MRG Data that Revolutionizes the Fundamentals of Radiation Protection over 100 Year and the Theoretical Reproduction & Interpretation by the WAM Model

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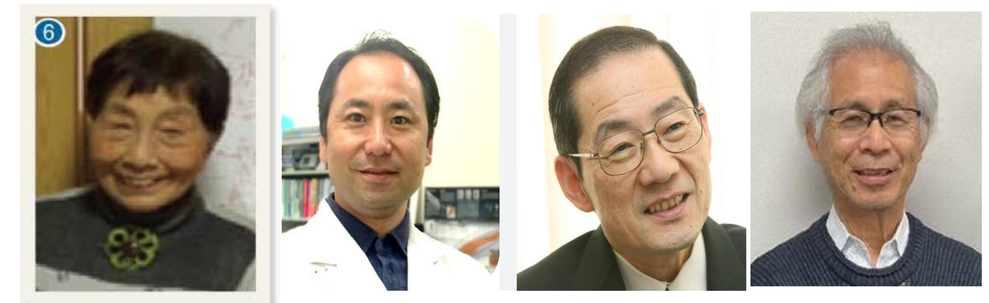
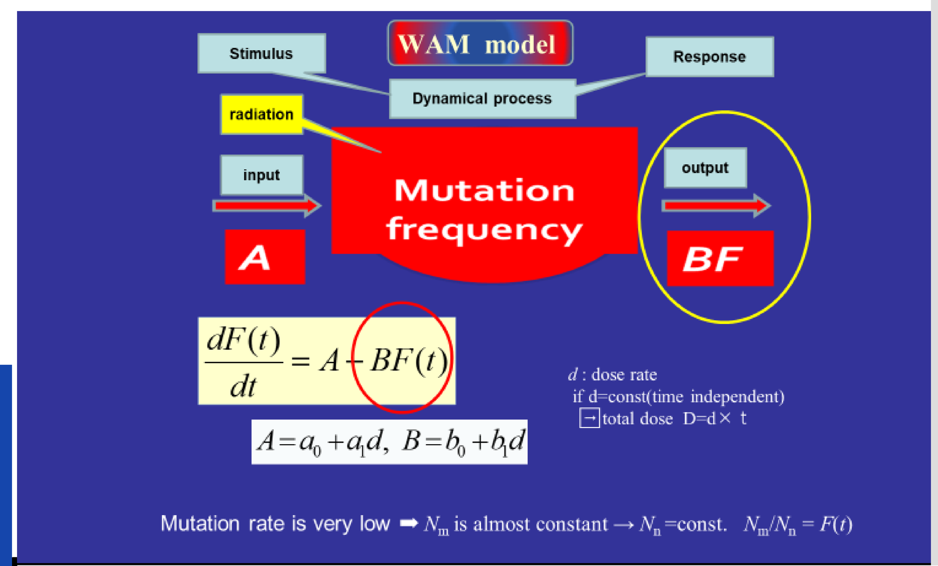


Biological effects caused by radiation exposure

From the view point of Modern molecular biology
Two important exp/of mutation frequency exp.
SLT (Special Locus Test)

1. Hermann Joseph Muller's Exp. (1927)
ARTIFICIAL TRANSMUTATION OF THE GENE.
Muller, Hermann Joseph. 1927.
Science, Vol. 66, p. 84.

2. William L. Russell's Exp.(1950s~1980)
Mutation frequencies in male mice and the estimation of genetic hazards of radiation in men.
W. L. Russell and E. M. Kelly. 1982,
Proceedings of the National Academy of Sciences, Vol. 79(2), 542-544



Prediction by WAM model : if dose rate (d) is constant …

Solution of WAM equation

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

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

if d is constant - Under an environment that constantly exposed at a certain dose rate

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

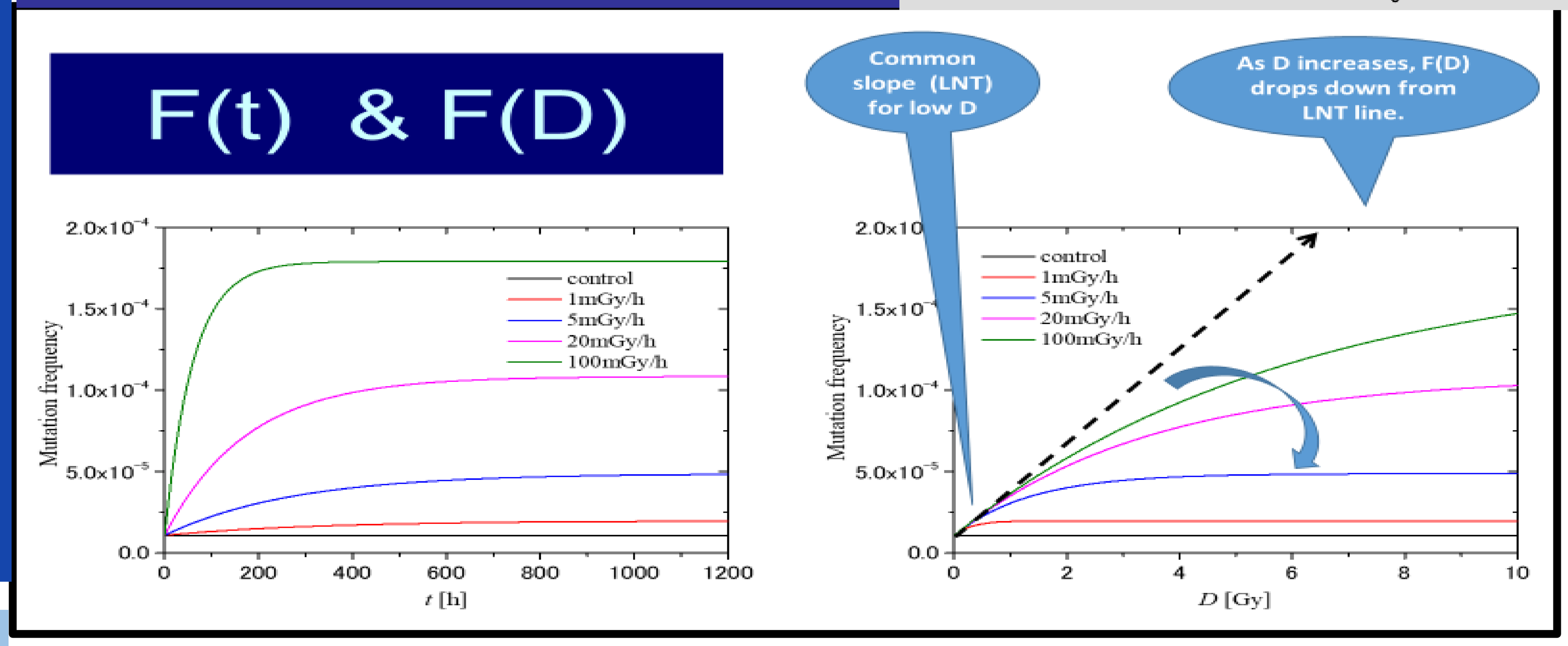
$$F_s = F(\infty : d = 0) = \frac{a_0}{b_0}$$

The INT or LQM has been the basic principle of for almost 100 years.
They depend only on total does and failed to explain the exclusive mechanism or cancer growth effect in estimating biological risk for the former or in clinical planning for the latter.
We need dynamical equation, as a consequence it predicts dose rate dependence.
The t-dependence is essential to overcome the difficulty

LNT : confirmed only by Drosophila data
How about animals : more like human
→ mouse →Mega-mouse project
with various dose rate

NAS（BEAR）→BEIR →UNSCEAR→ICRP

F(t) & F(D)

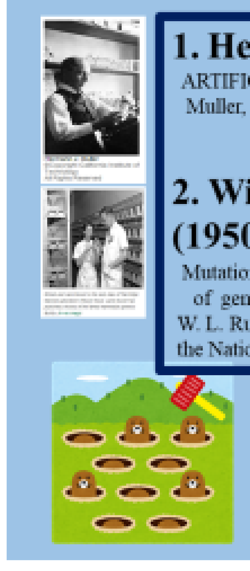


Muller Russell Gondo Exp.

For almost 100 years, we have had almost no reliable data to testify the dose dependence of mutation frequency, especially we need the experiments with low dose rate radiation exposure which are expected to show the deviation of LNT prediction. People had never recognized this, because LNT demands only the total dose dependence. Dose and Dose rate dependence.

MRG Data

Gondo et.al.（2023）
Whole-genome sequencing (WGS) technique
mice under low dose-rate radiation environments at Tokai University and IES.



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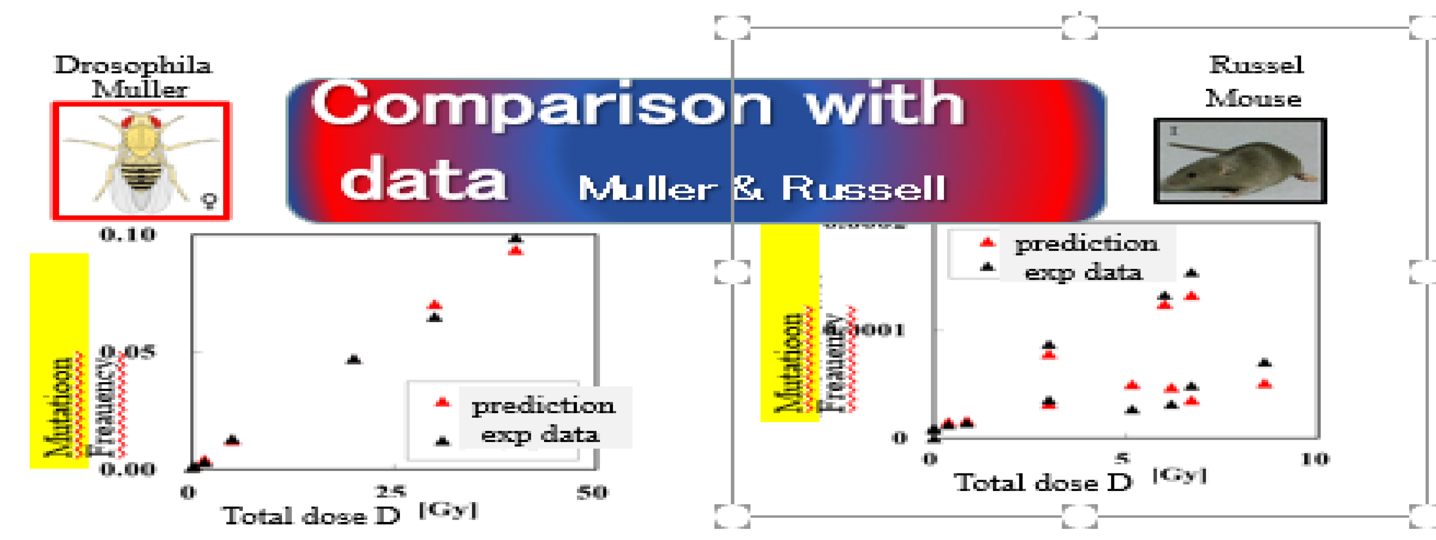
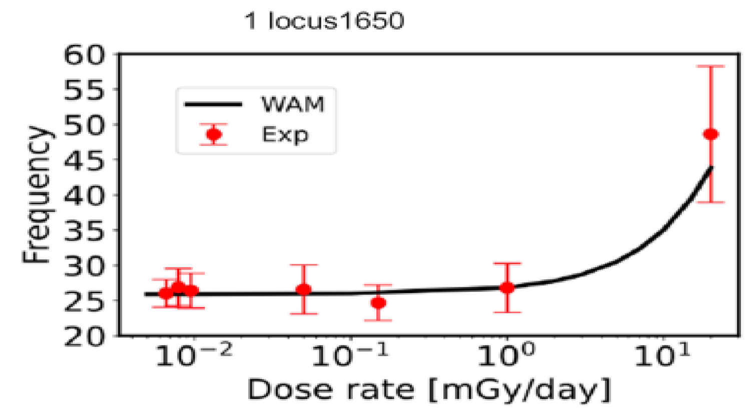
Unlike the days when Russell and Muller used the special locus test (SLT) by focusing on phenotype and painstakingly search for mutations, advances in science and technology have made whole-genome analysis possible. It is now no longer necessary to experiment on a million animals.

Comparison with data Muller & Russell



Comparison with data: Gondo data

N=1.08X10 -5/1650X2X2X10⁹
1 locus1650



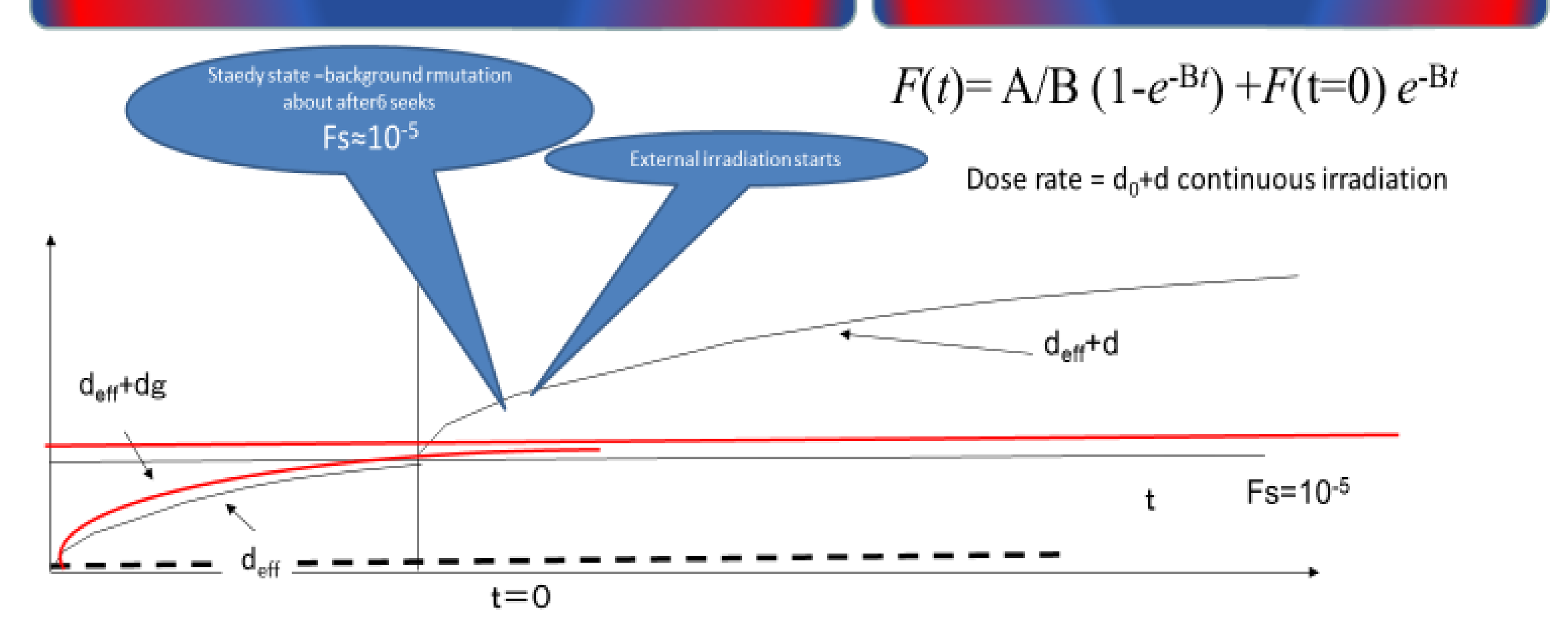
The effect of natural radiation is less than 1/1000! of the control term. Therefore, when mice are continuously irradiated for a long time over generations, as in the case of the current Gondo experiment, the additional dose rates can be renormalized to the control values. On the other hand, in the case of Russell's and Muller's experiments, when the irradiation time is set and the irradiation is stopped at a finite time, it is necessary to calculate with time-dependent d as described above.

What is the control value?

Spontaneous mutation frequency

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

Dose rate = d_0+d continuous irradiation



The definition of d_{eff} is the dose rate corresponding to the one that causes the endogenous mutation. Therefore, it is equivalent to performing an irradiation experiment at a dose rate of d_{eff} until t=0 and then at d+d $_{eff}$. On the other hand, in the Gondo experiment, since continuous irradiation was performed at the dose rate dg from the beginning, it corresponded to the irradiation procedure at the dose rate of dg+d_{eff} (red line).

We confirm that both the control and the external radiation exposure procedure can be calculated from the same WAM equation.

Characteristic Quantities

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

- **spotaneous mutation frequency**

$$F_s = \frac{a_0}{b_0} = \frac{3.24 \cdot 10^{-8}}{3.00 \cdot 10^{-3}} = 1.08 \cdot 10^{-5}$$

- **critical time**

$$T_c \approx \left(1 - 0.051\frac{d}{d_{eff}}\right) \cdot 3.33 \cdot 10^2 [hr]$$

$$D_c = t_c \cdot d$$

- **effective dose-rate**

$$\Rightarrow a_o = a_1 d_{eff}$$

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

$$d_{eff} = d_n + d_o$$

Spontaneous mutation frequency

Natural radiation

$$A = a_0 + a_1 d, \quad \Rightarrow a_o = a_1 d_{eff}$$

Conclusion

For almost a century, definitive conclusions about dose rate effects have remained pending due to a lack of time course data. Gondo's data presented dose rate effects in the region of low dose rates. Definitely, this groundbreaking result strongly calls for a review of LNT LQM.

A review of the basic risk calculation formula LQM (LNT) is essential for the 2028 Main Recomm

1NDR=0.001mGy/day
d_{eff}=1mGy/hr
=24mGy/day=24000 NDR

WAM provides us with a guiding tool for radio protection

Propose an easy-to-understandable unit