Laboratory of Genome Instability

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Main text :

Learn “Life” to Medaka Fish.

When the first cells were born, molecular oxygen (O2) did not exist in the atmosphere of the Earth. So, the all living cells have been basically in a reduced state, not oxidized. Plant cells released O2 into the atmosphere as a byproduct of photosynthesis, which was a terrible poison to the ancient cells. However, poisonous means high chemical reactivity of O2 and before long aerobic bacteria appeared that can successfully obtain energy from O2. It is widely believed that mitochondria began as an intracellular symbiosis of these ancient aerobic bacteria. The cells of our body now live on energy from controlled oxidation with O2. In other words, we live on a precise balance of oxidation and reduction. If this elaborate balance is disturbed, the cells are unable to perform their physiological functions, which in turn has a negative impact on the health of the individual animal. We are revealing the physiological effects of weak but chronic oxidative stress on individual animals and exploring the practical ways to reduce it, with Japanese medaka fish.

[Research Theme]

We are studying the biological effects of low dose and low dose-rate chronic irradiation of ionizing radiation (IR) with Japanese medaka (*Oryzias latipes*), the regenerative process of IR-injured retina of zebrafish (*Danio rerio*), and the biological effects of weak ultrasonication on spinach (*Spinacia oleracea*).

We also maintain a collection of 74 populations of natural wild medaka collected from all over Japan (except Hokkaido), and study the intraspecific genetic diversity of Asian medaka to explore the machineries of animal evolution. Bodies of both animal and plant individuals are highly structured and are dynamic complex systems of living cells those differentiate in the various ways. We believe that histological analysis to obtain information on structure of the system and transcriptome analysis to describe the dynamics of the system will be prerequisite to understand the system. The motto of our laboratory is to flexibly select experimental materials and methods according to the aim of the experiments, and to conduct hand-made experiments with wisdom and ingenuity while devising experimental sets.

The following research topics are currently in progress:

**(1) Biological effects of oxidative stress by low dose and low dose-rate chronic irradiation of IR on medaka**

The accident of the Fukushima Daiichi Nuclear Power Plant in 2011 caused the radioactive contamination of a wide area of East Japan and there is still an urgent need to understand the health effects of long-term exposure to low dose and low dose-rate irradiation of IR on both humans and ecosystems. As researchers of biological effects of IR, we believe that this issue is our inevitable responsibility. The large cohort studies of atomic bomb survivors during World War II have recognized that exposure to low doses of IR below 100 mSv does not significantly increase the risk of future cancer. According to the dose-rate effect hypothesis, it was considered that genomic mutations would not occur in IR exposures of 100 mSv or less (because even if IR exposure induced mutations in the cells, the cells would repaire them) and that no significant effects on genome would be induced, and the physiological effects of chronic exposure to low dose and low dose-rate irradiation of IR were remained to be addressed. We are studying the physiological effects induced in adult Japanese medaka after chronic exposure to low dose and low dose-rate irradiation of gamma-rays by histological and transcriptomic analyses.

（Picture 1, 2）

Picture 1：Fish rearing indoor facility in Kashiwa campus

Picture 2：Medaka fish in the tank for chronic low dose and low dose-rate irradiation of gamma-rays (@ Radiation Biology Center, Kyoto University）

**(2) Elucidation of the effects of chronic oxidative stress on animal individual health**

The most powerful environmental factor that affects the health of an individual animal is food. The foods that animals, including us, have eaten were live plants and animals or those immediately after they were captured and died. Especially for animals, after they die, their bodies will be rapidly oxidized by O2 in the atmosphere. For a long time in the past, human has eaten fresh plants and fresh animals that were not oxidized and our body has been designed to do so. When we eat plants and animals that have been dead and oxidized (unfresh foods or preserved foods), it would tilt the oxidization/reduction balance of our body to the oxidized side, as it we eat oxidative stress. Chronic exposure to low dose and low dose-rate irradiation of IR can be interpreted as a chronic exposure to oxidative stress, since low level reactive oxygen species are chronically produced during the irradiation. We hypothesize that improving the oxidization/reduction balance of the animal body by eating fresh, non-oxidized foods can reduce the effects of chronic exposure to low dose, low dose-rate irradiation of IR, and are trying to examine this hypothesis with medaka.

**(3) Elucidation of the biological effects of weak ultrasonication on living organisms**

We are developing ultrasonic cleaning devises to clean foodstuffs such as vegetables, fruits, meats, and seafoods (Japanese patent number P6095057). We found that when leafy vegetables such as spinach are cleaned with ultrasonic waves, they absorb water and open up, and ethylene signaling is suppressed, so that their stomata remain closed, keeping them crisp and fresh for a longer time (Oda et al., 2021, doi.org/10.1016/j.fochms.2021.100026).

Until recently, ultrasound treatment has long been used in the life sciences as a method to crush cells and tissues and recover proteins and the other biochemical molecules, but novel and unrevealed biological effects of ultrasound, such as promotion of germination and activation of bone regeneration, are beginning to be reported very recently.

**(4) Elucidation of the machinery of intraspecific diversity in medaka (*Oryzias latipes*)**

As shown by the fact that medaka living on the Sea of Japan side of the Japanese archipelago (northern Japan population) and those living on the Pacific side (southern Japan population) are listed as different species in some fish illustrated books, medaka have a great deal of genetic diversity within them. It is revealed that medaka came to the Japanese archipelago from the Continent more than 4 million years ago; medaka is a great neighbor to the Japanese. Because medaka are small and not tasty, they have never been important as a fishery resource for the Japanese people, although they have been very close to the Japanese people's lives. Thanks to these fortunes, the medaka populations that have naturally formed have still survived throughout the Japanese archipelago without significant disturbance by human. We have maintained 74 populations of natural medaka collected from all over Japan 35 years ago. This is a living library of medaka genomes, each with a slightly different genome and exhibiting a variety of characteristic traits. We are looking for evidences that epigenetics contributed to speciation in medaka.

(Picture 3, 4)

Picture 3: Activation of spinach after ultrasonic washing

Picture 4: Outdoor medaka rearing facility