A great approach for understanding living things: Mechanobiology

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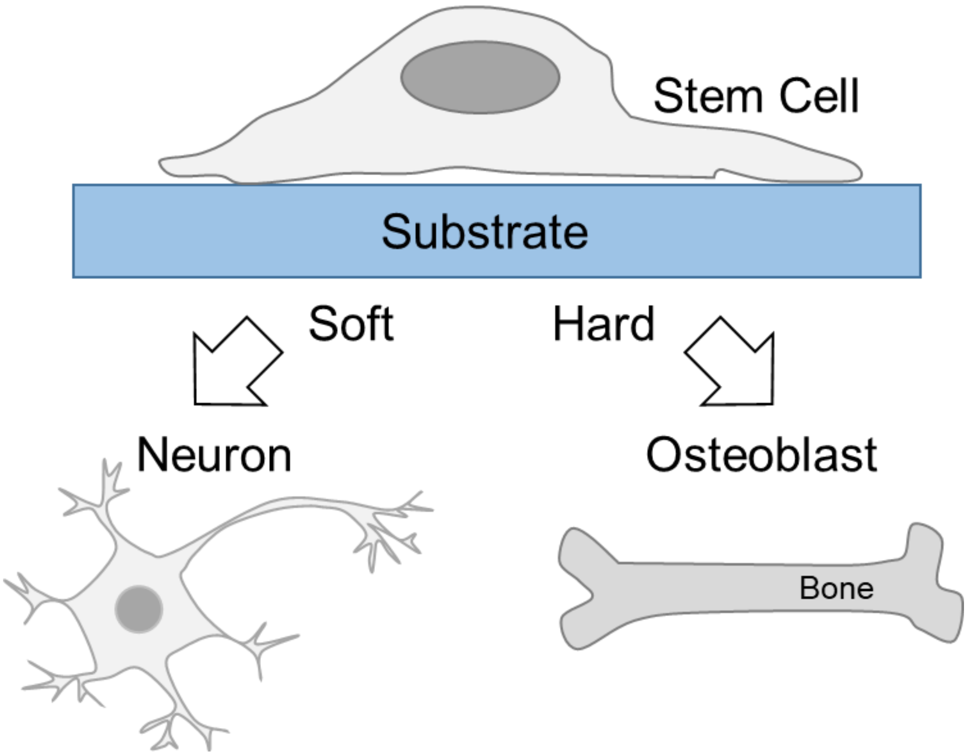

The mechanisms of life are so enigmatic that many scientists are working to unravel them. Among them, the mechanisms of cell differentiation and organ formation are attractive questions. Cell differentiation is the process of transforming stem cells into cells with specific functions, such as neurons or muscle cells. Organ formation describes the processes involved in the early development of an organ. Research in this field has developed rapidly with the development of biological and physical techniques such as genetic modification, and fluorescent imaging in recent years. A certain kind of biology called mechanobiology is attracting attention by utilizing these technologies. Mechanobiology is a field that studies the role of physical forces in various biological phenomena such as cell differentiation and organ formation. The idea of mechanobiology itself was proposed in *On Growth and Form*, written by biologist

D'Arcy Wentworth Thompson in 1917. This book showed that physical forces are involved in the formation of animals and plants. In addition, the book proposed that we can apply the ideas of physics and mathematics to understand these phenomena. However, at that time, some essential technologies such as genetic modification, fluorescence imaging, and mechanical measurement were not yet developed, so it was impossible to conduct detailed mechanobiology studies. In other words, although the importance of mechanobiology was recognized, it was impossible to measure the force-related phenomena in detail due to technical problems. The development of measurement and analysis technologies has made it possible to conduct detailed mechanobiological studies and uncover some force-related biological processes.

Although chemical signals, enzymatic reactions, and physical forces are central matters for understanding biology, most people may associate biological research with chemical signals or enzymatic reactions. These studies are so important that many scientists have studied them. However, the importance of investigating the role of physical forces in living organisms is also unquestionable. Without ways for our bodies to respond to external stimuli, we cannot feel anything.

Mechanobiology research has been made at various scales: biomolecules, cells, organs, and individuals. Although these scale hierarchies cannot be divided because they influence each other, we regard them as divided for convenience. At the biomolecular scale, many force-responsive biomolecules have been found such as Piezo1, Piezo2, kinesin, and actin. Among them, Piezo1 and Piezo2 have recently attracted much attention from researchers. They are ion channels activated by mechanical stimuli and were discovered by Ardem Patapoutian's research group [1]. Ion channels are proteins that exist in biological membranes and are responsible for the permeation of ions such as calcium and sodium ions. Many people knew that stimuli such as temperature and touch are sent to the brain in the form of electricity through nerve cells, however, it was not well understood how temperature and tactile stimuli are converted into the form of electricity. These discovery has advanced our understanding of how tactile stimuli are detected. Their research was highly evaluated and the 2021 Nobel Prize in Physiology or Medicine is awarded to David Julius and Ardem Patapoutian for their discoveries. Many experiments have been conducted to study the response of Piezo proteins to force after their discovery [2]. For example, microfluidic devices with micrometer-scale channels have been used to simulate the shear stresses that cells in blood vessels are exposed to. These studies have shown that Piezo proteins are involved in various biological phenomena such as vascular formation and muscle growth. These biological phenomena are so crucial that further research is required. At the cellular scale, it has been shown that physical forces are involved in essential phenomena such as cell motility and cell differentiation. For example, substrate elasticity determines stem cell lineage specification [3]. On the soft substrate, stem cells become neurons and on the hard substrate, they become osteoblasts. Osteoblasts are cells with a role in bone formation in bone tissue. Those differences prove that cells change their behavior depending on mechanical stimuli. Thus, even by looking at typical life phenomena involving physical forces in cells and biomolecules, we can see how physical forces play an essential role in living organisms.

The field of mechanobiology has the potential to make a significant impact in the field of medicine. In recent years, the technology to create organs from certain types of cells called regenerative medicine is attracting a lot of attention. Thus, there have been efforts to create organs from cells that can differentiate into all cell types, such as iPS cells and ES cells. If further studies on cellular and biomolecular response mechanisms to mechanical stimuli are conducted, it may be possible to control the organ formation using chemical and mechanical stimuli. In addition, it could help in the development of molecularly targeted drugs. For example, since the Piezo protein is known to be involved in pain, the development of drugs that target the Piezo protein could help people suffering from chronic pain.

Even in life, which should be one of the most familiar, many mysteries remain, and further research is needed to uncover them. Most basic research, including mechanobiology, has the potential to improve our lives. The day may come when further mechanobiology research at various size scales will reveal the role of physical forces in living organisms in an integrated manner.

References

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