Synopsis of Original Research Paper

Exploring skin aging mechanisms and anti-aging factors using small fish

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In this study, we used small fish to elucidate the mechanism of skin aging and to explore for anti-aging factors. Animal tissues, including skin, are constantly exposed to external disturbances such as environmental changes and ultraviolet light, as well as internal disturbances such as replication errors and mutations, resulting in the frequent generation of a variety of pathological cells. However, it is poorly understood how animal tissues respond to the appearance of pathological cells. Therefore, to investigate this, we used zebrafish and mice as models. As a result, we found an immune cell-independent mechanism for eliminating pathological cells. Specifically, we showed that neighboring normal cells sense the appearance of pathological cells using intercellular tension and induce cell death, and that the elimination mechanism is conserved across species. In addition, we also explored the systemic mechanisms of skin aging. In previous skin aging studies, the slow aging rate of mice, a representative experimental model, has been a bottleneck. Therefore, in this study, we used the ultra-short-lived small fish *Nothobranchius furzeri*, which ages the fastest among all vertebrates that can be kept in captivity. We revealed that signals from germ cells suppress the synthesis of activated vitamin D in the liver in males, that this control promotes skin aging, and that administration of activated vitamin D can suppress skin aging. Thus, our research using small fish revealed new mechanisms for maintaining tissue homeostasis and skin aging.