How is it that cells are lost from the body?

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[My basic science approach]

Organisms make many proteins written in their genes. From my own experience, I had a vague feeling that no protein is not interesting to study. The words of two scientists made it clear to me why I felt this way.

When Spanish developmental geneticist Ginés Morata was a graduate student, he proposed the idea of cell competition, in which cells of the same type compete with each other to form the body and select the best-adapted cells. He introduced concepts like natural selection into developmental research. In an interview about biological research, Morata said the following (Current Biology 16, R976-7, 2006).

The "science activity is a delightful one, and the goal is to find out how nature solves the problems of various organisms. The solutions organisms have taken are unexpected and often not elegant. Organisms have devised many ingenious solutions, but I believe they were by chance and necessity, not planned. Who could have predicted that most genomic DNA would be of unknown function or that introns would separate the protein-coding genes? (omitted). To the students, you don't have to invent anything, but the organisms have already done the inventing; you just have to find the solution chosen by evolution. (omitted). Science is creative, and how much time one spends obsessing over a problem is important to its progress. Even if a subject seems trivial at first glance, it is a scientist who can discover unexpected and interesting aspects from it,"


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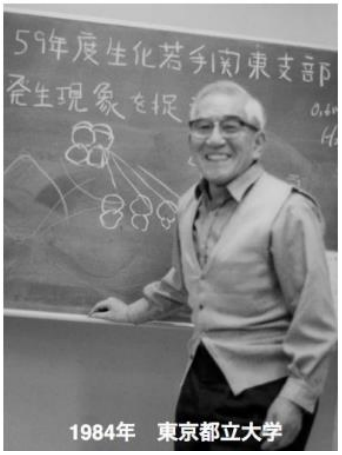
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Dr. Katsuma Dan, who studied the development of sea urchins at Tokyo Metropolitan University, says in his book "Talking with Sea Urchin.

As I continued my work, the theme that had initially confronted me gradually came over to me. Now it seems as if the smaller cell of the unequal cell division appeal to me. This voiceless appeal is directed to me, and I feel that no one else would understand it unless I understand it. In this sense, all my research on sea urchins has been translating their language into human language, like deciphering the letters left behind by departed

people and not creating something new. It is painful to face a theme while trying to understand it. However, when the theme becomes the breath, you breathe and the blood that flows through your veins, there is no room for impatience or pedantry.

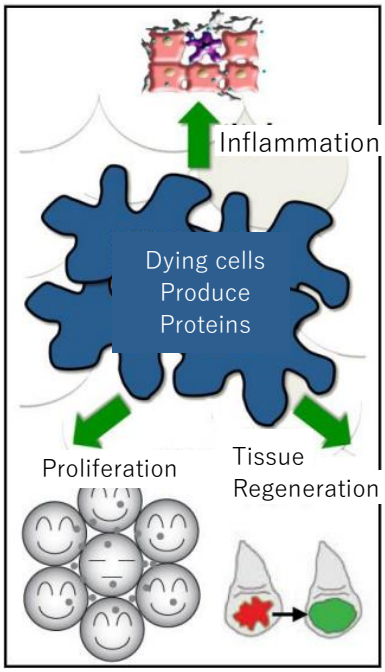
From the words of these two developmental biologists, I think that the mechanisms that organisms have created over their long evolution have endless discoveries and charms no matter where they are explored. The reason why classics and works of art are new to all ages is that they contain solutions for expressions that allow so many perspectives. Creatures have a mechanism that has endured a more extended history than any human-made work. I want to decipher even one of these fascinating mechanisms.

[About my research]

Our bodies start from a single fertilized egg and reach 37 trillion cells in an adult. However, many cells are lost during development. This seemingly futile phenomenon is called programmed cell death. Programmed cell death occurs even after birth, and large numbers of blood, intestinal, and skin cells are lost every day. Today's me has many cells that are different from yesterday's me. We live our lives without being aware of cell death, but this is because cells are replenished in the same amount as they are lost, and the life and death of cells maintain the body. So how and why does cell death occur? This is my research theme.

Development is a creative process in which cells increase and produce individualized cells such as nerves and muscles. Thus, few people noticed that cells were lost in the process and were interested in the meaning of cell loss. Even if noticed, cell death mainly was interpreted negatively that it was lost because it happened to be out of order. In the 1970s, researchers in the nematode worm (*C. elegans*) observed all cell divisions during development and found that in *C. elegans*, 1090 cells are born, and 131 are lost at a particular time and place. Programmed cell death had indeed occurred. In 1986, the gene required for all 131 cell deaths was identified, and later similar sequences of gene was found in human and mouse. In 1993, I discovered that the mammalian gene with sequences similar to the cell death gene in *C. elegans* cause cell death in mammalian cells. The gene found in *C. elegans* was also utilized to induce cell death in human, and it turned out that cell death in mammals is also controlled by genes (called apoptosis). This made it possible to conduct experiments to answer a question that had been unapproachable before: "What is the purpose of apoptosis? This is because it is now possible to inactivate apoptotic genes in the body and observe apoptotic proteins by *in vivo* imaging. As a result, it has

become clear that dying cells send out messages and actively communicate with the body. Cell death selectively eliminates error cells that arise during development, and it also produces proteins that stimulate proliferation so that lost cells can be properly replaced by healthy surrounding cells. Dying cells also produce proteins that promote tissue regeneration. In some cases, toxic substances are also released, causing inflammation.



If you think about it, the dead cells send out messages to those around them that make the cycle of cell birth and cell death possible during development and in adult life. Perhaps life is possible because of death. In disease, many life phenomena are related to the loss of cells, such as the death of cells that do not need to die or cancer due to the over proliferation of cells that should die. From the research that explores messages from dead cells and clarifies the active role of cell death, I would like to understand the mechanism of development, body maintenance, and diseases.