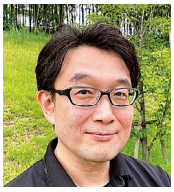
Medical & healthcare, Drug discovery

Understanding the molecular basis governing the sex difference in health-span and identifying anti-aging medicine



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Researchmap https://researchmap.jp/read0148831?lang=en

Abstract

To prevent age-related decline and extending healthy life expectancy, it is essential to clarify the principles governing aging and lifespan and to identify anti-aging medicine. However, in aging study, the lifespan of the organism is the rate-limiting factor. For example, when using mice, one analysis takes 2 to 3 years. We have focused on the African turquoise killifish as a new experimental animal that can solve this problem. Not only does this fish exhibit an aging phenotype similar to that of humans, but it also has a lifespan of only a few months, allowing aging and lifespan analysis to be performed in a short period of time. In this study, we used killifish to successfully identify the mechanism behind sex differences in lifespan, which has been a long-standing issue in aging and lifespan research. Specifically, we found that germ cells drive sex-dependent differences in lifespan. Furthermore, we succeeded to identify vitamin D as an anti-aging hormone.

Background & Results

It is known that females live longer than males in many animals, including humans, but the mechanism by which this gender difference in lifespan occurs remains unclear. In this study, we used the killifish, a small, extremely short-lived fish, as an experimental model to elucidate that germ cells cause gender differences in lifespan. Specifically, killifish females live longer than males, just like humans, but when germ cells are removed, the lifespan of females decreases and that of males increases, resulting in males and females having similar lifespans (Fig 1). Furthermore, we found that the different functions of germ cells in males and females drive sex-dependent difference in lifespan. Specifically, in females where germ cells were removed, the female hormone estrogen was significantly reduced, and insulin/IGF signaling was abnormally activated, suggesting that female germ cells suppress aging by activating estrogen signaling and suppressing insulin/IGF signaling. On the other hand, in males, germ cell removal promoted the synthesis of active vitamin D in the liver, suppressing aging of muscles and skin. In other words, it was suggested that male germ cells shorten lifespan by suppressing active vitamin D synthesis. We also discovered that treatment with an appropriate amount of active vitamin D to killifish extended the lifespan of both males and females (Fig 2). This is the first study to show that vitamin D extends the lifespan of vertebrates, and suggests that vitamin D is an anti-aging hormone (Science Advances 2024).

Significance of the research and Future perspective

By utilizing characteristic animals, we aim to accelerate the clarification of fundamental mechanisms controlling aging. Based on our discoveries, we would like to develop preemptive medicine preventing aging to extend human healthspan.

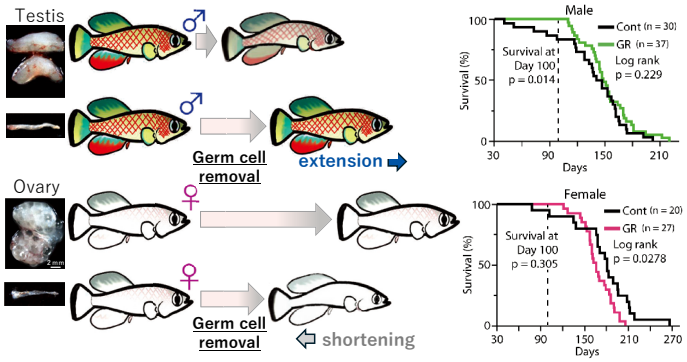

Fig 1) Germ cells drive sex-dependent differences in lifespan

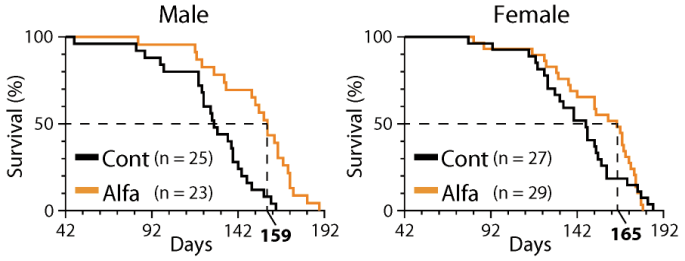

Fig 2) VitaminD extends lifespan

Patent	
Treatise	Abe, Kota; Ishitani, Tohru et al. Sex-dependent regulation of vertebrate somatic growth and aging by germ cells. Science Advances. 2024, 10(24), eadi1621. doi: 10.1126/sciadv.adi1621 Ogamino, Shohei; Ishitani, Tohru et al. Dynamics of Wnt/β-catenin reporter activity throughout whole life in a naturally short-lived vertebrate. NPJ Aging 2024, 10(1), 23. doi: 10.1038/s41514-024-00149-1 Oginuma, Msasayuki; Ishitani, Tohru et al. Rapid reverse genetics systems for N. furzeri, a suitable model organism to study vertebrate aging. Scientific Reports 2022, 12(1), 11628. doi: 10.1038/s41598-022-15972-3
URL	http://www.biken.osaka-u.ac.jp/en/achievement/research/2022/178
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