universal Declaration on the Human Genome and Human Rights[27] (1997) was the first international instrument to condemn human reproductive cloning as a practice against human dignity. Article 11 of this Declaration states: "*Practices which are contrary to human dignity*[28]*, such as reproductive cloning of human beings, shall not be permitted…*" This position is shared by the World Health Organization, the European Parliament, and several other inter organizations. Some see the increase in control of what kind of genome we want to pass on to our children as a positive development. National instruments require people to use genetics to have 'better' children.

Ethics of cloning

In bioethics[29], the ethics of cloning refers to a variety of ethical positions regarding the practice and possibilities of cloning, especially human cloning. While many of these views are religious[30] in origin, the questions raised by cloning are faced by secular perspectives as well. Human therapeutic and reproductive cloning are not commercially used; animals are currently cloned in laboratories and in livestock production. Advocates support the development of therapeutic cloning in order to generate tissues and whole organs to treat patients who otherwise cannot obtain transplants,[31] to avoid the need for immunosuppressive drugs, and to stave off the effects of aging. Advocates for reproductive cloning believe that parents who cannot otherwise procreate should have access to the technology. Opposition to therapeutic cloning mainly centers around the status of embryonic stem cells, which has connections with the abortion debate.

Some opponents of reproductive cloning have concerns that technology is not yet developed enough to be safe - for example, the position of the American Association for the Advancement of Science[32,33] as of 2014, while others emphasize that reproductive cloning could be prone to abuse (leading to the generation of humans whose organs and tissues would be harvested), and have concerns about how cloned individuals could integrate with families and with society at large. Religious groups are divided into two, one with opposing technology as usurping God's (in monotheistic traditions) place; others support therapeutic cloning's potential life-saving benefits.

Current law

In 2015, it was reported that about 70 countries had banned human cloning.

India

India does not have a specific law regarding cloning, but it has guidelines prohibiting whole human cloning or reproductive cloning. India allows therapeutic cloning and the use of embryonic stem cells for research purposes[34]. In terms of section 39A of the Human Tissue Act 65 of 1983, genetic manipulation of gametes or zygotes outside the human body is absolutely prohibited. A zygote is the cell resulting from the fusion of two gametes; thus fertilized ovum. Section 39A thus prohibits human cloning.

United Kingdom

On January 14, 2001, the British government enacted The Human Fertilization and Embryology (Research Purposes) Regulations 2001 to amend the original Act 1990 by extending the permissible scope of embryo research to permit research to include stem cells studies and nuclear replacement, thus legalizing therapeutic cloning.

The Human Reproductive Cloning Act 2001 explicitly prohibited reproductive cloning. The first license was granted on August 11, 2004, to researchers at the University of Newcastle to allow them to investigate treatments for diabetes, disease, and Alzheimer's disease.
The Human Fertilization and Embryology Act 2008, a major review of fertility legislation, repealed the 2001 Cloning Act by making amendments of similar effect to the 1990 Act. The 2008 Act allows regulated experiments on hybrid human-animal embryos for research purposes.. These legislative developments reflect the UK's attempt to balance scientific advancement with ethical oversight, particularly in the context of emerging biotechnologies. In March 2005, a non-binding United Nations Declaration on Human Cloning, calling for the ban of all forms of human cloning contrary to human dignity, was adopted.

United States
The Patients First Act of 2017 (HR 2918, 115th Congress) aims to promote stem cell research, using cells that are "ethically obtained", that could contribute to a better understanding of diseases and therapies, and promote the "derivation of pluripotent stem cell[35,36] lines without the creation of human embryos.

Conclusion
This systematic review highlights the evolving landscape of cloning technologies, particularly Somatic Cell Nuclear Transfer (SCNT) and induced pluripotent stem cells (iPSCs). While SCNT remains the gold standard for producing genetically identical organisms and offers distinct advantages in speed and mitochondrial therapy, it is constrained by low success rates and ethical controversies. Reprogramming through iPSCs, though more ethically acceptable, requires longer derivation times and lacks mitochondrial applicability.
Significant advancements have been made in understanding human development, disease modelling, and regenerative medicine through cloning research. Legislative measures, such as those in the United Kingdom, underscore the need for carefully regulated scientific exploration. Continued interdisciplinary research, policy refinement, and ethical discourse are imperative to unlocking the full potential of cloning in modern biomedicine.
Cloning remains a technologically exciting but practically limited tool in modern genetics. While animal cloning has progressed, human cloning is still in its infancy. Enhanced techniques and ethical clarity are essential for advancing this field responsibly.

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