

Apoptosis in Embryonic Development ^[1]

By: Bartlett, Zane Keywords: [Apoptosis](#) ^[2]

Apoptosis, or programmed cell death, is a mechanism in embryonic development that occurs naturally in organisms. Apoptosis is a different process from cell necrosis, which is uncontrolled cell death usually after infection or specific trauma. As cells rapidly proliferate during development, some of them undergo [apoptosis](#) ^[3], which is necessary for many stages in development, including [neural development](#) ^[4], [reduction](#) ^[5] in [egg](#) ^[6] cells (oocytes) at birth, as well as the shaping of fingers and vestigial organs in [humans](#) ^[7] and other animals. [Sydney Brenner](#) ^[8], H. Robert Horvitz, and John E. Sulston received the Nobel Prize in Physiology or Medicine in 2002 for their work on the genetic [regulation](#) ^[9] of organ development and programmed cell death. Research on cell lineages before and after embryonic development may lead to new ways to reduce or promote cell death, which can be important in preventing diseases such as Alzheimer's or cancer.

Karl Vogt observed the phenomenon of [apoptosis](#) ^[3] in Neuchâtel, Switzerland, in 1842, but Vogt did not use the term [apoptosis](#) ^[3]. Vogt noticed in midwife toad ([*Alytes obstetricans*](#) ^[10]) embryos that cells in the [notochord](#) ^[11], a cartilaginous skeletal structure, disappeared and were replaced by cells of the vertebrae. Although Vogt documented that some cells disappeared during development, he did not focus his research on that phenomenon. Researchers did not give [apoptosis](#) ^[3] very much attention until 1885 when Walther Flemming, who worked at the University of Kiel in Kiel, Germany, used more advanced staining techniques on the cell [nucleus](#) ^[12] to observe what he called chromatolysis, the diminishing of nuclear material in dying cells. Chromatolysis is part of the process of [apoptosis](#) ^[3], but Flemming's research was overshadowed until biologist Alfred Glücksmann, who worked at the [Strangeways Research Laboratory](#) ^[13] in Cambridge, England, published a review on cell death literature in 1951.

In his review, Glücksmann hypothesized that for an organism to grow and develop, cell death must occur. At the time of Glücksmann's review, many scientists interpreted dead cells as metabolic byproducts of cells undergoing [mitosis](#) ^[14], or cellular replication. Glücksmann presented evidence from past embryological research that described planned cell death as an aspect of normal development. Glücksmann's hypothesis remained largely unnoticed for more than twenty years. However, John F. Kerr, Andrew H. Wyllie, and Alastair R. Currie, pathologists working at the University of Aberdeen in Aberdeen, Scotland, referenced Glücksmann's review as motivation to develop their own research on [apoptosis](#) ^[3] in 1972.

Kerr had first studied cell death in 1965 when he noticed atrophy, or shrinkage, in [rat](#) ^[15] liver cells under an electron [microscope](#) ^[16]. Kerr noticed that the shrinkage was distinct from necrosis due to trauma, which normally causes the cell to rupture and release its contents. A few years later, Kerr and his colleagues noted common patterns involved in cell death related to their research and recorded in previous experiments and reviews, including Glücksmann's work. Kerr and his team framed their research focus as about programmed cell death, a concept that Richard Lockshin and Carroll Williams at St. John's University New York City, New York, had used in 1964. Kerr and his colleagues coined the term [apoptosis](#) ^[3] to describe programmed cell death. They claimed that cell death from [apoptosis](#) ^[3] was not accidental, and that it followed the same pattern in both developing and developed cells. With their 1972 article, Kerr and his team brought the idea of [apoptosis](#) ^[3] to greater scientific attention.

Kerr, Wyllie, and Currie's research clarified the process of [apoptosis](#) ^[3] as a series of specific steps, later verified by other researchers. First, cells undergoing [apoptosis](#) ^[3] begin to shrink in size and lose physical connections with neighboring cells. Second, the [chromatin](#) ^[17], or the combination of DNA and protein within the cell [nucleus](#) ^[12], condenses and enzymes begin to fragment the [chromatin](#) ^[17] within the cell. Third, the cell membrane bulges irregularly, or blebs. Fourth, the [nucleus](#) ^[12] collapses and breaks into fragments containing pieces of [chromatin](#) ^[17], while the cell continues to bleb. Fifth, the cell breaks into several smaller membrane bodies that contain various cellular fragments, called apoptotic bodies. Lastly, white blood cells, also called phagocytes, or neighboring cells engulf the apoptotic bodies and break them down. The organism suffers no major injury as a result.

After Kerr, Wyllie, and Currie published their research, scientists accepted [apoptosis](#) ^[3] as a mechanism in cellular development and began to study its significance in development and disease. For example, since the 1970s [Sydney Brenner](#) ^[8] in Berkeley, California, Robert Horvitz in Cambridge, Massachusetts, and John Sulston in Cambridge, England, conducted much of their early research on the nematode [Caenorhabditis elegans](#) ^[18] (*C. elegans*). Through diagrams of cell lineages and careful documentation, Brenner, Horvitz, and Sulston predicted when cell death would occur, and they identified some of the [genes](#) ^[19] involved in the [regulation](#) ^[9] of cell death. In particular, Horvitz noted that *C. elegans* neurological development included a large amount of [apoptosis](#) ^[3], with 105 of the 131 programmed cell deaths occurring in neural cells. Brenner, Horvitz, and Sulston received the [Nobel Prize in Physiology or Medicine](#) ^[20] in 2002 for their work in genetic [regulation](#) ^[9] of organ development and programmed cell death.

Research conducted after Brenner, Horvitz, and Sulston published their findings on *C. elegans* reinforced the theory that

programmed cell death through [apoptosis](#)^[3] is essential for development in animals. In 1993, scientists working with Horvitz found that a gene in mice was very similar to the gene that codes for an enzyme that causes cell death during development in *C. elegans*. The research showed that the [apoptosis](#)^[3] observed in *C. elegans* also occurs in mammals.

In 1997, Michael Jacobson and researchers at the MRC Lab of Molecular Biology in Cambridge, England, outlined the importance of cell death in animals in the article "Programmed Cell Death in Animal Development". Jacobson and colleagues claimed that the primary functions of [apoptosis](#)^[3] are to sculpt the organism by deleting unwanted structures, controlling the number of cells, and eliminating nonfunctional, harmful, abnormal, or misplaced cells. Absence of [apoptosis](#)^[3] can include malformations of digits, decreased neurological function, malformations of the heart, or even cancer. For example, soft tissue cells between the fingers and toes undergo [apoptosis](#)^[3] in order to separate the digits from each other during development. The proper formation of heart loops also relies on the process of [apoptosis](#)^[3].

In his article "The Apoptotic Oocyte," Gary Wessel from Brown University in Providence, Rhode Island, discusses the role of [apoptosis](#)^[3] in human females. Human female oocytes undergo [apoptosis](#)^[3] during development and after birth. Scientists estimate that seven to eight million oocytes are formed in the [fetus](#)^[21], which are reduced to about 100,000 oocytes at birth, and then only a few hundred at the onset of menopause.

Apoptosis occurs not only during embryonic development, but also after birth. In [humans](#)^[7] for example, brain cells undergo [apoptosis](#)^[3] prior to and following birth to eliminate excess brain cells and streamline nerve impulses. Apoptosis also occurs in some cells that the body identifies as cancerous to prevent the spread of the cancer and kill the cancerous cells. However, unregulated [apoptosis](#)^[3] can cause disorders, such as Alzheimer's disease and amyotrophic lateral sclerosis, which is a motor [neuron](#)^[22] disease.

Sources

1. Barres, Ben A., and Martin C. Raff. "Axonal Control of Oligodendrocyte Development." *The Journal of Cell Biology* 147 (1999): 1123–8. <http://jcb.rupress.org/content/147/6/1123.full>^[23] (Accessed June 7, 2017).
2. Brenner, Sydney. "The genetics of *Caenorhabditis elegans*." *Genetics* 77 (1974): 71–94. <http://www.genetics.org/content/genetics/77/1/71.full.pdf>^[24] (Accessed June 7, 2017).
3. Clarke, Peter G. H., and Stephanie Clarke. "Nineteenth Century Research on Naturally Occurring Cell Death and Related Phenomena." *Anatomy and Embryology* 193 (1996): 81–99.
4. Flemming, Walther. *Über die Bildung von Richtungsfiguren in Säugethiereiern Beim Untergang Graaf'scher Follikel* [On Formation of Directional Figures in Mammalian Animals When the Graafian Follicle Disappears]. Kiel: 1885.
5. Glücksmann, Alfred. "Cell Deaths in Normal Vertebrate Ontogeny." *Biological Reviews* 26 (1951): 59–86.
6. Honig, Lawrence S., and Roger N. Rosenberg. "Apoptosis and Neurologic Disease." *The American Journal of Medicine* 108 (2000): 317–30.
7. Kerr, John F. "A Histochemical Study of Hypertrophy and Ischaemic Injury of Rat Liver with Special Reference to Changes in Lysosomes." *The Journal of Pathology and Bacteriology* 90 (1965): 419–35.
8. Kerr, John F., Andrew H. Wyllie, and Alastair R. Currie. "Apoptosis: A Basic Biological Phenomenon with Wide-Ranging Implications in Tissue Kinetics." *British Journal of Cancer* 26 (1972): 239–57. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2008650/pdf/brjncancer00355-0003.pdf>^[25] (Accessed June 7, 2017).
9. Jacobson, Michael D., Miguel Weil, and Martin C. Raff. "Programmed Cell Death in Animal Development." *Cell* 88 (1997): 347–54. <http://www.sciencedirect.com/science/article/pii/S0092867400818735>^[26] (Accessed June 7, 2017).
10. Lockshin, Richard A., and Carroll M. Williams. "Programmed Cell Death—II. Endocrine Potentiation of the Breakdown of the Intersegmental Muscles of Silkworms." *Journal of Insect Physiology* 10 (1964): 643–9.
11. Nobel Media. "The Nobel Prize in Physiology or Medicine 2002." *Nobelprize.org*. http://www.nobelprize.org/nobel_prizes/medicine/laureates/2002/^[27] (Accessed March 15, 2014).
12. Peter, Marcus E., Armin E. Heufelder, and Michael O. Hengartner. "Advances in Apoptosis Research." *Proceedings of the National Academy of Sciences*^[28] 94 (1997): 12736–7. <http://www.pnas.org/content/94/24/12736.full>^[29] (Accessed June 7, 2017).
13. Reynaud, Karine, and Marc-Antoine Driancourt. "Oocyte Attrition." *Molecular and Cellular Endocrinology* 163 (2000): 101–8.
14. Sulston, John, and Sydney Brenner^[8]. "The DNA of *Caenorhabditis Elegans*." *Genetics* 77 (1974): 95–104. <http://www.genetics.org/content/genetics/77/1/95.full.pdf>^[30] (Accessed June 7, 2017).
15. Vogt, Karl Christoph. *Untersuchungen Über Die Entwicklungsgeschichte der Geburtshelferkröte (Alytes Obstetricans)* [Investigations on The Developmental History of the Midwife Toad (Alytes Obstetricans)]. Solothurn: Jent & Gassmann, 1842. https://books.google.com/books/about/Untersuchungen_über_die_Entwicklungsges.html?id=FjtOAAAaAAJ^[31] (Accessed June 7, 2017).
16. Wessel, Gary M. "The Apoptotic Oocyte." *Molecular Reproduction and Development* 77 (2010).
17. Yuan, Junying, Shai Shaham, Stephane Ledoux, Hilary M. Ellis, and H. Robert Horvitz. "The *C. Elegans* Cell Death Gene *Ced-3* Encodes a Protein Similar to Mammalian Interleukin-1 β -Converting Enzyme." *Cell* 75 (1993): 641–52.

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