Origins of Apoptosis: Selfish Genes or Intelligent Design?

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Abstract

Apoptosis is a complex biochemical mechanism whereby a specific cell destroys itself under certain conditions, without injury to the cells around it. A literature review reveals that neo-Darwinists have been unable to explain how the mechanism for apoptosis could have evolved in a step-by-step process. The mechanism of apoptosis regulates cell life for the advantage of the organism as a whole and not for the mere advantage to the genes, as Dawkins proposed. Apoptosis supports the concepts of irreducible complexity and intelligent design.

Introduction

Cells can be eliminated by two means: necrosis (the death of a cell caused by injury or disease) and apoptosis (programmed cell death). Apoptosis is a critically important mechanism used by all multicellular organisms to eliminate unneeded or harmful cells including cancerous and precancerous cells (Shi, 2002; Steller, 1995; Huang and Strasser, 2000 p. 839; Weinrauch and Zychlinsky, 1999). Apoptosis also plays a critical role in normal development, in physiological balance (homeostasis) and in cell turnover (Elmore, 2007; Ashkenazi and Dixit, 1998).

From the embryo stage forward, cell division and apoptosis must be finely balanced and synchronized to maintain health and life. For example, after a sunburn, apoptosis destroys damaged cells that could become cancerous, allowing them to be replaced. Apoptosis results in cellular shrinkage, mitochondrial breakdown, release of cytochrome C, development of blebs on the cell surface, and recycling of cell components.

Definitions

Irreducible complexity is "A single system composed of several interacting parts that contribute to the basic function of the system, where the removal of any one of the parts causes the system to effectively cease functioning" (Behe, 1996, p. 9). An example of irreducible complexity is the fact that the chemical element carbon *must* have six protons. If one proton is removed, carbon no longer exists, but rather boron results. *Intelligent design* involves a set of criteria used to evaluate the physical world to determine if intelligence is responsible for some event. A common example in forensics is that it must be determined if a dead body died as the result of disease, accident, or intelligent action—specifically in legal terms suicide or homicide.

Steps Involved in Apoptosis

Three pathways triggering apoptosis are now known. The first is the *extrinsic* or *death receptor pathway* triggered by a signal from outside of the cell (a death ligand that binds to a death receptor). The second is the *intrinsic pathway* triggered by a signal from within the cell caused by factors including radiation, toxins, and hypoxia. The last is the *perforin pathway* caused by cytotoxic T cells. These three pathways trigger the *execution pathway* or the pathway actually causing the cell's destruction (Elmore, 2007).

A cell undergoing apoptosis always displays a certain set of characteristic traits, including cell shrinkage and pyknosis, the contraction of the cell nucleus into a compact mass that effectively ac-

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cepts stain (Elmore, 2007). The actual Apoptosis begins when proteases known as initiator caspases are activated inside a cell as a result of proteolytic processing that causes other proteases to digest specific cell components (Hengartner, 1998). Proteases called *caspases* function in apoptosis by directing complex specialized molecules to lyse the cell's chromatin, destroy its nucleoskeleton, destroy the enzymes that replicate and repair DNA, and activate CAD. CAD refers to the three enzymes, **c**arbamoyl phosphate synthase, **a**spartate transcarbamylase, and **d**ihydroorotase, that cut DNA up into small, roughly equal-sized portions of 200 base pairs (Rupinder et al., 2007).

Caspases also activate enzymes that digest the cytoskeleton, destroy the cell's ability to adhere to other cells, and eventually break the cell into small fragments (Barinaga, 1998). They even cause a phospholipid to move from the apoptotic cell membrane's inner surface to its outer surface to attract phagocytes. The fact that "all known caspases share a similar conformation at the substrate-binding grove" indicates irreducible complexity because a specific complex design is required for the system to function and no complexity gradations in their design are known in the living world (Shi, 2002, p. 460). All known organisms where apoptosis occurs require this caspase system to function properly (Rupinder et al., 2007).

A second group of proteases involved in apoptosis includes the protein-cleavage enzyme called "Interleukin-I converting enzyme-like proteases," abbreviated ICE-like proteases. The ICE-like proteases help to destroy the cell by digesting essential proteins and certain structural components in the cell's genetic material to prevent the cell from repairing itself (Martin et al., 1995). This double assault on the cell ensures both its death and its safe destruction without adversely affecting other cells.

Another step in apoptosis involves the cell sending attractants such as phosphatidyl serine (called "eat me" signals) from the inner cell membrane leaflet to the outer cell membrane leaflet in order to attract phagocytes. Normal cell to cell interactions, such as the ability to adhere to other cells, are also rapidly lost in cells undergoing apoptosis. The cell then gradually becomes more spherical, and its cell membrane undulates, forming protrusions or bulges called *blebs* (see Figure 1). The cell soon fragments and its membrane remnants encapsulate the cell fragments, which are at this stage known as *apoptotic bodies* (Veggeberg, 1995). This reduces the amount of leakage of the apoptotic cell's toxins or noxious contents (Elmore, 2007).

The cell fragments display antigens that cause them to be ingested by scavenger macrophages that reside in all tissues and by other local scavenger cells. The cell fragments are then broken down by lysosomal organelles and the cell's

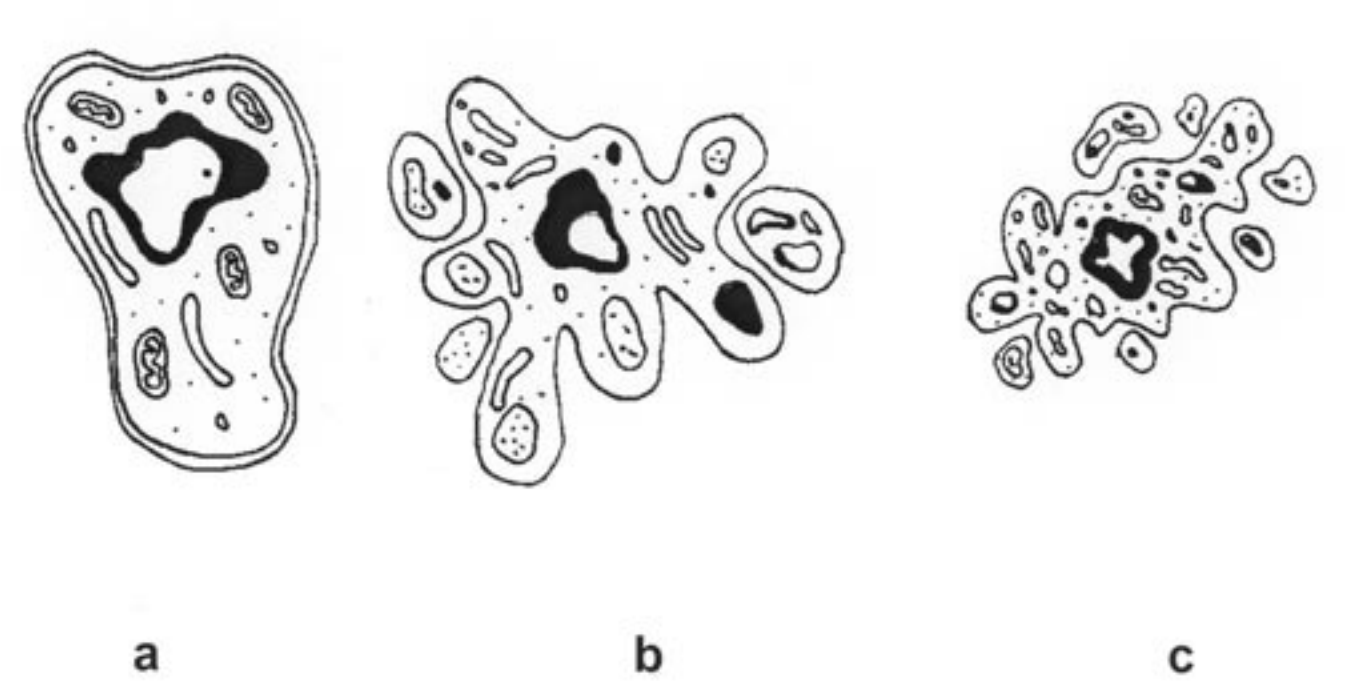

Figure 1. Steps in apoptosis. a. The cell's chromatin, a mixture of chromosomes and proteins, begins to condense. b. Here the cell membrane loses its structural integrity. Protuberances called "blebs" appear on the surface surrounding the cell. c. The cell shrinks and its DNA becomes fragmented. The cell parts are then recycled. Adapted from Medina (1996, p 37).

nutrients are recycled without triggering the inflammatory response typical of necrosis. The entire apoptotic process takes only about an hour, which is one reason why it went undiscovered by biologists until recently (Raff, 1996).

History of Apoptosis Research

The existence of apoptosis has been theorized since the dawn of cell theory but was described only recently. It once was assumed that cell death invariably resulted in negative consequences in the body, but by the 1950s, research had demonstrated that certain cells were systematically eliminated as a *normal* part of development. Examples include the tadpole's tail, the webbing between the fingers in human embryos, and the change in breast tissue after a mother stops breast feeding (Duke et al., 1996). Apoptosis also organizes the brain by eliminating neurons that do not make proper connections to other nerve cells. Apoptosis even causes the loss of large groups of cells, such as the dropping-off of flower petals. This latter role for apoptosis is the source of the term now used to label the entire process (apoptosis is Greek for *falling off*). The term apoptosis was first used only in 1972 (Elmore, 2007).

A breakthrough paper published in 1972 outlined the first evidence for apoptosis in precancerous cells (Kerr, Wyllie, and Currie, 1972). Unfortunately, this paper remained largely unnoticed until the early 1980s. The work of Robert Horvitz on *Caenorhabditis elegans* (an oft-studied nematode) was also critically important in understanding apoptosis (Veggeberg, 1995).

The Significance of Apoptosis

Apoptosis occurs at the expense of an individual cell and its genome, but benefits the entire organism. All eukaryotic cells contain all of the genes needed to self-destruct and will do so unless these genes are damaged, as with cancer cells, or unless the cell receives signals from other cells to block apoptosis (Raff, 1996). Maintaining a strict balance between cell division and cell death benefits the organism in numerous ways. Living on the edge of cell suicide ensures that all damaged cells are rapidly destroyed and that their corpses are expediently and effectively engulfed by neighboring cells (Adams and Cory, 1998; Wu, 1996).

Apoptosis is especially important in understanding many complex cellular processes, such as how insulin-like growth factor I and other proteins can control and eliminate select cells. Knowledge of apoptosis is required to understand how *p53* and other critically important tumor suppressor genes function (Mercer et al., 2007). These tumor suppressor genes regulate the repair of damaged DNA, but if the damage is too extensive the genes cause apoptosis to destroy the cell.

Problems Associated with Misregulation of Apoptosis

Aberrant regulation of apoptosis can allow cells with mutations (such as cancerous cells) to continue to divide and consequently such aberrant regulation contributes to cancer progression and other diseases. Misregulation of apoptosis can cause the destruction of cells that are not damaged, as during and after a heart attack. If damaged cells that could be repaired are destroyed, unnecessary heart damage results.

Misregulation of apoptosis can contribute to other disorders, such as tumors and certain autoimmune diseases like rheumatoid arthritis (Rupinder et al., 2007; Barinaga, 1998). Even Alzheimer's as well as Parkinson's and Huntington's diseases are all believed to involve a condition that causes specific neuron to commit suicide prematurely (Fesik, 2000). It is also believed that apoptosis is used to fine-tune the immune system by eliminating T-cells that attack the person's own cells, a step necessary to develop normal autoimmunity.

Necrosis and Apoptosis Compared

Accidental cell destruction, known as *necrosis*, is normally undesirable. But apoptosis, when properly regulated, is beneficial. The word *necrotic* comes from a Greek word meaning *to kill*. Cell death by necrosis occurs when a cell is severely injured by physical or chemical means, such as by oxygen deprivation. In necrosis, cells usually swell and lyse, releasing cytoplasmic material that triggers an inflammatory response in the intercellular matrix (Elmore, 2007). A major contrast between necrosis and apoptosis is that, in necrotic death the cell is a passive victim, but in apoptosis the cell is an active participant, even expending its own energy to achieve its own demise (Zamzami and Kroemer, 2001). Whether a cell dies by necrosis or apoptosis depends partly on factors including the cell death signal specifics, the physiological environment, the tissue, and the stage of the cell development (Elmore, 2007, p. 496).

Mitochondria play a critical and central role in mediating the intrinsic apoptosis pathway (Hengartner, 1998a). In necrotic death, the mitochondria and other cell organelles are often the first to swell and rupture, followed by the lysis of the entire cell. In apoptosis, instead of the cell *swelling*, internal mechanisms such as the action of caspases, cause the cell to *shrink*. As the apoptosized cell shrinks, it pulls away from its neighboring cells. As a result, the apoptotic cell normally does not trigger an inflammatory response. The nucleus also shrinks dramatically in apoptosis, and the chromatin condenses into distinct blobs that then migrate to the nuclear envelope (Duke et al., 1996, p. 80).

Exceptions to the usual elimination of cells by apoptosis involve a few cell types, such as those making up the eye lens. In an adult, the eye lens consists primarily of cell carcasses. The lens forms by cells slowly dying, and during this time most of the cytoplasm is gradually replaced by a crystalline protein (Duke et al., 1996). Other examples include skin cells which, as they mature, replace their contents with keratin protein, acquire a water-resistant coating, die, and are eventually sloughed off to be replaced by the cells moving up from below.

Apoptosis of T-Lymphocytes

The specifics of apoptosis also vary according to the cell type. More is known about apoptosis of T-lymphocytes than most other cell types. T-cells arise from bone marrow precursors, migrate to the thymus as thymocytes, and then develop into specialized T-cells that display receptor molecules that enable mature T-cells to detect specific antigens (McColl et al., 2007; Gregory, 1995). Thymocytes that either fail to produce functional receptors, or produce receptors that respond to self-cells, are also destroyed by apoptosis. Specifically, the thymocytes that are destroyed are those that bind too strongly to the molecules displayed in the thymus, which means that they may target healthy tissue later, causing an autoimmune disease (Golstein et al., 1991). Defective apoptosis may allow some of these auto-reactive cells to survive, resulting in malfunctioning of the immune system (Fesik, 2000). The best examples are the various autoimmune diseases.

Death Receptors

Apoptosis is triggered either by controlled deprivation of certain cell survival factors, or by a mechanism involving a so-called death receptor such as Fas, Apo 1, CD95 and many other protein death receptors. These protein receptors all belong to the tumor necrosis factor (TNF) gene superfamily, which are collectively called death ligands. Some growth receptors, such as the Nerve Growth Factor (NGF) receptor, also contain a death domain to help regulate growth and repair (Ashkenazi and Dixit, 1998). The ligands that bind to these receptors all activate apoptosis and, thus far, all appear to be structurally similar. As is true of many proteins used in apoptosis, they do not manifest a graduation from simple to complex as expected by neo-Darwinism.

Factors Controlling Apoptosis

Cell death can be triggered by external or internal chemical cell messages, growth, survival factors, or even conflicting signals that regulate cell division (Fesik, 2000). Cells that become infected by viruses often trigger apoptosis. Apoptosis can be triggered by a number of other mechanisms, including the *p*53 and other tumor-suppressor genes. Cells with DNA damaged by mutagens trigger production of p53 protein, which then activates a set of steps that may include apoptosis, thereby leading to the destruction of the cell carrying the mutation. These many mechanisms that function to repair (or to destroy) cells with mutations is a major problem for neo-Darwinism. If repair worked perfectly, evolution could not occur. Without repair, life as we know it could not exist (Elmore, 2007).

Specific signals known to trigger apoptosis vary according to the cell type and other factors that result in selective elimination of specific cells (Huang and Strasser, 2000). Apoptosis can even be triggered simply by time. Keratinocytes—a type of skin cell—undergo senescence via apoptosis about 21 days after they begin to migrate outward toward the skin surface.

Cell sensitivity and susceptibility to apoptosis vary according to several factors. A set of protein molecules tightly regulate apoptosis in complex ways; some facilitate promotion, while others result in inhibition (Korsmeyer, 1995). The protein family called Bcl-2 inhibits apoptosis, while another family of related proteins, including Bad, Bak, Bok, Bik, and Bid proteins, all promote apoptosis (see Figure 2). A balance of promotion and inhibition factors is required to ensure that apoptosis is triggered only when needed and is blocked when not needed (Zamzami and Kroemer, 2001).

Apoptosis Proteins

The many functions of the proteins involved in apoptosis are now being actively investigated, and more are discovered each year. Lewin (1997, p. 1128) noted that the functions of one of the most studied apoptosis regulator families, Bcl-2, are still "mysterious" but most regulate the signals that lead to caspase activation (Huang and Strasser, 2000). The Bcl-2 family of proteins includes both pro- and anti-apoptotic molecules that play a pivotal role in determining if a cell will live or die (Gross et al., 1999). Bcl-2 has a C-terminal anchor that is also found not only on outer nuclear but also on mitochondrial and endoplasmic reticulum membranes—indicating that it likely controls a wide variety of cell functions (Gross et al., 1999).

Cell death can be blocked by the production of high levels of apoptosis-inhibiting Bcl-2 protein (Hartwell and Kastan, 1994; Hartwell and Weinert, 1989). In lymphocytes, the *bcl-2* gene blocks apoptosis, while the *bax* gene promotes it. Normally Bcl-2 and Bax protein are produced in nearly equal amounts in the cell, eventually binding together to form heterodimers, negating their effects (Veggeberg, 1995). Lack of balance between the two can cause major problems: too much Bcl-2 protein may contribute to cancer and too much Bax protein results in premature cell death (Adams and Cory, 1998).

Certain normal cells, which would cause devastating effects if they were lost, such as heart cells, produce relatively

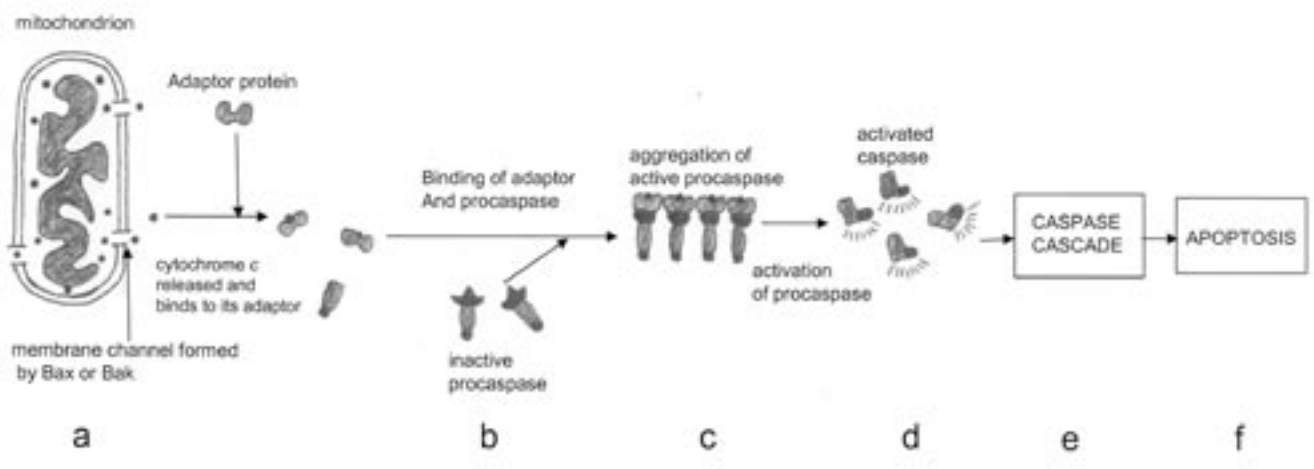

Figure 2. Apoptosis as regulated by the Bcl-2 family of intracellular proteins. (a) The death-promoting Bcl family of proteins, including Bak and Bax, form channels in the outer mitochondrial membrane. (b) The cell releases cytochrome C into the cytosol which then binds to an adaptor protein. (c) The adaptor protein then promotes both the aggregation and the activation of procapase. (d) Once activated, the caspase enzyme triggers a cascade (e) that leads to, (f) Apoptosis. Adapted from Alberts (2004, p. 628).

high levels of Bcl-2 protein. They are thus less likely to be destroyed by apoptosis and are more likely to be repaired (Mercer et al., 2007). If they become cancerous, these cells may give rise to aggressive tumors. Melanocyte cells produce the pigment melanin that darkens the epidermis, protecting the dermis from ultraviolet radiation damage. If melanocytes perished too easily, the loss of protection function that results causes other cells to be at a much greater risk of sustaining UV damage. But melanocytes manufacture large amounts of Bcl-2, and as a result, they normally undergo apoptosis only in extreme cases. Consequently, when melanocytes become cancerous, the cancer is not destroyed by apoptosis because of this factor, and hence melanoma is often lethal in a short time.

Cells (such as heart muscle cells) that are not prone to UV damage produce very small amounts of apoptosis-inhibiting Bcl-2 protein. Therefore, they tend to undergo apoptotic destruction quite readily. This system normally protects these cells against cancer, but lack of proper balance can also work against the body's best interest (Mercer et al., 2007).

Apoptosis and Viral Infections

Apoptosis likewise functions during viral infections in several ways. In order to reproduce, the virus must shut down the cell's ability to manufacture all proteins *except* those necessary to produce more viruses. The host's own protein synthesis is thus blocked, which can trigger apoptosis, killing both the cell and the virus (Fesik, 2000). This normally protects the cell from a wide variety of viruses.

To prevent this, the Epstein-Barr virus, which causes mononucleosis, and certain other viruses, possess apoptosis-suppressing genes that code for a pseudo Bcl-2 protein that is structurally similar to the Bcl-2 protein. It can even function as normal Bcl-2 protein, inhibiting apoptosis (Williams and Smith, 1993). In some cases, the Epstein-Barr virus can cause the cell to increase its production of Bcl-2, which blocks apoptosis long enough to allow the virus to reproduce effectively.

Apoptosis and Cancer

Cancer is the loss of normal control over cell division, differentiation, and other cell functions. It is caused by damage to the cell's DNA. For cancer to develop, the apoptosis mechanism must be disrupted or delayed long enough to allow some cells to accumulate enough mutations so that they are able to divide uncontrollably and, eventually metastasize (Fesik, 2000). The result is the production of cells that possess genetic mutations, and therefore function abnormally. These cancer cells have not sustained enough damage to cause them to die. In cancer cells, the genetic damage usually leads to an inability to induce apoptosis because the gene that codes either for the p53 protein, or some other tumor suppressor gene, is mutated or inactivated (Wang et al., 1995). Cancer cells may then become immune to normal apoptosis triggers.

Knowledge of the relationship between apoptosis and cancer can facilitate our exploitation of apoptotic mechanisms to diagnose precancerous conditions. It may also aid in determin-

ing the location of the cancer. The best example is follicular lymphoma, caused by a translocation of a *bcl-2* gene from chromosome 14 to 18 confers immortality on immune system B-cells, which can then accumulate to dangerous levels similar to leukemia.

Damage resulting from oxygen free radicals is a major cause of mutation that can in turn lead to cancer, aging, cataracts, atherosclerosis and other diseases. Oxygen free-radicals can also trigger apoptosis if the damage is not sufficient to destroy the cell by necrosis. A diet high in free radical neutralizers, such as vitamins A, C, E and selenium, can reduce free-radical damage.

Use of Apoptosis to Treat Cancer

Programmed cell death is affected by many of the same genes that control the cell division cycle (Maddika et al., 2007). A functional approach to the study of programmed cell death has involved viruses that are inactivated as pathogens by removing their disease-causing genes. Genes that function to fight disease are then spliced into the virus genome. The virus then is able to splice its new anti-virus genes into the DNA genome of the cells that it infects.

An example of how this approach is used to kill cancer cells involves injecting tumors with modified herpes viruses-containing genes that trigger apoptosis. Virus genes that can be inserted into the cell's genome include the "suicide genes," causing these cells to be highly susceptible to drugs, such as ganciclovir, which is used to treat herpes (Hartwell and Kastan, 1994). This approach infects the cells with a virus that gives them a pseudo-disease. Then drugs that are effective in killing "pseudo-diseased" cells are utilized to kill the infected cells. Treated subjects are also injected with a stimulant that is used to intensify the effect of the "suicide gene." A problem yet to be overcome is that the modified herpes virus still triggers the immune system, which then attacks the modified virus and interferes with the effect of the suicide gene. It is necessary to develop techniques to determine how virus genes can remain hidden, or how the immune system can be prevented from detecting and destroying these viruses. Viruses can also be used to taxi working genes into a cell to replace or "fix" damaged genes that lead to cancer.

Implications of Apoptosis for Intelligent Design

Only a small amount of the knowledge about the biological world known today was known in the 1800s when William Paley penned his argument from design seen in a pocket watch. What has been learned since then has eloquently supported Paley's thesis that design is strong evidence for a Designer. The level of the complexity in the cell is now known to exceed the level of complexity existing above the cellular level. Apoptosis is only one of many thousands of complex cellular systems that are now being researched. I did a computer search of over 15 million records from two databases and uncovered almost 70,000 articles on apoptosis. But only four of these 70,000 were remotely relevant to the evolution of apoptosis. None of these contained any empirical evidence that would contradict Behe's (1996) or Paley's conclusions (Blackstone and Green, 1999; Wiens et al., 2000; Aravinch et al., 1999).

One of the three articles that mentioned evolution was a highly speculative discussion of the role of mitochondrial cytochrome C in apoptosis (Blackstone and Green, 1999). The authors speculated that apoptosis in more complex animals may be a vestige of evolutionary conflicts between the supposed endosymbiosis of the mitochondrial organelle and its cellular host. But endosymbiosis, the belief that organelles in metazoan cells arose by ancestral cells capturing microbes, is itself an idea that suffers from several major problems (Bergman, 1998).

In another article, Wiens et al. (2000) evaluated sequence comparisons of certain organic molecules involved in apoptosis, such as the Bcl-2 superfamily. They found a high similarity between certain metazoan organisms and vertebrates. A third author tried to explain how neo-Darwinism can account for two opposite solutions to the problem of virus survival. In some cases, viruses inhibit apoptosis, and in others, viruses can stimulate apoptosis (Krakauer and Payne, 1997). In none of these articles was a substantial case made for the macroevolutionary origin of apoptosis.

The last article located (Kroemer, 1997) was the first major attempt to explain the evolution of apoptosis. Kroemer used endosymbiosis theory in an attempt to explain how apoptosis could have evolved. His discussion effectively illustrates the difficulties in the evolution of apoptosis. He also attempts to speculate on the evolutionary relationship of necrosis to apoptosis but only serves to accentuation the many differences between the two systems. With few exceptions (such as blastomeres and eye lens cells), all cells in multicellular animals are designed to undergo apoptosis unless blocked by signals from other cells (Raff, 1996). This fact is used as evidence that it evolved very early in unicellar organs. A problem with all evolution scenarios is that apoptosis would benefit only multicellular organisms because it would end the gene line of a unicellular creature.

As far as is known, apoptosis functions in very similar ways in all life forms, and no evidence exists for the origin of apoptosis by evolution. Although the system varies somewhat in different life forms, a life form either has a complete, complex, functioning apoptosis system or lacks it entirely. Research on the apoptotic molecular machinery has shown that all protein domain architectures are based on the same "highly conserved" domains. This term "highly

conserved" simply means that the DNA code used to produce protein is very similar in both so called "primitive" and "advanced" life forms (Aravind et al., 2001)—a fact that strongly supports the conclusion that these basic domains were designed. In Darwinian terms, the apoptosis mechanism is "evolutionarily conserved" (Shi, 2002, p.459) meaning that a similar system is found throughout all life forms as would be expected if they were all created.

Apoptosis also supports the irreducibly complex supposition that postulates a certain level of complexity must exist for the system to function at all (Elmore, 2007). Because the process of apoptosis is similar in all organisms, significant similarity would be expected to exist between human apoptosis genes and those of the so-called "primitive" or "simple" animals. Proteins that have similar functions would be expected to have very similar designs in all organisms from worms to humans, and this is what is found. The apoptosis system is one more example of a detailed set of irreducibly complex biochemical mechanisms that have no Darwinistic explanation (Behe, 1996).

All of the estimated 200,000 kinds of proteins in humans must appropriately interact with each other so that each one can carry out its assigned function, while not interfering with the function of other proteins or cellular processes. If a single protein is altered, it could have adverse consequences on the entire cell. If the change renders the needed protein non-functional, a cell function will be prevented, and that would likely result in an altered protein, which would interfere with the function of other structures (Zubay et al., 1995; Yockey, 1992; Branden and Tooze, 1999). This chain of events is especially true for systems apparently designed to destroy a cell, such as apoptosis.

The discovery of apoptosis also argues against neo-Darwinism because this mechanism is lethal to the cell if all the many checks and balances are not in place as a complete set. The enzymes and mechanisms that apoptosis use to destroy the cell, if not tightly controlled, can easily malfunction and damage or kill normal healthy cells, as sometimes does happen. Therefore, it is difficult to envision a Darwinian mechanism that enables mutations to develop the apoptosis system, yet keeps the system properly controlled and functional so as not to consistently destroy the very populations that apoptosis is supposedly evolving to benefit. As with the evolution of DNA repair mechanisms (Bergman, 2005), the activity of apoptosis would be antagonistic to the same evolutionary mechanism that supposedly constructed it.

Apoptosis and the "Selfish-Gene Hypothesis"

Apoptosis may be one evidence against the selfish-gene hypothesis, which postulates that the gene's ultimate purpose is only to perpetuate itself. In this view, plant and animal bodies are only survival machines "created by our genes," and the "predominant quality to be expected in a successful gene is ruthless selfishness" (Dawkins, 1976, p. 2). This ruthless selfishness of genes means that they "care" only about their own propagation, and ultimately use the whole body for their one goal. In Wilson's words: "The organism is only DNA's way of making more DNA" (1975, p. 3). More than any other contemporary scientist, Dawkins has popularized the idea that all living things are mere vehicles for genes, whose sole biological purpose is the propagation of their own DNA. Its basic thesis is that genes

> swarm in huge colonies…safe inside gigantic lumbering robots, sealed off from the outside world, manipulating it by remote control. They are in you and me; they created us body and mind; and their preservation is the ultimate rationale for our existence…we [the phenotypes or individual organism] are their survival machines (Dawkins, as quoted in Milner, 1990, p. 402).

This gene selectionism thesis has been so widely accepted that it is "frequently referred to simply as 'modern Darwinism'" (Johnson, 2000, p. 106). Dawkins teaches that all activities of life exist ultimately for the purpose of preserving and spreading the ruthlessly selfish genes.

Evolution is a very plastic theory. Although Darwinists acknowledge that neo-Darwinism normally would tend to favor the survival of each cell so that it could pass on its genes, some have attempted to explain the apoptotic mechanism within the selfish-gene hypothesis (Dawkins, 1976). Dawkins noted that, if diseased cells die, the organism as a whole has a net advantage of living longer, and thereby passing its genes to its offspring. One problem with this explanation of apoptosis' origin is that apoptosis is not critical in many cells until after the organism's reproductive age is past. Another problem is that many of the numerous cells destroyed by apoptosis do not affect an organism's survivability. Other methods that would be in harmony with the selfish-gene theory could achieve the same goal, such as having a more elaborate repair system and possessing more protection against cell damage so that fewer cells would need to be destroyed.

The body produces many structures by removal of cells, making the body, not the DNA, of greatest biological importance. If DNA were of the greater biological importance, a means would have been favored to evolve the required trait embryologically—a means that would be more in harmony with the selfish gene theory, rather than by relying on apoptosis to remove certain cells after they have developed. Apoptosis is actually a default option that must be bypassed in order for the cell to continue in its mitotic pathway. Unless overridden

by the proper signal, the cell will always enter apoptosis. This is contrary to what would be expected from a neo-Darwinism origin for the system.

Among the many other problems facing Dawkin's "selfish gene" theory is the fact that the genes by themselves are useless. They are only the software, and without the cell machinery involving hundreds of enzymes and complex structures such as the ribosomes (the "hardware"), life could not function. Genes are only part of the survival unit, and the complex cell organization as a unit is required for survival (Morange, 2002). The old central dogma was: DNA → RNA → proteins. The new dogma is: The genome as a unit → gene products → structure and function → pathways and physiology (Morange, 2002), all which fits with an origin by a creator.

Genes are also inactivated and controlled by non-genetic factors—a process called *epigenetic control*. The X chromosome dosage compensation in females, where one of the two X chromosomes in each somatic cell is randomly inactivated by methylation early in development, is an example. Margulis and Sagan (2002) make a strong case against the selfish gene hypothesis by arguing that the entire biosphere cooperates to the degree that it functions as a unit, a concept called the Gaia hypothesis (2002). They conclude that a gene is never "a self" but "only a piece of DNA long enough to have a function" and that the "time has come in serious biology to abandon words like 'selfish genes' and replace them with 'meaningful terms'" (Margulis and Sagan, 2002, pp. 16–17).

Summary

Recent research has found a "vastly" greater level of complexity in the genome than previously believed only a decade ago (Aravind et al., 2001). Apoptosis is an extremely complex genetic and biochemical system that is only one of many examples where the genes put the organism first, not the reverse as Dawkins selfish gene model predicts. Neither the germ cell line nor the somatic cell line of the affected cell benefit because apoptosis destroys both forever; thus, only the organism can benefit. Often not only inferior cells die, as neo-Darwinism teaches, but cells that are either detrimental to the organism, or cells that are unneeded by the organism die because they are in the wrong place at the wrong time (Elmore, 2007).

Furthermore, evolution is unable to explain the origin of this system, which analysis has shown both the mechanism and the genes involved are very similar in all eukaryotes so far researched (Elmore, 2007). Thus, this supports the claim that apoptosis is irreducibly complex. Apoptosis is an extremely complex genetic and biochemical organization that is only one of many thousands of examples of an irreducibly complex system that regulates cell life for the benefit of the organism as a whole.

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