

State of Research and Perspective on Adaptive Response to Low Doses of Ionizing Radiation in Japan

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Abstract

In a review article entitled "Physical Benefits from Low Levels of Ionizing Radiation," published in *Health Physics* in December of 1982, Professor T.D. Luckey of the University of Missouri, asserted the "radiation hormesis" with 200 references.

This resulted in the first International Symposium on Radiation Hormesis in Oakland, California (August 1985). CRIEPI consulted many specialists about Luckey's paper and studied many other papers such as Lorenz, 1954; Luckey, 1980, Liu et al., 1985.

Radiation hormesis research in Japan has been based on the rationale that if Luckey's claim were to be true, radiation management in Japan has been extremely erroneous.

CRIEPI organized a Hormesis Research Steering Committee composed of leading specialists in the field concerned, and began research in cooperation with a number of universities, as well as the National Cancer Research Institute, and the National Institute of Radiological Sciences. After obtaining interesting results in various experiments on the health effects of exposure to low doses of radiation, we have proceeded on an expanded program, which involves fourteen universities and two research institutes throughout Japan.

The interesting results we obtained can be categorized in five groups.

1. Enhancement of immune systems such as lymphocytes and suppression of cancer,
2. Radio-adaptive response relating to the activation of DNA repair and apoptosis,
3. Rejuvenation of cells such as increase of SOD and cell membrane permeability,
4. Radiation effect on neuro-transmitting system through increase of key enzymes,
5. Others, including the therapy of adult-disease such as diabetes and hypertension.

We are now carrying out experimental activities on the effects of low-dose radiation on mammals. After several years of research activities, we are recognizing Luckey's claim. Some basic surveys including Hiroshima Nagasaki and animal experiments in Japan have brought us valuable informations on the health effects of low-dose radiation. The followings are some topical research informations obtained across Japan.

Topics of Low Dose Radiation Research

(1) Survey of A-bomb Survivors

The follow up data of people who received radiation from the Atomic Bomb show us an interesting feature especially in the low dose range. A certain optimum dose

for the suppression of leukemia was shown through the survey of the people of Hiroshima and Nagasaki exposed to the radiation of the Atomic Bomb.

(2) The Beneficial Effect of Misasa Spa

Professor Emeritus of Osaka University Dr. Kondo and Dr. Tanooka, former Chairman of Japan Radiation Research Society, conducted statistical comparisons of cancer of the people of Misasa villages (i.e. high radon levels in drinking water), adjacent villages and Japan. The result was meaningful especially on the suppression of total cancer.

(3) Medical Application: Treatment of Cancer

Professor Sakamoto used low dose radiation to cure and to suppress the reappearance of cancer in the hospital of Tohoku University. For example, he applied 10 cGy three times weekly for several weeks successfully against liver cancer and lymphatic tumors. He applied whole body or half body low level dose combined with local high dose irradiation to treat non-hodgkin's lymphoma. The low survival rate of 36% in patients with non-hodgkin's lymphoma after five years of the therapy improved to a 90% survival rate with a low dose treatment schema. Some analytical results demonstrate an increase of the ratio of the helper T cells to suppressor T cells.

(4) Cell Rejuvenation

Yamaoka of CRIEPI found cell rejuvenation on the properties of cell membranes and superoxide dismutase activities by 25 cGy to 50 cGy of irradiation.

After low dose of X-ray whole body irradiation, increase of SOD enzyme and decrease of Lipid-peroxide had been kept more than six weeks.

(5) Adaptive Response

Ikushima of Kyoto Univ. examined the radio-adaptive response. Yonezawa of University of Osaka prefecture confirmed two phases of radio-adaptive responses by using a priming dose and survival after a sublethal dose administration. He found that a low enhanced resistance to sublethal x-radiation given two months after 5 to 10 cGy whole body dose, and two weeks after 30 to 50 cGy also.

(6) Response of p53

Professor Onishi of Nara Medical College discovered a marked increase of stress protein production by p53 genes. Dose of 10 to 25 cGy were effective.

(7) Importance of Low Dose Steady Irradiation

Prof. Nomura confirmed the importance of steady low dose irradiation for gene repairing activities, giving evidence that steady low dose administration is essential for obtaining beneficial health effects.

Research Program on the Adaptive Response to Low Dose Radiation in Japan

CRIEPI is running with fourteen Universities on twelve research subjects of adaptive responses, intending to examine the extensive range of biological functions related to low-dose radiation.

The subjects being interested in the research program are as follows:

- (1) SOD response, Lipid-peroxide reduction, and membrane permeability
- (2) Cell apoptosis and anti-cancer effects

- (3) P53 response and its effects
- (4) Response of the central nervous system
- (5) Responses of the intercellular signal transduction
- (6) Enhancement of immune system inhibitory effects on carcinogenesis
- (7) Inhibitory effects of diseases of grown up people such as diabetes
- (8) Effects on the energy metabolism regulation
- (9) Radioadaptive response by DNA repair and apoptosis
- (10) Enzyme response and stress relaxation
- (11) Repair mechanism of DNA aberrations
- (12) Epidemiological analysis of atomic bomb survivors

Closing Remarks

Formation of ions, free electrons and free radicals by ionizing radiation enhances and creates many comprehensive bio-chemical reactions, followed by significant biological responses.

Animal tests results give us a certain scientific synopsis on the adaptive response to low dose effect on carcinogenesis and malignant tumor. Suppression of cell aging. Activation of biological defense mechanisms.

We have such an impression that a certain low dose radiation raises some vitalizations of basic biological functions. The recent progress of analytical technique on the observation of DNA structural responses greatly contributes the unbelievable success of our research on the adaptive responses of low dose radiation.

Analysis of the history of the evolution of living materials through a billion of years shows us all kinds of environmental conditions were put in the extremity of positive utilization without exception in our physical processes, air, water, sun light, temperature, salt, and radiation. This pursuit of the extremity of the positive utilization of the all kinds of environmental factor through the process of evolution is the life itself, in a sense. It is obvious the natural radiation back ground on the earth was fairly higher than present situation in the past days.

On this sense, the adaptive response is the fundamental characteristics of lives. All kinds of damages caused by environmental influence, diseases, loss of power are to be overcome by enhancement of DNA repair and apoptosis activities. This is the way of adaptive response.

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