【Grant-in-Aid for Scientific Research(S)】

Integrated Science and Innovative Science (New multidisciplinary fields)

Title of Project：Visualization of radiation induced mutagenesis in vivo

Hiroshi Mitani
(The University of Tokyo,Graduate School of Frontier Sciences, Professor)

Research Area：Risk science of radiation

Keyword：Radiation, Mutagenesis, Medaka, Mouse, Apoptosis

【Purpose and Background of the Research】

A complex network of signaling proteins sense radiation-induced DNA damage and activates the cellular response, which activates cell-cycle checkpoint, DNA repair and apoptosis. The defects in this process lead to mutation, cancer, and cellular death. However, the comparison of mutation frequency among cells in various kind of tissue is very hard to study. In this project, we will establish the now bioimaging assay systems using Medaka and mouse to measure the radiation-induced mutation frequencies quantitatively, and examine the following objectives.

1) Identification of genes that determine the frequency of radiation-induced mutation in vivo.
2) The contribution of metabolic condition and environmental stress on radiation-induced mutagenesis in vivo.
3) Screening of antiradiation drugs which reduce radiation induced mutation frequency and apoptosis.

【Research Methods】

1) Visualization of radiation induced mutation in vivo
GFP tagged reporter gene and expression repressor target gene will be introduced in to mouse and medaka. The deletion mutation in target gene will enhance the expression of reporter gene. The spontaneous and radiation-induced mutation will be quantified using flow cytometry.

2) Establishment new strain for detection of radiation-induced mutation
The assay system described above will be introduced into Medaka and mouse embryos to establish the transgenic strains to determine the mutation frequency of cells in vivo.

3) Visualization of DNA damage response in vivo.
The transgenic Medaka with GFP expression construct regulated by promoter of stress-inducible gene will be established. The radiation-inducible GFP signals in vivo will be measured quantitatively.

4) Isolation of new mutant strains with DNA repair defects
New DNA repair deficient Medaka mutant strains will be isolated from Tilling library。The in vivo mutation in these strains will be measured and the suppression of mutation frequency by antiradiation drugs will be compared to that observed in wild type strain.

【Expected Research Achievements and Scientific Significance】

Because of very low frequency of mutation after irradiation with non-lethal dose of radiation, it is hard to analyze mutation frequency quantitatively. The main purpose of this project is development of new assay system for mutation in both vivo. Medaka is an ideal model for large-scale sampling and similar assay also will be applicable to mouse. And we will screen drugs, which can modify radiation-induced mutation frequency in vivo.

【Publications Relevant to the Project】

Aizawa,K.et al. (2007) Responses of embryonic germ cells of the radiation-sensitive Medaka mutant to γ-irradiation. J. Radat. Res. 48, 121-128.

Mitani,H et al.(2006) The Medaka Genome: Why we need the multiple fish models in vertebrate functional genomics. Genome Dynamics vol2."Structure and Evolution of Vertebrate Genomes" Edited by Volff JN. Karger Publishers Basel p.165-182.

【Term of Project】 FY2009-2013

【Budget Allocation】 76,300 Thousand Yen

【Homepage Address and Other Contact Information】

http://park.itc.u-tokyo.ac.jp/K-medaka/index.html