ResearchGate

See discussions, stats, and author profiles for this publication at: https://www.researchgate.net/publication/343059802

Hela Cells and Immortality

Article · September 2017

DOI: 10.7537/marscbj070317.11

CITATIONS
2

READS
9,004

1 author:

Hongbao Ma
Brookdale University Hospital

261 PUBLICATIONS **2,256** CITATIONS

SEE PROFILE

All content following this page was uploaded by Hongbao Ma on 26 November 2020.

The user has requested enhancement of the downloaded file.

PREOMICS EXHIBIT 1037 - IPR2024-01473
PREOMICS v. THE BRIGHAM & WOMEN'S HOSPITAL
Page 1 of 9

Hela Cells and Immortality

Dr. Ma Hongbao

Brookdale University Hospital & Medical Center, Brooklyn, NY 11212, USA
ma8080@gmail.com; 718-404-5362

Abstract: Immortality is the eternal life, the ability to live forever. The most important is the biological immortality, where the living body will live without die. Other people believe that life extension is a more achievable goal in the short term, with immortality awaiting further research breakthroughs. HeLa is an immortal cell line used in scientific researches and applications. It is the oldest and most commonly used human cell line. The line was derived from cervical cancer cells taken on February 8, 1951 from Henrietta Lacks, a patient who died of her cancer on October 4, 1951. The cell line was found to be durable which let researchers can use it in scientific research easily. The cells from Lacks' cancerous cervical tumor were taken without her knowledge or consent. Cell biologist George Otto Gey found that the cells could be kept alive, and a single cell was isolated then multiplied from them. Finally the cell was developed as a cell line. This cell line was labeled as HeLa, the first two letters of the patient's first and last name (Henrietta Lacks), and the HeLa became the name of the cell line.
[Ma H. **Hela Cells and Immortality.** *Cancer Biology* 2017;7(3):71-78]. ISSN: 2150-1041 (print); ISSN: 2150-105X (online). http://www.cancerbio.net. 11. doi:10.7537/marscbj070317.11.

Key words: cancer; immortality; DNA; eternal; life; stem cell; cell; protein

Life is unique in the known universe, and the life forms are ranging from bacteria to human existing in the world for a long history (Ma and Cherng, 2005). The nature of life and the life immortality are always attracting for the human society, in the whole human history in now.

The most important is the biological immortality, where the living body will live without die. However, in the earth, all the living body must be dye. Immortality is the eternal life, the ability to live forever, at least that we know. Even, some people believe that life extension is a more achievable goal in the short term, with immortality awaiting further research breakthroughs, everyone must face the die seriously. One more point, even the absence of aging would provide humans with biological immortality, but not invulnerability to death by physical trauma; although mind uploading could solve that issue if it proved possible.

Biological immortality is a biological state in which the rate of mortality from senescence is stable or decreasing. Various unicellular and multicellular species, including some vertebrates, achieve this state either throughout their existence or after living long enough. A biologically immortal living being can still die from means other than senescence, such as through injury or disease. The rate of mortality may cease to increase in old age, but in most cases that rate is typically very high. As a hypothetical example, there is only a 50% chance of a human surviving another year at age 110 or greater. People are interested even pursues the immortality all the time in the human time, and people are interested in immortality now.

The term is also used by biologists to describe cells that are not subject to the Hayflick limit on how many times they can divide. The Hayflick limit or Hayflick phenomenon is the number of times a normal human cell population will divide until cell division stops. Empirical evidence shows that the telomeres associated with each cell's DNA will get slightly shorter with each new cell division until they shorten to a critical length. The Hayflick limit has been found to correlate with the length of the telomere region at the end of a strand of DNA. During the process of DNA replication, small segments of DNA at each end of the DNA strand (telomeres) are unable to be copied and are lost after each time DNA is duplicated. The telomere region of DNA does not code for any protein; it is simply a repeated code on the end region of DNA that is lost. After many divisions, the telomeres become depleted and the cell begins apoptosis. This is a mechanism that prevents replication error that would cause mutations in DNA. Once the telomeres are depleted, due to the cell dividing many times, it will no longer divide. This is when the cell has reached its Hayflick limit. The Hayflick limit process does not take place in most cancer cells due to an enzyme called telomerase. This enzyme maintains telomere length, which results in the telomeres of cancer cells never shortening. This gives these cells infinite replicative potential. A proposed treatment for cancer is the usage of telomerase inhibitors that would prevent the restoration of the telomere, allowing the cell to die like other body cells. On the other hand, telomerase activators might repair or extend the telomeres of healthy cells, thus extending their Hayflick limit. Telomerase activation might also lengthen the telomeres of immune system cells enough

PREOMICS EXHIBIT 1037 - IPR2024-01473
PREOMICS v. THE BRIGHAM & WOMEN'S HOSPITAL
Page 2 of 9

to prevent cancerous cells from developing from cells with very short telomeres. The cancer telomerase may be used in the application of human immortality.

In religious contexts, immortality is often stated to be one of the promises of God (or other deities) to human beings who show goodness or else follow divine law. What form an unending human life would take, or whether an immaterial soul exists and possesses immortality, has been a major point of focus of religion, as well as the subject of speculation, fantasy, and debate.

HeLa is an immortal cell line used in scientific researches and applications. It is the oldest and most commonly used human cell line. The line was derived from cervical cancer cells taken on February 8, 1951 from Henrietta Lacks, a patient who died of her cancer on October 4, 1951. The cell line was found to be durable which let researchers can use it in scientific research easily. This is very useful cell line in scientific research and in the application.

The cells from Lacks' cancerous cervical tumor were taken without her knowledge or consent. Cell biologist George Otto Gey found that the cells could be kept alive, and a single cell was isolated then multiplied from them. Finally the cell was developed as a cell line. This cell line was labeled as HeLa, the first two letters of the patient's first and last name (Henrietta Lacks), and the HeLa became the name of the cell line.

The HeLa cells were the first human cells grown in a lab that were naturally immortal, meaning that they do not die after a set number of cell divisions, not senescence.

The stable growth of HeLa enabled the researcher Jonas Salk at the University of Minnesota hospital to successfully grow polio virus, enabling the development of a vaccine. In 1952, Jonas Salk in the hospital of University of Minnesota developed a vaccine for polio using Hela cells. To test Salk's new vaccine, the cells were put into mass production in the first-ever cell production factory.

In 1953, HeLa cells were the first human cells successfully cloned and the demanding of the HeLa cells quickly grew in the biomedical researches and industry after then. Up to now, the scientists have grown an estimated 20 tons of HeLa cells. The HeLa cell lines are known to overtake other cell cultures in laboratory settings and it is estimated that HeLa cells, at one point, contaminated millions of dollars worth of biological research.

The Hela cells were propagated by George Otto Gey shortly before Ms. Henrietta Lacks died of her cancer in year 1951. This was the first human cell line to prove successful in vitro, which was a scientific achievement with profound future benefit to medical research. Gey freely donated these cells along with the techniques that his lab developed to any scientist requesting them simply for the benefit of science. Neither Lacks nor her family gave permission to harvest the cells but, at that time, permission was neither required nor customarily sought. The cells were later commercialized, although never patented in their original form. There was no requirement at that time to inform patients or their relatives about such matters because discarded material or material obtained during surgery, diagnosis, or therapy was the property of the physician or the medical institution. This issue and Lacks' situation were brought up in the Supreme Court of California case of Moore v. Regents of the University of California. The court ruled that a person's discarded tissue and cells are not his or her property and can be commercialized.

At first, the HeLa cell line was said to be named after a Helen Lane or Helen Larson. Starting in the 1970s the Lacks family was contacted by researchers trying to find out why the HeLa cells had contaminated other cell lines in laboratories. These cells are treated as cancer cells, as they are descended from a biopsy taken from a visible lesion on the cervix as part of Lacks' diagnosis of cancer.

HeLa cells, like other cell lines, are termed immortal in that they can divide an unlimited number of times in a laboratory cell culture plate as long as fundamental cell survival conditions are met. There are many strains of HeLa cells as they continue to mutate in cell cultures, but all HeLa cells are descended from the same tumor cells removed from Lacks. The total number of HeLa cells that have been propagated in cell culture far exceeds the total number of cells that were in Henrietta Lacks' body.

HeLa cells were used by Jonas Salk to test the first polio vaccine in the 1950s. They were observed to be easily infected by poliomyelitis, causing infected cells to die. This made HeLa cells highly desirable for polio vaccine testing since results could be easily obtained. A large volume of HeLa cells were needed for the testing of Salk’s polio vaccine, prompting the US National Foundation for Infantile Paralysis (NFIP) to find a facility capable of mass-producing HeLa cells. In the spring of 1953, a cell culture factory was established at Tuskegee University to supply Salk and other labs with HeLa cells. Less than a year later, Salk’s vaccine was ready for human trials. HeLa cells were also the first human cells to be successfully cloned in 1953 by Theodore Puck and Philip I Marcus at the University of Colorado, Denver, USA. Since that time, HeLa cells have continually been used for research into cancer, AIDS, the effects of radiation and toxic substances, gene mapping, and countless other scientific pursuits.

The photo of Henrietta Lacks and her husband David Lacks is shown in Figure 1.

PREOMICS EXHIBIT 1037 - IPR2024-01473
PREOMICS v. THE BRIGHAM & WOMEN’S HOSPITAL
Page 3 of 9

Figure 1. Henrietta Lacks and her husband David Lacks.

HeLa cells have been used in testing how parvo virus infects cells of humans, HeLa, dogs, and cats. These cells have also been used to study viruses such as the oropouche virus. The oropouche virus causes the disruption of cells in culture, where cells begin to degenerate shortly after they are infected, causing viral induction of apoptosis. HeLa cells have been used to study the expression of the papillomavirus E2 and apoptosis. HeLa cells have also been used to study canine distemper virus to induce apoptosis in cancer cell lines, which could play an important role in developing treatments for tumor cells resistant to radiation and chemotherapy. HeLa cells have also been used in a number of cancer studies, including those involving sex steroid hormones such as estradiol, estrogen, and estrogen receptors, along with estrogen-like compounds such as quercetin and its cancer reducing properties. There have also been studies on HeLa cells, the effects of flavonoids and antioxidants with estradiol on cancer cell proliferation. HeLa cells were used to investigate the phytochemical compounds and the fundamental mechanism of the

PREOMICS EXHIBIT 1037 - IPR2024-01473
PREOMICS v. THE BRIGHAM & WOMEN'S HOSPITAL
Page 4 of 9

anticancer activity of the ethanolic extract of mango peel. The ethanolic extract of mango peel was found to contain various phenolic compounds and to activate death of human cervical malignant HeLa cells through apoptosis, which suggests that the ethanolic extract of mango peel may help to prevent cervical cancer as well as other types of cancers.

In 2011, HeLa cells were used in tests of novel heptamethine dyes IR-808 and other analogs which are currently being explored for their unique uses in medical diagnostics, the development of theranostics, the individualized treatment of cancer patients with the aid of PDT, co-administration with other drugs, and irradiation. HeLa cells have been used in research involving fullerenes to induce apoptosis as a part of photodynamic therapy, as well as in *in vitro* cancer research using cell lines. Further HeLa cells have also been used to define cancer markers in RNA, and have been used to establish an RNAi Based Identification System and Interference of Specific Cancer Cells.

The HeLa cell line was derived for use in cancer research. These cells proliferate abnormally rapidly, even compared to other cancer cells. Like many other cancer cells, HeLa cells have an active version of telomerase during cell division, which prevents the incremental shortening of telomeres that is implicated in aging and eventual cell death. In this way, the cells circumvent the Hayflick limit, which is the limited number of cell divisions that most normal cells can undergo before becoming senescent.

HeLa cells are rapidly dividing cancer cells, and the number of chromosomes varied during cancer formation and cell culture. The current estimate (excluding very tiny fragments) is a hypertriploid chromosome number (3n+) which means 76 to 80 total chromosomes (rather than the normal diploid number of 46) with 22–25 clonally abnormal chromosomes, known as HeLa signature chromosomes. The signature chromosomes can be derived from multiple original chromosomes, making challenging summary counts based on original numbering.

The complete genome of the HeLa cells was sequenced and published on March 11 of 2013 without the Lacks family's knowledge. Concerns were raised by the family, so the authors voluntarily withheld access to the sequence data. Jay Shendure led a HeLa sequencing project at the University of Washington (USA) which produced a paper that had been accepted for publication in March of 2013, but that was also put on hold while the Lacks family's privacy concerns were being addressed. On August 7 of 2013, NIH director Francis Collins announced a policy of controlled access to the cell line genome based on an agreement reached after three meetings with the Lacks family. A data-access committee will review requests from researchers for access to the genome sequence under the criteria that the study is for medical research and the users will abide by terms in the HeLa Genome Data Use Agreement, which includes that all NIH-funded researchers will deposit the data into a single database for future sharing. The committee consists of six members including representatives from the medical, scientific, and bioethics fields, as well as two members of the Lacks family.

HeLa cells are sometimes difficult to control because of their adaptation to growth in tissue culture plates. Through improper maintenance, they have been known to contaminate other cell cultures in the same laboratory, interfering with biological research and forcing researchers to declare many results invalid. The degree of HeLa cell contamination among other cell types is unknown because few researchers test the identity or purity of already established cell lines.

Henrietta Lacks was a black tobacco farmer from southern Virginia who got cervical cancer when she was 30. A doctor at Johns Hopkins took a piece of her tumor without telling her and sent it down the hall to scientists there who had been trying to grow tissues in culture for decades without success. No one knows why, but her cells never died. Henrietta's cells were the first immortal human cells ever grown in culture.

Henrietta's daughter is Deborah.

Twenty-five years after Henrietta died, a scientist discovered that many cell cultures thought to be from other tissue types, including breast and prostate cells, were in fact HeLa cells. It turned out that HeLa cells could float on dust particles in the air and travel on unwashed hands and contaminate other cultures. It became an enormous controversy. In the midst of that, one group of scientists tracked down Henrietta's relatives to take some samples with hopes that they could use the family's DNA to make a map of Henrietta's genes so they could tell which cell cultures were HeLa and which weren't, to begin straightening out the contamination problem.

So a postdoc called Henrietta's husband one day. But he had a third-grade education and didn't even know what a cell was. The way he understood the phone call was: "We've got your wife. She's alive in a laboratory. We've been doing research on her for the last 25 years. And now we have to test your kids to see if they have cancer." Which wasn't what the researcher said at all. The scientists didn't know that the family didn't understand. From that point on, though, the family got sucked into this world of research they didn't understand, and the cells, in a sense, took over their lives.

This was most true for Henrietta's daughter. Deborah never knew her mother, as she was an infant when Henrietta died. She had always wanted to know who her mother was but no one ever talked about Henrietta. So when Deborah found out that this part of

PREOMICS EXHIBIT 1037 - IPR2024-01473
PREOMICS v. THE BRIGHAM & WOMEN'S HOSPITAL
Page 5 of 9

her mother was still alive she became desperate to understand what that meant: Did it hurt her mother when scientists injected her cells with viruses and toxins? Had scientists cloned her mother? And could those cells help scientists tell her about her mother, like what her favorite color was and if she liked to dance.

Deborah's brothers, though, didn't think much about the cells until they found out there was money involved. HeLa cells were the first human biological materials ever bought and sold, which helped launch a multi-billion-dollar industry. When Deborah's brothers found out that people were selling vials of their mother's cells, and that the family didn't get any of the resulting money, they got very angry. Henrietta's family has lived in poverty most of their lives, and many of them can't afford health insurance. One of her sons was homeless and living on the streets of Baltimore. So the family launched a campaign to get some of what they felt they were owed financially. It consumed their lives in that way.

For scientists, one of the lessons is that there are human beings behind every biological sample used in the laboratory. So much of science today revolves around using human biological tissue of some kind. For scientists, cells are often just like tubes or fruit flies, and they're just inanimate tools that are always there in the lab. The people behind those samples often have their own thoughts and feelings about what should happen to their tissues, but they're usually left out of the equation.

The story of HeLa cells and what happened with Henrietta has often been held up as an example of a racist white scientist doing something malicious to a black woman. But that's not accurate. The real story is much more subtle and complicated. What is very true about science is that there are human beings behind it and sometimes even with the best of intentions things go wrong.

The HeLa cell line was derived for use in cancer research. These cells proliferate abnormally rapidly, even compared to other cancer cells. Like many other cancer cells, HeLa cells have an active version of telomerase during cell division, which prevents the incremental shortening of telomeres that is implicated in aging and eventual cell death. In this way, the cells circumvent the Hayflick limit, which is the limited number of cell divisions that most normal cells can undergo before becoming senescent.

Horizontal gene transfer from human papillomavirus 18 (HPV18) to human cervical cells created the HeLa genome, which is different from Henrietta Lacks' genome in various ways, including its number of chromosomes. HeLa cells are rapidly dividing cancer cells, and the number of chromosomes varied during cancer formation and cell culture. The current estimate (excluding very tiny fragments) is a "hypertriploid chromosome number (3n+)" which means 76 to 80 total chromosomes (rather than the normal diploid number of 46) with 22–25 clonally abnormal chromosomes, known as HeLa signature chromosomes." The signature chromosomes can be derived from multiple original chromosomes, making challenging summary counts based on original numbering. Researchers have also noted how stable these aberrant karyotypes can be:

Human papillomaviruses (HPVs) are frequently integrated into the cellular DNA in cervical cancers. We mapped by FISH five HPV18 integration sites: three on normal chromosomes 8 at 8q24 and two on derivative chromosomes, der (5)t (5; 22;8) (q11; q11q13; q24) and der (22)t (8; 22) (q24; q13), which have chromosome 8q24 material. An 8q24 copy number increase was detected by CGH. Dual-color FISH with a c-MYC probe map ping to 8q24 revealed colocalization with HPV18 at all integration sites, indicating that dispersion and amplification of the c-MYC gene sequences occurred after and was most likely triggered by the viral insertion at a single integration site. Numerical and structural chromosomal aberrations identified by SKY, genomic imbalances detected by CGH, as well as FISH localization of HPV18 integration at the c-MYC locus in HeLa cells are common and representative for advanced stage cervical cell carcinomas. The HeLa genome has been remarkably stable after years of continuous cultivation; therefore, the genetic alterations detected may have been present in the primary tumor and reflect events that are relevant to the development of cervical cancer.

The complete genome of the HeLa cells was sequenced and published on 11 March 2013 without the Lacks family's knowledge. Concerns were raised by the family, so the authors voluntarily withheld access to the sequence data. Jay Shendure led a HeLa sequencing project at the University of Washington which produced a paper that had been accepted for publication in March 2013—but that was also put on hold while the Lacks family's privacy concerns were being addressed. On 7 August 2013, NIH director Francis Collins announced a policy of controlled access to the cell line genome based on an agreement reached after three meetings with the Lacks family. A data-access committee will review requests from researchers for access to the genome sequence under the criteria that the study is for medical research and the users will abide by terms in the HeLa Genome Data Use Agreement, which includes that all NIH-funded researchers will deposit the data into a single database for future sharing. The committee consists of six members including representatives from the medical, scientific, and bioethics fields, as well as two

PREOMICS EXHIBIT 1037 - IPR2024-01473
PREOMICS v. THE BRIGHAM & WOMEN'S HOSPITAL
Page 6 of 9

members of the Lacks family. In an interview, Collins praised the Lacks family's willingness to participate in this situation that was thrust upon them. He described the whole experience with them as 'powerful', saying that it brought together 'science, scientific history and ethical concerns' in a unique way.

HeLa cells are sometimes difficult to control because of their adaptation to growth in tissue culture plates. Through improper maintenance, they have been known to contaminate other cell cultures in the same laboratory, interfering with biological research and forcing researchers to declare many results invalid. The degree of HeLa cell contamination among other cell types is unknown because few researchers test the identity or purity of already established cell lines. It has been demonstrated that a substantial fraction of *in vitro* cell lines are contaminated with HeLa cells; estimates range from 10% to 20%. Stanley Gartler (1967) and Walter Nelson-Rees (1975) were the first to publish on the contamination of various cell lines by HeLa.

Science writer Michael Gold wrote about the HeLa cell contamination problem in his book *A Conspiracy of Cells*. He describes Nelson-Rees's identification of this pervasive worldwide problem — affecting even the laboratories of the best physicians, scientists, and researchers, including Jonas Salk — and many possibly career-ending efforts to address it. According to Gold, the HeLa contamination problem almost led to a Cold War incident. The USSR and the USA had begun to cooperate in the war on cancer launched by President Richard Nixon, only to find that the exchanged cells were contaminated by HeLa. Gold contends that the HeLa problem was amplified by emotions, egos, and a reluctance to admit mistakes. Nelson-Rees explains:

It's all human – an unwillingness to throw away hours and hours of what was thought to be good research... worries about jeopardizing another grant that's being applied for, the hurrying to come out with a paper first. And it isn't limited to biology and cancer research. Scientists in many endeavors all make mistakes, and they all have the same problems.

Rather than focus on how to resolve the problem of HeLa cell contamination, many scientists and science writers continue to document this problem as simply a contamination issue — caused not by human error or shortcomings but by the hardiness, proliferating, or overpowering nature of HeLa. Recent data suggest that cross-contaminations are still a major ongoing problem with modern cell cultures. Taken directly from the International Cell Line Authentication Committee (ICLAC) webpage:

Regrettably, cross-contamination and misidentification are still common within the research community. Many cell lines were cross-contaminated during establishment; this means that all work using those cell lines has incorrectly used the contaminant – which may come from a different species or a different tissue.... A cell line is considered to be misidentified if it no longer corresponds to the individual from whom it was first established. Many cases of misidentification are caused by cross-contamination, where another, faster growing, cell line is introduced into that culture.

HeLa was described by Leigh Van Valen as an example of the contemporary creation of a new species, dubbed *Helacyton gartleri*, due to their ability to replicate indefinitely, and their non-human number of chromosomes. The species was named after Stanley M. Gartler, whom Van Valen credits with discovering "the remarkable success of this species." His argument for speciation depends on these points:

- The chromosomal incompatibility of HeLa cells with humans.
- The ecological niche of HeLa cells.
- Their ability to persist and expand well beyond the desires of human cultivators.
- HeLa can be defined as a species as it has its own clonal karyotype.

Van Valen proposed the new family Helacytidae and the genus Helacyton, as well as proposing a new species for HeLa cells in the same paper.

However, this proposal has not been taken seriously by other prominent evolutionary biologists, nor by scientists in other disciplines. Van Valen's argument of HeLa being a new species does not fulfill the criteria for an independent unicellular asexually reproducing species because of the notorious instability of HeLa's karyotype and their lack of a strict ancestral-descendant lineage.

Why are HeLa cells immortal? They have an active telomerase during cell division which prevents the shortening of telomeres. Telomeres are repetitive sequences found at the end of chromosomes to protect them from damage and fusing with other chromosomes. During the replication process, the machinery of enzymes involved cannot reach the end of the chromosome so with each cell division, the telomere repeats get shorter. In differentiated cells telomerase, which is responsible to prevent the shortening of telomeres is inactive. This is the phenomenon behind aging. So these HeLa cells, are highly proliferative human cancer cell line with an active telomerase. That's why they are immortal. Normal cells have a problem called hayflick limit which mean that they divide till certain generations and die. The reason behind this is the telomeres present on chromosome shorten as the cell divide. where as in cancer cells like Hela, HepG2 etc., the telomeres remain same (mutations in telomeres/telomerase) instead of getting shortened

PREOMICS EXHIBIT 1037 - IPR2024-01473
PREOMICS v. THE BRIGHAM & WOMEN'S HOSPITAL
Page 7 of 9

there by evading apoptosis (programmed cell death). Almost every cancer cell lines is immortal.

The Hayflick limit or Hayflick phenomenon is the number of times a normal human cell population will divide until cell division stops. Empirical evidence shows that the telomeres associated with each cell's DNA will get slightly shorter with each new cell division until they shorten to a critical length.

The concept of the Hayflick limit was advanced by American anatomist Leonard Hayflick in 1961, at the Wistar Institute in Philadelphia, Pennsylvania, USA. Hayflick demonstrated that a population of normal human fetal cells in a cell culture will divide between 40 and 60 times. The population will then enter a senescence phase, which refutes the contention by Nobel laureate Alexis Carrel that normal cells are immortal. Each mitosis slightly shortens each of the telomeres on the DNA of the cells. Telomere shortening in humans eventually makes cell division impossible, and this aging of the cell population appears to correlate with the overall physical aging of the human body.

Australian Nobel laureate Sir Macfarlane Burnet coined the name Hayflick limit in his book *Intrinsic Mutagenesis: A Genetic Approach to Ageing*, published in 1974.

The HeLa cells are cancerous which are slightly different than normal cells. There isn't anything special about her cancer cells as opposed to other cancer cells, hers were just the first that were actively cultured properly. Cancer cells reproduce very quickly, and some do not experience the shortening of the DNA strand after many replications which allows them to continue to replicate (Unlike a normal DNA strand which has telomeres at the ends of the DNA strand which protect the important DNA proteins from being removed as it is shortened each time).

Although the premise that biological aging can be halted or reversed by foreseeable technology remains controversial, research into developing possible therapeutic interventions is underway. Among the principal drivers of international collaboration in such research is the SENS Research Foundation, a non-profit organization that advocates a number of what it claims are plausible research pathways that might lead to engineered negligible senescence in humans.

In 2015, Elizabeth Parrish, CEO of BioViva, treated herself using gene therapy, with the goal of not just halting, but reversing aging. She has since reported feeling more energetic, but long-term study of the treatment is ongoing.

For several decades, researchers have also pursued various forms of suspended animation as a means by which to indefinitely extend mammalian lifespan. Some scientists have voiced support for the feasibility of the cryopreservation of humans, known as cryonics. Cryonics is predicated on the concept that some people considered clinically dead by today's medicolegal standards are not actually dead according to information-theoretic death and can, in principle, be resuscitated given sufficient technological advances.

Similar proposals involving suspended animation include chemical brain preservation. The non-profit Brain Preservation Foundation offers a cash prize valued at over $100,000 for demonstrations of techniques that would allow for high-fidelity, long-term storage of a mammalian brain.

In early 2017, Harvard scientists headed by biologist David Sinclair announced they have tested a compound called NAD+ on mice and have successfully reversed the cellular aging process and can protect the DNA from future damage. The old mouse and young mouse cells are indistinguishable", David was quoted. Human trials are to begin shortly in what the team expect is 6 months at Brigham and Women's Hospital, in Boston.

Turritopsis nutricula is a hydrozoan that can revert to the sexually immature (polyp stage) after becoming sexually mature. It is the only known metazoan capable of reverting completely to a sexually immature, colonial stage after having reached sexual maturity as a solitary stage. It does this through the cell development process of transdifferentiation. This cycle can repeat indefinitely that offers it biologically immortal. To study the reason of the biological immortality of *Turritopsis nutricula* possibly supplies the way finding the biological immortality for human. *Turritopsis nutricula* is a species of jellyfish with a very unusual quality: it is biologically immortal. Also known as the immortal jellyfish, this fascinating animal, in theory, has the ability to sustain life indefinitely, so long as its nerve center remains intact (Ma and Yang, 2010).

The above contents are the collected information from Internet and public resources to offer to the people for the convenient reading and information disseminating and sharing.

As the nature will, to live eternally is an extracting dream in all the human history. Stem cell is the original of life and all cells come from stem cells. Germline stem cell (GSC) is the cell in the earliest of the cell stage. It is possible to inject the GSC into adult human body to get the eternal life. For a person, the most attracting will is to live longer, and the extreme dream is to live eternally. The number two important will for a person is to live happily. Humankind has a history longer than millions of years, and people never stopped the efforts to find a way to live eternally, no matter he/she was a beggar or an emper. There were many ways people considered as the way to keep life

PREOMICS EXHIBIT 1037 - IPR2024-01473
PREOMICS v. THE BRIGHAM & WOMEN'S HOSPITAL
Page 8 of 9

longer, even eternal, but people never got the eternal goal (Ma and Cherng, 2007).

References

1. Baidu. http://www.baidu.com. 2017.
2. Google. http://www.google.com. 2017.
3. Ma H, *Chen G.* Stem cell. The Journal of American Science 2005;1(2):90-92.
4. Ma H, Cherng S. *Eternal Life and Stem Cell.* Nature and Science. 2007;5(1):81-96.
5. Ma H, Cherng S. Nature of Life. Life Science Journal 2005;2(1):7-15.
6. Ma H, Yang Y. Turritopsis nutricula. Nature and Science 2010;8(2):15-20. http://www.sciencepub.net/nature/ns0802/03_1279_hongbao_turritopsis_ns0802_15_20.pdf.
7. Ma H. The Nature of Time and Space. Nature and science 2003;1(1):1-11. Nature and science 2007;5(1):81-96.
8. Marsland Press. http://www.sciencepub.net. 2017.
9. National Center for Biotechnology Information, U.S. National Library of Medicine. http://www.ncbi.nlm.nih.gov/pubmed. 2017.
10. Sarah Zielinski. Henrietta Lacks' 'Immortal' Cells. http://www.smithsonianmag.com/science-nature/henrietta-lacks-immortal-cells-6421299. 2010.
11. Why are HeLa cells "immortal"? https://www.quora.com/Why-are-HeLa-cells-immortal. 2016.
12. Wikipedia. HeLa. https://en.wikipedia.org/wiki/HeLa. 2017.
13. Wikipedia. http://en.wikipedia.org. 2017.
14. Wikipedia. The free encyclopedia. http://en.wikipedia.org. 2017.

9/25/2017

PREOMICS EXHIBIT 1037 - IPR2024-01473
PREOMICS v. THE BRIGHAM & WOMEN'S HOSPITAL
Page 9 of 9

View publication stats