Prolongation of Life Span of Disease Model Mice by Low Dose Rate Irradiation

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Effects of Low Dose Rate Irradiation on Mice

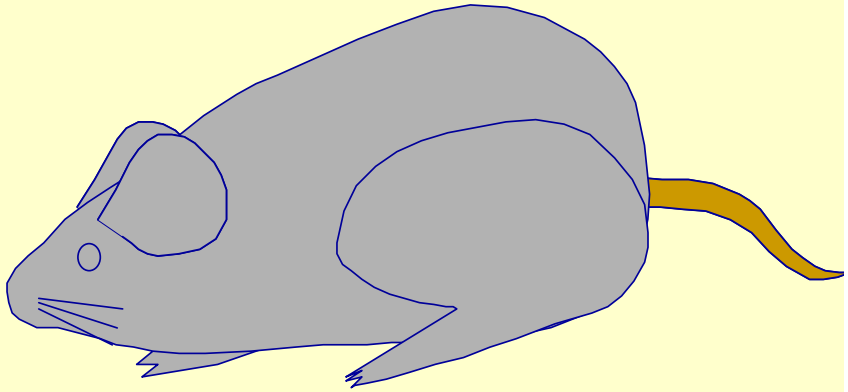
- Suppression of Tumorigenesis
  - Radiation-Induced Thymic Lymphoma
  - Chemically-Induced Skin Tumor
- Suppression of Disease Development
  - Diabetes, Type I and Type II
  - Fatty Liver by CCl_4
- **Life Span Prolongation**

1. Type II Diabetes

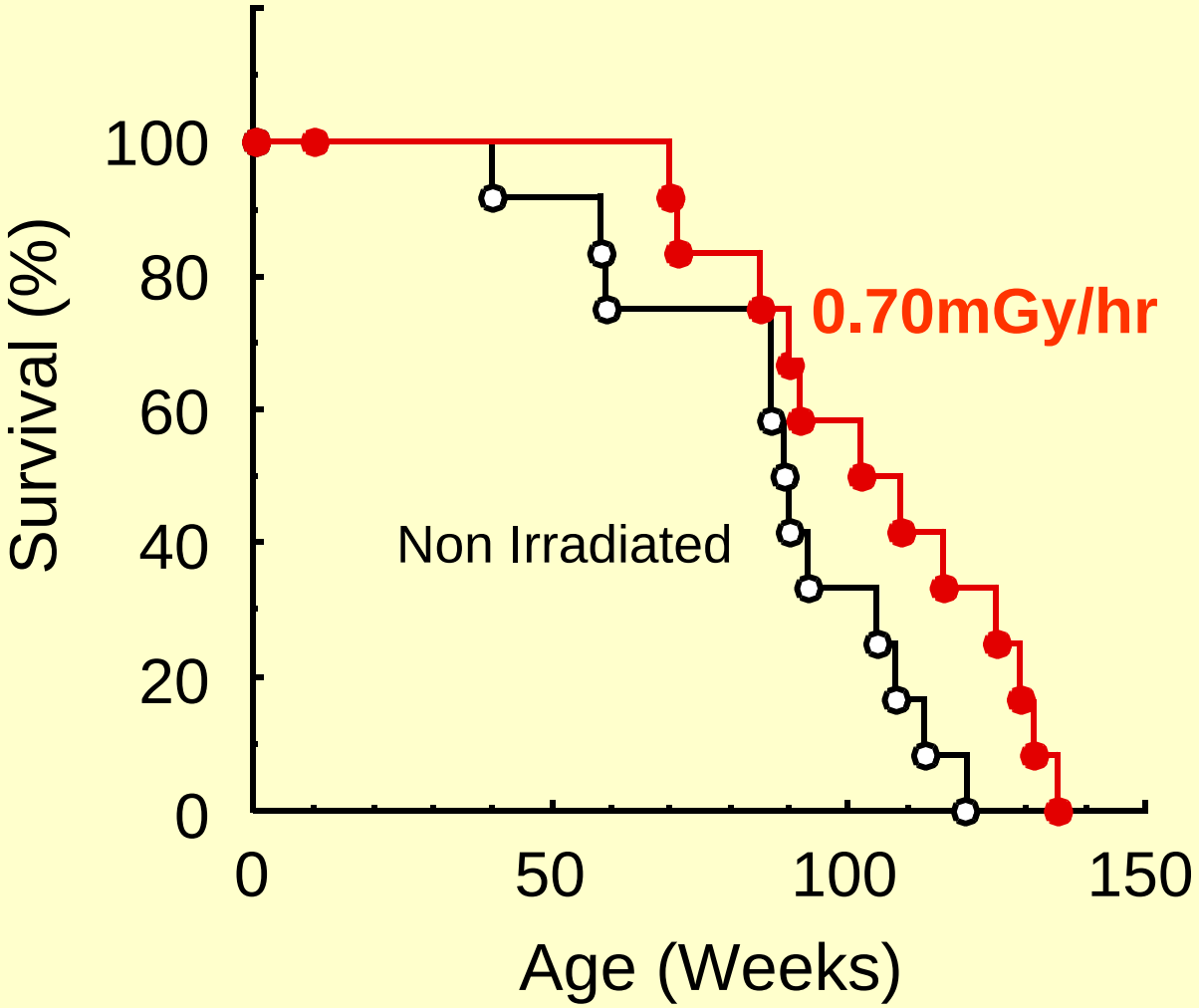
Female BKS.Cg-+*Lepr*^{db}/+*Lepr*^{db}/Jcl
(C57BL/KsJ-db/db)

Dose Rate: 0.70mGy/ hr

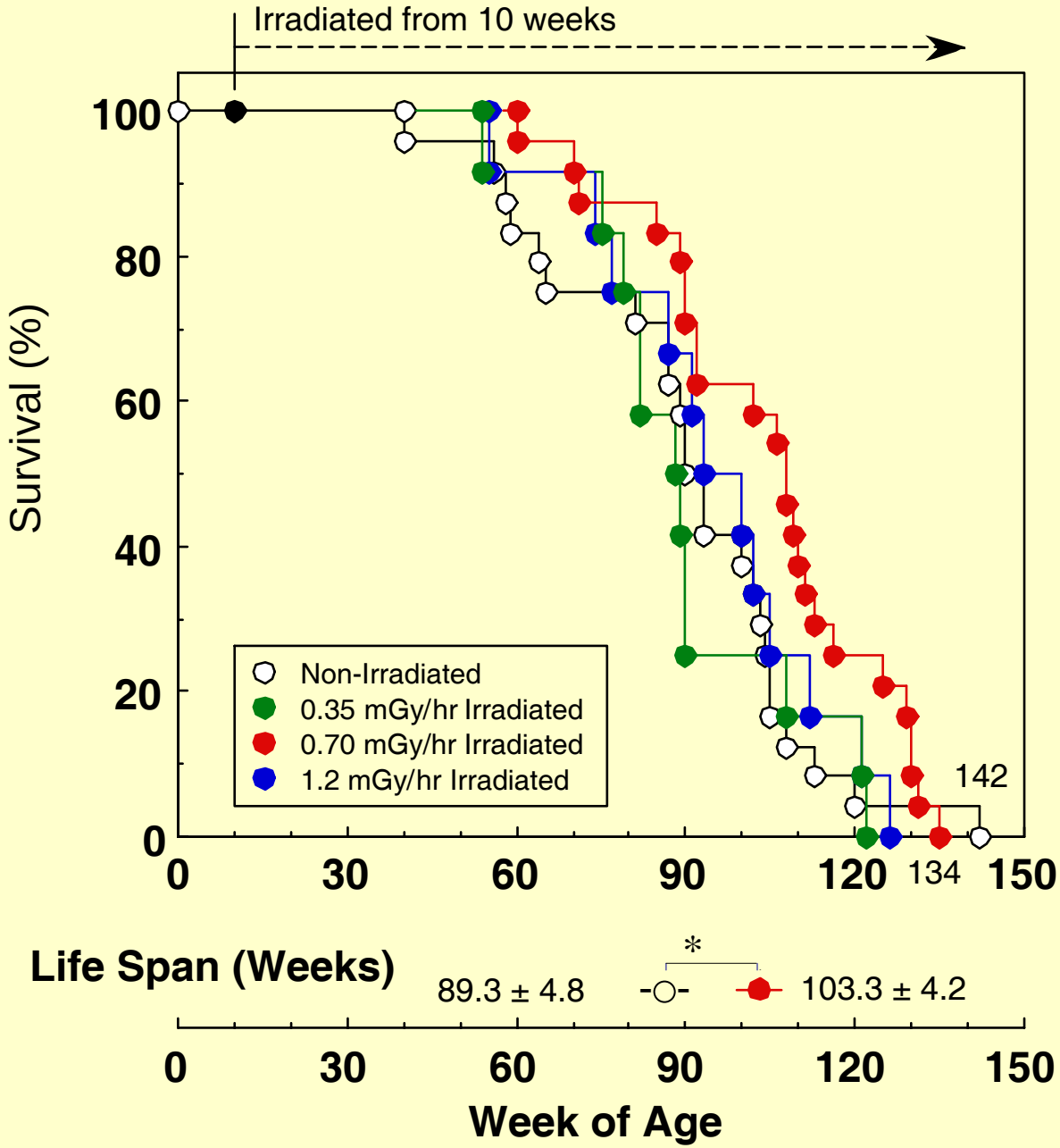
(10 Weeks Old at the Beginning of the Irradiation)



Prolongation of Life Span of db/db Mice by Low Dose Rate Irradiation

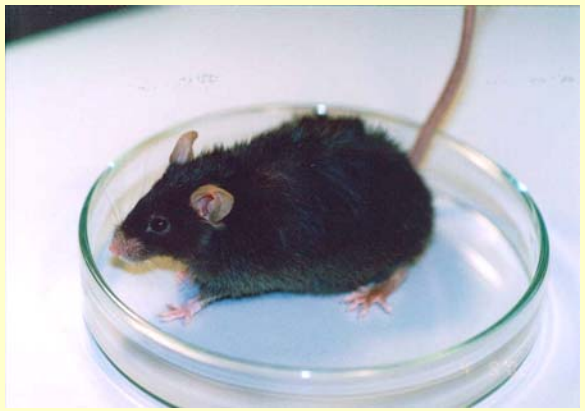
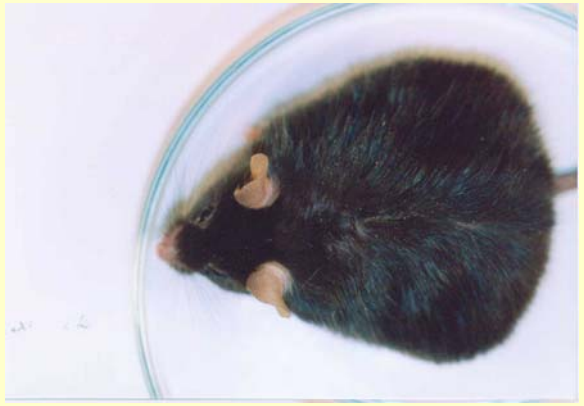


Effects of Low Dose Rate Irradiation on Life Span of *db* Mice

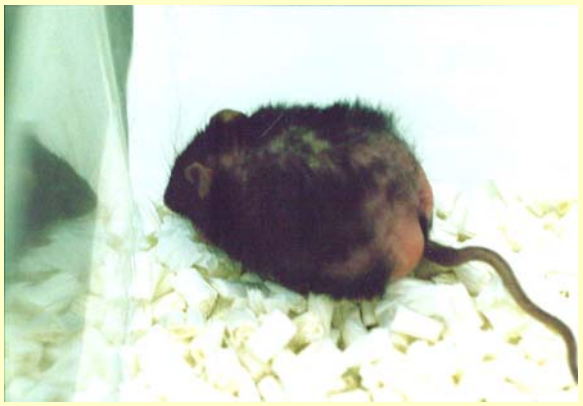


Appearance of *db/db* Mice at 90 Weeks of Age

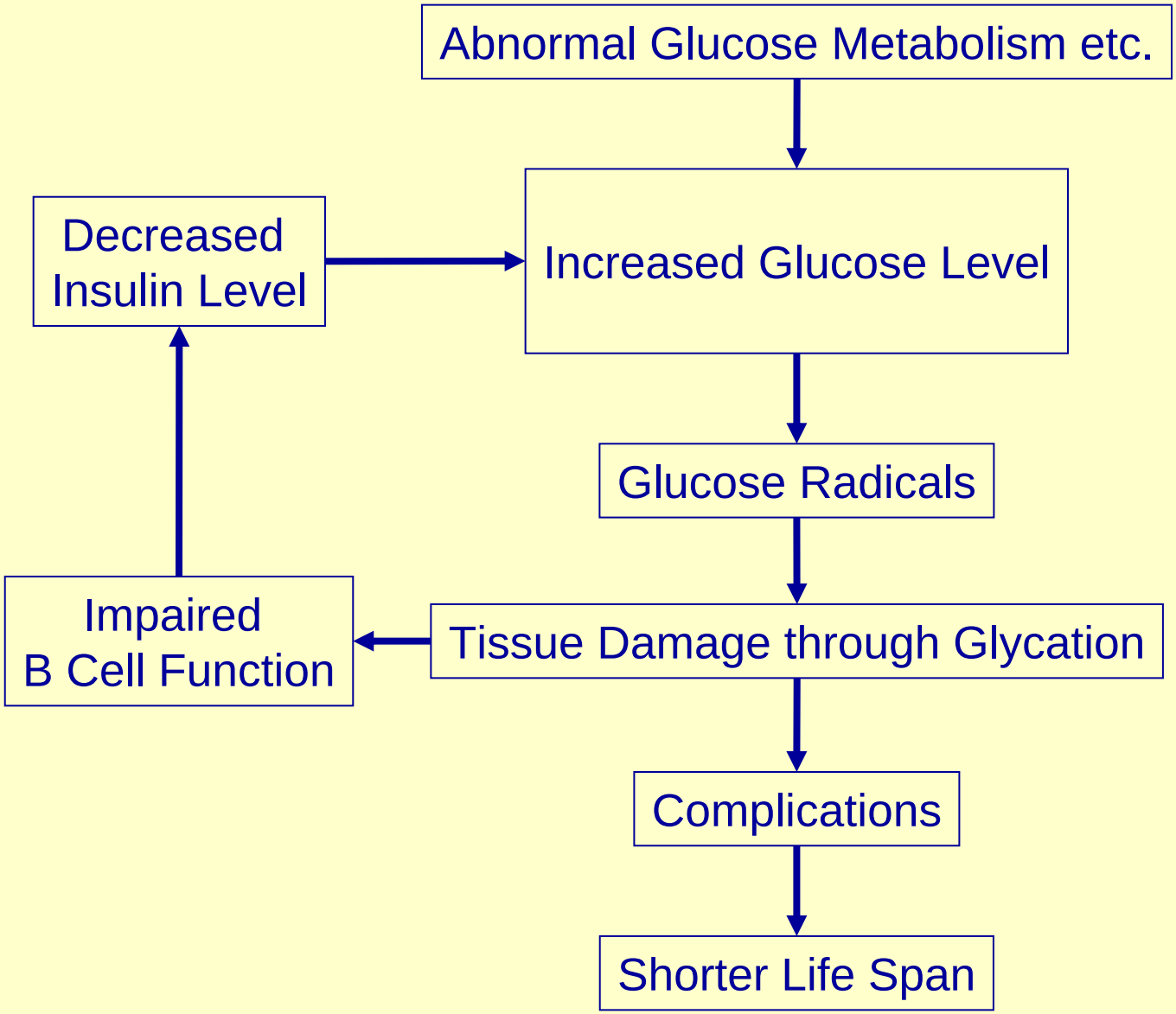
Irradiated

Non-Irradiated



Possible Mechanism for Life Span Prolongation in Diabetic Mice



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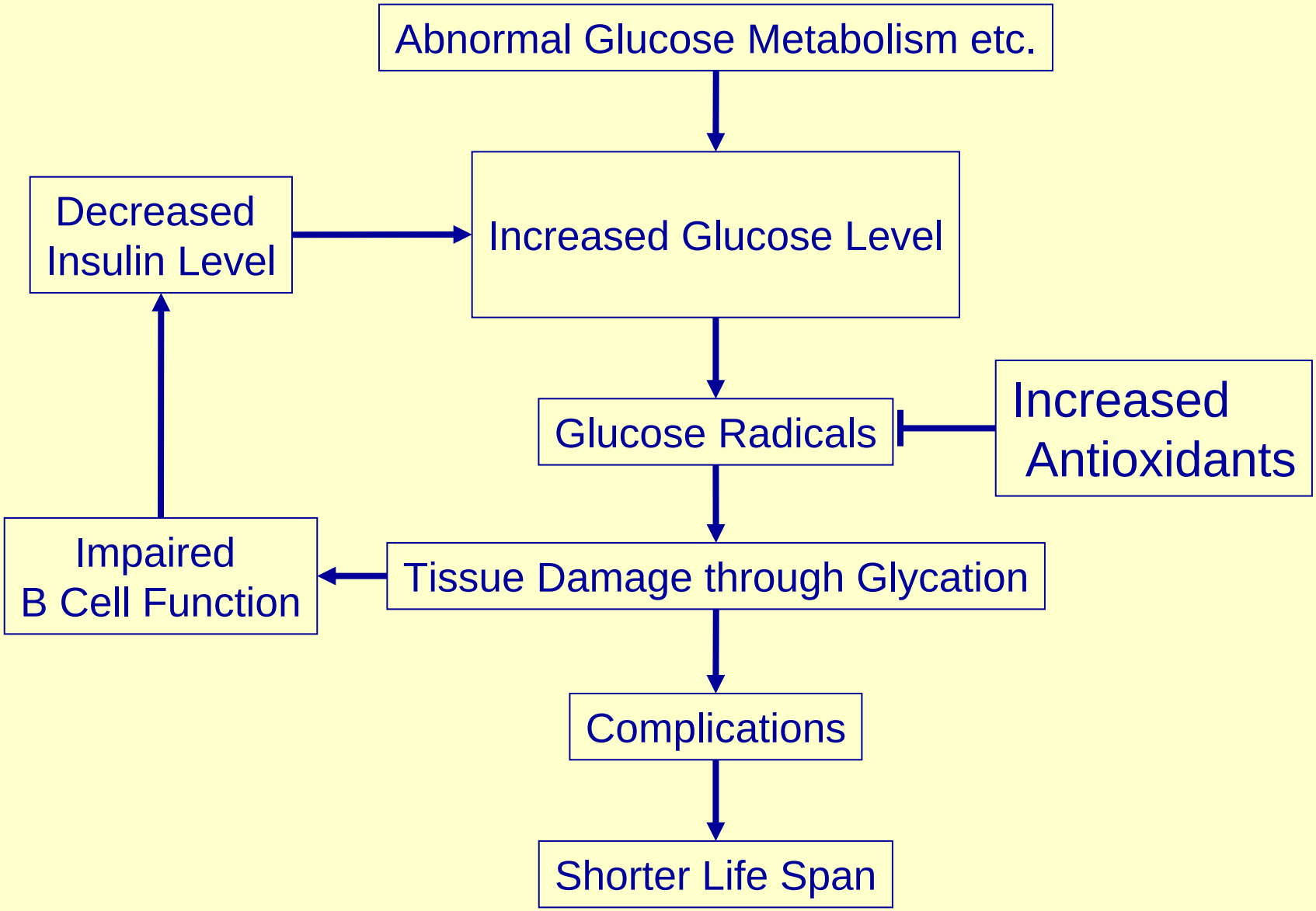
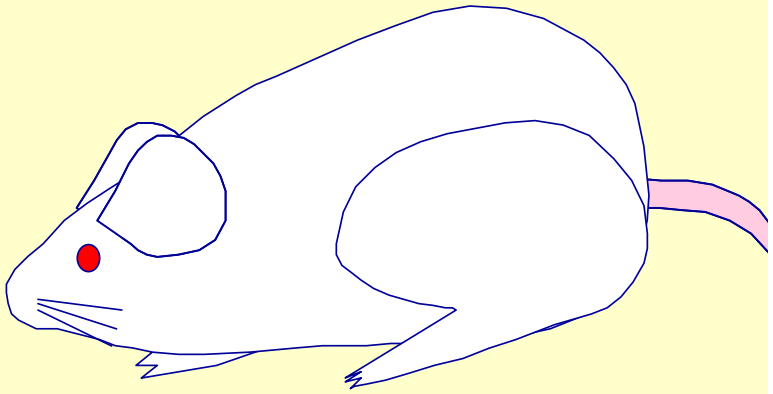


2. Severe Autoimmune Diseases

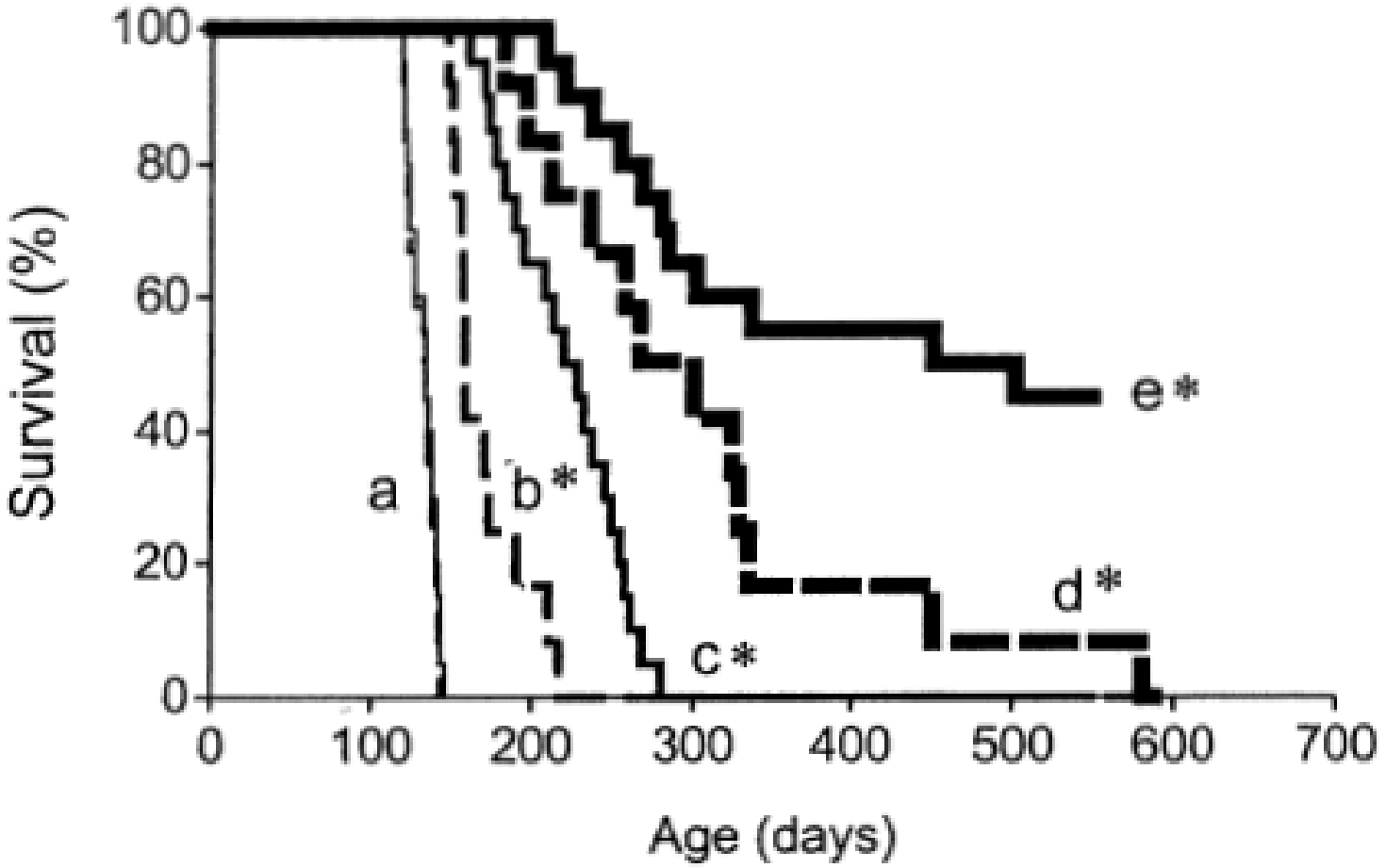
Female MRL-*lpr/lpr* Mice

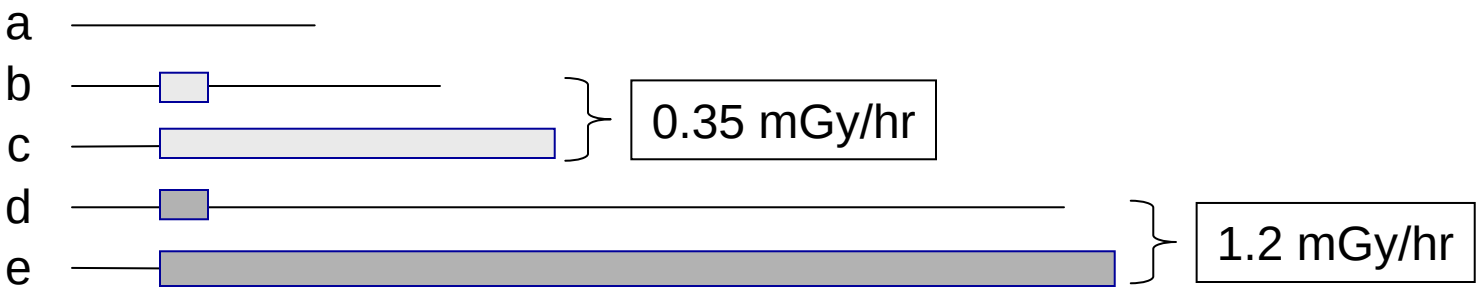
Lack in Apoptosis, Which Removes Self-Attacking Lymphocytes.

Dose Rate: 0.35 or 1.2mGy/ hr
Duration: 7wk to 12wk of Age
or
Life Span Long



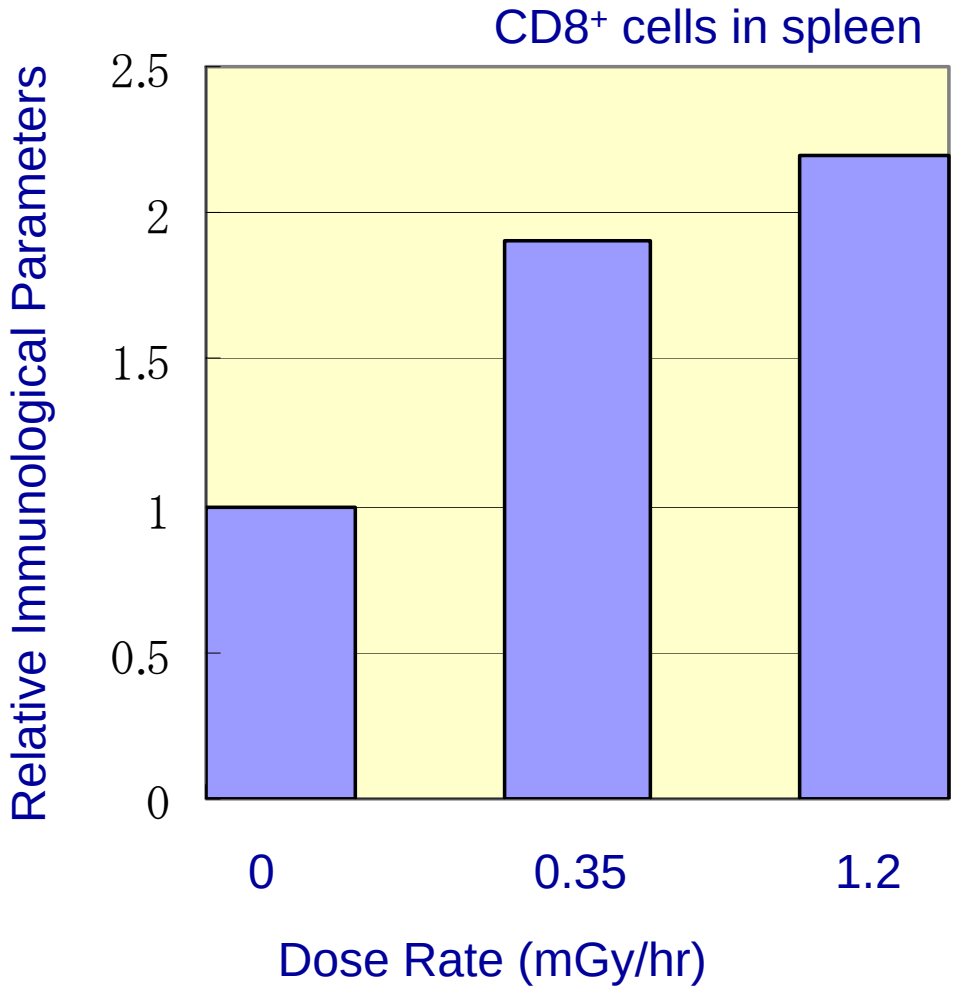
Prolongation of life span in MRL-*lpr/lpr* mice with chronic low dose rate irradiation





Effects of Low Dose Rate Irradiation on Immunological Parameters

(Measured after 7 wk irradiation)



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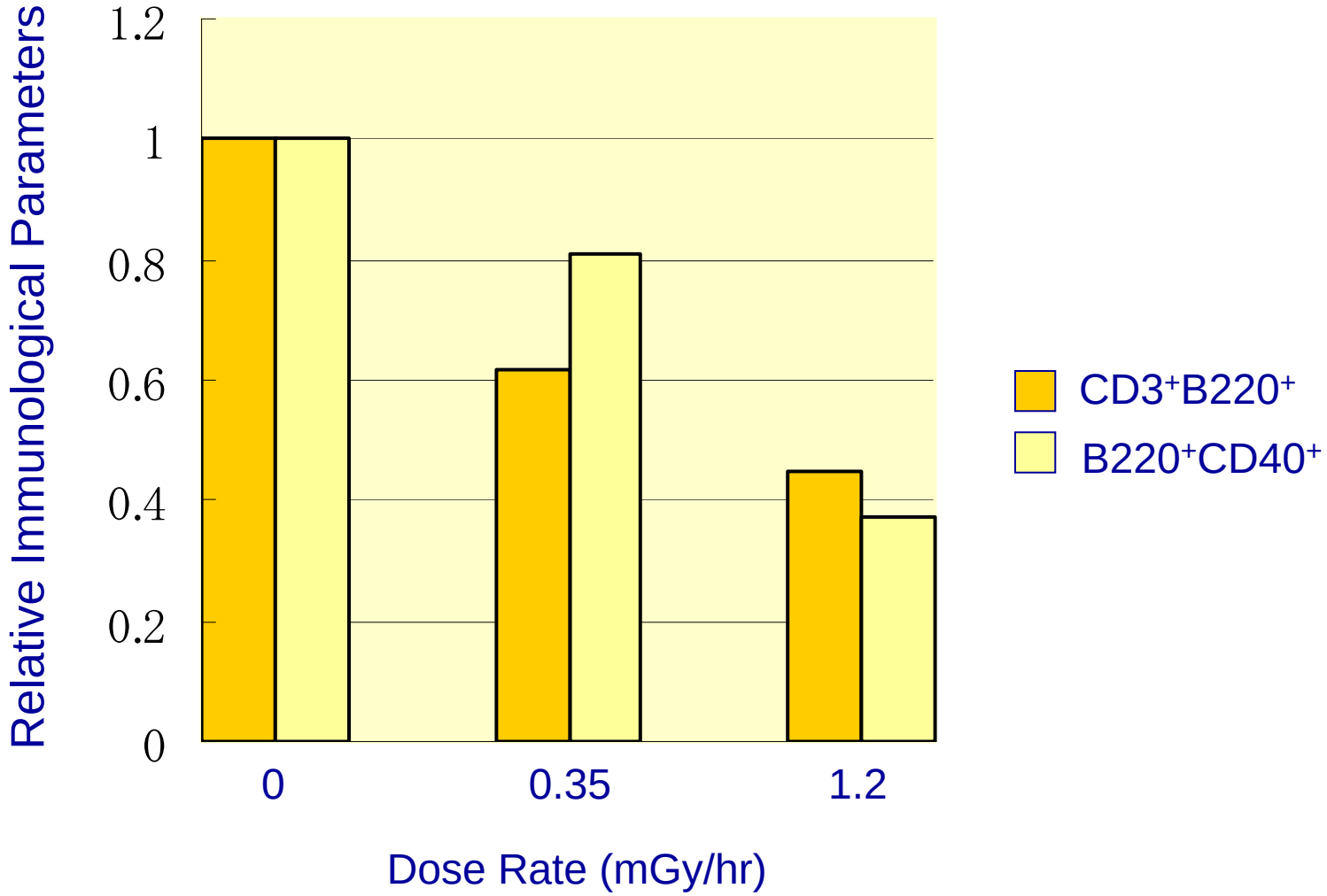


3. Klotho: A Premature Aging Model Mouse

Established in An Attempt to make disease model mice by shot-gun strategy.

Short life.

Show symptoms similar to premature aging syndromes.

Responsible gene is involved in calcium metabolism.

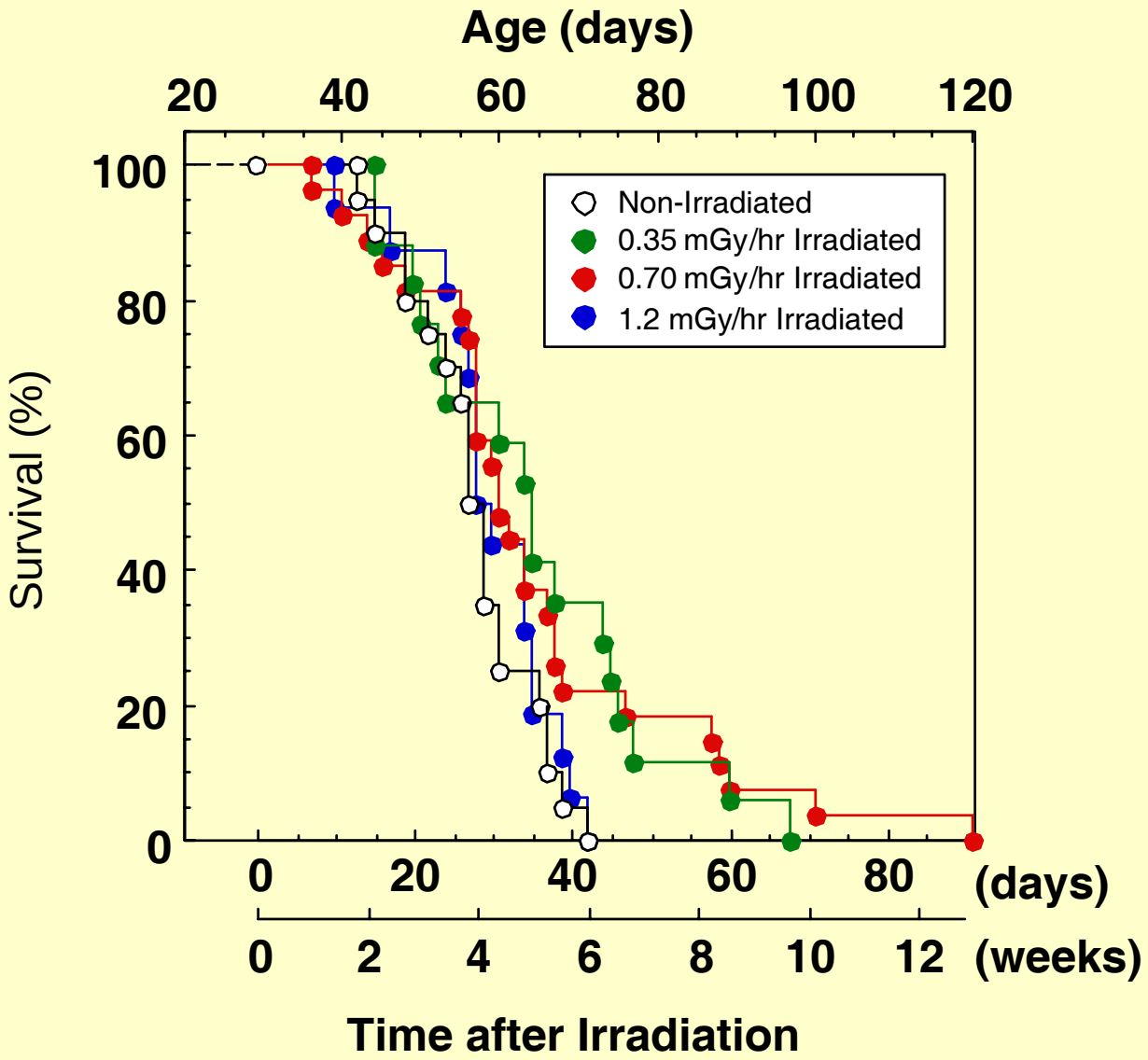
For Examination of Low Dose Rate Effect,

Female 4 wks old

Dose Rates 0.35, 0.70 or 1.2 mGy/hr ^{137}Cs Gamma-Rays

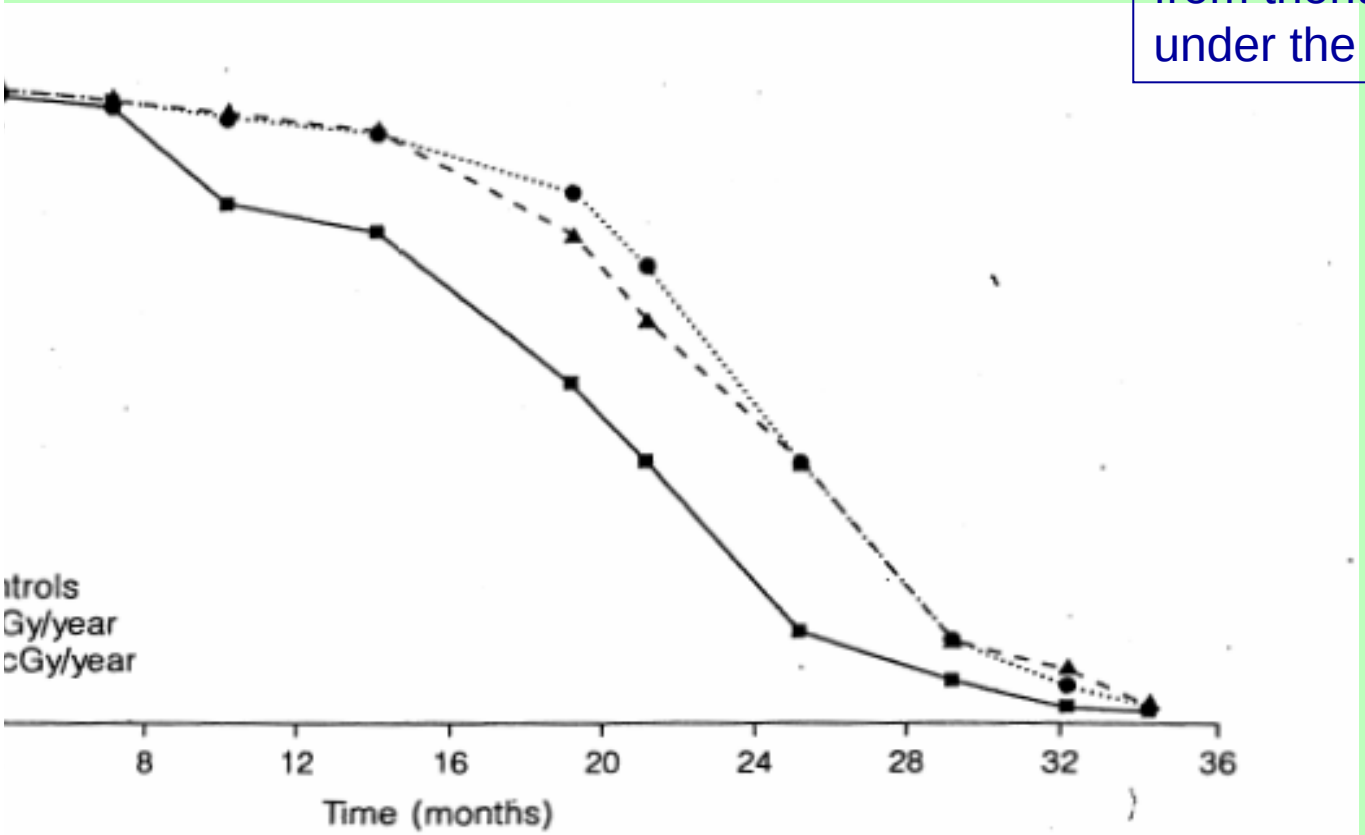
Life Long Irradiation from 4th week of age

Effects of Low Dose Rate Irradiation on Life Span of *klotho* mice



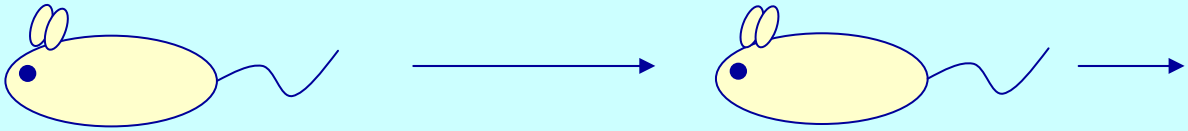
Effects of very low dose rate gamma irradiation on life span in C57BL/6 mice (1)

Irradiated with gamma rays from thorium nitrate placed under the floor of cages.



Caratero et al., Gerontology 44, 272-276 (1998)

Research Institute of Environmental Sciences (Rokkasho, Aomori)



natural death
& autopsy,
pathology

Starts at
50 days old

Stops at
450 days old

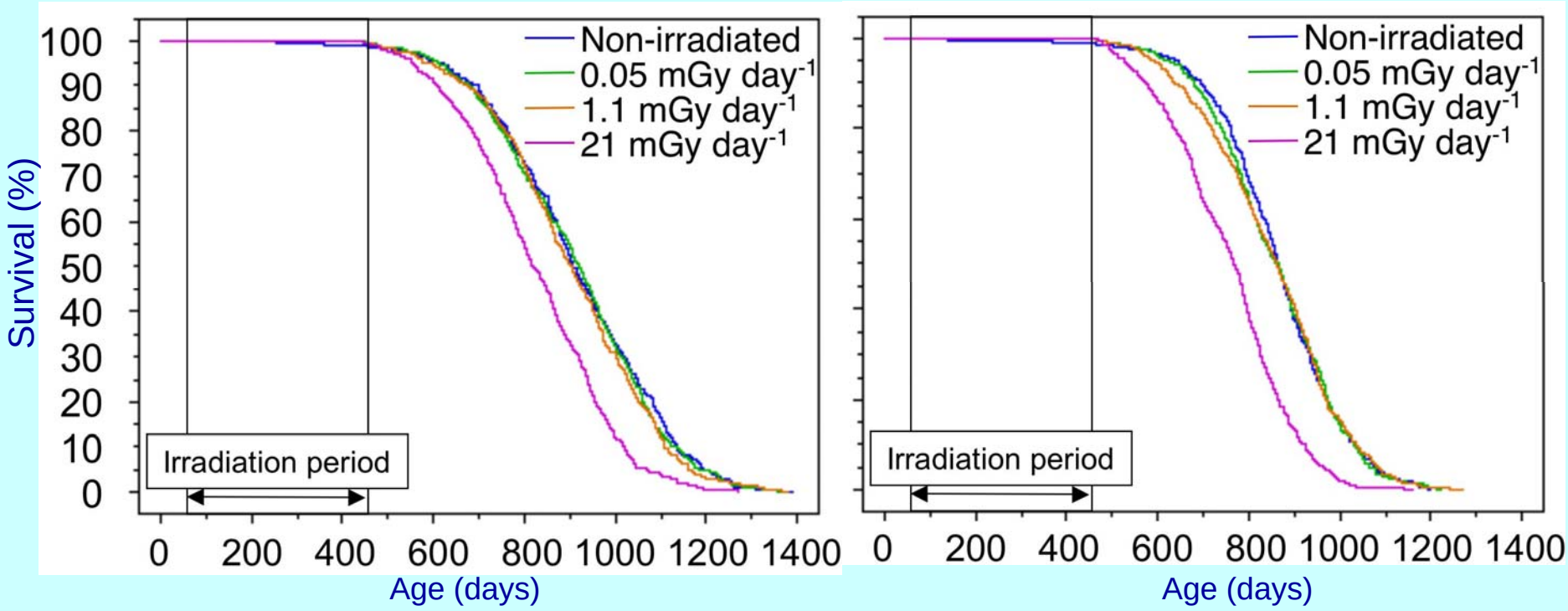
continuous exposure to low dose rate radiation

0 mGy/day
0.05 mGy/day
1.1 mGy/day
21 mGy/day

Survival curves of B6C3F1 mice

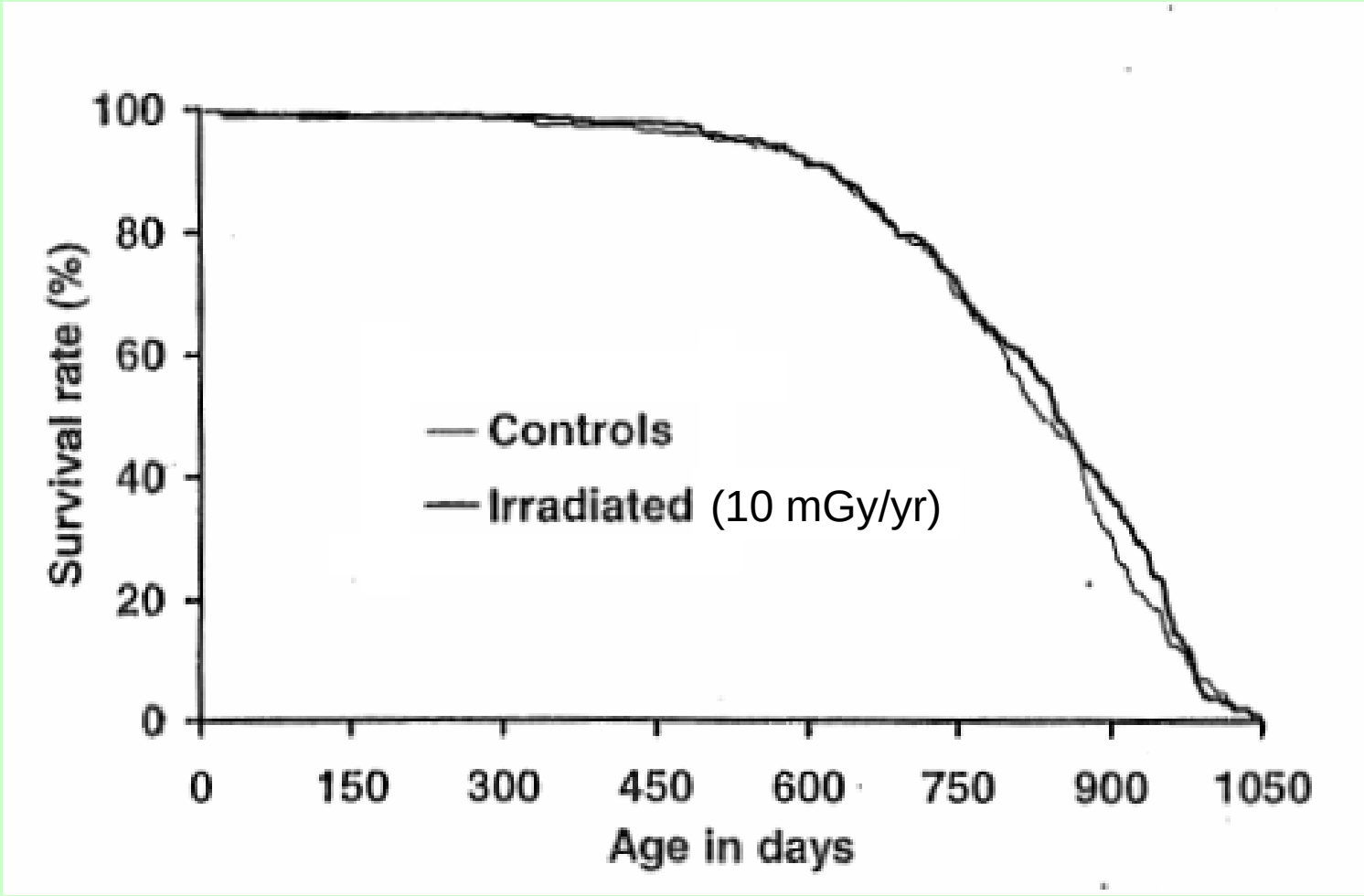
A : Male

B : Female



Tanaka, S. *et.al. Rad. Res.* 160: 376 - 79. (2003)

Effects of very low dose rate gamma irradiation on life span in C57BL/6 mice (2)



Courtade et al.
Int. J. Radiat. Biol. 78, 845-855 (2002)

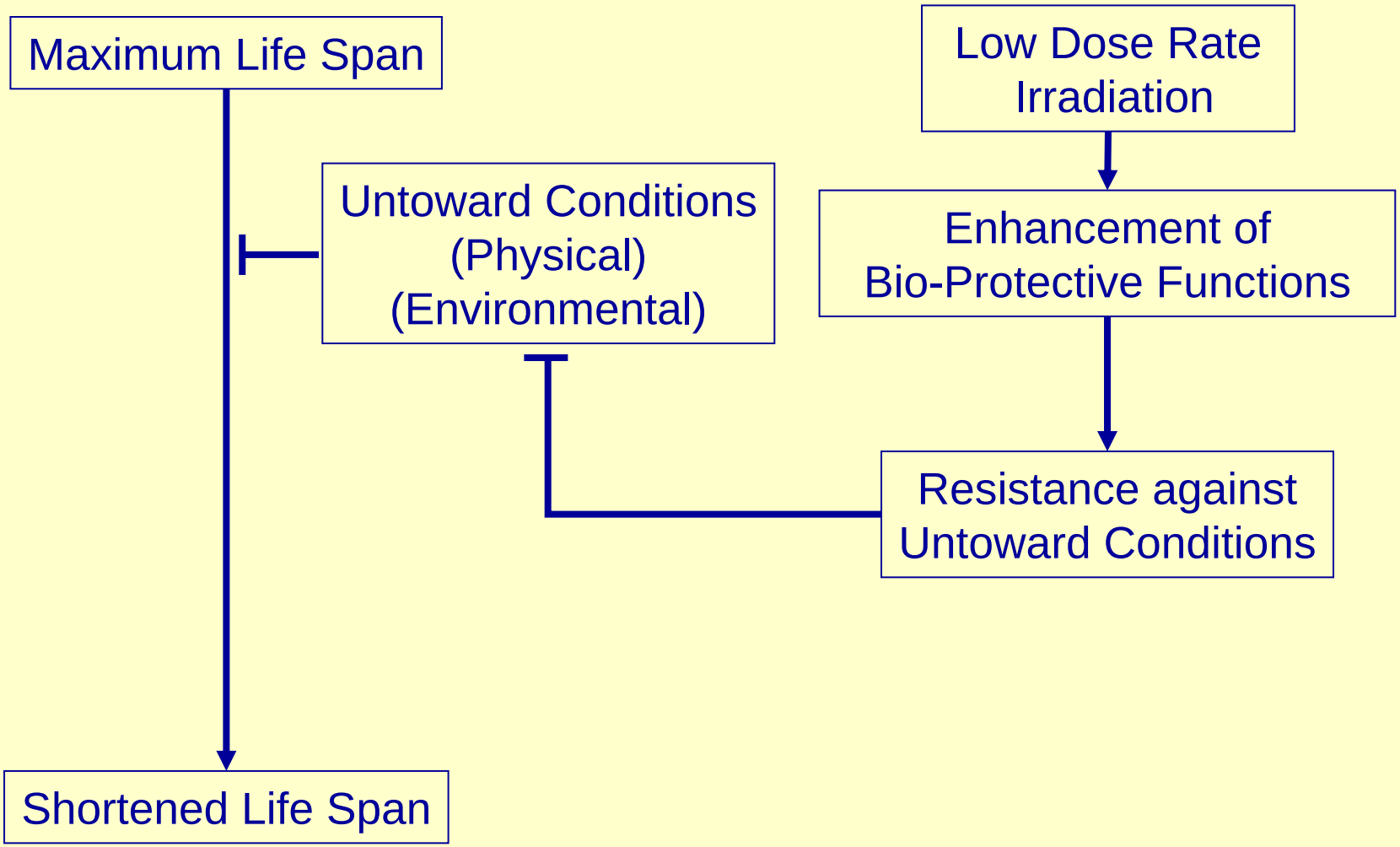
Summary of Effects of Very Low Dose Rate Irradiation on C57BL/6 Mice

Dose Rate (cGy/yr)	50 % Survival Time (months)	Conditions for Animal Care
0	20	Conventional More Crowded
7	24	Same as above
14	24	Same as above
0	27	SPF Less Crowded
10	27	Same as above

Summary of Effects of Low Dose Rate Irradiation on Life Span in Mice

Strain	Conditions for Animal Care	Life Span Prolongation
db	SPF	Yes
lpr	SPF	Yes
klotho	SPF	Yes
C57BL/6	Conventional	Yes
C57BL/6	SPF	No
B6C3F1	SPF	No

Low Dose Rate Irradiation and Life Span

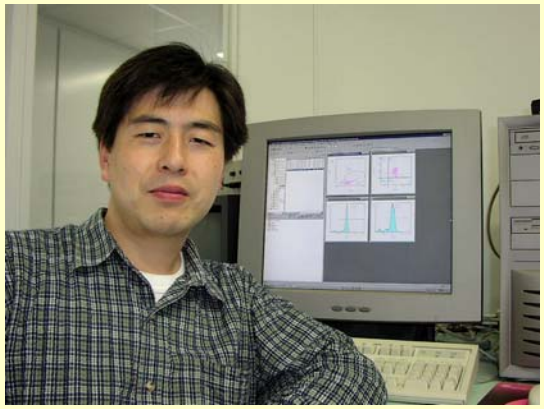


Collaborators in CRIEPI

T. Iwasaki

Y. Hoshi

T. Nomura



Y. Ino

H. Tanooka