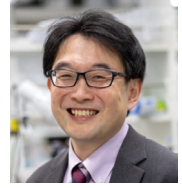




# A cell-cell communication system which enables highly reproducible construction of healthy body

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<https://researchmap.jp/read0148831?lang=en>

## Abstract

It is well known that defective cells generated in the adult body can cause diseases such as cancer. In this study, we discovered that defective cells are frequently generated during the developmental process, and that a mechanism exists to detect and eliminate these defective cells, enabling the reproducible construction of healthy bodies.

## Background & Results

To generate a healthy body, various cells must be arranged in an orderly fashion during development. However, during this process, active cell division, proliferation, and migration can result in replication errors and fluctuations in signal transduction. So, how can we reproducibly construct bodies with consistent shape and function in the presence of these fluctuations? To answer this question, we need to analyze the irregular fluctuations that arise within animals and the mechanisms that address them, but conventional techniques have not yet been able to do so. Using zebrafish, a small fish suitable for imaging, we have succeeded for the first time in capturing the activity of the cellular coordination mechanisms that resolve fluctuations. Specifically, in animal embryos, the cell fate control mechanism known as Wnt signaling is activated or inactivated in appropriate locations to induce appropriate neurons. However, our analysis revealed that defective cells (fluctuating cells) frequently arise in which Wnt signaling is activated or inactivated in inappropriate locations. Detailed analysis revealed that embryonic cells monitor each other's status through intercellular tension. When a defective cell emerges, the resulting fluctuations in intercellular tension allow neighboring cells to sense the defective cell's appearance and induce its apoptosis. We also found that the activity of Shh signaling, which controls the positioning of spinal neurons and muscle cells, fluctuates frequently and uncontrollably, and that these fluctuations are contained by a similar mechanism. Importantly, when this mechanism is forcibly suppressed, naturally occurring defective cells accumulate, resulting in the formation of neurons and muscle cells in the wrong places, causing abnormalities in motor development and, in some individuals, tumors and premature aging symptoms as they grow. Thus, we found that this defective cell elimination mechanism plays an essential role in cre-

ating a body that is highly reproducible and sustained in health. We also identified Foxo3 and other marker molecules for this defective cell elimination mechanism.

## Significance of the research and Future perspective

This study suggests that the causes of adult disease and aging may originate during embryonic development. It also suggests that a similar mechanism for eliminating defective cells may be active in adults, preventing the onset of diseases such as cancer. By using the markers identified in this study to clarify the lifelong function of this mechanism, it may be possible to uncover a new defense mechanism that does not involve immune cells.

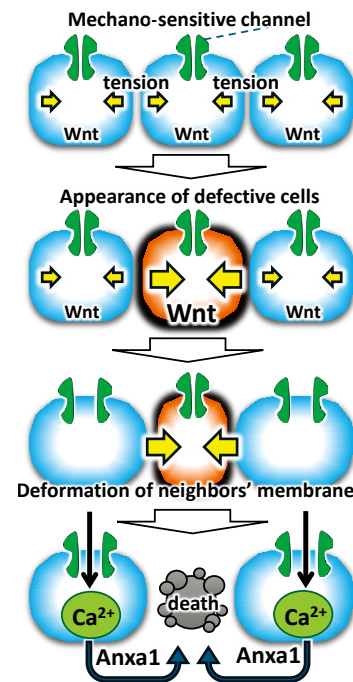


Fig.1) appearance and elimination of defective cells

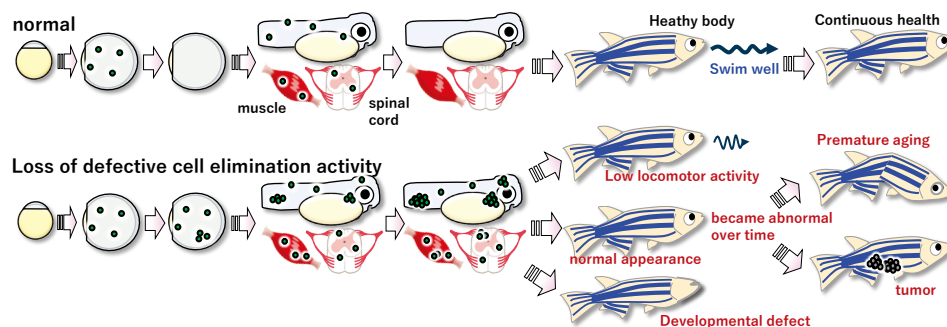


Fig.2) Defective cell elimination ensure lifelong health.

### Patent

### Treatise

### URL

### Keyword

Aoki, Kana; Ishitani, Tohru et al. Mechano-gradients drive morphogen-noise correction to ensure robust patterning. *Science Advances*. 2024, 10, 2357. doi: 10.1126/sciadv.adp2357

Matsumoto, Kana; Akieda, Yuki; Ishitani, Tohru et al. Foxo3-mediated physiological cell competition ensures robust tissue patterning throughout vertebrate development. *Nature Communications*. 2024, 15, 10662. doi: 10.1038/s41467-024-55108-x

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defective cell elimination system, cell competition, cell-cell communication