Cancer and Immortality

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Abstract: Immortality is eternal life, being exempt from death, unending existence. Some modern species may possess biological immortality. Cancer is the general name for a group of more than 100 diseases. Although there are many kinds of cancer, all cancers start because abnormal cells grow out of control. Untreated cancers can cause serious illness and death. The body is made up of trillions of living cells. Normal body cells grow, divide, and die in an orderly fashion. During the early years of a person's life, normal cells divide faster to allow the person to grow. After the person becomes an adult, most cells divide only to replace worn-out or dying cells or to repair injuries. This article introduces recent research reports as references in the related studies. Cancer has a closed relationship to the life Immortality.

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Immortality is eternal life, being exempt from death, unending existence. Some modern species may possess biological immortality.

Certain scientists, futurists, and philosophers have theorized about the immortality of the human body, with some suggesting that human immortality may be achievable in the first few decades of the 21st century. Other advocates believe that life extension is a more achievable goal in the short term, with immortality awaiting further research breakthroughs. The absence of aging would provide humans with biological immortality, but not invulnerability to death by disease or physical trauma; although mind uploading could solve that issue if it proved possible. Whether the process of internal endoimmortality is delivered within the upcoming years depends chiefly on research in the former view and perhaps is an awaited goal in the latter case.

In religious contexts, immortality is often stated to be one of the promises of 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.

Cancer is the general name for a group of more than 100 diseases. Although there are many kinds of cancer, all cancers start because abnormal cells grow out of control. Cancers can cause serious illness and death. The body is made up of trillions of living cells. Normal body cells grow, divide, and die in an orderly fashion. During the early years of a person's life, normal cells divide faster to allow the person to grow. After the person becomes an adult, most cells divide only to replace worn-out or dying cells or to repair injuries.

Cell senescence is a permanent growth stop or slow. Cultured cancer cells including metastatic melanoma cells often appear immortal, that means proliferate indefinitely, while uncultured benign nevi often show senescence. Primary melanomas are typically precrisis, with immortalization/telomere maintenance as a late event. Even some cancer cells could be immortal, most cancer cells seem unable to multiply limitlessly and spread throughout the body.

Telomeres are the caps that protect the ends of chromosomes and they shorten every time a cell divides. In a telomere crisis, the tips become so short that the cell mistakes them for DNA breaks and tries to repair them, generating freak cells that die or become dormant.

Some senescence markers in cells are important, such as β-galactosidase, nuclear p16, and heterochromatic foci/aggregates.

Cell senescence is a major tumor suppressor mechanism and a target of familial melanoma genes, while conversely, immortality is widely considered a hallmark of cancer. However, it is unclear whether early cancers are immortal.

Normal mammalian somatic cells enter senescence following either extensive proliferation, activation of an oncogene, or cellular stresses including oxidative or DNA. Cells of various kinds of benign, static neoplasms in vivo show markers of senescence, for example, in melanocytic nevi, which generally carry activating v-*raf* murine sarcoma viral oncogene homolog B1 (*BRAF)* or neuroblastoma *RAS* viral oncogene homolog (*NRAS)* mutations. It is proposed that clonal proliferation initiated by an oncogene is normally limited by oncogene-induced

senescence, giving a benign lesion rather than a growing cancer.

Several signaling pathways can mediate cell senescence. Telomere shortening is strongly implicated in human replicative senescence: DNA-damage signaling from short telomeres activates p53, transcriptionally upregulating the cyclin-dependent kinase inhibitor (CDKI) p21. Replicative and oncogene-induced senescence also often involve another major tumor suppressor and CDKI, p16. p16 affects permanent cell arrest by inhibiting cyclin-dependent kinase 4 and thereby activating the retinoblastoma (RB) family of growth inhibitors.

p16 is encoded at the locus most commonly mutated in familial melanoma, *CDKN2A*, underlining its importance in melanoma. *CDKN2A* also encodes another protein, alternative reading frame, another effector of senescence, although not clearly so in human cells. Melanoma-associated mutations of p16 were confirmed to disable cell senescence in melanoma cells.

It is generally proposed that cellular immortalization is required for cancer development. However, this has not been proven for all types of cancer, especially early cancers. In the case of melanoma, many immortal cell lines have been derived from metastatic melanomas, but fewer from primary melanomas. Primary cutaneous melanocytic lesions can be classified into four stages: benign nevi or moles, dysplastic nevi, radial growth-phase (RGP) melanomas, which grow in the epidermis with micro- or no invasion, and vertical growth-phase (VGP) melanomas, which invade the deeper dermis and appear competent for metastasis.

The molecular requirements for immortalization specifically of human melanocytes have been established in recent years. As expected from its role in melanoma susceptibility, p16 appears important and defects in the p16/RB pathway in melanocytes lead to lifespan extension; however, the cells can then still become arrested, by a p53-dependent route. Human melanomas, while often retaining wild-type p53, may show downstream suppression of p53 signaling by various routes including TBX2 or DEK overexpression or LKB1/STK11 deficiency. However, disruption of both the RB and p53 pathways is still not sufficient for immortalization. It is a stage of continuing cell division balanced by extensive cell death, as the unprotected chromosome ends can be ligated to each other by the DNA repair machinery. Telomeric crisis has been described as a stage in the progression of human breast, pancreatic, colorectal, and other cancers. Escape from telomeric crisis, in culture or in cancer development, requires telomere maintenance, which permits immortality and which is usually achieved, either as a rare natural event (in cancers) or artificially, by upregulated expression of telomerase reverse transcriptase (TERT), the catalytic subunit of telomerase. Telomere maintenance combined with a defect in the p16/RB pathway appears necessary and sufficient for full immortalization of human

With one very special exception, every cell in your body is a prisoner to developmental decisions made long before birth, committed without choice to being a particular tissue — if muscle, every time the muscle cell divides, its descendents are muscle cells too. After about 50 divisions the tissue cells die. Only the cells whose descendents become gametes — eggs and sperm — escape this fate. Called embryonic stem cells, they are immortal, and able to form every kind of cell in your body. Last year scientists learned how these unusual cells escape death, and in the last few months they have learned how to culture them in the laboratory. This long-sought advance has at last given us an answer to the question of why we grow old.

As with many scientific advances, progress came when scientists learned to ask the right question. Dr. Leonard Hayflick, now of the University of California, San Francisco, has that honor. He discovered in 1961 that when cells are taken from the body and grown in tissue culture on a laboratory dish, there is a limit to how long the cell line lives — after about 50 divisions, the aging cell line dies. Called the Hayflick limit, this inability to survive past a certain number of cell divisions has puzzled developmental biologists for decades. What causes the cells, after so many successful divisions, to abruptly throw in the towel? How does a cell know its time is up?

Over the last 18 months we have learned the answers to these questions. The key breakthrough came when researchers succeeded in making cells violate the Hayflick limit — in essence, they learned how to make human body cells growing in tissue culture immortal. The secret to immortality proved to be a short tag of DNA stuck on the tips of the cell's chromosomes. Called a telomere, this segment of DNA plays a key role in cell division. The telomere provides a place for the cell's DNA-copying machinery to latch onto the chromosome when the time comes each generation for the chromosomal DNA to be copied into daughter chromosomes. However, every time the machinery attaches, the short bit of the telomere where the machinery sits down on the DNA is not itself copied, so the telomere gets a little shorter each time the cell divides. When the telomere reaches a minimal length after some 50 divisions, the cell can no longer replicate its DNA and lapses into senescence. So how were scientists able to make cells immortal? The secret to producing cell immortality lay in their realizing that all cells possess a gene, known as the telomerase gene, which can add

DNA back to the tip of telomeres, restoring them to their original youthful length. In almost all cells this gene is turned off early in development, rendered permanently inactive in an event that commits that cell to eventual sure death. This sad decision is a very necessary one, as it protects the adult human body from developing tumors whenever a cell's division controls are disabled. Only when this added protection against runaway growth is also lost, the switch stopping production of telomerase turned back "ON," can a cell proceed beyond a few divisions and become a cancer cell. Cancer cells are immortal because they produce telomerase.

In the human body, only two kinds of body cells are immortal, able to divide without limit. Cancer cells are one. The other kind of immortal cell is the embryonic stem cell. The cells derived from recently fertilized human eggs, before they implant in the uterus, are called embryonic stem cells and have the power to develop into all of the 210 different kinds of cells in the body. Most of them last only fleetingly as stem cells, soon turning into more specialized cells and loosing their telomerase activity. A few, however, are set aside, protected from the influences that trigger differentiation and shutting down of the telomerase gene. Called germ line cells, these embryonic stem cells have a fully functional telomerase gene and continue to divide, producing eggs and sperm that in their turn produce more stem cells in the next generation.

HeLa is a cell type in an immortal cell line used in scientific research. 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 remarkably durable and prolific which warrants its extensive use in scientific research.

The cells from Lacks' cancerous cervical tumor were taken without her knowledge or consent. Cell biologist George Otto Gey found that they could be kept alive, and was able to isolate one specific cell, multiply it, and develop a cell line. As was custom for Gey's lab assistant, she labeled the culture 'HeLa', the first two letters of the patient's first and last name; this became the name of the cell line.

These 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 (i.e. lack of senescence). These cells could be used for conducting a multitude of medical experiments—if the cells died, they could simply be discarded and the experiment attempted again on fresh cells from the culture. This represented an enormous boon to medical and biological research.

The stable growth of HeLa enabled a researcher at the University of Minnesota hospital to successfully grow polio virus, enabling the development of a vaccine, and by 1952, Jonas Salk developed a vaccine for polio using these 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 demand for the HeLa cells quickly grew in the nascent biomedical industry. Since the cells' first mass replications, they have been used by scientists in various types of investigations including disease research, gene mapping, and effects of toxic substances and radiation on humans. Additionally, HeLa cells have been used to test human sensitivity to tape, glue, cosmetics, and many other products.

Scientists have grown an estimated 20 tons of HeLa cells, and there are almost 11,000 patents involving these 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.

Constitutional (hereditary) genetic variation and somatic genetic alterations acquired during transformation to the neoplastic phenotype are both critical determinants of cancer outcome, and can ultimately have a significant effect on cancer survivorship. This article discusses the role of constitutional and somatic genetics in determining outcome and survivorship following a diagnosis of cancer using illustrative examples primarily from the hematologic malignancies (Allan, 2008).

Germline genetics, gender and hormonal-signaling pathways are all well described modifiers of cancer risk and progression. Although an improved understanding of how germline genetic variants interact with other cancer risk factors may allow better prevention and treatment of human cancer, measuring and quantifying these interactions is challenging. In other areas of research, Information Theory has been used to quantitatively describe similar multivariate interactions. We implemented a novel information-theoretic analysis to measure the joint effect of a high frequency germline genetic variant of the p53 tumor suppressor pathway (MDM2 SNP309 T/G) and gender on clinical cancer phenotypes. This analysis quantitatively describes synergistic interactions among gender, the MDM2 SNP309 locus, and the age of onset of tumorigenesis in p53 mutation carriers. These results offer a molecular and genetic basis for the observed sexual dimorphism of cancer risk in p53 mutation carriers and a model is proposed that suggests a novel cancer prevention strategy for p53 mutation carriers (Atwal, et al, 2008).

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