

Low-Dose-Radiation-Activated Natural Protection against Cancer and Other Diseases

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Contents

- Nuclear physics, radiation, and life
- Current vs. past natural background radiation exposures
- Current low-dose-radiation risk assessment paradigm: Linear-no-threshold
- Systems biology perspective on low-dose-radiation risks
- Radiation activated-natural-protection (ANP) a biological basis for radiation hormesis
- Implications of radiation ANP for managing radiological and chemical terrorism incidents
- Conclusions

Nuclear Physics, Radiation, and Life

- The laws of nuclear physics (known and unknown) gave us radiation (ionizing and non-ionizing) (*Gerald Looney 2003*).
- Radiation-related **nucleosynthesis** within stars, supernova, and during the big bang gave us H, C, O, N and the other elements.
- **All life therefore appears to be due, at least in part, to radiation reactions!**

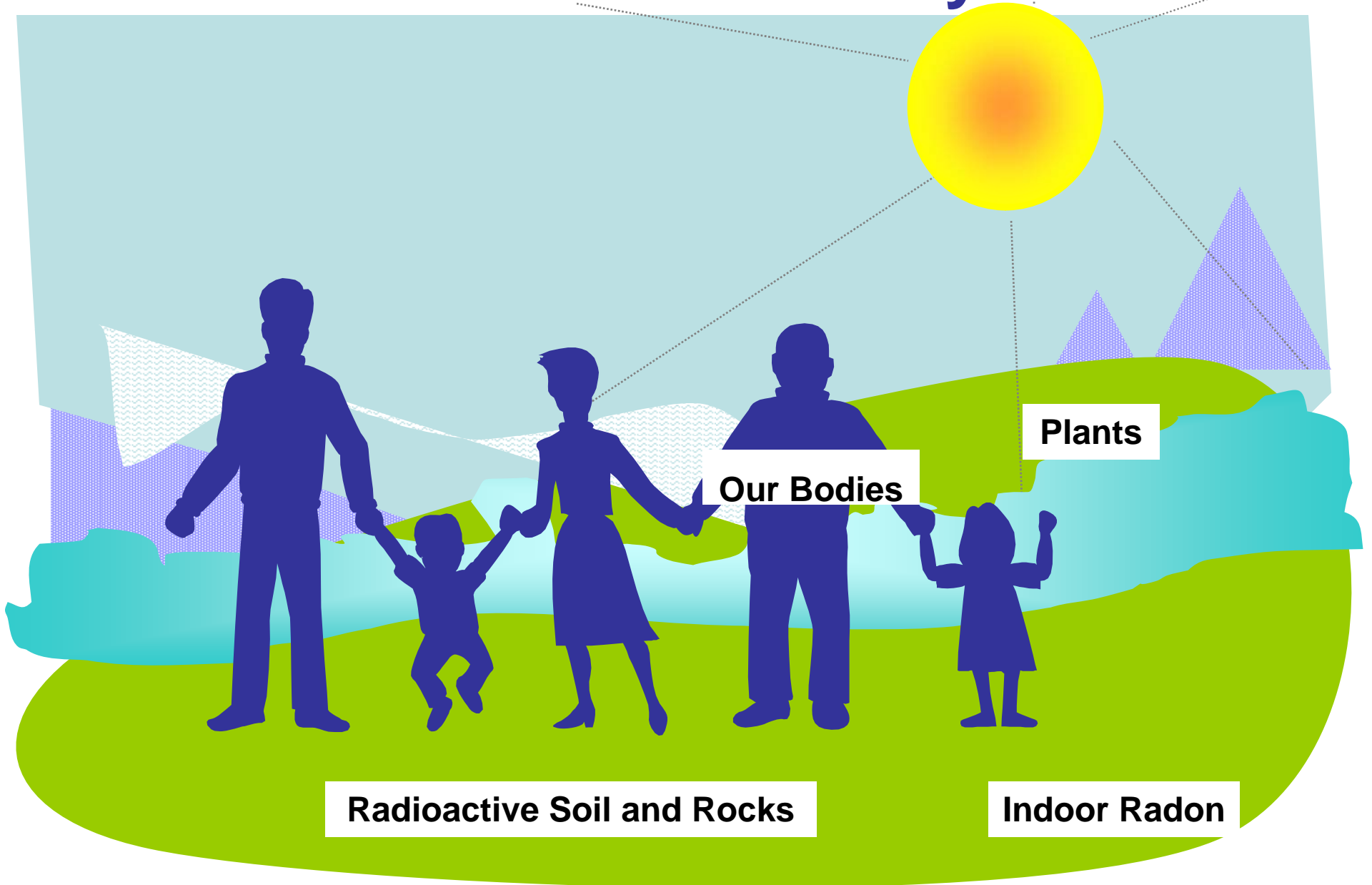
<http://www.sepp.org/Archive/NewSEPP/Hormesis-Looney.htm>

Big Radiation Secret (Looney, 2003)

- “And ... the biggest surprise and best-kept secret of all: a man isolated in ... a chamber and secure from extrinsic background radiation would still experience significant intrinsic irradiation from himself.
- The human body, rather than being a chaste and inviolate vessel of biologic purity devoid of and unpenetrated by ionizing radiation, is actually its own radioactive repository and beehive of ionizing rays...”

<http://www.sepp.org/Archive/NewSEPP/Hormesis-Looney.htm>

Natural Radiation is Everywhere



Natural Radioactivity from Potassium-40

- Largest source of natural radioactivity for humans, followed by carbon-14.
- Physical half-life of 1.25 billion years.
- Mainly (88.8%) undergoes beta decay (0.51 MeV average energy) to stable calcium-40.

Natural Radioactivity from Potassium-40 in 1 Pound of Food

Food	Disintegrations per second (Becquerel)	Beta particle emissions per minute
Red meat	50	2682
Carrot	57	3040
White potato	57	3040
Banana	59	3147
Lima bean	78	4148
Brazil nut	94	5007

Based on information from <http://physics.isu.edu/radinf/natural.htm>

Natural Radioactivity in the Body of A Typical 70kg Adult Human

Nuclide	Approx. Total Mass	Disintegrations per day
Uranium isotopes	90 micrograms	95 thousand
Thorium isotopes	30 micrograms	9.5 thousand
Potassium-40	17 milligrams	380 million
Radium isotopes	31 picograms	95 thousand
Carbon-14	22 nanograms	320 million
Tritium isotopes	0.06 picograms	2 million
Polonium isotopes	0.2 picograms	3.2 million

Based on information from <http://physics.isu.edu/radinf/natural.htm>

Natural Background Radiation was Much Higher When Mammalian Life Forms Arose on Earth

“While generations of students and scientists have learned about radioactive decay and the half-lives of various radioactive elements and isotopes, virtually no one has turned the telescope around and discussed or documented the reverse view: The same number of half-life years taken back into the past produces a double-life, a doubling of radioactivity for these elements, and an incremental terrestrial background level many times higher than today's levels.” (*Looney 2003*)

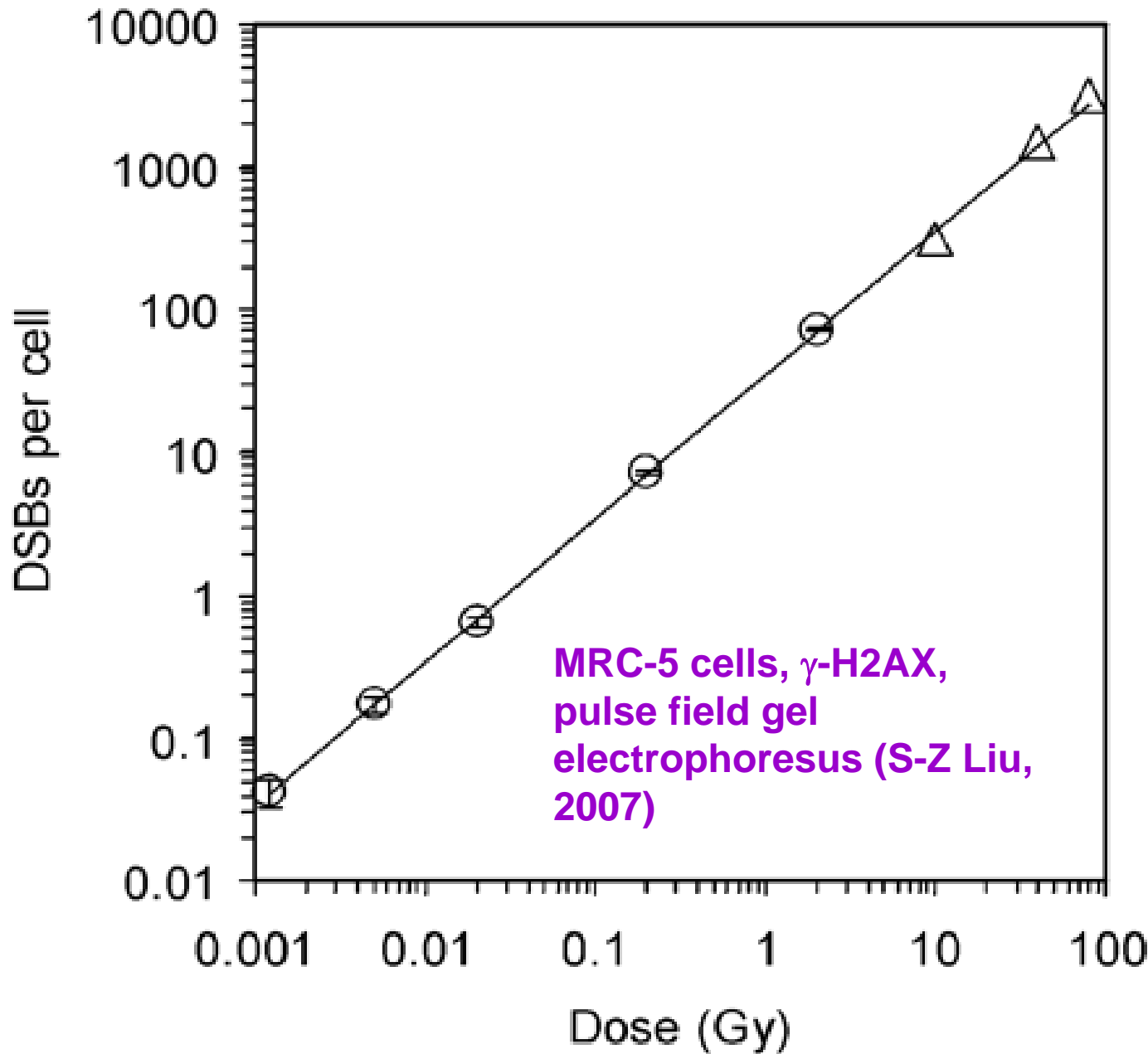
Protective Processes that Arose During Higher Natural Radiation Environments on Earth

Evolution in high natural radiation environments have provided mammals with:

- DNA repair
- Apoptosis
- Cell repopulation
- Immune system defenses

Do these processes therefore operate more efficiently in higher than current natural radiation environments?

**Current LNT Risk Assessment
Paradigm which Ignores Natural
Protection Against Radiation Harm**



LNT Dogma:
DNA double-strand breaks are an **LNT** function of radiation dose; thus, cancer induction is also an LNT function of dose.

Risk Implication of LNT Model

- Any amount of radiation will cause cancers in a very large population.
- Doubling the radiation dose doubles the number of cancer cases.
- Allows use of weighted doses, fixed risk coefficients, and back-of-the-envelope calculations of cancer risk.
- Such back-of-the-envelope calculations following the Chernobyl accident led to predictions of up to hundreds of thousands of cancer deaths.
- The predicted large number of deaths did not occur.

LNT-Based Radiation Protection System

- **Equivalent dose:** A weighted tissue-specific dose that is intended to account for the different effectiveness of different radiation types.
- **Effective dose:** A weighted dose intended to relate non-uniform exposure to uniform gamma-ray exposure over the body.
- The indicated doses are justified based on the LNT hypothesis.
- **Typical dose units:** sievert (Sv) and millisievert (mSv)
- Humans are protected by limiting effective dose.

Radiation Limits (Metting 2006)

- Public drinking water (EPA): 0.04 mSv/y
- Releases to air (EPA): 0.1 mSv/y
- Security personnel scanners (ANSI): 0.25 mSv/y
- Public exposure (DOE, NRC): 1 mSv/y
- DOE administrative control: 20 mSv/y
- Worker exposure (DOE, NRC): 50 mSv/y

Average background radiation exposure in the U.S. is approximately 3 mSv/y

Systems Radiation Biology

Perspective for Cancer Induction

- Although the risk of DSB rises linearly with dose, a second risk relates to the probability that initial DSB will lead to cancer.
- The second risk is a nonlinear function of dose and is influenced by protective signaling (L. Feinendegen).
- The protective signaling provides a biological basis for radiation activated natural protection against diseases.

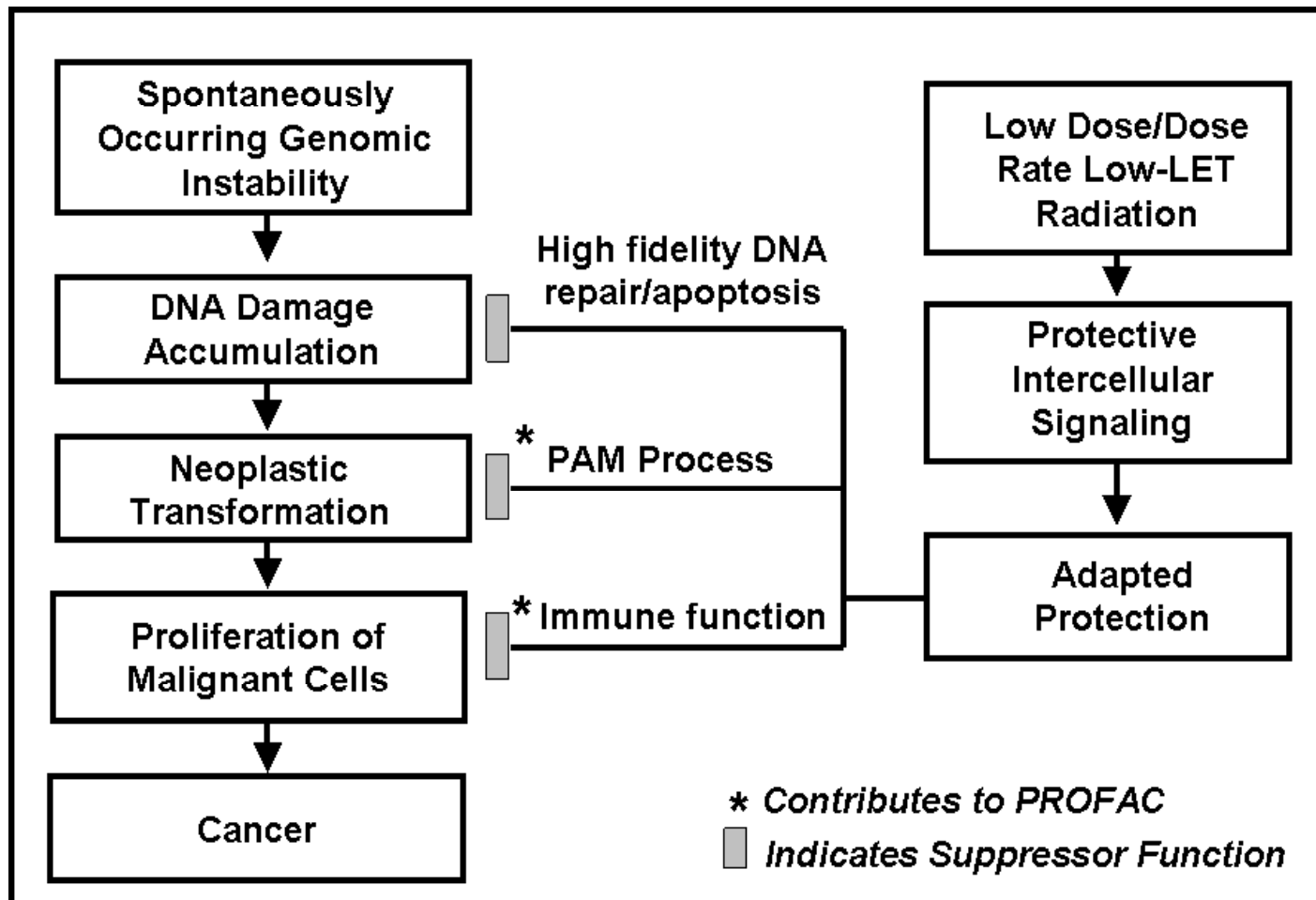
Added Low-Dose, Low-LET Radiation Protects Us

- Protects against chromosomal damage (Ed Azzam's group)!
- Protects against mutation induction (Pam Sykes' group), even when the low dose follows a large dose (Tanya Day's work)!
- Protects against neoplastic transformation (Les Redpath's group)!
- Protects against high dose chemical- and radiation-induced cancer (Kazou Sakai's group)!
- Enhances immune system defense (Shu-Zheng Liu's group)!

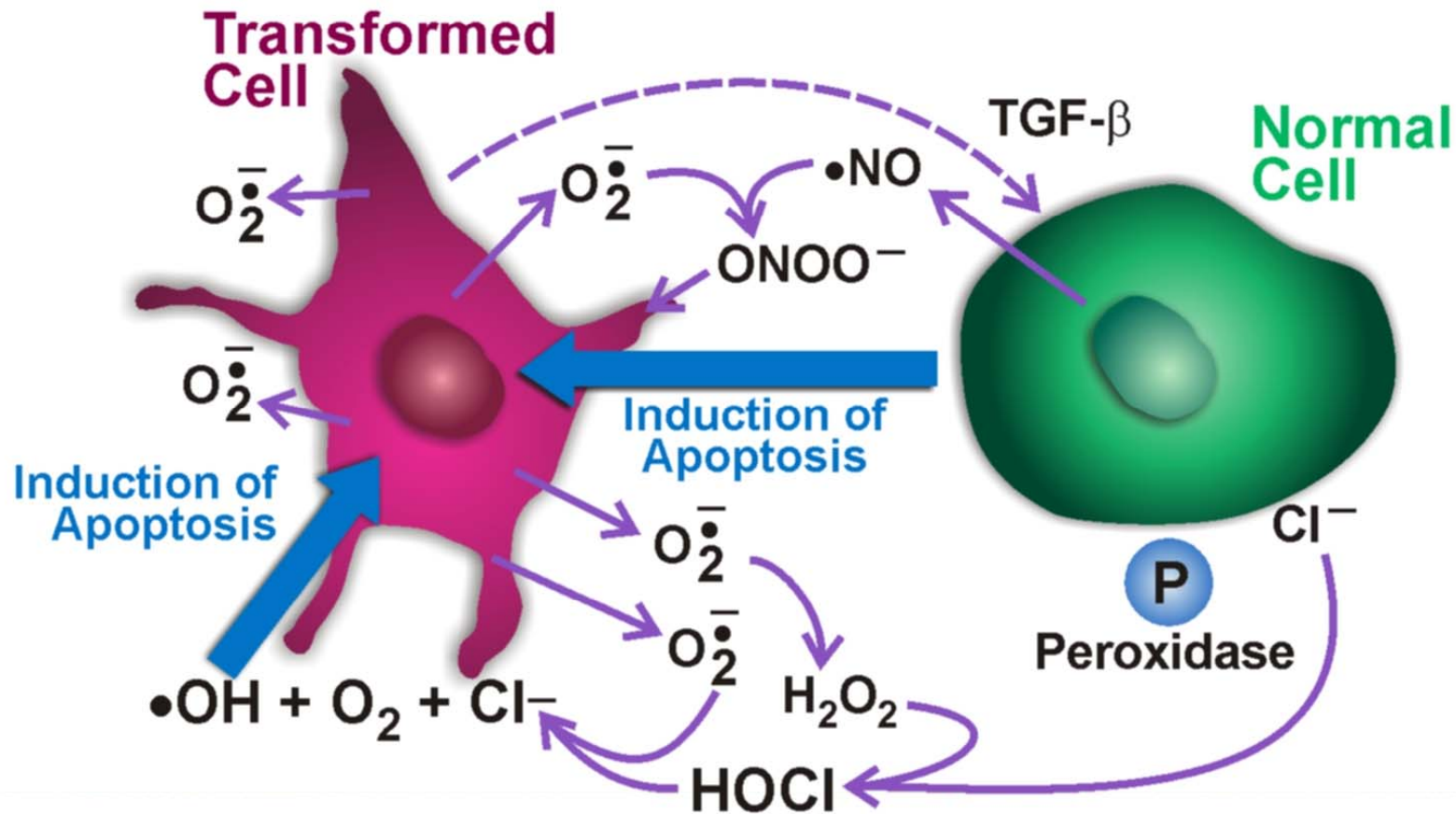
Added Low-LET Radiation Protects Us (continued)

- Suppresses cancer induction by alpha radiation (Chuck Sanders group)!
- Suppresses metastasis of existing cancer (Kiyohiko Sakamoto's group)!
- Suppresses growth of transplanted lymphoma cells (Kaushala Prasad Misra's group)!
- Extends tumor latent period (Ron Mitchel's group)!
- Protects against diseases other than cancer (Kazuo Sakai's group)!

Systems Radiation Biology Related Activated Natural Protection (ANP)



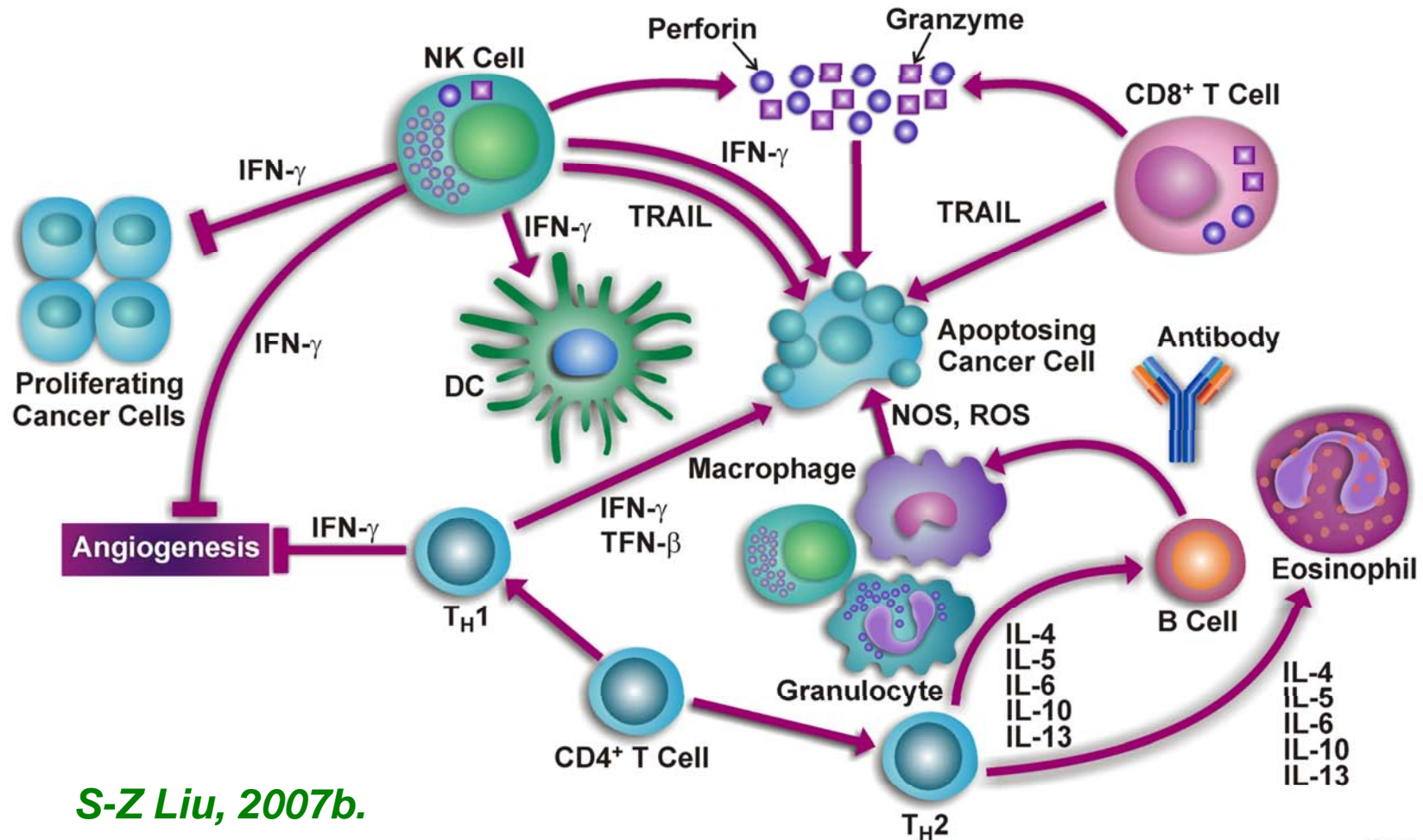
Protective Apoptosis Mediated (PAM) Process in Fibroblast



6781-3

G. Bauer 2000: epigenetic pathways.

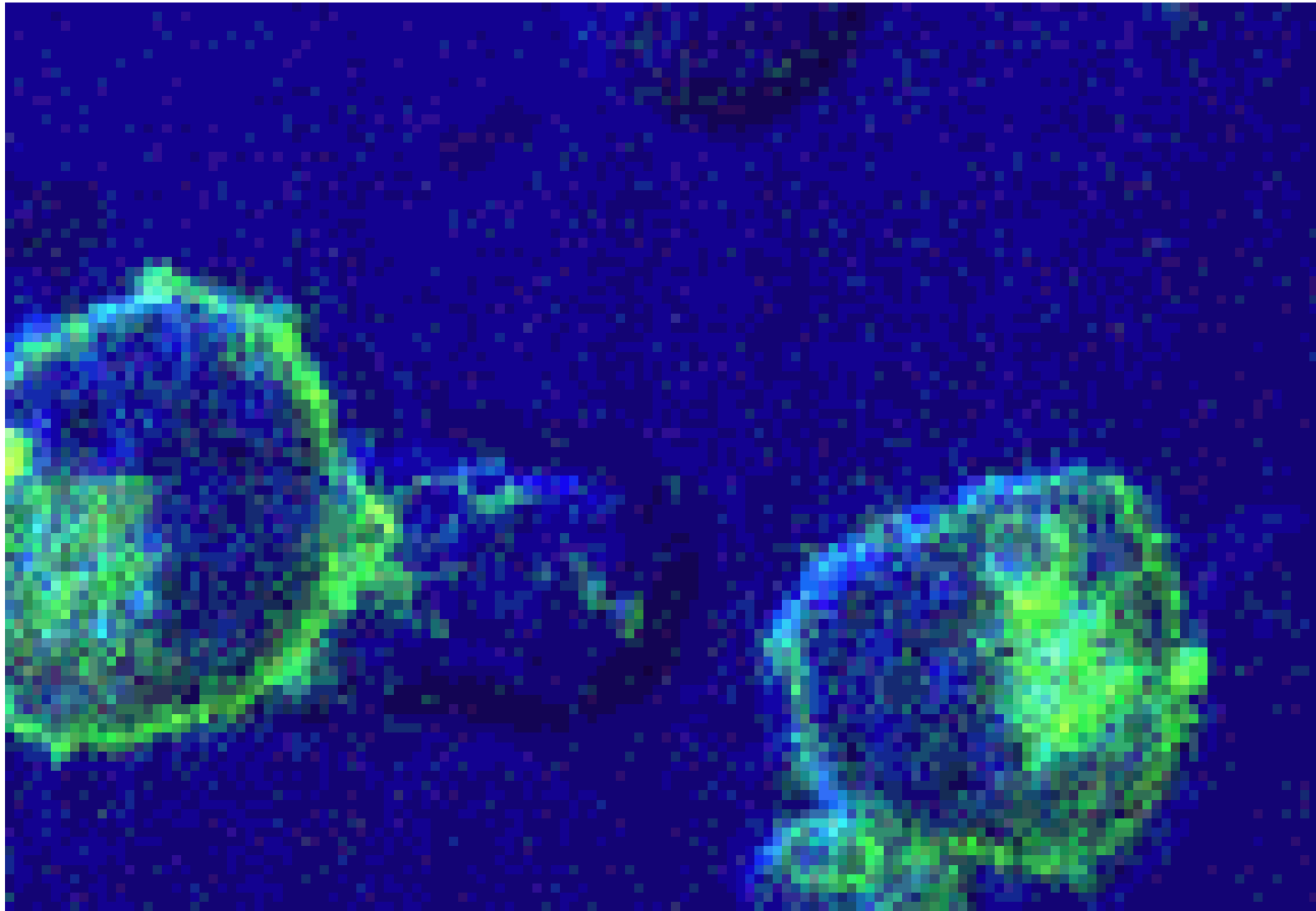
Systems-Biology-Related Tumor Control Stimulated by Low-Dose Radiation



S-Z Liu, 2007b.

G. Dranoff. Nat Rev Cancer 4: 11-22, 2004.

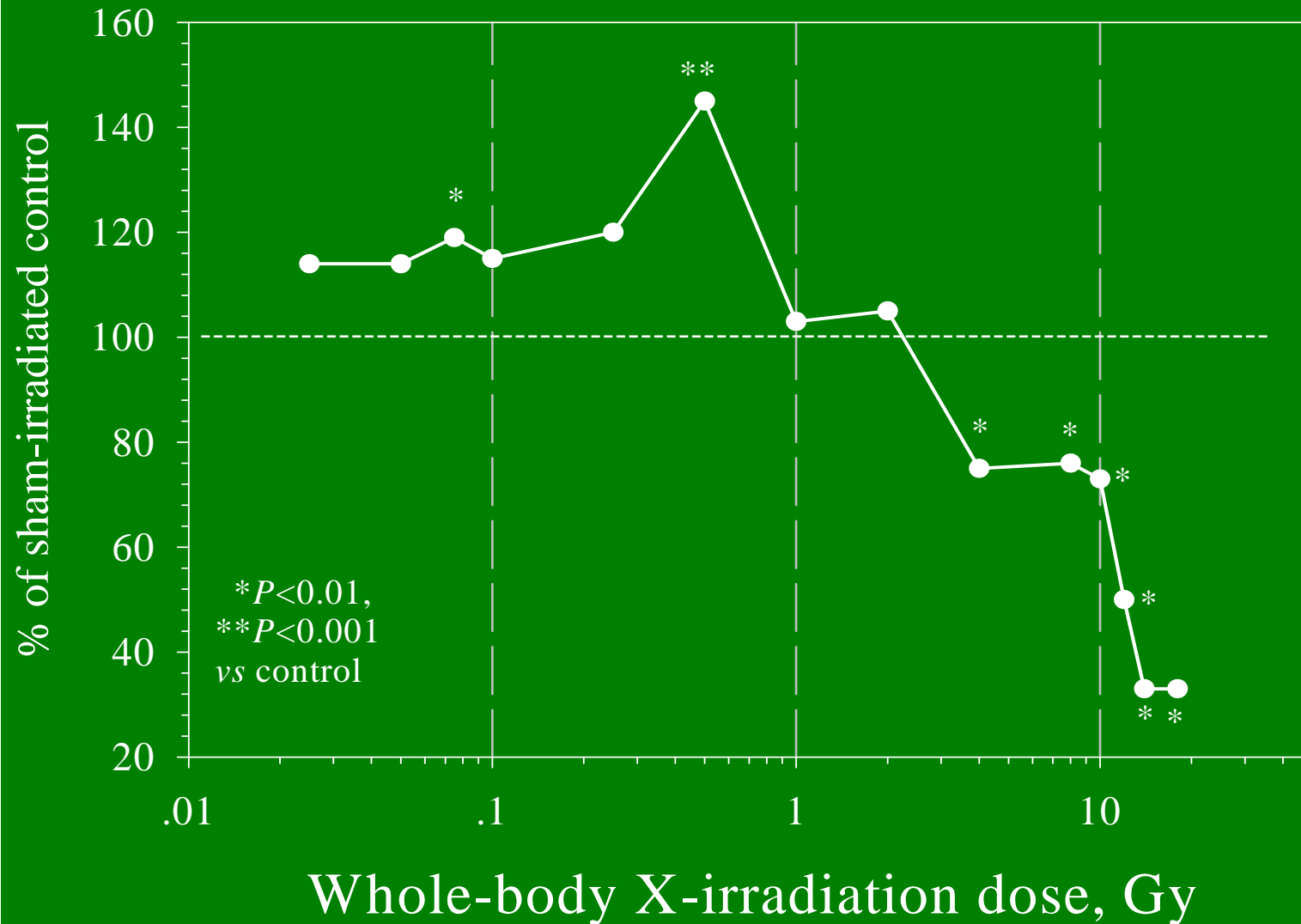
Cytotoxic T Lymphocyte Destroying Cancer Cell (*S-Z Liu, 2007*)



Low-Dose X-Ray Stimulated Cellular Immunity in Mice (*S-Z Liu, 2007*)

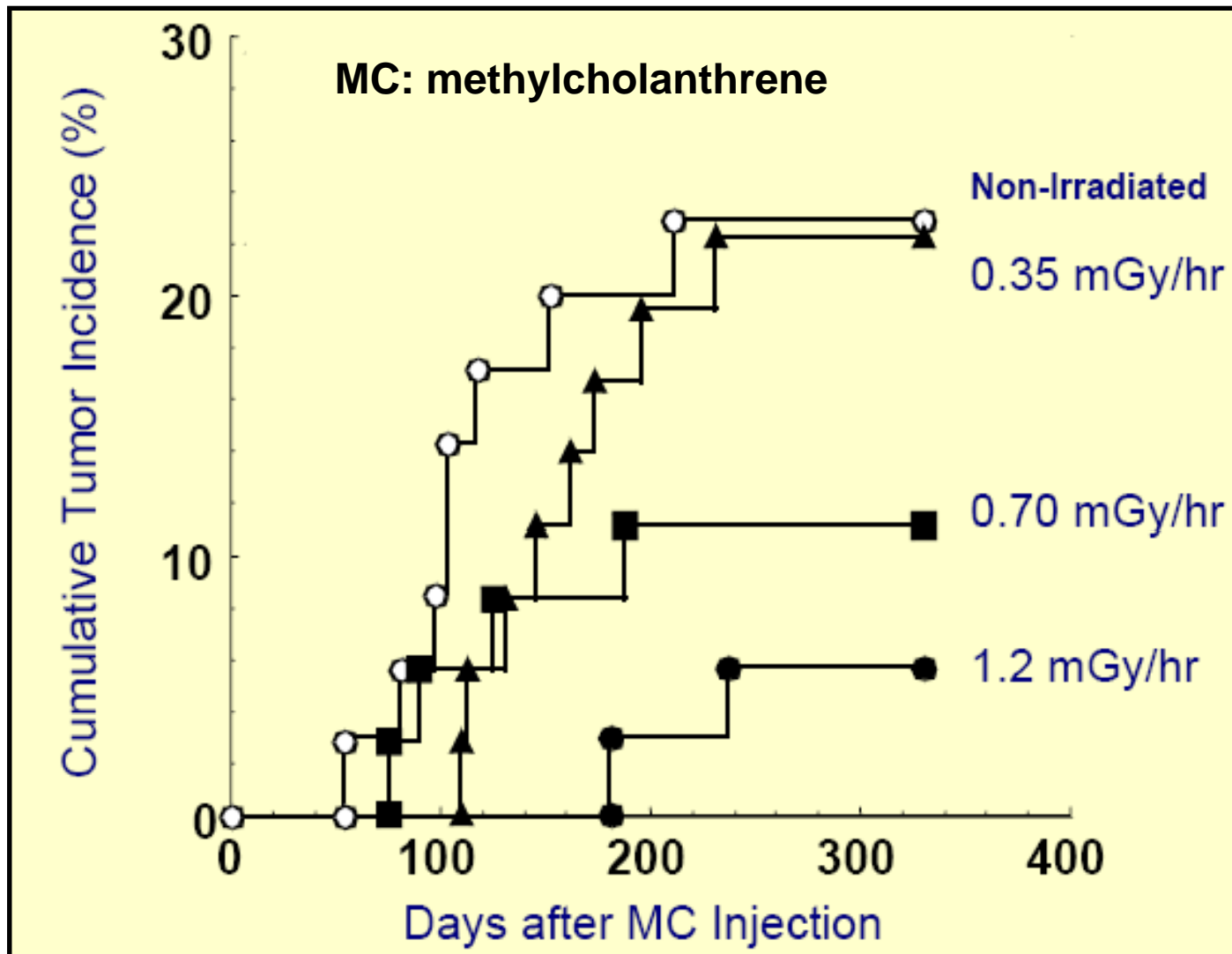
Parameter	Dose (mGy)	Change (%)	P value
NK activity	75	+19	< 0.05
Mac. activity	75	+52	< 0.05
Cytotoxic T Lymphocytes	75	+40	< 0.01
Antibody depen. cell mediated cytotoxicity	75	+30	< 0.05
T cell proliferat.	77	+101	< 0.01

NK activity of mouse splenocytes 24h after whole-body X-irradiation



(*Fan XH and Liu S-Z. JNBUMS 1989,*

Low-Dose-Rate Gamma Ray ANP against MC-Induced Skin Tumors



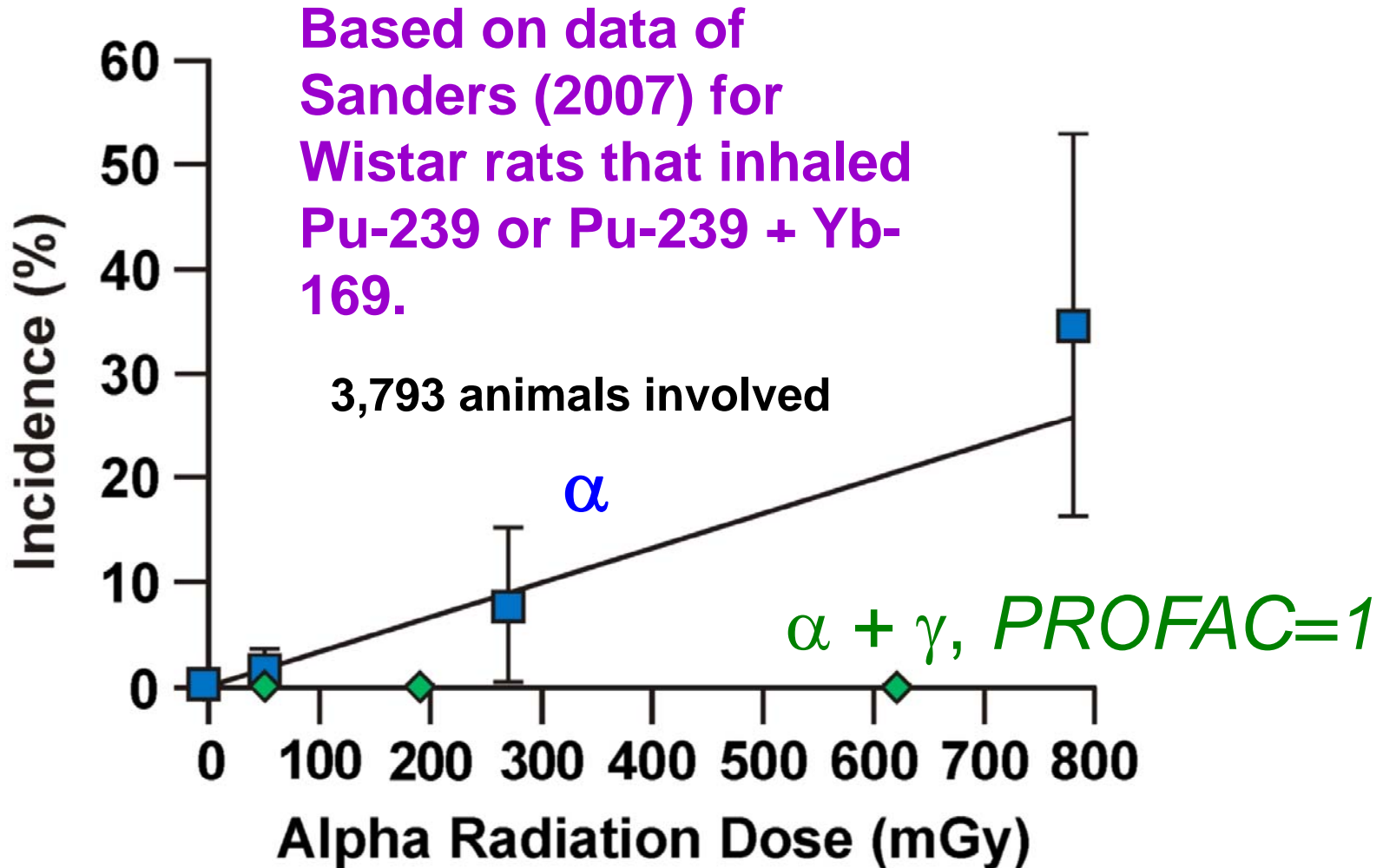
K. Sakai, 2005 International Dose-Response Conference presentation

Gamma-Ray ANP Against Diseases Among Nuclear Shipyard Workers

Cause of Death	SMR	p value	PROFAC
Allergic, endocrine, metabolic	0.69 ± 0.12	4.9 x 10 ⁻³	0.31
All respiratory disease	0.62 ± 0.08	1.0 x 10 ⁻⁶	0.38
Pneumonia	0.68 ± 0.04	< 10 ⁻¹⁴	0.32
Emphysema	0.63 ± 0.26	7.7 x 10 ⁻²	0.37
Asthma	0.30 ± 0.43	5.2 x 10 ⁻²	0.70
All infectious & parasitic	0.86 ± 0.72	4.2 x 10 ⁻¹	0.14
Total mortality	0.78 ± 0.04	1.9 x 10 ⁻⁸	0.22

Based on combining SMR data from Sponsler and Cameron (2005).

Gamma-Ray ANP Against Alpha Radiation Induced Lung Cancer



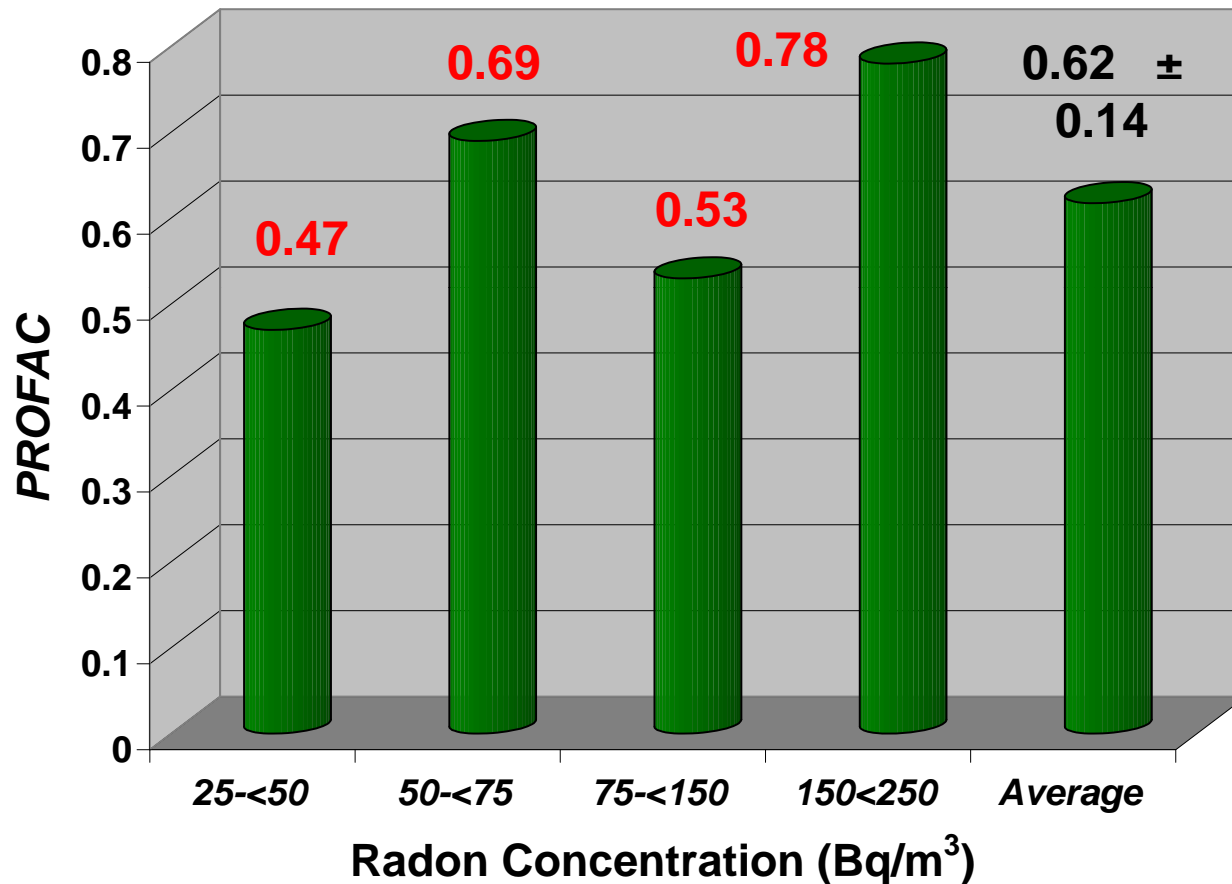
Protection Factors (*PROFAC*) for Radon-Spa Areas in Japan (Misasa)

Cancer Site or Type	<i>PROFAC</i>	
	Females	Males
Leukemia	0.47 ± 0.016	0.56 ± 0.016
Stomach	0.55 ± 0.016	0.60 ± 0.016
Breast	0.74 ± 0.014	(results not reported)
Lung	0.81 ± 0.012	0.53 ± 0.016
Colon/rectum	0.86 ± 0.011	0.70 ± 0.015

Radon exposure involves a beta/gamma component, which is considered protective. *Data from Mifune et al. 1992*



Central Estimate of Indoor Radon *PROFAC* Against Lung Cancer



Based on data from Thompson et al. Health Physics 94:228-241, 2008.

Implications of Radiation ANP for Reducing Harm from Radiological and Nuclear Weapons

- Low dose, sparsely ionizing radiation could be used to enhanced hematological recovery following lethal whole body irradiation as a result of radiological or nuclear incidents (*Lu Cai, 2008*).
- Survivors of high radiation and chemical doses from radiological, nuclear, and chemical weapons could be at a high risk for cancer occurrence.
- Using repeated low doses or low-dose-rate exposure to sparsely ionizing radiation alone or in combination with other cancer preventative agents could reduce the number of cancer occurrences.
- Research is needed on determining optimal scheduling of doses and protective agent combinations.
- Age, genetic characteristics, and other factors may be important.

Conclusions

- Radiation ANP appears to be an evolutionary gift derived from the higher natural background levels that previously existed on Earth.
- Radiation ANP includes molecular (DNA repair), cellular (PAM process), immune system components.
- Radiation ANP provides a biological basis for radiation hormesis, since low doses and dose rates stimulate protection while high doses and dose rates are inhibitory.
- Low-dose, sparsely radiation could be used to enhance hematological recovery after lethal damage to bone marrow from radiological or nuclear terrorism incidents.

Conclusions (continued)

- Radiation ANP could be used in preventing cancer among high-risk individuals following terrorist or other incidents involving high radiation or genotoxic chemical exposures.
- Age, genetic characteristics, and other factors may be important determinants of the level of protection afforded.
- More research is needed related to using low-dose radiation to prevent disease occurrences for high-risk individuals.

International Collaborations

- Dietrich Averbeck, France
- Ed Azzam, USA
- Georg Bauer, Germany
- Doug Boreham, Canada
- Shu-Zheng Liu, China
- Jerry Cuttler, Canada
- Kaushala Prasad Misra, India
- Ron Mitchel, Canada
- Les Redpath, USA
- K. Noy Rithidech. USA
- Kazou Sakai, Japan
- Chuck Sanders, Korea
- Maurice Tubiana, France

Acknowledgements

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Other Related Presentations

<http://www.radiation-scott.org>

Backup Slides

Ionizing Photon Radiation Bursts from Thunder Storms

- 10-20 MeV photon radiation bursts are associated with thunder storms.
- The ionizing radiation arises just before a lightening strike and can travel kilometer distances.

Hamish Johnson, Physics World

<http://physicsworld.com/cws/article/news/31092>



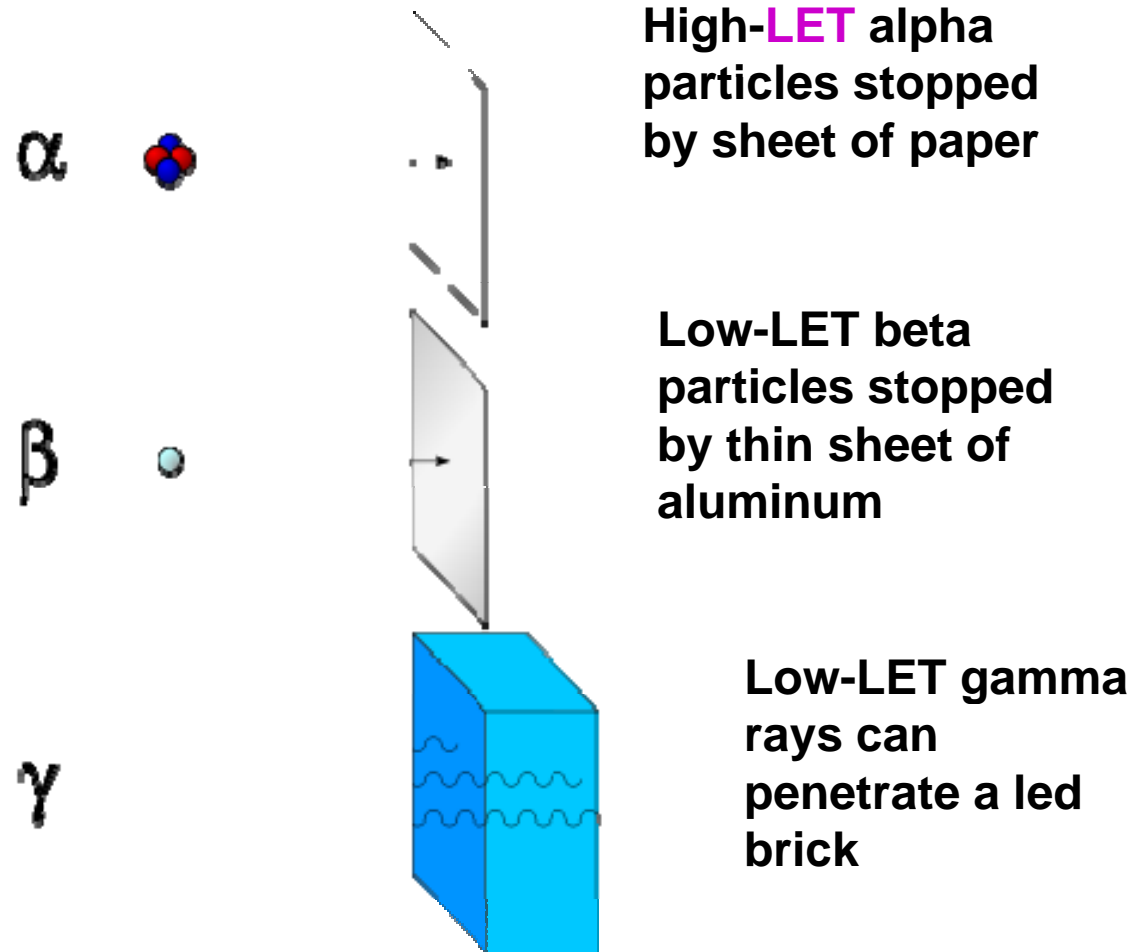
Photo from:

<http://www.pbs.org/wgbh/nova/sciencenow/3214/02-works.html>

Sources of Natural Background Radiation (BEIR VII Report, 2006)

Exposure Pathway	Percentage contribution to the dose to humans
Cosmic rays, high-LET	4%
Ingestion, high-LET	5%
Inhalation, high-LET (radon)	52%
Cosmic rays, low-LET	12%
Ingestion, low-LET	7%
Earth surface, low-LET	20%

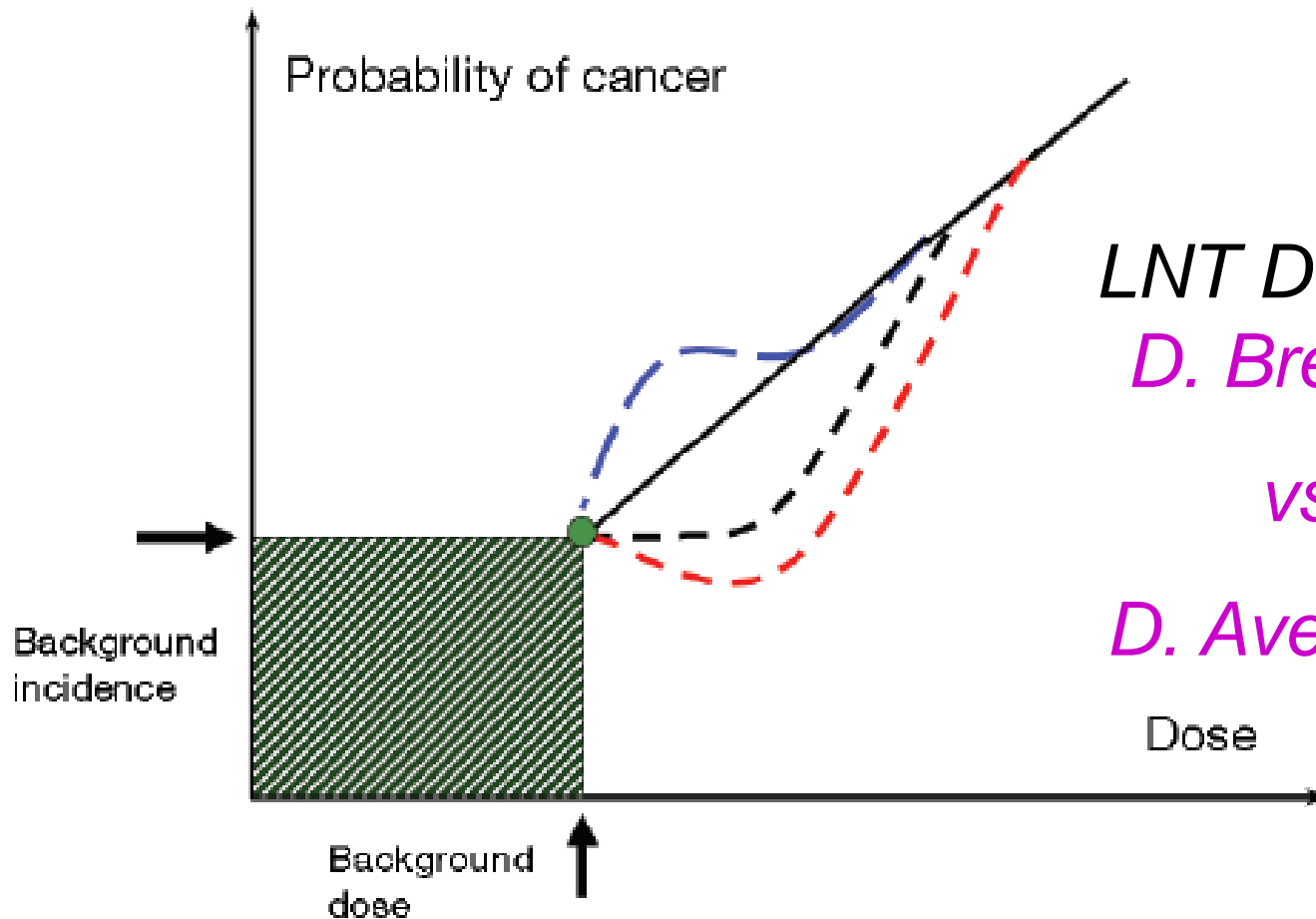
Radiation Penetration by Type



LET, linear energy transfer: average energy lost

NCRP 2008 Meeting in Washington, DC

Dose-Response Relationships



LNT Debate:

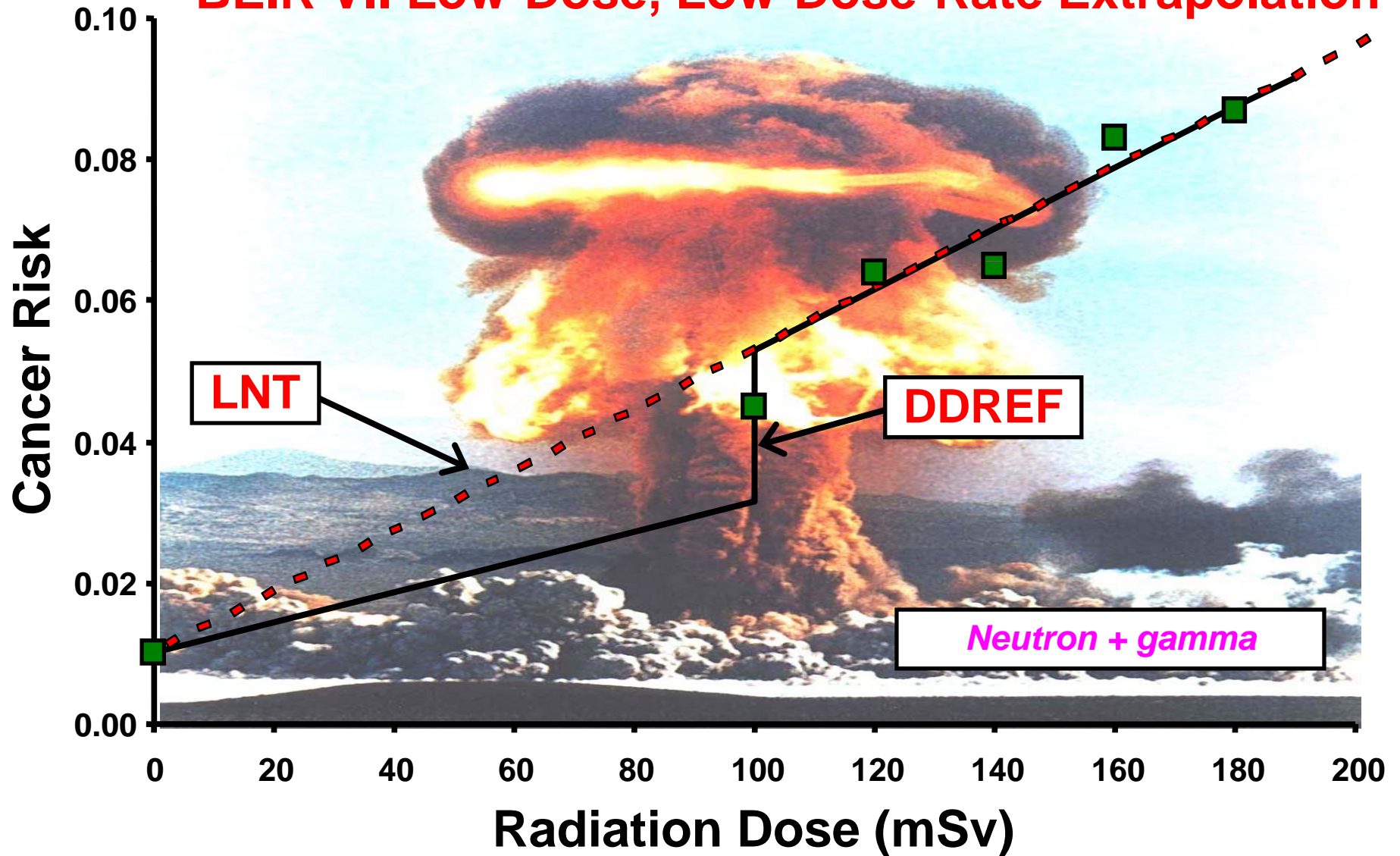
D. Brenner

vs.

D. Averbeck

Current Radiation Risk Assessment Paradigm: Linear No-Threshold

BEIR VII Low-Dose, Low-Dose-Rate Extrapolation



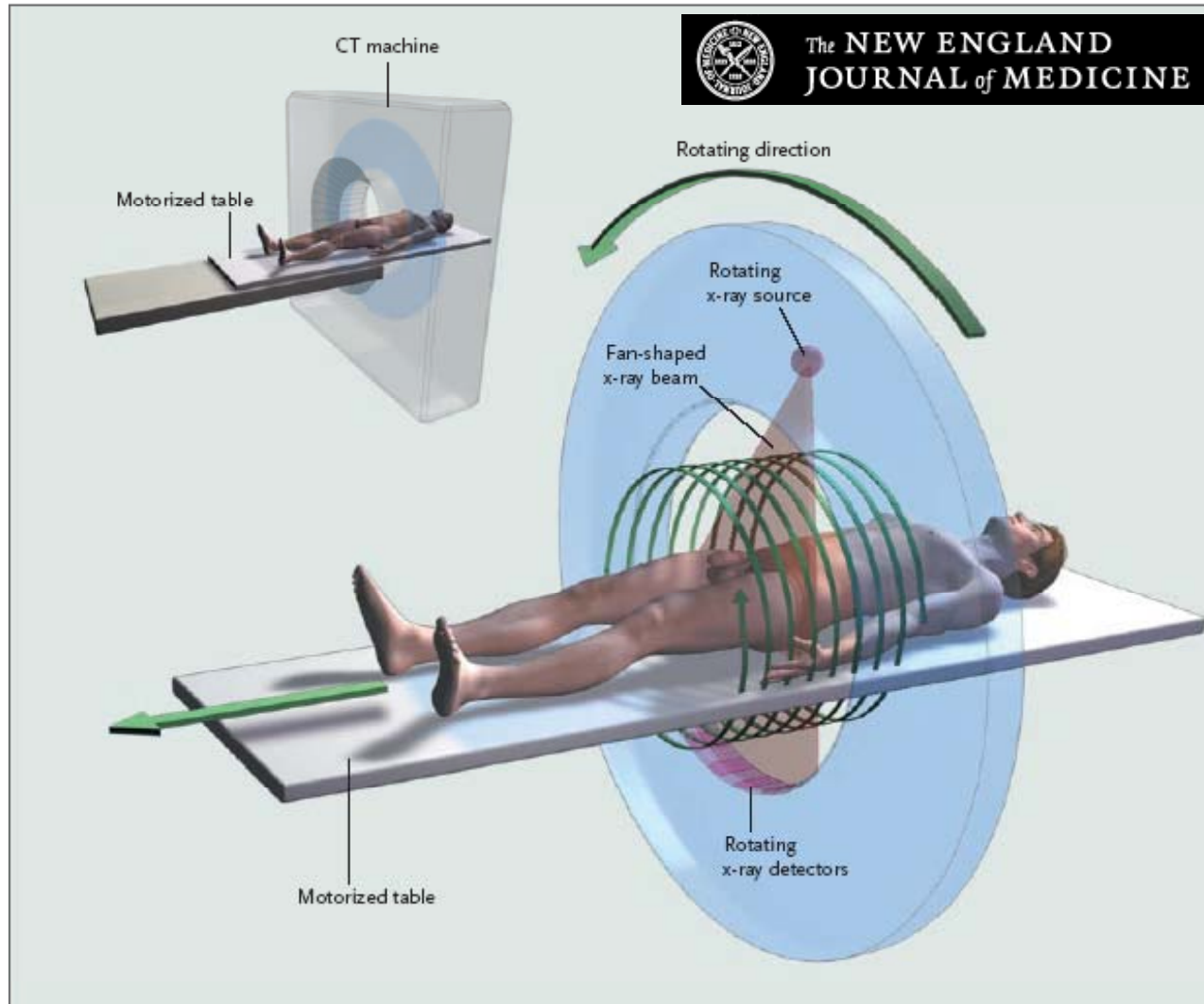
LNT-Associated Radiation Phobia Following a Dirty Bomb Incident



Radiation-Phobia-Associated Impacts:

- **Loss of lives** associated with frantic evacuations.
- **Severe injuries** during evacuations.
- **Increased suicides** and abortions.
- Increased **psychosomatic disorders**.
- Increased **drug/alcohol/cigarette abuse**.
- Permanent **abandonment of properties** with low-level contamination.

CT Scan



D. Brenner & E. Hall, NEJM 357:2277-84, 2007.

Typical Organ Radiation Doses from Radiologic Studies (Brenner & Hall 2007)

Study Type	Relevant Organ	Dose (mGy or mSv)
Dental radiography	Brain	0.005
Posterior-anterior chest radiography	Lung	0.01
Lateral chest radiography	Lung	0.15
Screening mammography	Breast	3
Adult abdominal CT	Stomach	10
Neonatal abdominal CT	Stomach	20

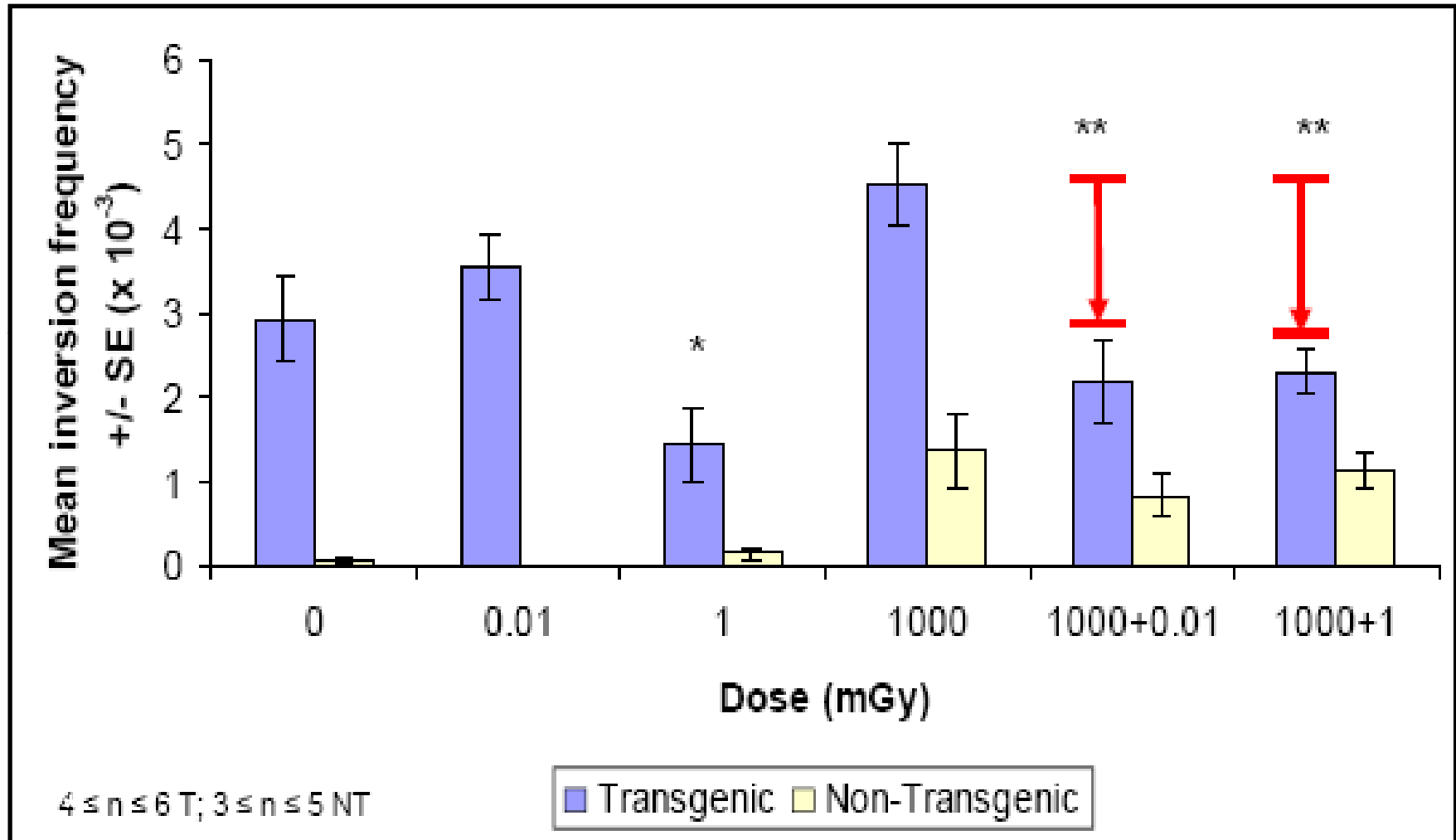
Hypothetical Cancer Cases for a Population of 50 Million Based on BEIR VII Risk Coefficient

Radiation Dose (mSv)	Hypothetical Average Individual Risk	Hypothetical Radiation-induced Cases
100	0.01	500 thousand
10	0.001	50 thousand
1	0.0001	5 thousand
0.1	0.00001	5 hundred

Evolutionarily-Derived Contributors to Low-Dose, Low-LET Radiation Induced Protection

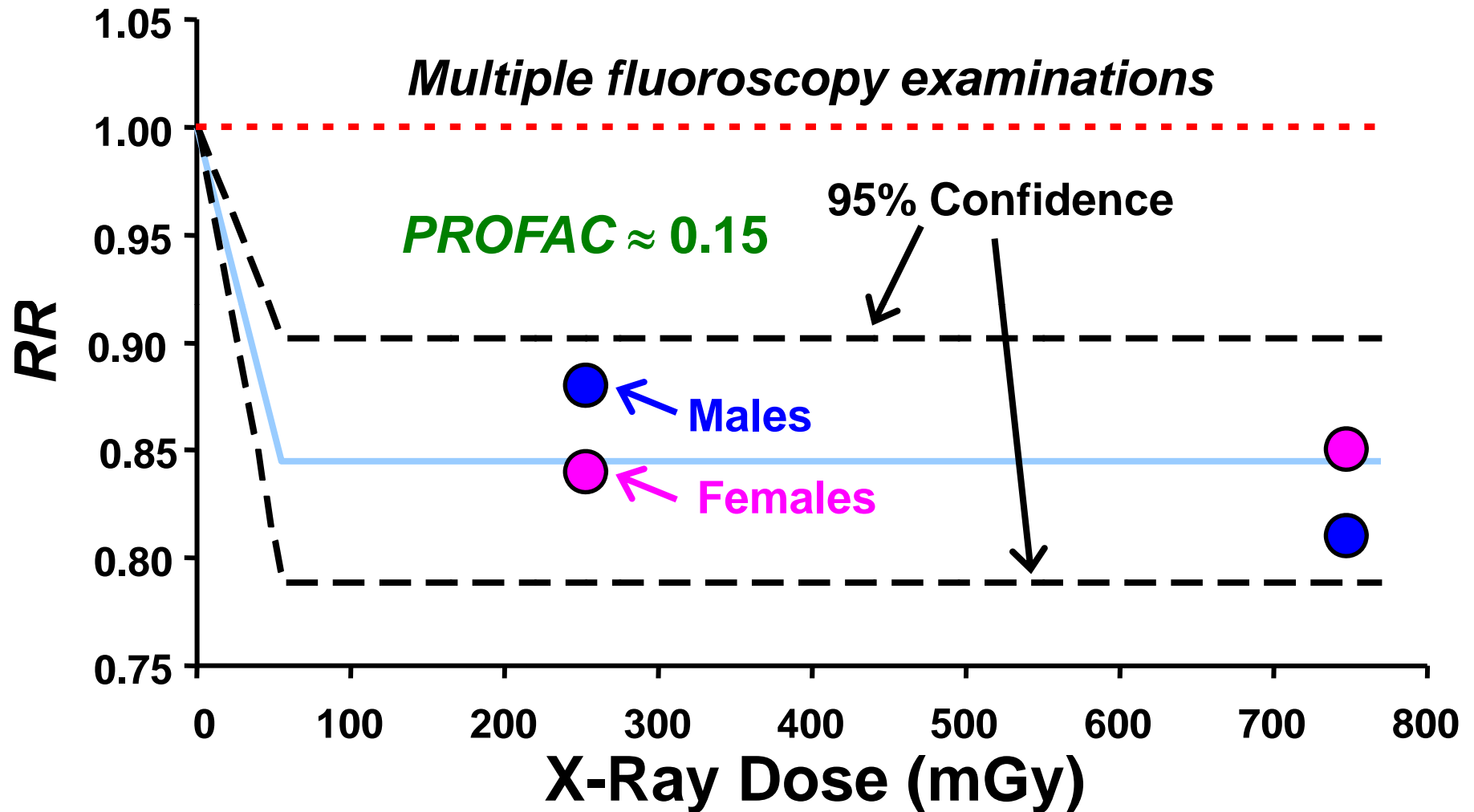
- Induced DNA DSB repair, for doses above a threshold, which may be dose-rate dependent (*W. Olipitz and colleagues*).
- Stimulated immunity against cancer (*S-Z Liu's group*).
- **P**rotective **a**poptosis **m**edicated (**PAM**) (*G. Bauer's group*).

Small Doses of Low-LET Radiation Protected From Inversion Mutations in pKZ1 Mice



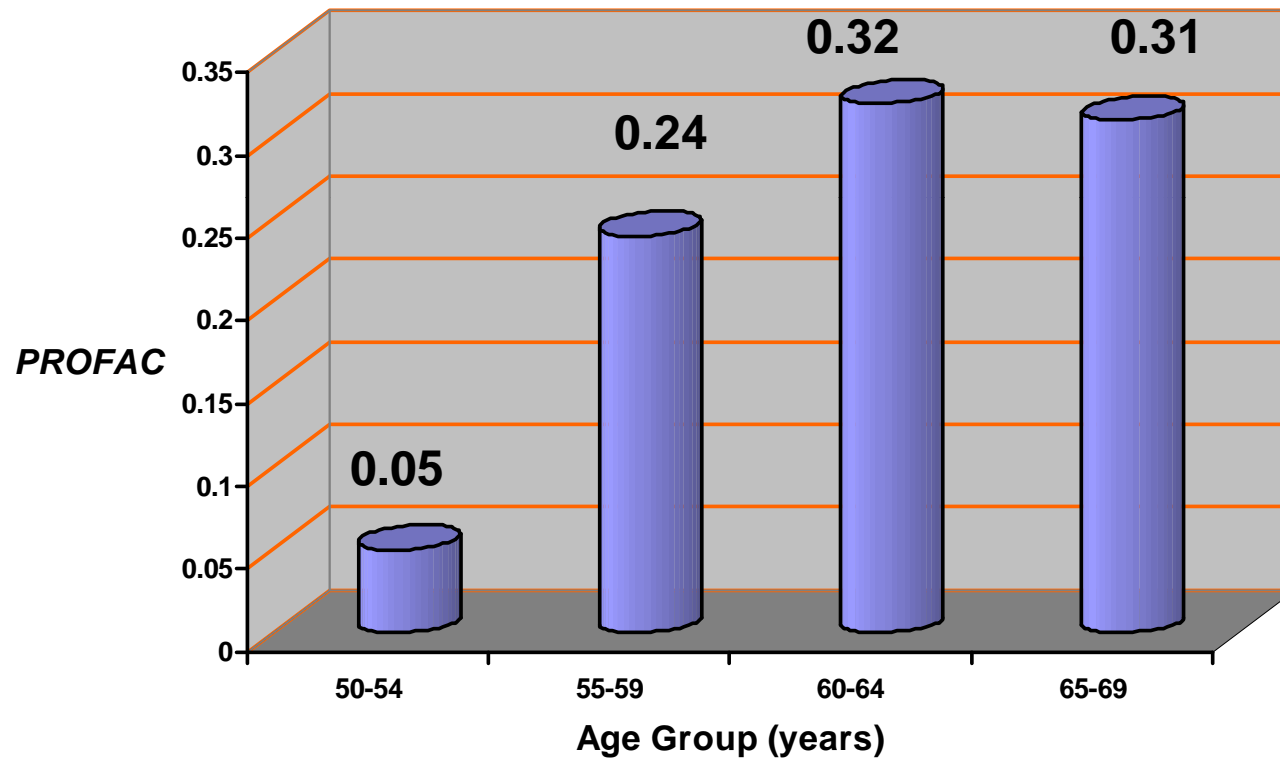
Small X-ray dose given hours after 1000 mGy dose protected T. Day, International Hormesis Conference 2006

Diagnostic X-Ray ANP Against Spontaneous Lung Cancer in Canadian TB Patients



Data from Howe GR. Radiat. Res. 142:295-304,1995. Similar findings have been reported for breast cancer (Miller. N. Engl. J. Med. 321:1285-1289, 1989)

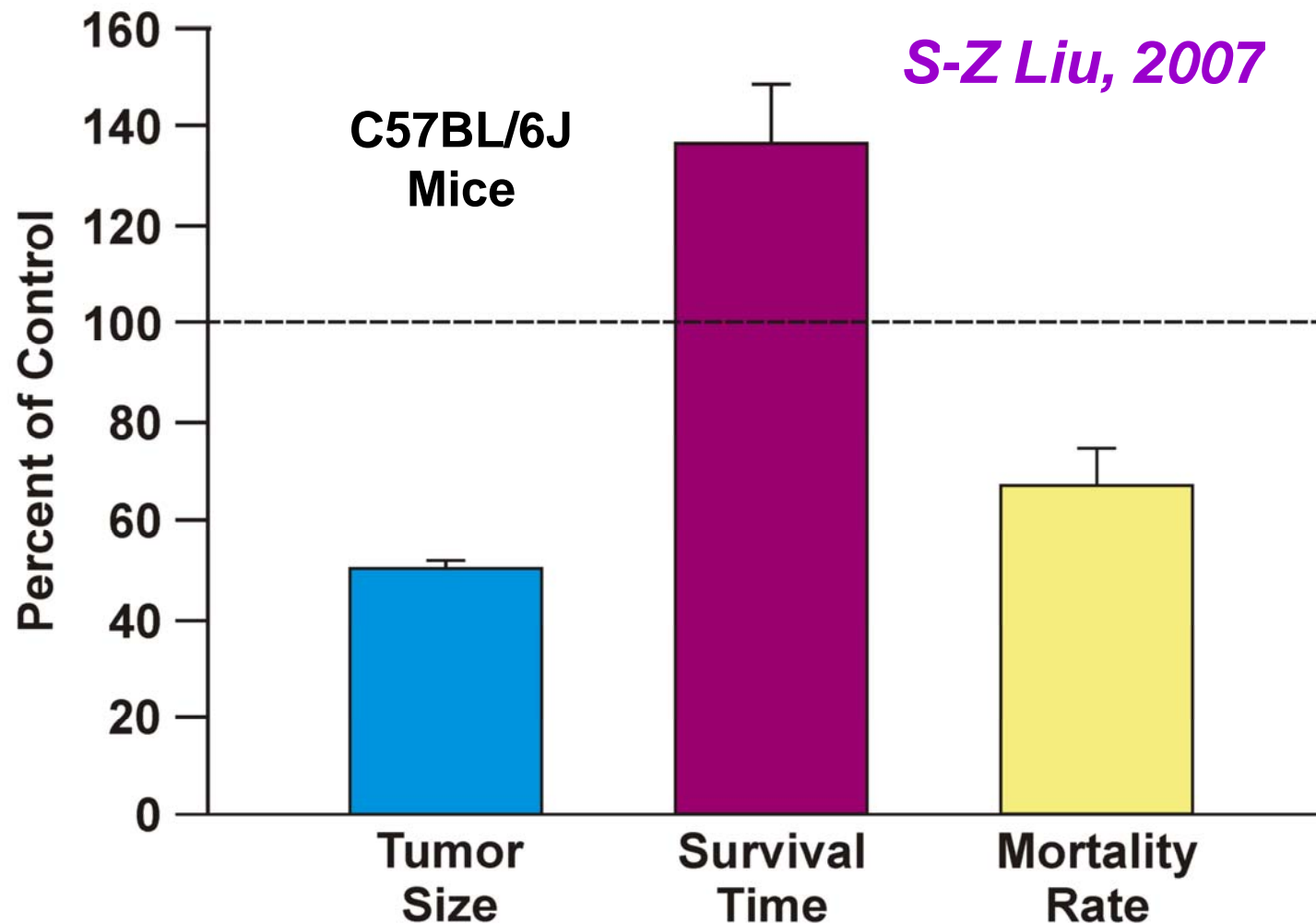
Upper Bound X-Ray *PROFAC* Against Breast Cancer



Based on data (after multiple mammograms) from L. Nyström et al. Lancet 359:909 - 919(2002).

Low-Dose X-Ray ANP Against Lung Cancer

75 mGy 24h before Lewis lung cancer cell implantation



Thymic Lymphoma Study of S-Z Liu

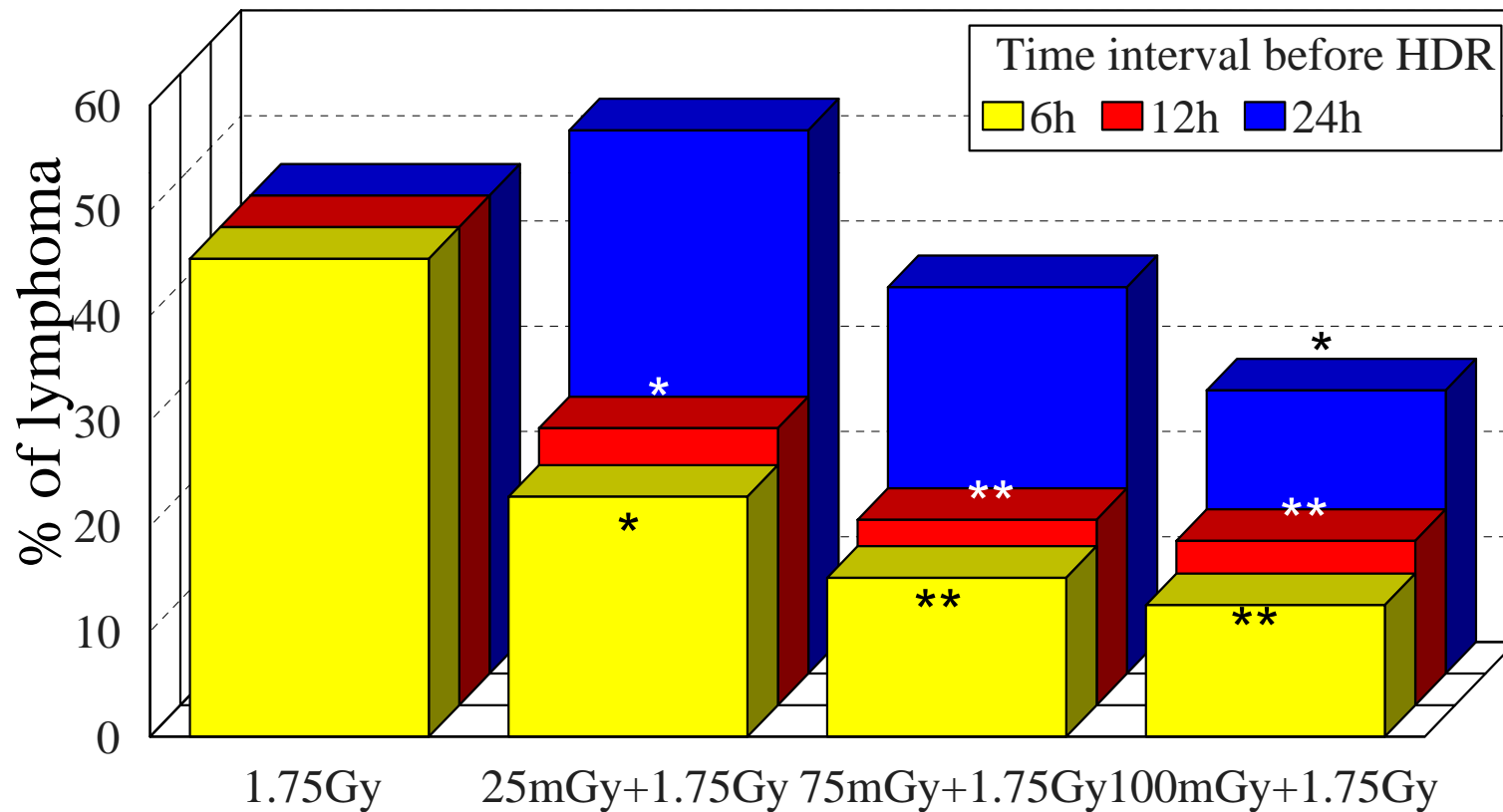
- Low dose X rays (25, 75, or 100 mGy) given before large X ray dose (1.75 Gy) to mice.
- Time interval between low and high dose was 6, 12, or 24 hours.
- Four cycles of dosing were given apparently to reduce acute toxicity.

S-Z Liu, 2007.

Low Dose ANP Against High Dose X-Ray Induced Thymic lymphoma in C57BL/6J Mice: Evidence for Stochastic Thresholds

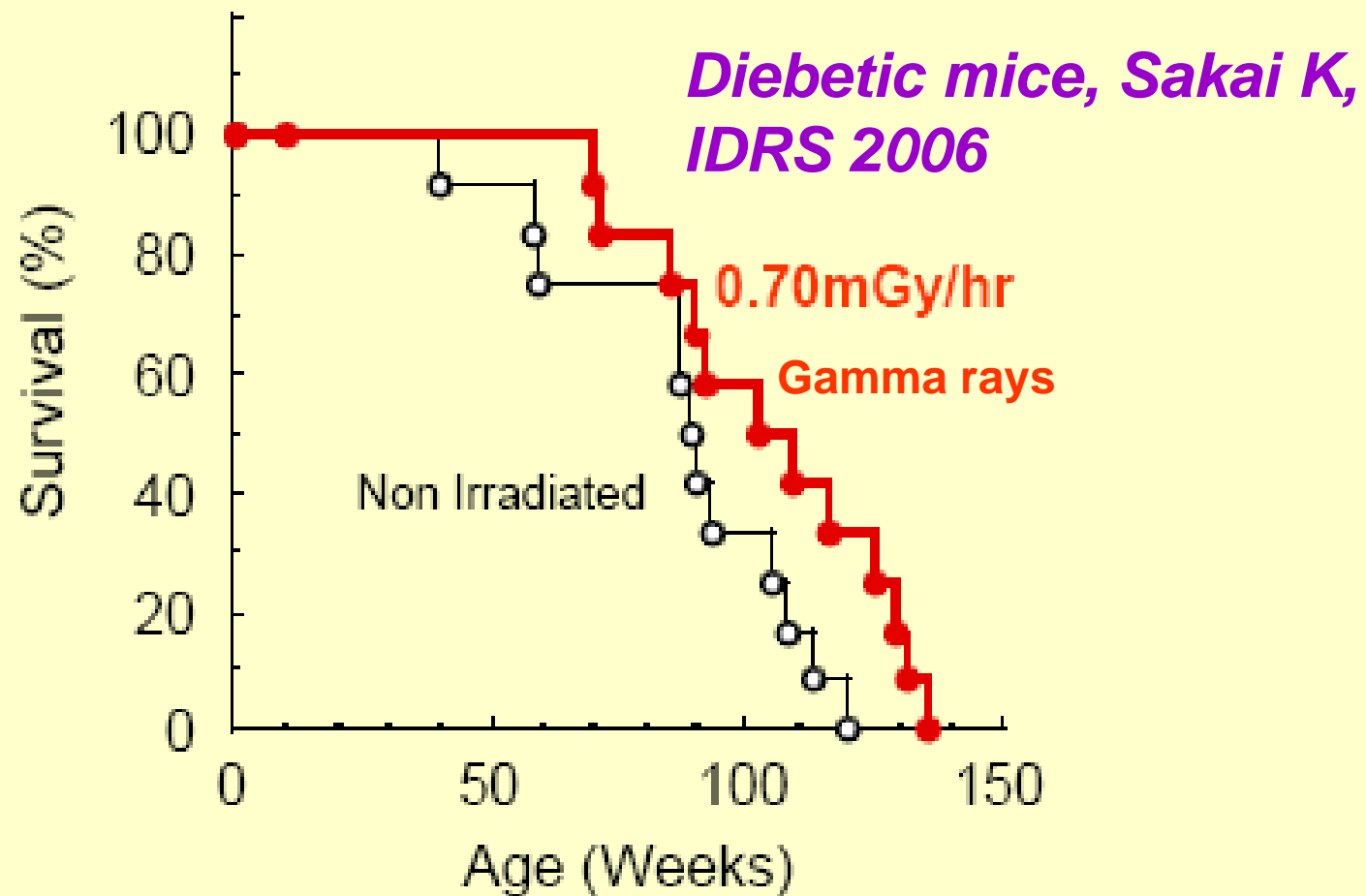
HDR=1.75 Gy x 4

S-Z Liu, 2007

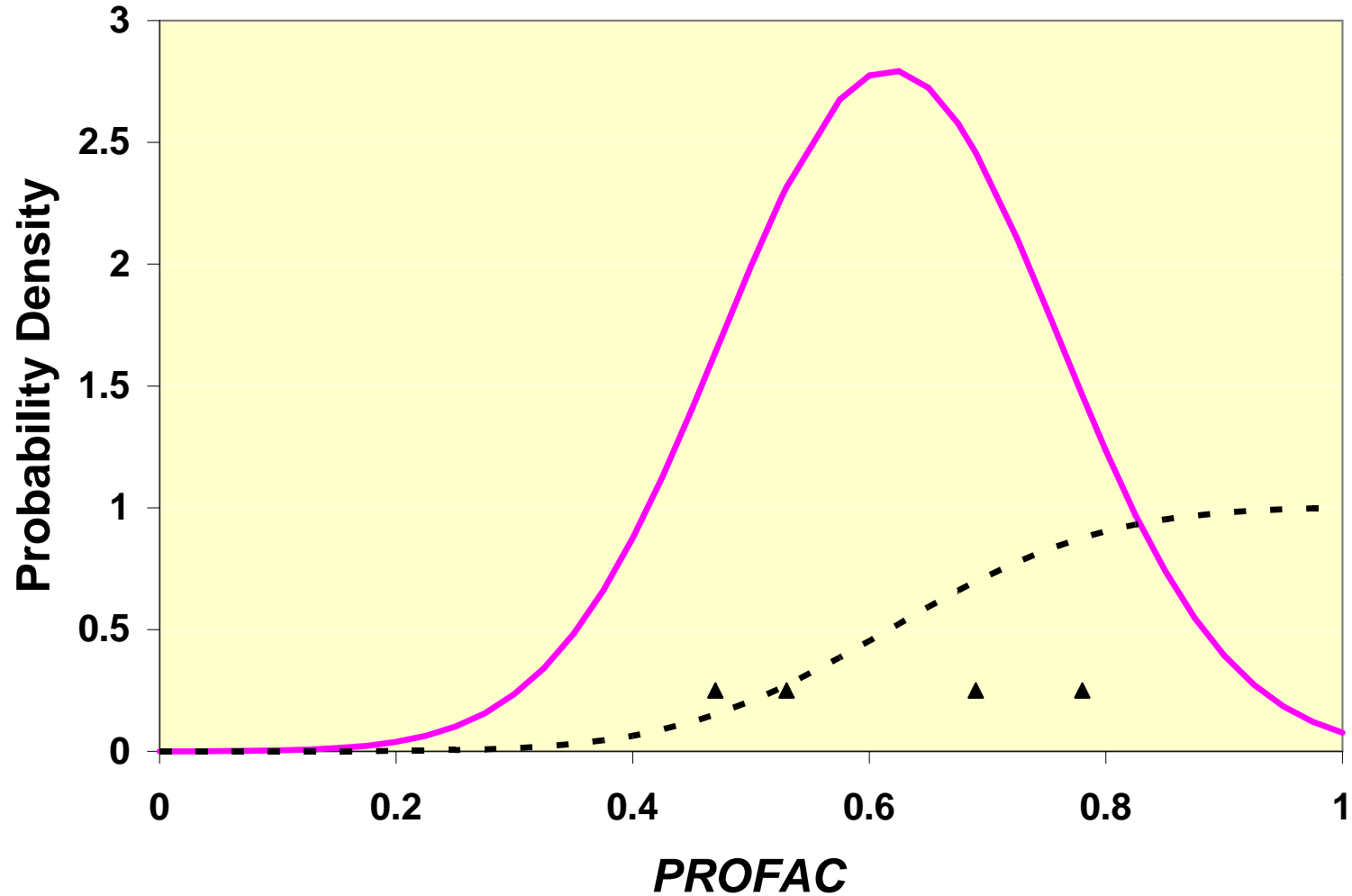


* $P < 0.05$, ** $P < 0.01$ vs 1.75Gy x 4

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



Indoor Radon Lung Cancer *PROFAC* Distribution



Based on data from Thompson et al. (2008).

Related Literature

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