Data that Revolutionizes the Fundamentals of Radiation Protection over 100 Years and WAM Model

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The content of the submitted poster session of ICRP2023 contains important messages and includes a new important proposal. We have therefore written this note in the hope that the proposals will be understood not only by radiation protection specialists but also by the general public. There we will make a quick survey of the WAM model that we have proposed, including the new proposal of radiation protection. Together with this report, we will also make a short review separately of the history of radiation protection to date

Abstracts contributed to this ICRP2023

Abstract- The content of the poster session

Abstract–

Gondo et.al. conducted whole-genome sequencing (WGS) experiments using mice under low dose-rate radiation environments at Tokai University and IES. The experiments were carried out over multiple generations at dose-rates of 0.05, 0.15, 1.0, and 20 mGy/day. Gondo is scheduled to present their findings orally at this conference [Y. Gondo et al., ICRP Tokyo conference oral presentation]. The obtained results were found quantitatively match the predictions of the WAM (Whack-a-Mole) model, which is presented at the conference[H. Toki et al., ICRP Tokyo conference abstract]. Following the famous Drosophila experiment by Muller in 1927, which demonstrated that mutations could occur in response to artificial external stimuli such as radiation, further analysis was conducted using data from the mega-mouse experiment, which involved mice that are more closely related to humans. Experiments were carried out newly by Gondo et.al. on mice using the WGS technology. We named the series of experimental data obtained by **Mueller, Russell, and Gondo as the MRG data**. The WGS study provided groundbreaking and accurate information regarding the effects of low-dose radiation on living organisms and demonstrate the resilience of the body's protective systems. **As a result, mutations in cells may occur, but at the same time, the organism possesses a mechanism to repair these mutations while maintaining a balance to sustain life. The WAM model clearly incorporates the characteristic of living organisms that involve maintaining equilibrium through the ability to generate mutations and repair them simultaneously** [M. Bando et al., International Journal of Radiation Biology 95 (2019) 1390-1403]. This interplay is expressed as a function of time, represented by a differential equation describing the mutation frequency F as dF/dt = A-BF. Here, A represents the stimuli such as reactive oxygen species or radiation, while B represents the term that represents the battle against these stimuli to counteract mutations. Here, A and B represent the magnitudes of mutation-inducing stimuli and protective stimuli per unit of time, respectively ($A = a_0 + a_1 d$, $B = b_0 + b_1 d$), where d represents the dose-rate. There are **three important quantities derived from the WAM equation. The saturation value** $F_s=A/B$ provides the mutation frequency per generation at low dose-rate. **The saturation time** $t_c=1/B$ provides the time to approach the saturation frequency. **The effective dose rate** $d_{eff}=a_0/a_1$ provides the dose to result in the endogenous mutation frequency. The effective dose d_{eff} derived from the mega-mouse experiment was about 1000 times the natural dose-rate, which was noticed by Muller already after the next year of the original 1927 paper. This fact was clearly demonstrated by Gondo et al., which indicated **that the mutation frequency was not much changed within the dose-rate until 100 times the natural dose-rate**. This finding also serves to clearly generalize the conventional approach of describing the effects of radiation as extrapolating down from the higher dose-rate experiments using LNT (linear no-threshold model) or LQM (linear-quadratic model). **These groundbreaking results reported in the Gondo data represent a paradigm shift in the history of radiation protection.**

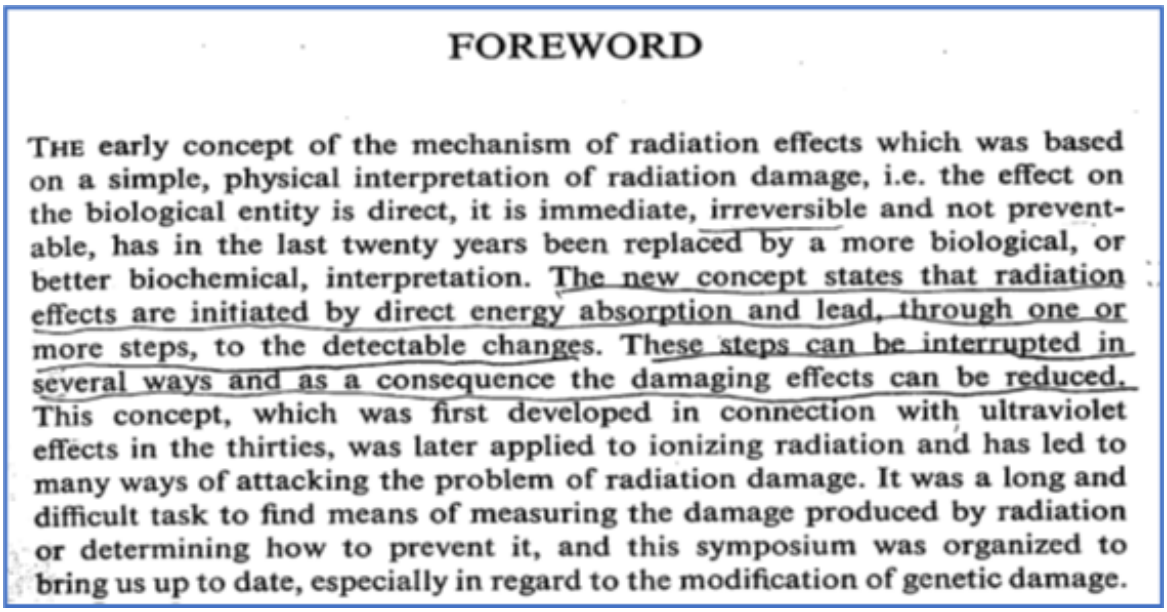
Keywords: WAM; MRGdata;Radiation Four; Five

1. INTRODUCTION

The primary concern for the general public exposed to low dose radiation exposure is the risk at low dose rates. While we acknowledge that we are regularly exposed to natural radiation[b] from the atmosphere as long as we inhabit this planet, we are routinely exposed to falling from the sky, it is natural to worry that the effects of extra exposure to man-made radiation will accumulate over the next 100 years of life and affect our own children and grandchildren. In contrast, according to the LNT/LQM, which has been the basis of radiation protection up to now, the risk of mutation is determined by the total dose exposed. According to this, 'radiation effects are cumulative'. Although it was not without opinion that there might be an effect of dose rate, the effect of dose rate was corrected by parameters such as DDREF, and the prevailing view was that "if the experiment cannot be reproduced, the LQM is sufficient because the parameters can be taken appropriately", and as a simple and convenient formula it has been used for 100 years as the standard The LQM has been used as a standard for 100 years as a simple and convenient formula. The LQM has thus been used as a standard for radiation protection for 100 years. And it has been addressed by the ALARA principle of 'as little radiation as possible'.

However, a crucial issue is actually missing. That is, whether risks are really accumulating or not. This leads to the question of how this relates to dose-rate effects.

The latest data on genomic variation in low-dose-rate radiation exposure will be presented at ICRP 2023 (Gondo)[c]. This ground-breaking report provides clear evidence that radiation experiments up to very low dose rates on the order of 1 μGy/day hardly alter genomic variation (SNVs). SNVs hardly change even when the total dose reaches as high as 100 mGy. The Gondo experiment provided an important experimental fact that differed from previous experiments in that it showed that at low dose rates, even in regions where the total dose was considerably higher, very little mutation was seen. What makes this Gondo experiment ground-breaking?



FOREWORD

THE early concept of the mechanism of radiation effects which was based on a simple, physical interpretation of radiation damage, i.e. the effect on the biological entity is direct, it is immediate, irreversible and not preventable, has in the last twenty years been replaced by a more biological, or better biochemical, interpretation. The new concept states that radiation effects are initiated by direct energy absorption and lead, through one or more steps, to the detectable changes. These steps can be interrupted in several ways and as a consequence the damaging effects can be reduced. This concept, which was first developed in connection with ultraviolet effects in the thirties, was later applied to ionizing radiation and has led to many ways of attacking the problem of radiation damage. It was a long and difficult task to find means of measuring the damage produced by radiation or determining how to prevent it, and this symposium was organized to bring us up to date, especially in regard to the modification of genetic damage.

[b] Natural radiation dose rate about 1 μ Gy/day

[c] Y.Gondo, Oral talk presentation: Whole Genome Sequencing （WGS）; H. Toki et al, Statistical analysis of low dose rate mouse experiments with WGS technology and quantitative reproduction of mutation frequency using Whack-a-Mole Model. poster session

Fig. 1. The forwarded message of the Leiden Conference.

It is related to the shock caused by Russell's first experimental report[d] on the mega mouse experiment in 1958. This was reflected in the opening address at the Leiden International Conference[e], which was held immediately after this (Figure 1). The impact was felt even in Japan. Looking at the records of the Leiden conference, we can see the scientists' thoughts on whether mutations really accumulate in living organisms and to what extent repair mechanisms function. Unfortunately, this desire was inherited and not pursued. LNT and LQM, which have been established for the past 100 years, continue to have flaws to this day.

As the image has become established that cells that have mutated will continue to accumulate in the body, we have heard the fear of evacuees from Fukushima saying, “The devil is accumulating inside the body. It's scary." I want to see the reality clearly. At the beginning of irradiation, there is a tendency for mutations to increase in LNT as a result of the effects, but this is not the only reason. When I talked to a biology specialist, I was pretty much convinced that the mechanism is that the disease gradually subsides due to resistance within the body. Just as we were trying to build a model to formulate a model for risk estimation, we came to know the above history, and we, as physics majors, thought that we might be able to make a more realistic model. and started to investigate the biological effects caused by radiation. It was Lea who created a model to explain the experimental results of LNT observed in flies, called the [hit model]. Lea was a nuclear physicist who wrote an excellent textbook, which you can read for brilliant insights. Unfortunately, Lea passed away at a young age. The textbook[f] is a compilation of Lea's work by his pupil but had Lea lived longer, he would surely have moved on. It was with this in mind that I entered the field; the crucial flaw of the LNT is that it does not take into account the 'bio-toughness' of the organism. It is our Whack-A-Mole (WAM) model that we have proposed by taking account of biological recovery effects. I became more and more convinced as my colleagues increased that biologists were more and more aware of the common sense that living organisms maintain their biological activities by recovering or eliminating mutations in vivo, and we began to collaborate on this.

2. WHACK-A-MOLE (WAM) MODEL

2.1. Formulation

The WAM model incorporates the property that the ability to repair mutations maintains life in equilibrium. External stimuli cause cells to mutate, but the defence function maintains the stability of the organism. This struggle is the essence of life. The response of the organism to mutations in the body is a race against time, and to describe this competition, the time course of mutation frequency is important and the mutation frequency must be a function of time. The mutation frequency F, therefore follows a differential equation with respect to time.

[d] W.L. Russell, Liane Russell and Elizabeth M. Kelly, “Radiation Dose Rate and Mutation Frequency”, Science. Vol.129,P1546 (1958)

[e] Proceeding of an Internal Symposium 1960 held at the University of Leiden, the Netherland, Aug. 13-19. 1962 ” Repair From Genetic Radiation Damage and Differential Radiosensitivity in Gem Cells” , Edited by F.H. Sobels.

[f] D. E. Lea, Douglas Edward, "Radiation Biophysics" (Japanese translation by Yasu Nishiwaki), Iwanami Shoten, 1957. Incidentally, Nishiwaki also wanted to pursue nuclear physics, but nuclear research was prohibited in Japan at the time.

$$\frac{dF(t)}{dt} = A - BF(t), \quad A = a_0 + a_1 d, \; B = b_0 + b_1 d, \qquad (1)$$

A represents the mutation reaction rate in the body due to stimuli such as active oxygen and radiation, and B represents the rate at which mutated cells are eliminated in response to those stimuli. If there is an external stimulus (specifically, a stimulus due to radiation exposure), a term proportional to the dose rate d is added to A and B relative to the normal reaction rate. Not only does F increase (term A), but it also incorporates the effect of decreasing due to the presence of term B.

Let us consider the case where irradiation starts at time t = 0 and at a constant dose rate d. Let us examine the time variation of F at this time. By taking the initial mutation frequency F (t=0) , the solution of (1) is simply solved,

$$F(t) = \frac{A}{B}\left(1 - e^{-Bt}\right) + F(0)e^{-Bt} \qquad (2)$$

By using this simple model we analysed the data of flies and mice. What was surprising about the results was that we were able to reproduce much of the data from flies and mice using just four common parameters[g].

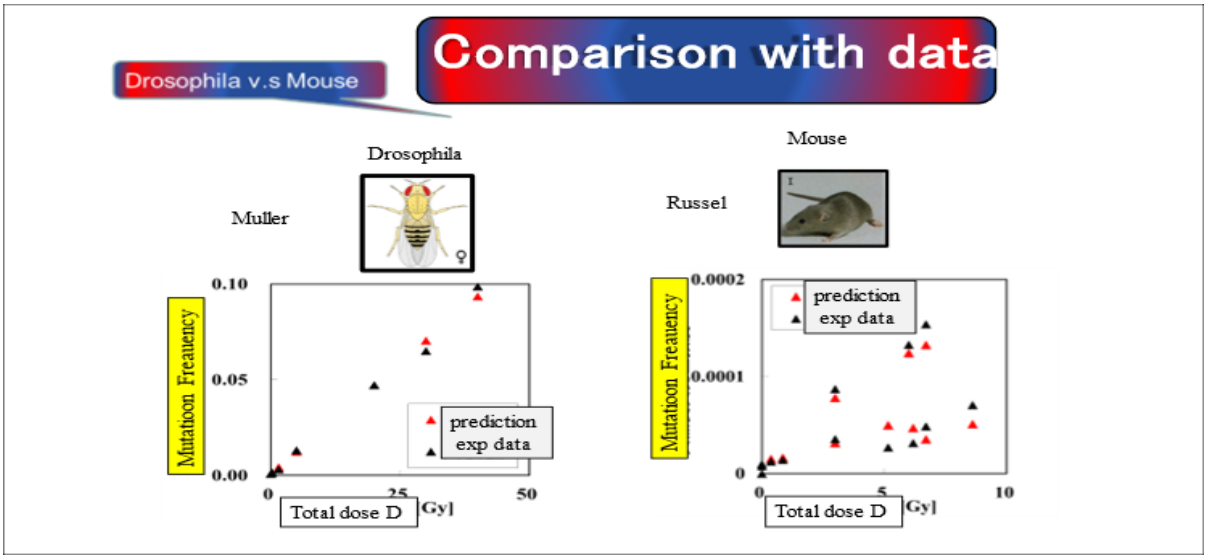


Fig. 2. Comparison of the fly and mouse data with WAM predictions.

$$a_0 = 3.23 \times 10^{-8}\ [1/\mathrm{hr}]$$
$$b_0 = 3.24 \times 10^{-3}\ [1/\mathrm{hr}]$$
$$a_1 = 2.91 \times 10^{-5}\ [1/\mathrm{Gy}]$$
$$b_1 = 1.00 \times 10^{-1}\ [1/\mathrm{Gy}$$

Fig. 3. The common 4 WAM parameters determined from mouse and fly data. .

[g] For the details go to the paper, M. Bando et.al "Study of mutation from DNA to biological evolution" International Journal of Radiation Biology Vol.95, No1 p014201.2049

The fact that the same mechanism is exhibited across species at the cellular level encouraged us to confirm that a unified description can operate at the cellular level. The set of four WAM parameters common to flies and mice thus determined gives us the basis for further discussion.

2.2. Characteristic quantities

In order to better understand the behaviour of the mutation frequency F using the WAM model, let us here explain the characteristics of WAM using diagrams. For this purpose, it is convenient to define the following characteristic quantities.
A simulator is also available on the website, which allows the readers to quickly obtain numerical calculations and graphs of the model.

Fig. 4. WAMSIM:http://radi.rirc.kyoto-u.ac.jp/wam ☛

2.2.1. Steady states Fs and Fs(∞)

From Eq.(2), we find,

$$F(\infty) = A/B = \frac{a_0 + a_1 d}{b_0 + b_1 d} \qquad (3)$$

Also from equation (1), we note that this is the value of F where dF/dt=0, and F becomes time-independent, that is, F is in a steady state. This means that in Equation (2), at t=∞, a steady state is achieved, and the mutant cells in a system do not accumulate. Note that this does not mean that mutant cells are not produced, but that there is a balance between generation and elimination. Figure 5 reproduces this situation. It can be seen that the steady-state value (3) increases as the dose rate increases.

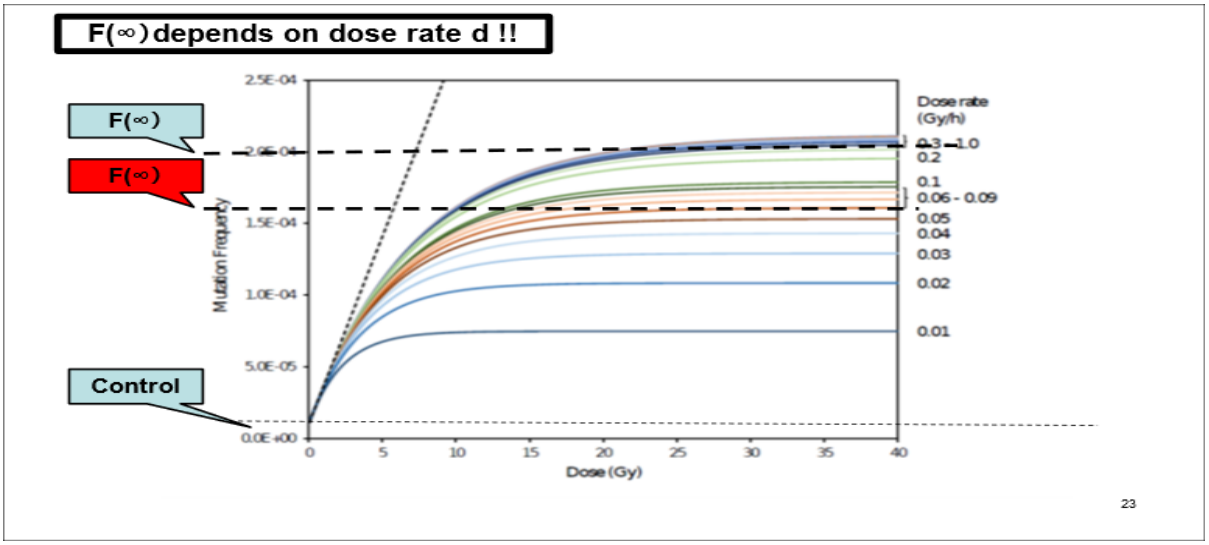


Fig. 5. The steady states F(∞) depends on the dose rate(varying 0.01-1.0 Gy/h) .

For the special case where d=0, that is, the external radiation irradiation is zero, we have the control value, Fs(0)$\stackrel{def}{=}$ Fs, the value of which is from the table (Fig.4),

$$F_s \equiv \frac{a_0}{b_0} \equiv \frac{3.24 \cdot 10^{-8}}{3.00 \cdot 10^{-3}} \equiv 1.08 \cdot 10^{-5} \qquad (4)$$

This is the value commonly referred to as the control term, which is the value that Muller, Russell, and Neel had already focused on. This control term has been confirmed to be of the same character as that of radiation-induced mutations. It is just this very fact that led Neel to propose the notion of 'doubling dose' (DD) since it was known that "induced mutations result in an add-on to spontaneous mutations, which are not specific induced mutations, but any of the existing spontaneous mutations ". Nevertheless, it has hitherto been treated separately from external stimuli. The value of Fs was also unexpectedly large, as Muller also pointed out, and raised the issue in a paper shortly after the 1927 paper[h], 'spontaneous mutations are nearly 10 000 times the value of the effect of natural radiation', and the focus was on control values throughout. This is why control data were carefully measured in the mega mouse experiments.

Indeed, the WAM enabled a unified understanding of control and external stimuli. We shall see later that this has been successfully demonstrated in the Gondo data. Clitical time: Tc

2.2.2. Critical Time Tc

As can be seen from equation (2), the time transition is determined by e^{-Bt},

$$F(t) - F(0) = (A/B - F(0))(1-e^{-Bt}) \qquad (5)$$

This equation shows the temporal evolution of the deviation of F(t) from the initial value.

Let us now consider the following case as F(0); if irradiation is stopped at t = 0, F(0) is large due to irradiation. ; conversely, if the proliferation starts from normal stem cells in one of the organs in the body. The initial value starts from F(0) = 0. Consider the time evolution of F in this case. Let us examine the time transition under the condition d = 0, i.e. (A, B) = (a0, b0), namely for the case of no external stimuli,

$$F(t) - F(0) = (Fs - F(0))(1-e^{-b_0 t}) \qquad (6)$$

Then we find that F(t) approaches to the control value Fs. The critical time Tc is defined as

$$T_c = 1/bo \approx 3.33 \cdot 10^2 [\mathrm{hr}] \qquad (7)$$

so that b_0Tc=1 where the value of Tc is from the table of Fig.3. This is illustrated in Fig. 6. It can be seen from this that, whatever the initial conditions, with time, the condition returns to normal: in about two weeks the difference is reduced by about one-third, and in about six weeks it returns to almost the original normal value. In fact, this should have been observed in the megamouse experiments[i].

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[h] H. J. Muller and L. M. Mott-Smith "EVIDENCE THAT NATURAL RADIOACTIVITYIS INADEQUATE TO EXPLAIN THE FREQUENCYQOF "NATURAL" MUTATIONS " Nature, 124, No. 3128 (1929)

[i] No mention of this is found in the reports of the Megamouse experiments. Russell and his colleagues did not pay any attention to the time dependence and only accurately described the total dose dependence. However, in the book, "Strange Glow-The Story of Radiation" written

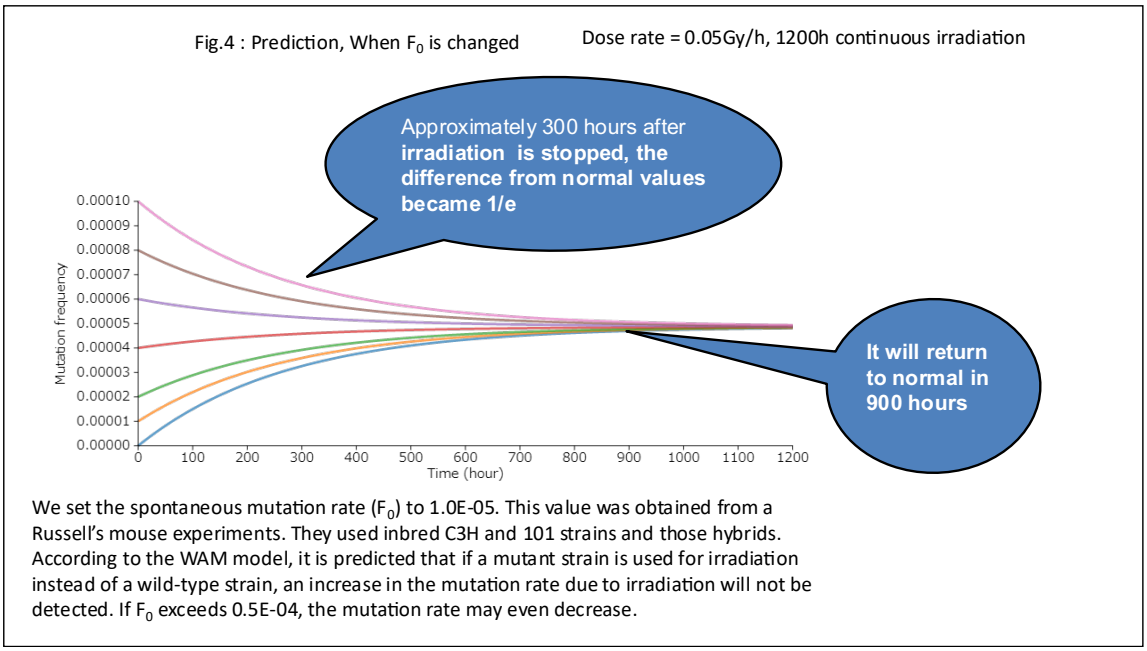


Fig. 6. The mutation frequency, F(t) approaches to normal control value Fs almost 6 weeks after the external irradiation stops.

This recovery effect can be recognized also in the processes during the irradiation period where the total dose D=d・t increases, so that the mutation frequency, which initially increases in proportion to the total dose D, begins to deviate from the LNT after about the critical time Tc has elapsed. If the time is taken horizontal axis, a deviation from the straight line can be seen at approximately a constant time Tc (Fig. 7 left), but if the horizontal axis is taken as the total dose (D = d x t), it can be seen that as the dose rate is stronger, F(t) begins to deviate from the straight line at a larger D (Fig. 7 right).

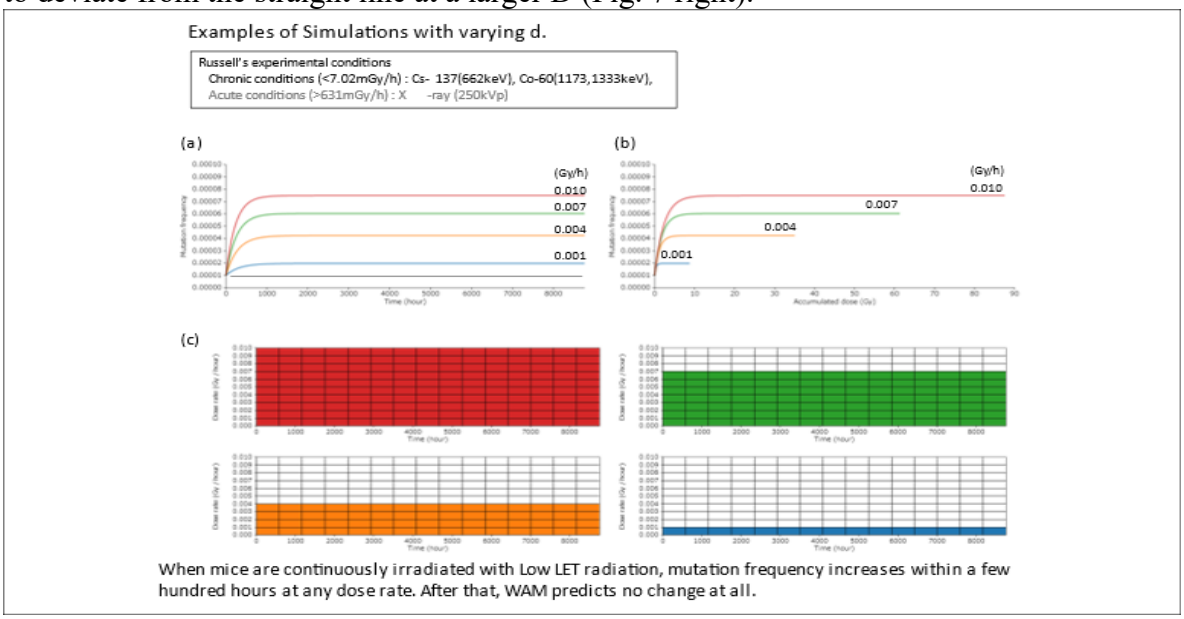


Fig. 7. Starting from Fs the mutation frequency F increases linearly with time t (or total dose D) with dose rate d. It begins to deviate from LNT around the critical time Tc(left) or Dc=Tc・d (right).

by science historian T. Jorgensen, the following is recorded. 'The longer the time between irradiation and mating, the more dramatically smaller the mutation' (p 228).

It should be noted here that we have already mentioned that the parameter values are common for flies and mice, but the lifetime is shorter in flies and relatively longer in mice. In humans, it is even longer. Due to the short lifespan in flies, irradiation experiments had to be carried out at high dose rates and for short durations of time. This meant that they could only observe LNTs in the range of their behavior. In contrast, mice have a long lifespan, so deviations from LNTs appeared gradually with each dose rate. This is precisely the function of the organism to reduce mutant cells, rather than accumulate them, after exposure to radiation. Of course, rapid irradiation can lead to the death of an individual before the relaxation time if a large dose of radiation is administered all at once. However, at low dose rates, F(t) will gradually settle to a steady state, even if aspects of LNT are initially observed. At this time, a deviation from the LNT can be observed, which was the reason why different experimental data were observed at different dose rates, even though the total dose was the same. The time of this deviation was the same for flies and mice, but the lifespan of the flies was too short to give long low-dose experimental results. This was the reason for the difference in data between mice and flies.

2.2.3. Effective dose rate equivalent to cause endogenous mutation

The cell mutations that occur within a living organism are, in a sense, compensation for acquiring the energy necessary to maintain its activities. This is represented by a0 in WAM model. As already mentioned, this value is common to both flies and mice. If we convert this value into ``the radiation dose rate that causes an equivalent mutation,'' how large will it be?

First let the parameter A be written as,

$$A = a_0 + a_1 d = a_1(d_{eff} + d), \quad (8)$$

where we define d_{eff} as “effective dose rate equivalent to cause endogenous mutation” ,which can be calculated as,

$$d_{\mathrm{eff}} = \frac{a_0}{a_1} = \frac{3.24 \cdot 10^{-8}}{2.94 \cdot 10^{-5}} = 1.10\ [\mathrm{mGy/hr}] \quad (9)$$

Which includes the contribution of natural radiation, dn

$$d_n = 0.001\,\mathrm{mGy/hr} = 0.024\,\mathrm{mGy/day} \quad (10)$$

Up to here, we have explained the characteristics of WAM and their meaning using three characteristic indicators. Even in the data obtained so far from flies and mice, if you look carefully, you can see the characteristics of WAM, and it is true that WAM is a simple and clear model that can honestly explain dose-rate effects and the existence of steady-state. However, we still need more conclusive evidence. Indeed, various questions have been raised regarding the WAM model.

(1) “Is there any conclusive evidence of the steady state?”

(2) "Isn't it still within the margin of error?"
(3) “Isn’t DDREF sufficient for the dose rate effect?”
(4) “Did you clearly explain why flies and mice are so different?”
(5) "Is there any evidence of a dose rate effect in the fly data?"

We desperately need definitive data to respond to these criticisms. Unfortunately, after Russell and Muller's experiments, there have been almost no experimental results that measured dose rates or changes over time.

3. MRG (MULLER RUSSELL GONDO) ANALYSIS

3-1 For **MORE THAN** half a century, there were no reliable data to prove the dose-rate dependence of mutation frequencies; even when deviations from LNT were visible, it was common practice to make do with LQMs that included a second-order term for the total dose; LNT-focused only on the total dose dependence and the importance of the time dependence of low-dose-rate experiments was not recognised. Moreover, the importance of the time dependence of low dose rate experiments was not recognized. Moreover, Large-scale experiments such as those on mega-mouse experiments will never be possible again. In order to carry out ultra-low dose rate irradiation experiments, which are expected to provide conclusive evidence, one must be prepared to take the risk of 'negative data'. The Gondo experiment was a daring challenge based on the advances in modern genome analysis. Although the budget was not enough for full analysis of the entire genome sequence, supplemented by theoretical estimation and produced excellent results. The Gondo group then presented data for the first time in the ultra-low dose rate region, clearly showing a region of mutation frequency that does not change over time.

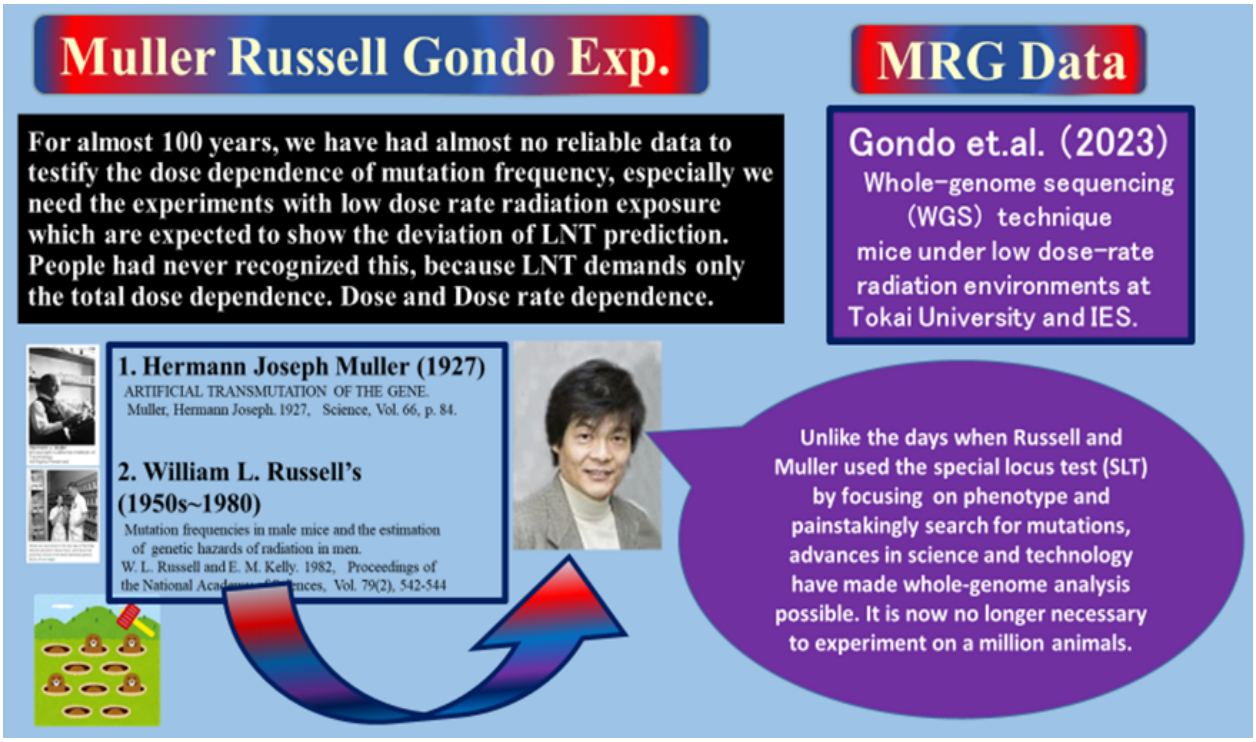


Fig. 8 . Muller Raassell Gondo data

The experimental results were in close agreement with the predictions of the Whack-a-Mole (WAM) model, and the conclusive evidence for the WAM model has been demonstrated **.**

How was this possible? This is partly because we constructed a 'successional experiment' over the lifespan of mice. And this demands a sea change in the concept of control. Experiments of continuous irradiation beyond the 'recovery time', so to speak, meant that the background natural radiation was a control term in areas of relatively high radiation. Thus, for the first time, it could be demonstrated that the WAM provided a theoretical framework that not only describes the effect of radiation on mutation frequency but also describes endogenous mutations in a unified way at the same time.

Let us recall that the content of A is expressed by three contributions: so-called endogenous mutations within the body, natural radiation d_n, and artificial radiation dose d_{EFF}.

$$A = a_1 (d_{eff} + d_n + d) \quad (11)$$

As already mentioned, the contribution of natural radiation d_n is approximately 1/10,000 of the endogenous mutation. The dose rate set in the Gondo experiment is in the ultra-low range comparable to natural radiation. The total dose is also distributed over an order of magnitude of data points. Figure 9 shows the difference between regions of the Gondo data in comparison with the diagram shown in the previous analysis (Figure 7). Since the Gondo data is in a very low dose region, it is concentrated almost near the origin.

3-2 Let's compare experimental data and theory. A detailed comparison of the results of long-term radiation-induced DNA mutations. The detailed comparison of WAM prediction and Gondo experimental data has been demonstrated in the report by Toki et al., so here we will explain the essence of the comparison of the results of the WAM model simulation described in §3 with the Gondo data. In the diagram of the total dose dependence of mutation frequency due to WAM (Figure 6) seen in §3, the contrast with LNT was important. Since it is not on a logarithmic scale, the range covered by the Gondo experiment is the area surrounded by the black circle in Figure 10A, which in normal memory is concentrated almost near the origin. Since this was a super-low dose rate irradiation experiment, the total dose are naturally concentrated near the origin.

Since the data has undergone a relaxation time, it has already almost reached a region of steady state, and the reader will notice that F is of the same order as natural radiation, dn = 0.024 mGy/day, as shown in equation (10). As was already mentioned, dn is of the order 1/10000 compared with the contribution of controls, it is clear that the influence of ultra-low dose rate irradiation experiments on F is of this order. Thus, we have confirmed a good agreement between the WAM results and the Gondo data. On the other hand, LNT demands that the total dose should increase in proportion to time (total dose D also), which clearly contradicts the Gondo data. This clearly indicates that it is absolutely impossible to use term A alone; term B is absolutely necessary, and it cannot be reproduced simply by adjusting the LNT parameters. Furthermore, accepting this fact, it can be derived that there is almost no change in long-term experiments with a dose rate of 1 mGy/day. On the contrary, WAM predicts that F (t) is almost the same as the case where external radiation is almost zero up to a dose rate of about 1 mGy/day. The Gondo experiment is very important data in that it showed that up to a certain dose rate, there is no effect even if the total dose becomes quite high, and WAM is important to be able to explain those phenomena.

It is worth noting that the mutation response and recovery rates determined from Muller's fly experiments and Russell's mouse data are almost identical across species. It is no exaggeration to say that such beautiful insight had already expressed by Neel, saying that

'DNA, is DNA' has been realised in the WAM after almost 100 years. By extension, this means that the Gondo data could be accurately predict and prove to be in excellent agreement with the experimental data. In this way, the WAM solved a century-old riddle and clearly demonstrated the deviation of LNT and LQM. We are convinced that this is an epoch-making result that will revolutionise the history of radiation protection, which has been formulated by treating controls differently.

Fig.10 Mutation frequency F per generation after organizing this data is indistinguishable from that of the control. Figure 11 shows this region plotted on a logarithmic scale and compared with the data and WAM results.

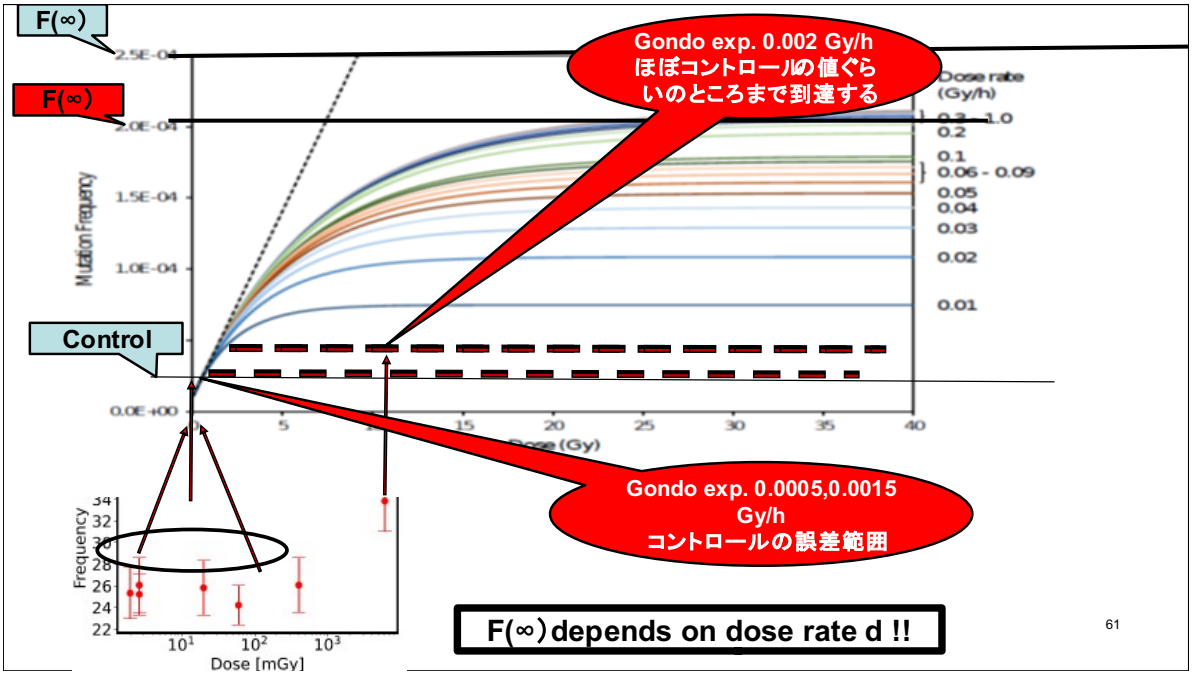


Fig.9 Dose dependence of Gondo data this data is indistinguishable from control.line

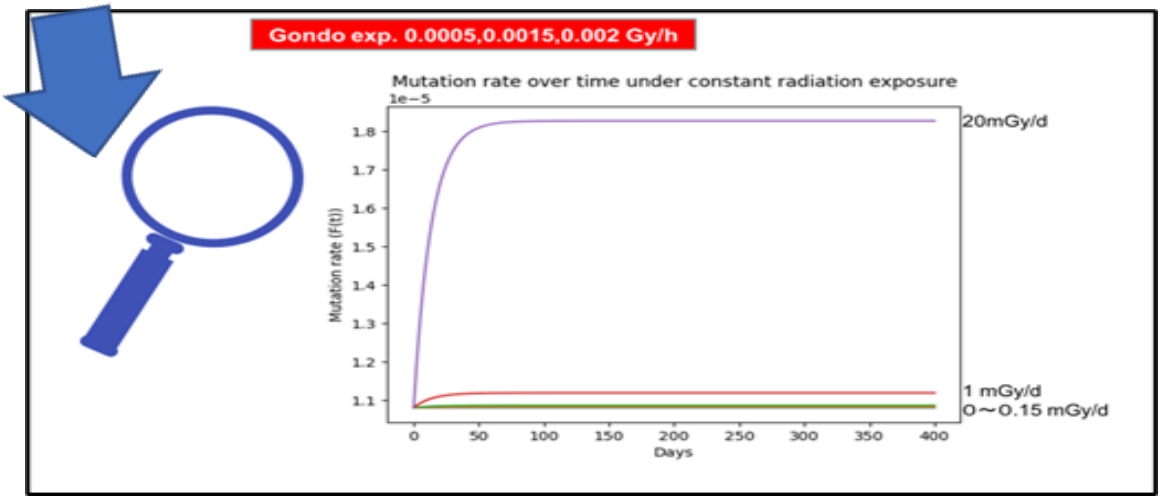


Fig.10 Enlarged view of Gondo data in Figure 8

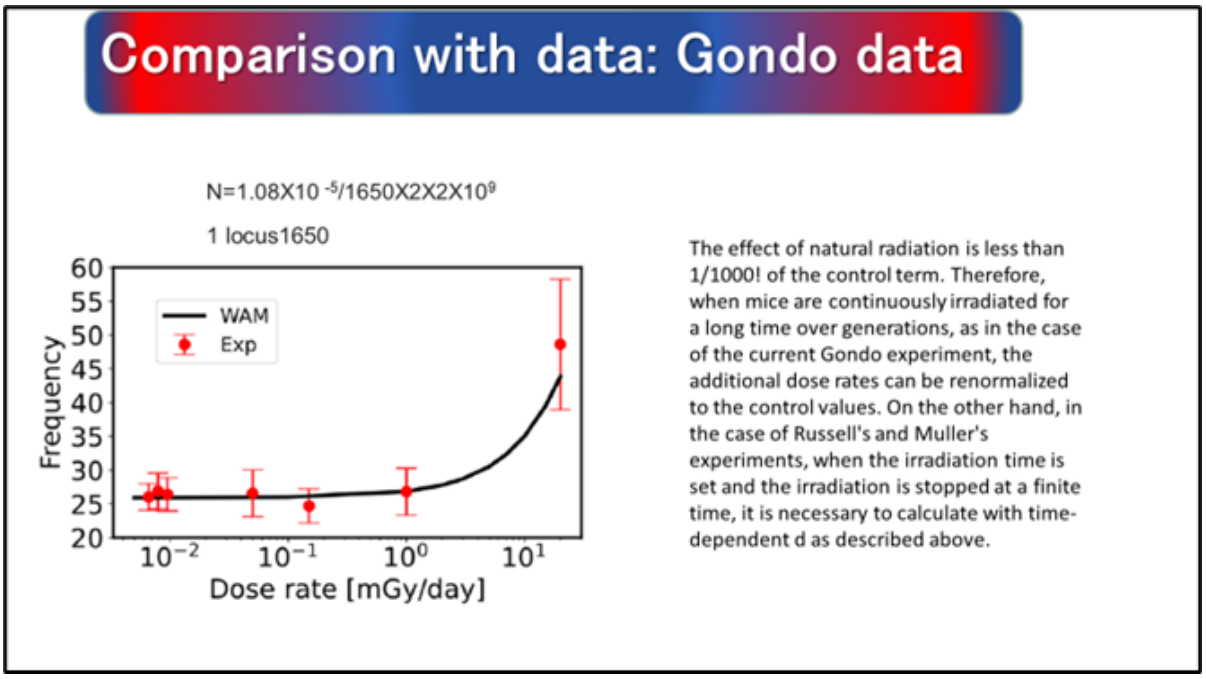


Figure 11 Comparison of WAM Results wi Gondo data.

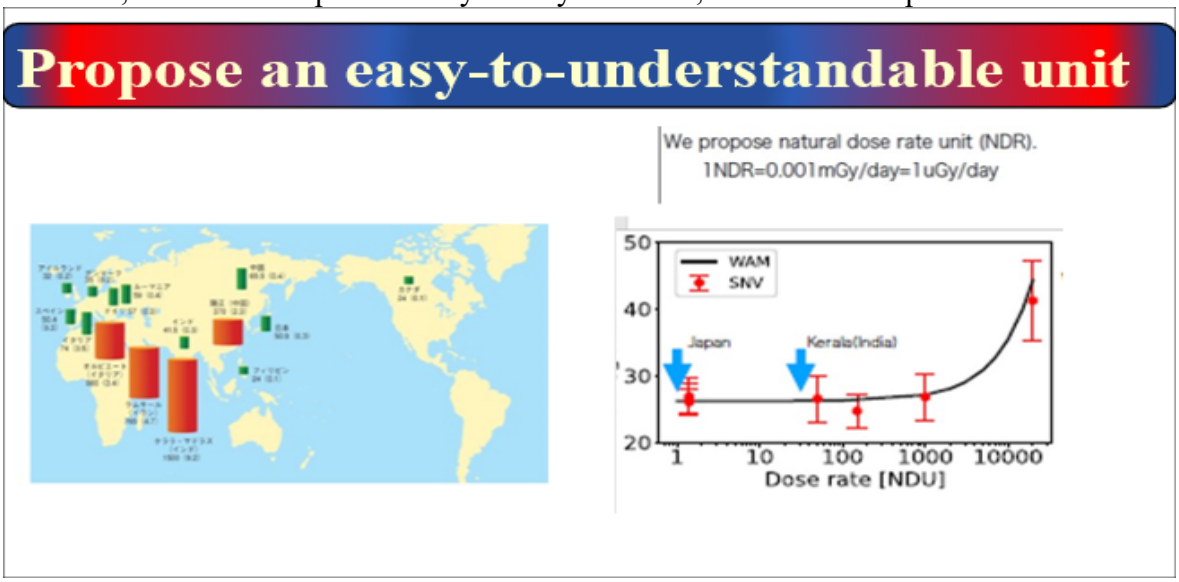
4 Proposal of Natural Dose-Rate Unit (NDR)

From the above considerations, the control ultimately caused the same amount of variation as irradiation at the "equivalent dose rate," and we were able to understand the variation due to natural radiation and external radiation irradiation in a unified manner. In this way, it is possible to predict mutation frequencies that take into account differences in natural radiation levels in high-dose areas around the world. The ``effects of extra dose", which until now relied on epidemiology, can now be estimated theoretically. Note again that the effect of natural radiation is less than 1/1000-10000 of the mutation rate in controls. In long-term, continuous radiation exposure experiments on mice, such as the Gondo experiment, the additional dose rate can be incorporated into natural variation. In fact, health impact studies are being conducted in ``High Background Radiation Areas" such as Kerala, Guarapari in Brazil, and Guangzhou in China. Figure 13 shows which areas fall under this area.It can be seen that the current experiment uses dose rate data that corresponds to these areas. Therefore, if you conduct experiments on mice in these areas, it can be assumed that the same result as the Gondo data is obtained.

Here we would like to propose that instead of using the conventional total dose Gy, we should instead display the dose rate, and display "how many times stronger is the intensity than natural radiation?" in units of {NRR}. I think this would allow the general public to understand without confusion. In any case, 10, 100, and 1000 are easy to understand, but millimeter and micro are difficult to distinguish because they cannot be distinguished with the naked eye. Figure 14 shows the radiation doses at various locations using this display. I used the NDR unit to draw dose rate maps at several locations on the ground and in space.

The reason for the 100-year-old mystery [why dose rate effects were seen in mouse experiments but not in fly experiments] has been clarified. The only way to solve the mystery is to actually check it out. Unfortunately, in the animal experiments that followed the MR experiments, only the total dose dependence was recorded, ignoring both dose rate

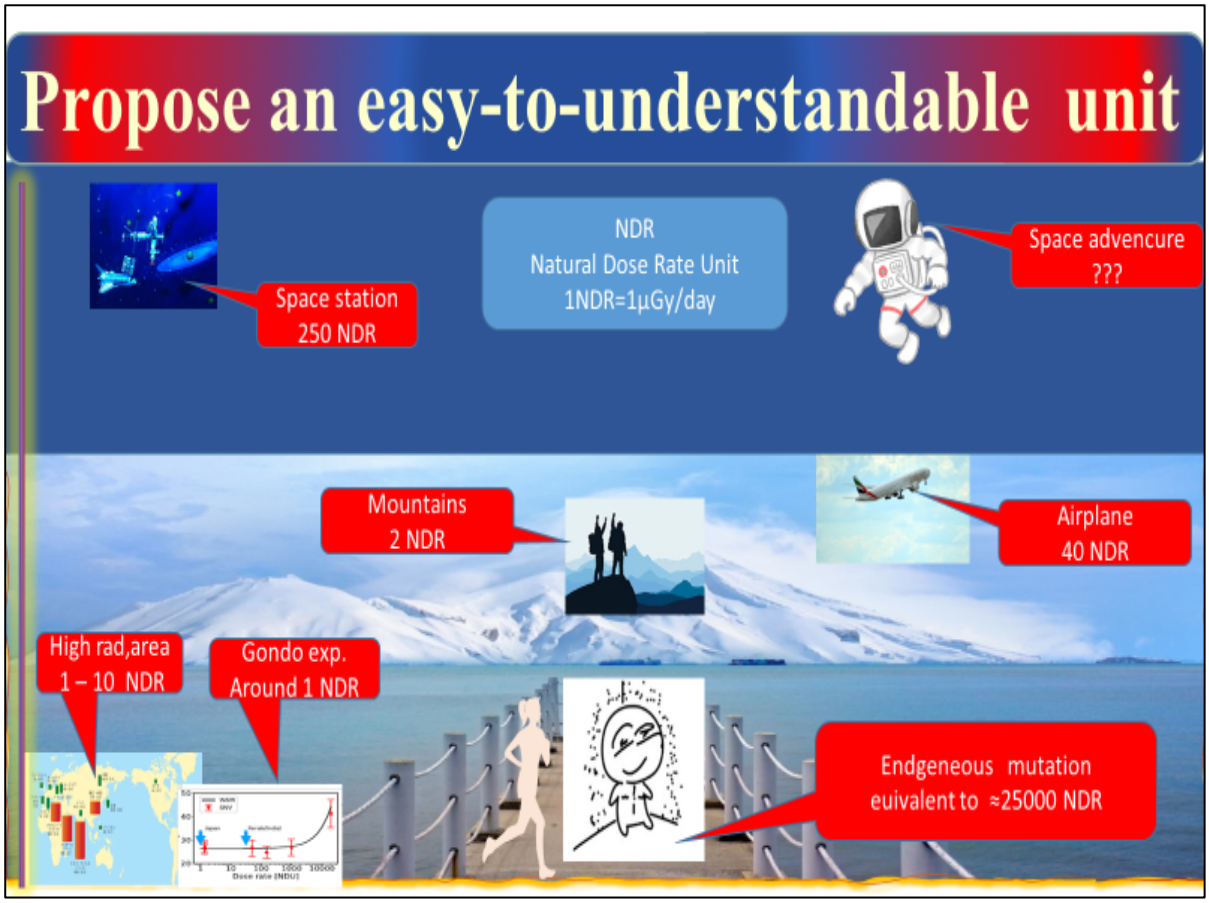
and time history. Even in Russell's report that looked at the effects of fractionation, the time course during irradiation was not mentioned at all in the paper. The only report we found was a book written by Timothy J. Jorgensen that mentions experiments on mice, stating that ``the longer the time between irradiation and mating, the more dramatically the mutations become smaller.'' has been written. The fact that only the total dose is recorded may be due to Mueller's influence. However, as an experimenter, I find it strange considering that it is common sense to leave protocols in place. Since Lee Russell was still alive, we visited her and asked her about her situation, but we were told that she was sleeping in the basement of Oak Ridge, buried among a vast amount of documents. There was talk that Mr. Higuchi, who specialized in the history of science, was interested and wanted to organize the materials, but since Lee passed away shortly after that, it has not been possible to confirm



4 CONCLUSION

The reason for the 100-year-old mystery [why dose rate effects were seen in mousxperiments but not in fly experiments] has been clarified. The only way to solve the mystery was to actually check it out. Unfortunately, in the animal experiments that followed the MR experiments, only the total dose dependence was recorded, ignoring both dose rate and time history. Even in Russell's report that looked at the effects of fractionation, the time course during irradiation was not mentioned at all in the paper. The only report we found was a book written by Timothy J. Jorgensen that mentions experiments on mice, stating that ``the longer the time between irradiation and mating, the more dramatically the mutations become smaller.'' has been written. The fact that only the total dose is recorded may be due to Mueller's influence. However, as an experimenter, I find it strange considering that it is common sense to leave protocols in place. Since Lee Russell was still alive, we visited her and asked her about her situation, but we were told that she was sleeping in the basement of Oak Ridge, buried among a vast amount of documents. There was talk that Mr. Higuchi, who specialized in the history of science, was interested and wanted to organize the materials, but since Lee passed away shortly after that, it has not been possible to confirm this. However, we are now in an era where the entire genome can be read. In this Gondo experiment, due to budget constraints, we had to be satisfied with the genome analysis of a dozen or so animals, but if we use at least 100 animals, we can expect to get data comparable to the megamouse experiment. Although radiation can cause mutations that are dangerous to life, as the Curies originally intended, it also serves as a savior, ``defeating cancer cells.'' Rapid cure for cancer was slow to spread in Japan due to the severe effects of the

atomic bombing. Radiation therapy is now becoming popular, including for prostate cancer. At a cancer treatment center located alongside Cancer Spring Eight in Hyogo Prefecture, patients receive about 2 GY of radiation per day, and then play tennis and lead normal lives. I was surprised to find out that this kind of treatment can be done without cutting. Radiation therapy will continue to be used more and more in medical settings. In this medical setting, radiation doses are of course focused on cancer cells, but sometimes irradiation is on the order of 20Gy or 40Gy. At this time, the passage of time is important information, but current LNT calculations do not know the history of time at all. It is useless if you want to know the time history. What should be the unified n be used uniformly in these settings. The results of any science can be used to benefit human welfare and health, but they can also be used to control of radiation protection and radiotherapy? WAM is a method that ca effectively. We study the biological effects of radiation in order to find a way to live wisely. Harm humanity. Human beings have learned how to live wisely by seeing through the nature of others, understanding the rules, and using them Looking back, research in radiobiology began immediately after the discovery of radioactivity in 1896. In 1927, he demonstrated for the first time that spontaneous mutations can occur even when exposed to an artificial external stimulus called radiation. Following this famous experiment, we applied the parameter set obtained from the analysis of the mouse experiment (mega mouse experiment), which is more similar to humans, to the data of Gondo et al., and found that the experimental value at a dose rate of 20 mGy/day was 95 We were able to reproduce this with a confidence level of 1.5%. This series of experimental data was collectively referred to as MRG data, an acronym for Mueller-Russel-Gondo. These results provided ground-breaking and accurate information for considering the effects of low-dose radiation on living organisms and also demonstrated the strength of living body protection systems. Life activities such as cell proliferation that take place within living



organisms constantly consume energy. With radiation maps in hand, humanity will venture into space.

Achonowledement

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