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Biology of Death — Some Pros and Cons:

Reconsidering What Apoptosis will Bring in the Future

Abstract

In recent years, the biology of death has received attention in biomedical field. The biology of death is an area of study to seek answers the fundamental question; why does cell of organisms die? The researches of cell death has progressed surely and steadily for the past two decades; and besides, researchers all over the world have tried to elucidate mechanisms of diseases and find wide application of this field. However, there will be a danger of losing sight of the meaningfulness of these researches. This paper is organized into six sections; introduction, the mechanism of Alzheimer's disease, cancer, AIDS, the possible future brought on by biology of death and conclusion.

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For a long time, all the researches in biomedical and molecular biology field had been conducted in order to elucidate how and why cell of organisms multiply and differentiate; in other words, how cell is alive. On the other hand, the biology of death focuses flatly different point of researches; how and why cell more like curry out suicide than die. Thus, the biology of death gave innovative point of view to all the biology-related fields in the way considering cell life from perspective of cell death for the first time; indeed, Nobel Prize in Physiology or Medicine 2002 was awarded jointly Sydney Brenner, H. Robert Horvitz and John E. Sulston for their discoveries concerning programmed cell death.

The first paper mentioning cell death was published in a journal of pathology. Crawford, Kerr and Currie (1972) stated that they found dying cells different from necrosis in the diseased tissues. Necrosis is the disorganized rupture of cells; in contrast, what they found under a microscope were ". . . cells . . . seen to be shrunk, and there was condensation and fragmentation of their nuclear chromatin" (para.7). From analysis of an observation, they advocated that there was another way of cell death via a certain

process aside from necrosis. They also said that ". . . [another way of cell death] should be known by a term that is descriptive of its functional significance — apoptosis" (para.9). Incidentally, apoptosis is the Greek word meaning falling of leaves from deciduous trees; it is proven later that apoptosis act on when trees drop their leaves. Apoptosis had not been realized for over a decade, because the research conducted by Crawford et al was anything more than observation by microscope; subsequently, Ellis and Horvitz (1986) discovered that there were specific genes giving a command to cause apoptosis in nematode C. elegance. They said that ". . . two genes, *ced-3* and *ced-4* . . . may be involved in determining which cells express the fate of cell death" (para.5) and concluded that apoptosis coined by Crawford et al was the cell death programmed by specific genes. Furthermore, Green and Reed (1998) came to understand that "the effectors of apoptosis are represented by a family of intracellular cysteine proteases known as caspases" (para.5). They found that although they inhibited caspase, apoptosis sometimes occurred under certain conditions. From this, they indicated that there were many other pathways of occurring apoptosis.

Thus, the mechanism of apoptosis has become elucidated step by step, and researchers have tackled an enigma of apoptosis programmed by specific genes in recent years. However the phenomenon of apoptosis raises one question; why does

apoptosis have to occur? Horvitz gave a brief answer that apoptosis occurs because cell recognized "self" by considering all the various factors together (as cited in "Why Does Programmed Cell Death," 1999). Hengartner also explained that cell recognized its condition; that is, harmful to rest of the organisms or not, and decided whether cell should die or not (as cited in "Why Does Programmed Cell Death," 1999). He added that "[c]ells that are not needed may never have had a function. In other cases, they may have lost their function, or may have competed and lost out to other cells" (as quoted in "Why Does Programmed Cell Death," 1999). Apoptosis is therefore very important in self-protection and self-limitation of cell that are involved in progression of many kinds of diseases. In fact, the researches of apoptosis have shown the new way to elucidate mechanism of many life-threatening diseases.

Mechanism of Alzheimer's Disease

Alzheimer's was a disease that researchers essentially didn't know about its mechanism; however, the study of Alzheimer's has been developed to find a complete therapy in recent years. Barinaga (1998) reported that apoptosis might be involved in Alzheimer's although that hadn't been totally proven yet. She mentioned that:

> [Two research] teams showed that [βamyloid], which builds up in the brain of people with Alzheimer's, causes cultured neurons to die by apoptosis — also

known as programmed cell death because it involves the activation of a genetic program for dismantling cells . . . (para.4).

However, the authenticity continues to be a matter of debate; in fact, Younkin said that "[t]here are problems looking in Alzheimer's brains and knowing whether you are looking at true apoptosis of is or just fragmentation of DNA that resembles apoptosis" (as quoted in Barinaga, 1998, para.5).

Mechanism of Cancer

Research of cancer also attracts a great deal of interest. People who die from cancer are over 70 million all over the world, and in Japan, two in three people will have a cancer and one in three people will die from cancer, so that the research of cancer faces an urgent need to elucidate its mechanism for all of us (Tanuma, 2010, chap.4). For a long time, cancer is focused on abnormal proliferation of cancer cell only, and researchers try to identify the genes that promote carcinogenesis action; still, it has been revealed in recent years that cancer is the internal situation having abnormalities in cancer suppressor genes; people who has cancer is defective in specific genes occurring apoptosis to cancer cell (Thompson, 1995, p.1458-1459). Biello (2006) also gave clear explanation that almost all the cells except cardiac muscle cells and nerve cells in brain commit suicide when they recognize that they are harmful or not needed (the

process is known as apoptosis), “but in cancer cells this mechanism has often been genetically disabled or otherwise broken, allowing tumors to proliferate” (para.1).

Mechanism of AIDS

According to survey (2009) done by WHO, there are 33.4 million people who acquire Acquired immunodeficiency syndrome known as AIDS; however, there are no curative therapies (http://www.who.int/hiv/en/). To achieve early development of therapies, its complex mechanism become elucidating. AIDS is a disease induced by HIV infection, and specifically, T helper cells acquire HIV infection. Gougeon and Montagnier (1993) said that infected T helper cells send a signal making uninfected T helper cell die; in other words, infected T helper cells induce apoptosis. Current researches indicated the reason why infected T helper cells didn’t die was that HIV blocked apoptosis (Tanuma, 2010, chap.4). All things considered, it is said that AIDS is a disease HIV-infected T helper cells forgetting apoptosis send a signal inducing apoptosis to uninfected T helper cells.

The Possible Future

As noted above, we had found the existence of apoptosis that is programmed by specific genes; afterwards, researchers changed in thinking; how to control apoptosis in order to eliminate fundamental cause of disease rather than how to get rid of abnormal

cells. In fact, many serious diseases can redefine in terms of fact that there are abnormalities of apoptosis in diseased cells. For instance, Alzheimer's, Parkinson's and amyotrophic lateral sclerosis known as ALS are caused because of occurring apoptosis too much; on the other hand, Cancer, autoimmune diseases and viral infections are caused because apoptosis, which should occur, is blocked. AIDS can be regarded as a disease associated with both the inhibition of apoptosis and the increased apoptosis. If we can find chemical compounds that inhibit the signal of death sending excessively or regain the power of death in order to make diseased cells die in the future, these diseases will be no longer diseases. This is not just a dream, I strongly said that it is a feasible dream; indeed, Lin (2008) stated that one of the polymer molecules, Flex-Het inducing apoptosis effectively inhibits the proliferation of lung cancer cells in mice. There is a person who approaches cancer from a different perspective. Hergenrother also stated that he found synthetic compound named PAC-1 having ability to activate procaspase-3, which inhibit apoptosis in cancer cells (as cited in Biello, 2006). I think it will be possible that we control basic function of cell, apoptosis in a positive way, apply to curative therapy and prevent a disease in the future.

Conclusion

Protect our life from death — for such occasions, researchers in biology-related

field face a new challenge day in, day out; therefore, I think it would be accurate to say that there aren't any symptomatic therapies, and people can recover fully from all the diseases in the future. Biology of death; that is, modern development of biomedical field will grant human wish to die a natural death; nevertheless, I can't categorically describe such future as good. Human beings have been conscious of the death, but we might have entered and have to keep going the new era that we can't feel approach of death. Although we can tamper apoptosis, which originally gives us death, and keep away from death, it doesn't mean we can evade death. If we really seek immortality or can prolong our life programmed by genes, as much as we like in the future, we will have a feeling of emptiness toward life. I strongly emphasize that what really needed for the age to come is not the immorality but knowing the meaningfulness of limited life through the biology of death.

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