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Research Article

WHAT IS THE FATE OF DNA AFTER DEATH?

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A B S T R A C T

We might all live on after we die.Animal studies reveal that some genes work after 48 hrs after death.Hundreds of genes actually wake up after you stop breathing.Some of them are usevally active in developing fetus, while others have been linked to cancer. This could explain the high risk of cancer in recipients of liver transplants. The donar organs might have activated by cancer genes after death.We entered from stone age to clone age. Landing on moon is easier than entering inside the cell**.** DNA contains the genetic blue print of an individual. Preserving DNA gives an opportunity to capture the information and establish a connection that will last forever. DNA contains valuable information about our ancestral and family roots. When a person dies, it also vanishes. Now the DNA is preserved similar to that of blood bank.75 % of the genetic diseases can be known by DNA. It is easy for the doctor to know the treatment plans. The deoxyribonucleic acid (DNA) is a reservoir of information in a cell and flow of information including genetic information from DNA to subsequent molecules including ribonucleic acid (RNA) and protein is referred as the central dogma.The transfer of information from nucleic acid to a nucleicid or from nucleic acid to protein may be possible but the transfer from protein to a protein or from protein to nucleic acid is impossible.

INTRODUCTION

The process of programmed cell death, or apoptosis, is generally characterized by distinct morphological characteristics and energy-dependent biochemical mechanisms.

Apoptosis plays a role in causing and preventing some important medical processes. In humans, apoptosis plays a major role in preventing cancer by causing cells with damaged DNA to commit "suicide" before they can become cancerous. It also plays a role in the atrophy of muscles, where the body decides that it's no longer a good idea to spend calories on maintaining muscle cells if the cells are not being regularly used.

Apoptosis is considered a vital component of various processes including normal cell turnover, proper development and functioning of the immune system, hormone-dependent atrophy, embryonic development and chemical-induced cell death. Inappropriate apoptosis is a factor in many human conditions including neuro degenerative diseases, ischemic damage, autoimmune disorders and many types of cancer. (1)

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Apoptosis translates to the "falling off" of leaves from a tree Hippocrates used the term to mean "the falling off of the bones". Galen extended its meaning to "the dropping of the scabs".

Apoptosis is a process of programmed cell death that occurs in multi cellular organisms (2) Between 50 and 70 billion cells die each day due to apoptosis in the average human adult (3) For an average child between the ages of 8 and 14, approximately 20 to 30 billion cells die a day (4)

The initiation of apoptosis is tightly regulated by activation mechanisms, because once apoptosis has begun, it inevitably leads to the death of the cell (5,6)

Intrinsic pathway (also called the mitochondrial pathway) and the extrinsic pathway (7) The *intrinsic pathway* is activated by intracellular signals generated when cells are stressed and depends on the release of proteins from the inter membrane space of mitochondria (8) The *extrinsic pathway* is activated by extracellular ligands binding to cell-surface death receptors, which leads to the formation of the death-inducing signaling complex(DISC) (9)

The intrinsic (Bcl-2 or mitochondrial) pathway of apoptosis functions in response to various types of intra cellular stress including growth factor withdrawal, DNA damage, unfolding

stresses in the endoplasmic reticulum and death receptor stimulation. Following the reception of stress signals, pro apoptotic BCL-2 family proteins are activated and subsequently interact with and inactivate anti apoptotic BCL-2 proteins. This interaction leads to the destabilization of the mitochondrial membrane and release of apoptotic factors.

In the extrinsic pathway, signal molecules known as ligands, which are released by other cells, bind to transmembrane death receptors on the target cell to induce apoptosis. For example, the immune system's natural killer cells possess the Fas ligand (FasL) on their surface (10). The binding of the FasL to Fas receptors (a death receptor) on the target cell will trigger multiple receptors to aggregate together on the surface of the target cell. The aggregation of these receptors recruits an adaptor protein known as Fas-associated death domain protein (FADD) on the cytoplasmic side of the receptors Active caspase-8 can also cleave BID protein to tBID, which acts as a signal on the membrane of mitochondria to facilitate the release of cytochrome c in the intrinsic pathway (11).

Apoptosis is the process of programmed cell death (PCD) that may occur in multicellular organisms(12) It is also becoming clear that mitosis and apoptosis are toggled or linked in some way and that the balance achieved depends on signals received from appropriate growth or survival factors(13)

Our cells face many dangers, from chemicals, viruses, and ionizing radiation. If cells are damaged in sensitive places by these attackers, the effects can be disastrous, leading to cancers. Cancer can be correctly defined as a group of cells that have undergone unregulated growth, and will often form a mass or lump, but may be distributed diffusely [14]. Most of the cancers result as a consequence of genetic mutations, as such mutations having direct influence and quantity and quality of protein production for smooth cellular functioning with DNA repair.There are two major categories of mutated genes; these are "oncogenes and tumor suppressor genes". Oncogenes are deviation from the normal genes, having direct influence in cell growth. The mutation in oncogenes may result in direct and continuous stimulation of the pathways such as cell surface growth factor receptors, intracellular signal transduction pathways, transcription factors, secreted growth factors that control cellular growth and division.Tumor suppressor genes are normal genes that control cell cycle, cell division and programmed cell death or apoptosis. An important difference between oncogenes and tumor suppressor genes is that oncogenes result from the activation of protooncogenes and is liable to cause cancer, but tumor suppressor genes cause cancer when they are inactivated . Balance between oncogenes and tumor suppressor genes for healthy living. Tumor suppressor genes such as P53 gene, which codes of P53 tumor suppressor protein, plays a significant role in normal cell division and DNA repair; and are plays an important role in detecting impaired growth signals or DNA damage in cells.(15)

In this scenario the P53 has become the focus of intensive cancer based research in laboratories around the world. Hence the P53 is considered as a critical tumor suppressor gene. There are many tumor suppressor genes that are associated with well defined clinical syndromes, with many more tumor suppressor genes still remains to be discovered. In this review article we have mainly focused in P53 and its interaction with MDM2, for future prospect to develop substances able to inhibit P53-MDM2 interaction, potentially as anti-cancer agents. P53 tumor suppressor genes P53 gene is located in chromosome 17 and was first identified as a transformation-related cellular protein which accumulates in the nuclei of cancer cells and binds tightly to the simian virus 40 (SV40) large T antigens [16]. The third stable domain studied thus far is the trans-activation domain; found near the end of each arm that activates the DNA-reading machinery [17]. Normal function of the P53 gene The P53 gene codes for the protein P53, which acts as a tumor suppressor, regulating cell division by keeping cells from growing and dividing too fast or in an uncontrolled way. Tumor protein P53 is found in the nucleus of the cells, where it binds directly to DNA. P53 determines the fate of the cell after DNA damage by inciting stimulus. So it plays a major role in repair or destruction of damaged DNA, preventing the formation of tumors in the future. Because tumor protein P53 is essential for regulating cell division and preventing tumor formation, it has been nicknamed as the "guardian of the genome" [18,19]. P53 as a positive cell regulator P53 has been demonstrated to have positive implication in cell growth and proliferation. In contrast cell growth with serum stimulation; there were high level of P53 mRNA with higher the rate of P53 protein synthesis increased markedly, mostly in the G1/S boundary just prior to initiation of DNA replication [20]. The experiments performed with normal resting T lymphocytes and normal diploid fibroblasts showed that P53 expression is always concomitant with induction of cell growth [21,22]. The level of P53 mRNA and protein is somewhat constant throughout the cell cycle when the cells are growing exponentially [23].. This inhibition was effective only when microinjection was performed at or around the time of growth stimulation, suggesting that P53 is critical for G0/G1 transition [24]. Antisense experiment which showed the inhibition of P53 expression prevented cell proliferation in both non-transformed NIH3T3 cells and transformed cells is also consistent with this result leading to the notion that wild type P53 is a positive regulator of cell proliferation [25]. Cancers - associated with the P53 gene Mutations in the TP53genes are the most common implicated factors responsible for about 50% of all the human cancers. TP53 mutations have been identified in different brain tumors, colorectal carcinoma, osteosarcoma, rhabdomyosarcoma and adrenocortical tumors. Most of these P53 mutations alter the single protein in tumor protein P53, leading to point mutation, resulting in formation of impaired proteins unable to bind DNA effectively. This impaired protein accumulates in the nucleus and halts the progression for self destruction in response to DNA damage.The damaged cells continue to grow and divide in an unregulated way, which can lead to cancerous tumors [26]. There are many queries to be uncovered how these genes play a role against cancers and their effective understanding for our benefit [27].. Most of these MDM2genes are increased by P53, this lead to a regulation loop that will keep P53 level very low in normal cells [28,29]. After genotoxic or non-genotoxic stresses, activation of P53 is a two-step process. First P53 protein level is increased through the inhibition of its interaction with MDM2 and the other negative regulators. Second, a series of modulator (kinases, acetylases) will activate P53 transcriptional activity. Downstream signaling includes a large series of genes that are activated by the trans-activating properties of P53.

Major Advances and Discoveries

German scientists Karl Vogats was first to describe the principle of apoptosis in 1842. In 1885, anatomist Walther Flemming delivered a more precise description of the process of programmed cell death. However, it was not until 1965 that the topic was resurrected. While studying tissues using electron microscopy, John Ross at University of Queensland was able to distinguish apoptosis from traumatic cell death.[6] Following the publication of a paper describing the phenomenon, Kerr was invited to join Alastair R Cure, as well as Andrew Wille, who was Currie's graduate student,[7] at University of Aberdeen. In 1972, the trio published a seminal article in the British Journal.[8] Kerr had initially used the term programmed cell necrosis, but in the article, the process of natural cell death was called *apoptosis*. Kerr, Wyllie and Currie credited James Cormack, a professor of Greek language at University of Aberdeen, with suggesting the term apoptosis. Kerr received the Paul ehtlich Prize on March 14, 2000, for his description of apoptosis. He shared the prize with Boston biologist H.Robert For many years, neither "apoptosis" nor "programmed cell death" was a highly cited term. Two discoveries brought cell death from obscurity to a major field of research: identification of components of the cell death control and effector mechanisms, and linkage of abnormalities in cell death to human disease, in particular cancer.

The 2002 Nobel prize in Medicine was awarded to Sidney Brenner, Horvitz and John E.Sulton for their work identifying genes that control apoptosis. The genes were identified by studies in the nematode C.elegans and homologues of these genes function in humans to regulate apoptosis.

In Greek, apoptosis translates to the "falling off" of leaves from a tree.[10] Cormack, professor of Greek language, reintroduced the term for medical use as it had a medical meaning for the Greeks over two thousand years before.Hippocrates used the term to mean "the falling off of the bones" Gallen" extended its meaning to "the dropping of the scabs". Cormack was no doubt aware of this usage when he suggested the name.

History and Mechanism

Ancient Egyptian mummies preserve many details of the deceased: facial features, signs of illness, even tattoos. But not, it seemed, DNA. After trying repeatedly to extract it, many scientists were convinced that the hot desert climate and, perhaps, the chemicals used in mummification destroyed any genetic material long ago.

Where as the mummies' soft tissue contained almost no DNA, the bones and teeth were chock full of genetic material. Ninety of the mummies yielded DNA once housed in mitochondria, the power plants of cells. Mitochondria carry only a few genes, but they are so plentiful that it's often easier to find their DNA than the single full human genome in a cell's nucleus. Still, because mitochondrial DNA is passed down from mother to child, it leaves out the story of the father's DNA. The nuclear genome, which contains DNA from both parents, is far more informative. (30)

Significance Gap in Research

The deoxyribonucleic acid (DNA) is a reservoir of information in a cell and flow of information including genetic information from DNA to subsequent molecules including ribonucleic acid (RNA) and protein is referred as the central dogma.(31).The transfer of information from nucleic acid to a nucleic acid or from nucleic acid to protein may be possible but the transfer from protein to a protein or from protein to nucleic acid is impossible. There is a gap in our understanding of cause or consequence between epigenetic gene transcription. Translational studies are needed to investigate epigenetic patterns in clinical material and from clinical trials to identify and validate prognostic markers. The extent to which epigenetic markers can be incorporated into risk models alongside genetic and life style factors is not yet known. Understanding how cancer risk factors impact on the epigenome and whether this provides a mechanism for increased risk associated with those exposures is poorly understood.

A genetic disorder is a disease caused in whole or in part by a change in the DNA sequence away from the normal sequence. Genetic disorders can be caused by a mutation in one gene (monogenic disorder), by mutations in multiple genes (multifactorial inheritance disorder), by a combination of gene mutations and environmental factors, or by damage to chromosomes (changes in the number or structure of entire chromosomes, the structures that carry genes).

Current Debate

DNA evidence may be more accurate and reliable than other forensic science, it still fundamentally probabilistic in nature and is prone to uncertainties at all stages of its production. Yet, because of the certainty attached to DNA evidence in public discourse, it can be used as a lever with which to challenge law's claims to truth-making authority, and to undermine public trust in the death penalty. A few abolitionists and other scholars have expressed misgivings about the abolitionist embrace of the innocence argument. We push this concern further, suggesting that both abolitionists and death penalty reformers, who seek to promote a "scientific" death penalty centered on DNA evidence, draw upon a mythologized notion of "science" as a producer of epistemic certainty.(32)

Ideas Where Research Go Next

The new study, led by Johannes Krause, a geneticist at the Max Planck Institute for the Science of Human History in Jena, Germany, used next-generation sequencing methods to read stretches of any DNA present in a sample and fish out those that resembled human DNA. The complete reads allowed the team to spot tell-tale damage patterns associated only with ancient DNA. That makes the new analysis much more reliable, says Hannes Schroeder, an ancient DNA researcher at the University of Copenhagen. "It succeeds where previous studies on Egyptian mummies have failed or fallen short.(30). DNA contains the genetic blue print of an individual. Preserving DNA gives an opportunity to capture the information and establish a connection that will last forever. DNA contains valuable information about our ancestral and family roots. When a person dies, it also vanishes. Now the DNA is preserved similar to that of blood bank.75 % of the genetic diseases can be known by DNA.It is easy for the doctor to know the treatment plans.

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