Low Doses, Cross Adaption and Multiple Stressors

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ADAPTIVE RESPONSE

Exposure
of cells or organisms to radiation
at a low dose and dose rate
(or to other mild stress)
induces mechanisms that protect
against the detrimental effects
of other events or agents,
including radiation

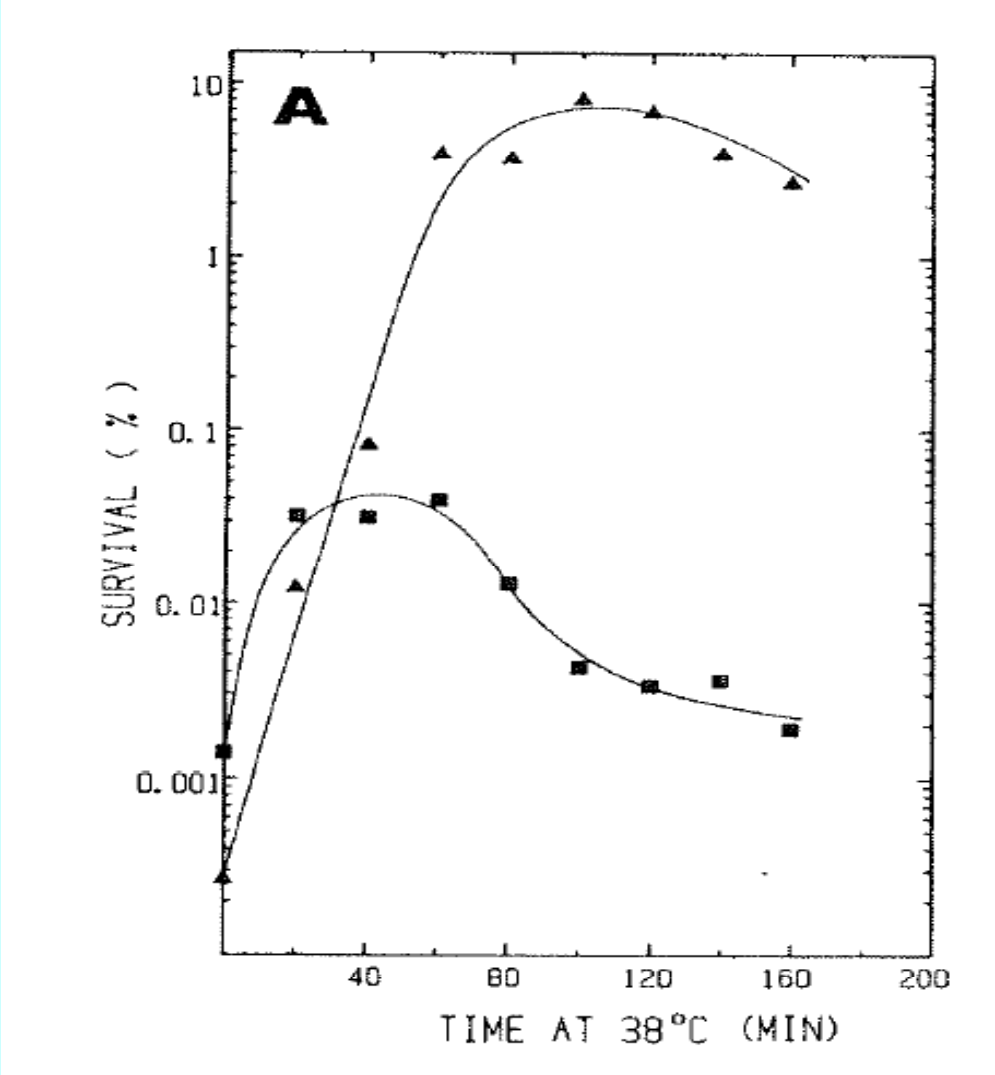
RELATIONSHIPS BETWEEN STRESSES AND EFFECTS

- Other stressors can modify radiation risk, and vice versa
- Adaptive responses to radiation are part of a general stress response
- Organisms are usually not exposed just once to a single stressor

QUESTION:

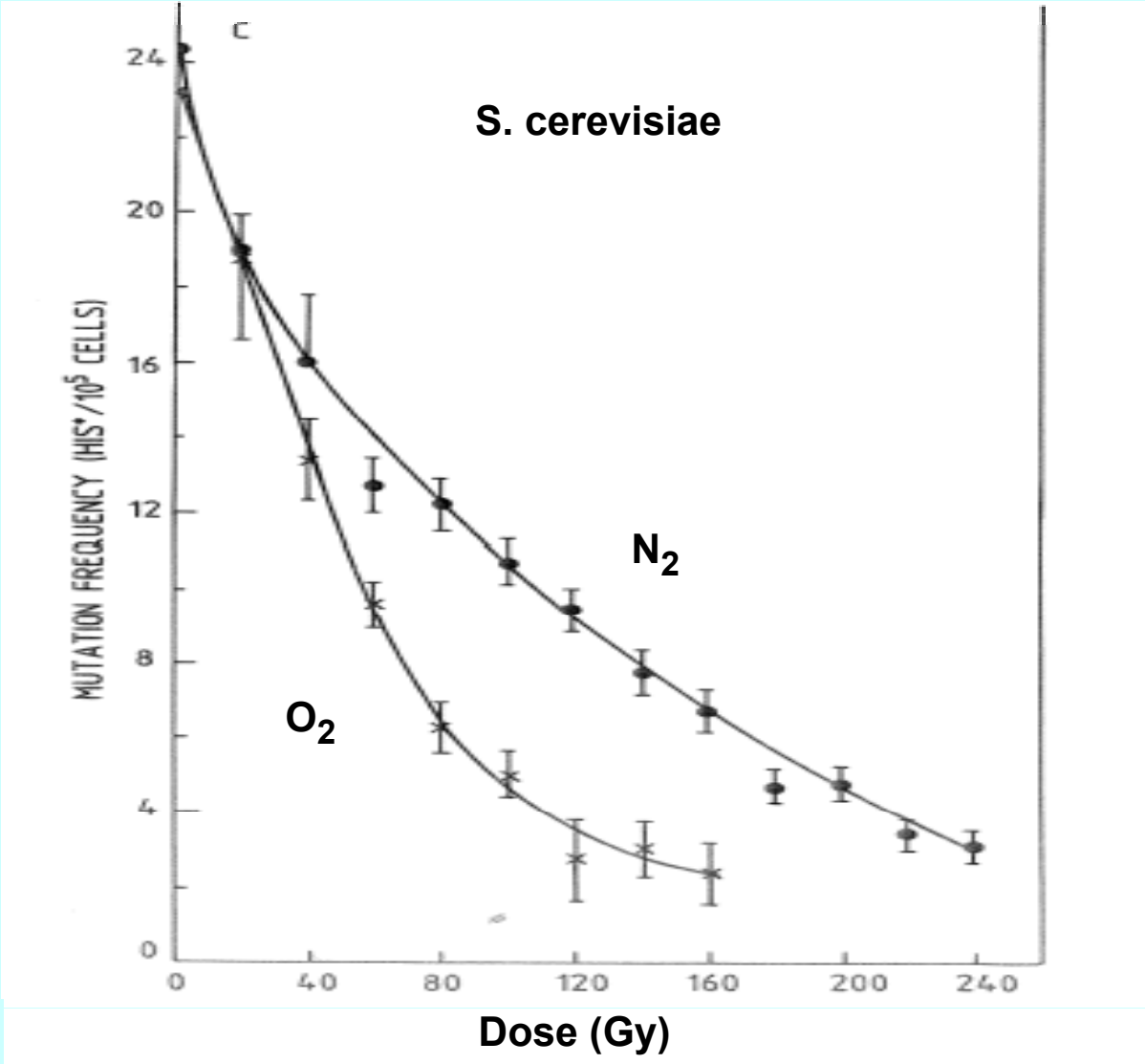
What are the protection limits and what influences them??

Adaption to Heat and Radiation from Heat Stress in Yeast



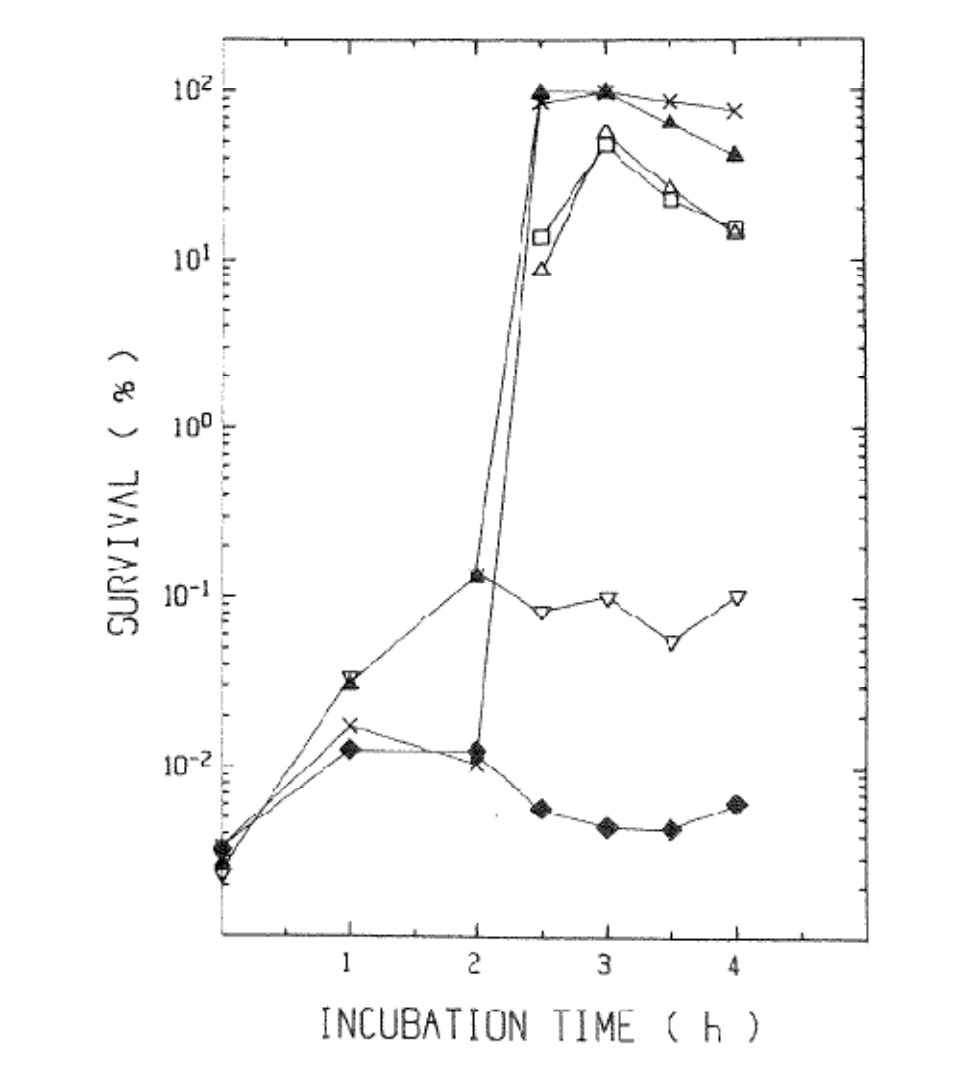
Mitchel and Morrison, Radiat. Res 92:182-187, 1982

Radiation-Induced Resistance to MNNG Mutation in Yeast



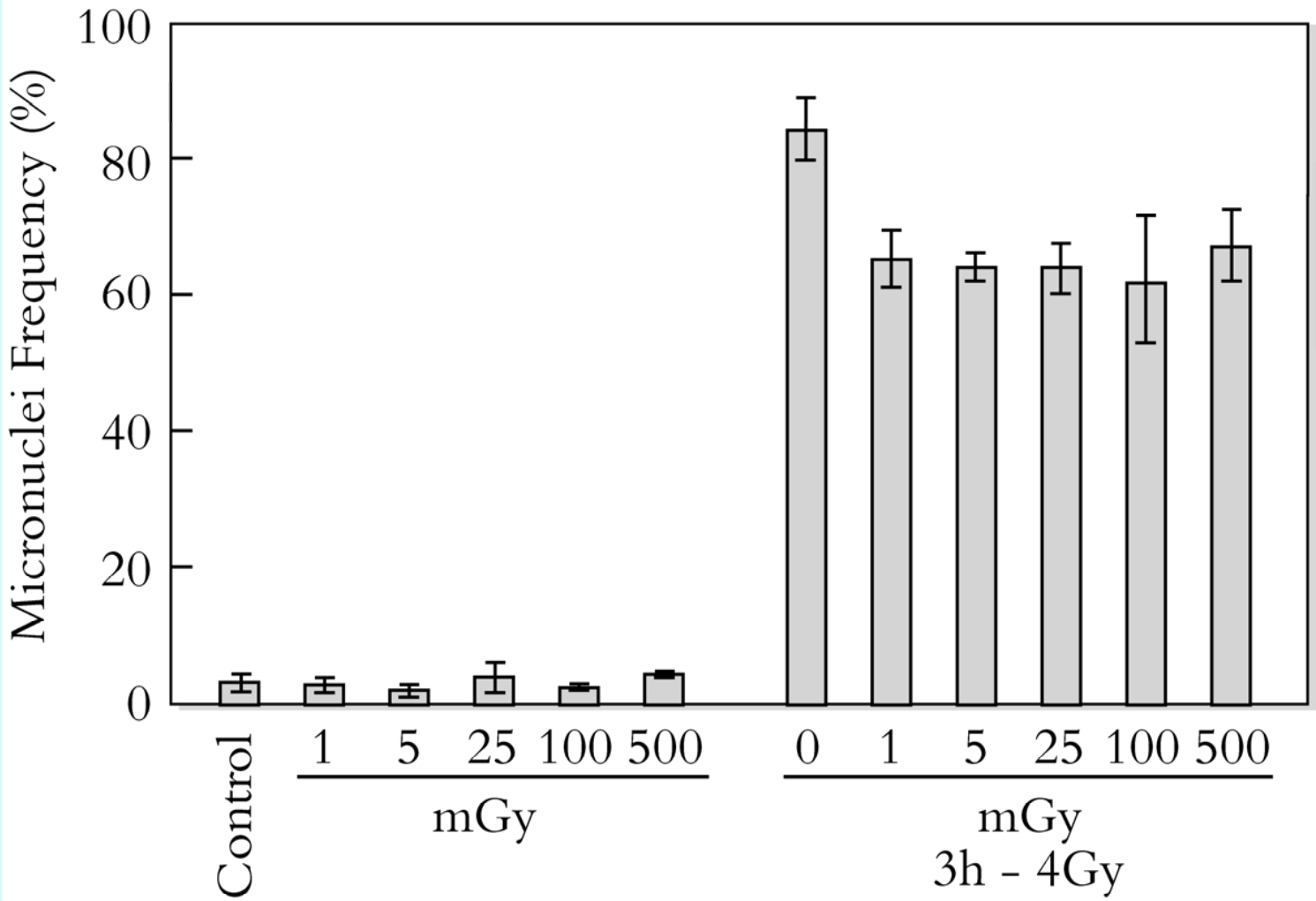
Mitchel and Morrison Mutat. Res. 183:149-159 (1987)

Lack Of Additivity for Adaption In Yeast By Heat and Radiation



Mitchel and Morrison Radiat. Res. 383-393 (1984)

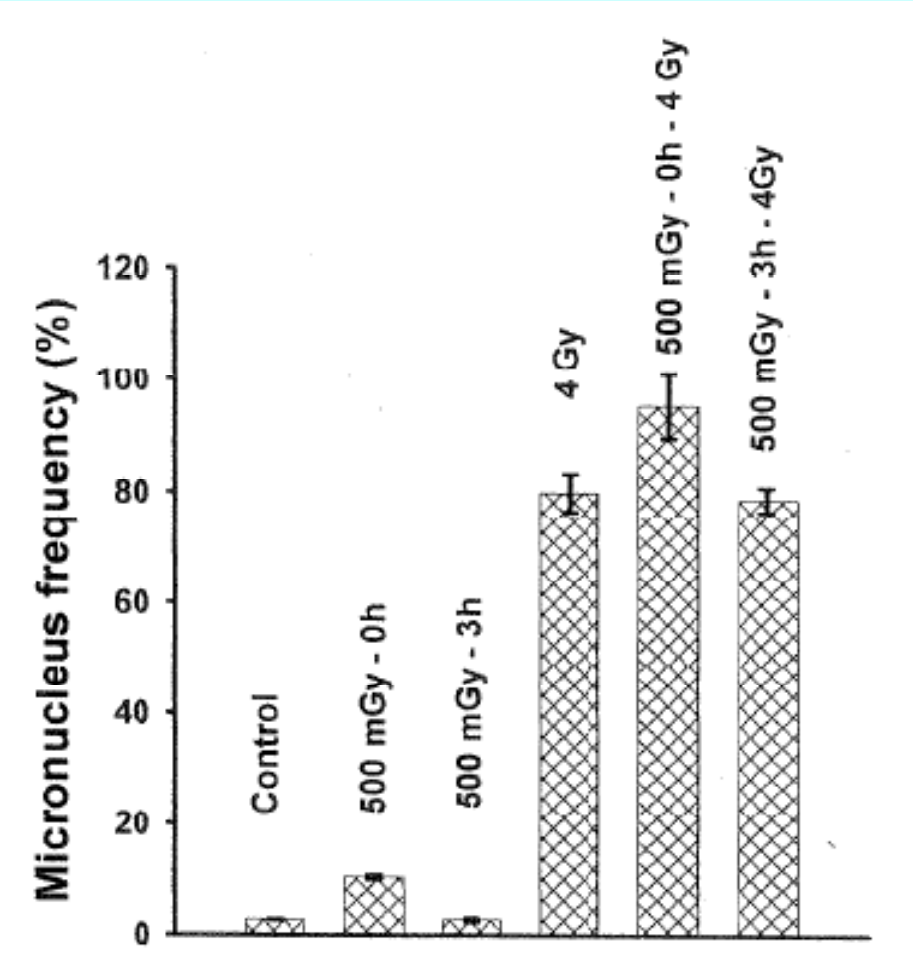
Repair of Broken Chromosomes in Human Cells Adapted by Exposure to Low Doses



1-3 mGy/min

Broome, Brown and Mitchel. Radiat. Res. 158, 181-186 (2002)

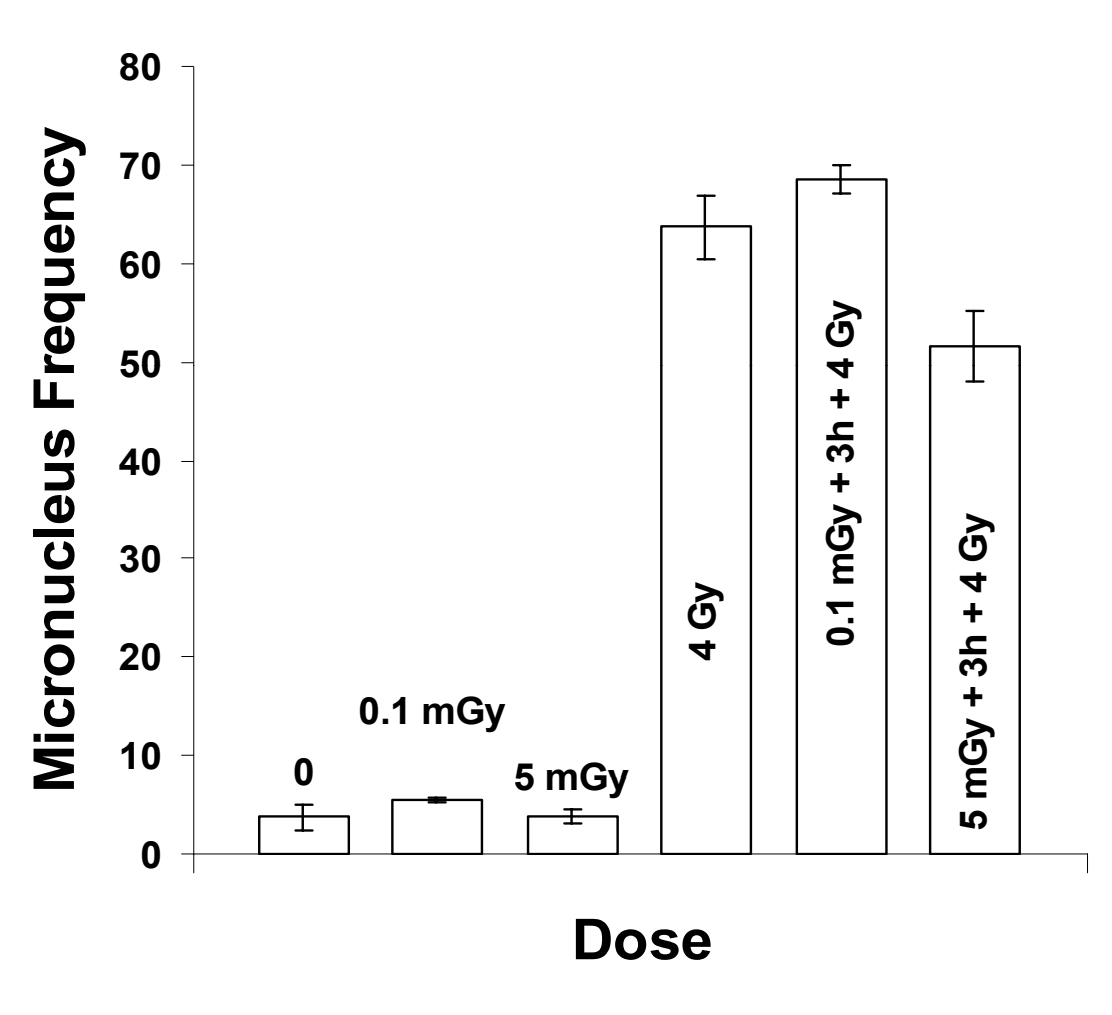
No Adaption in Human Cells at High Dose Rate



0.77 Gy/min
^{60}Co γ

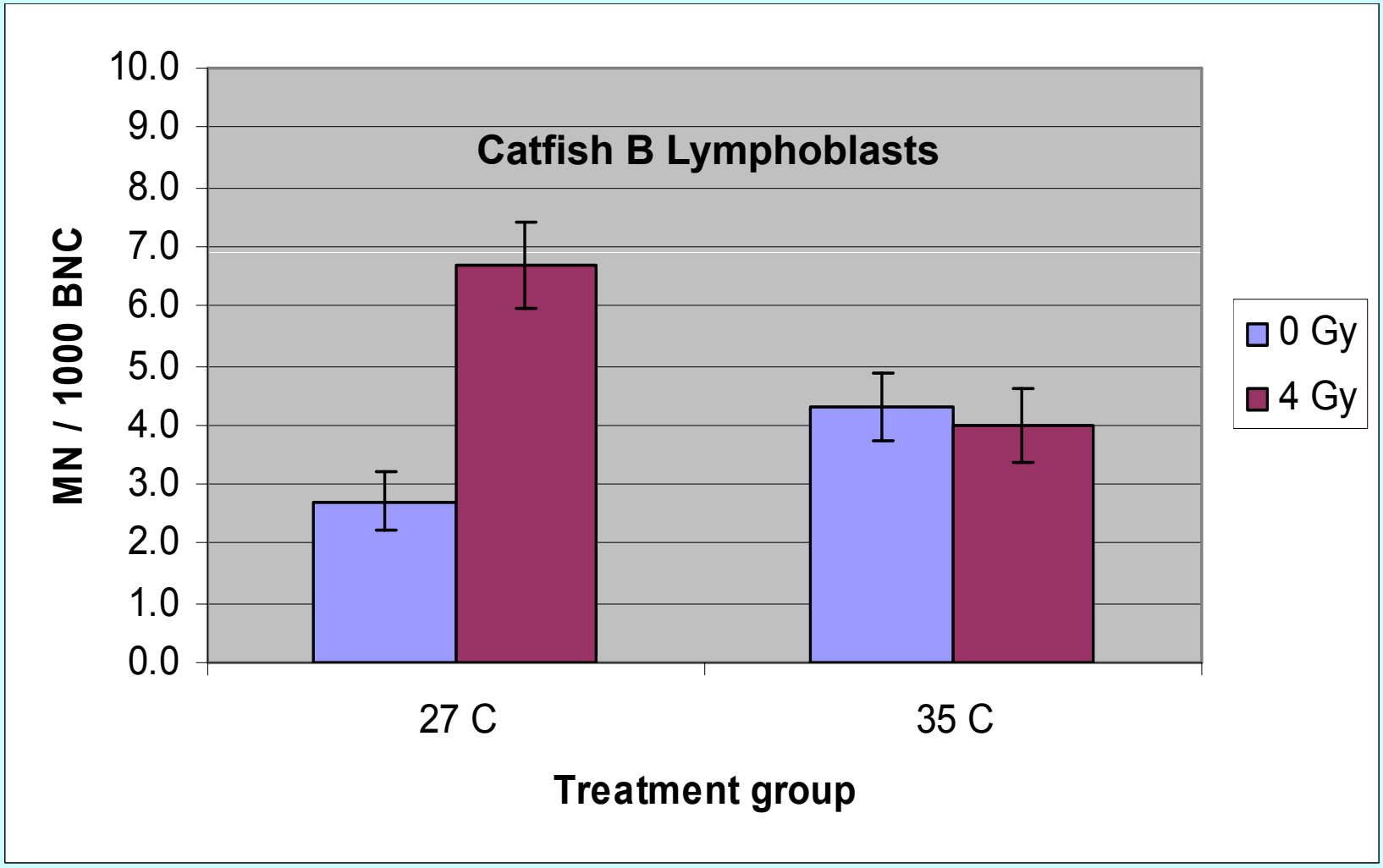
Broome, Brown and Mitchel. Radiat. Res. 158, 181-186 (2002)

Sub-critical Dose for Adaption in Human Cells

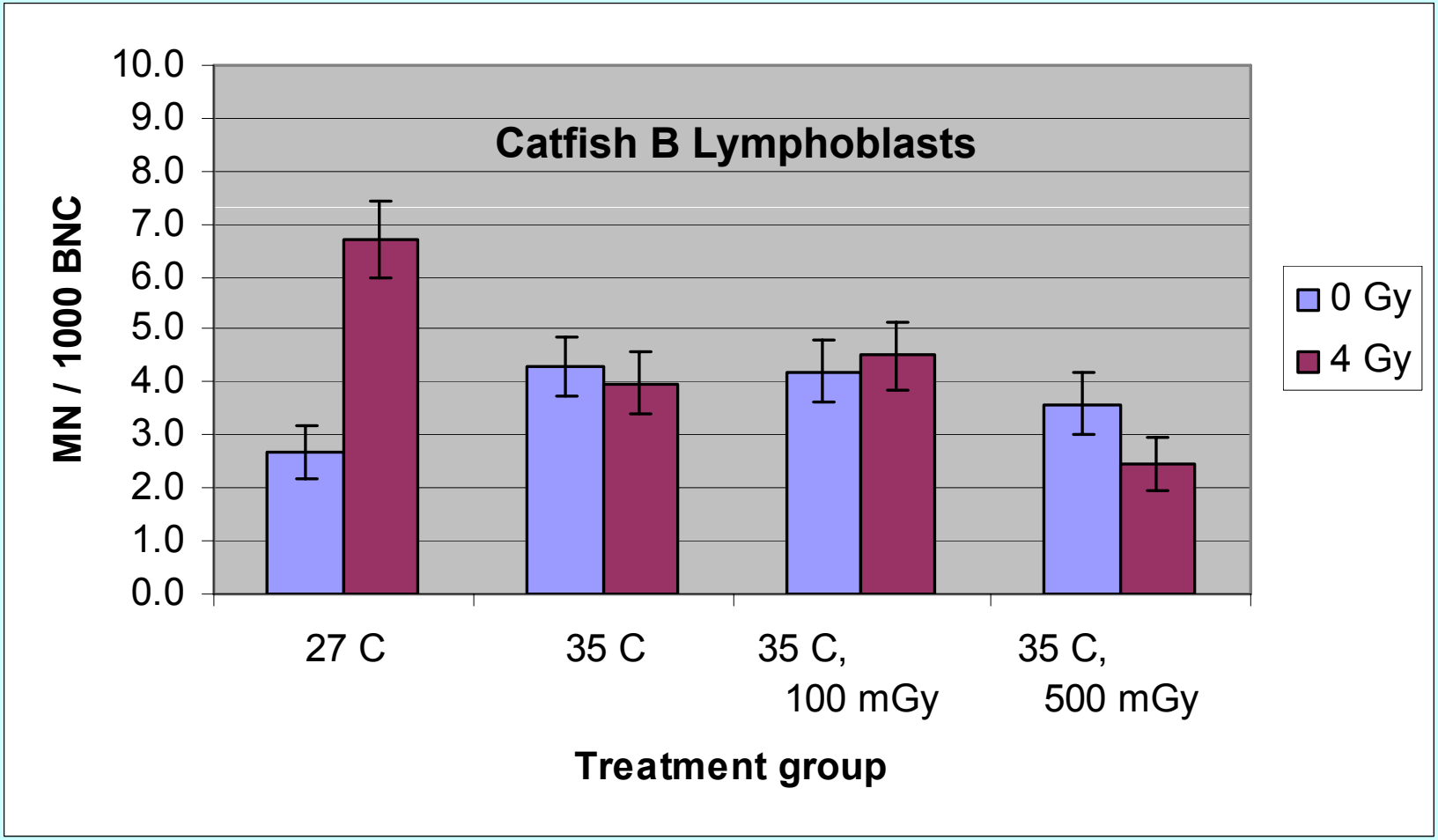


Broome, Brown and Mitchel. Radiat. Res. 158, 181-186 (2002)

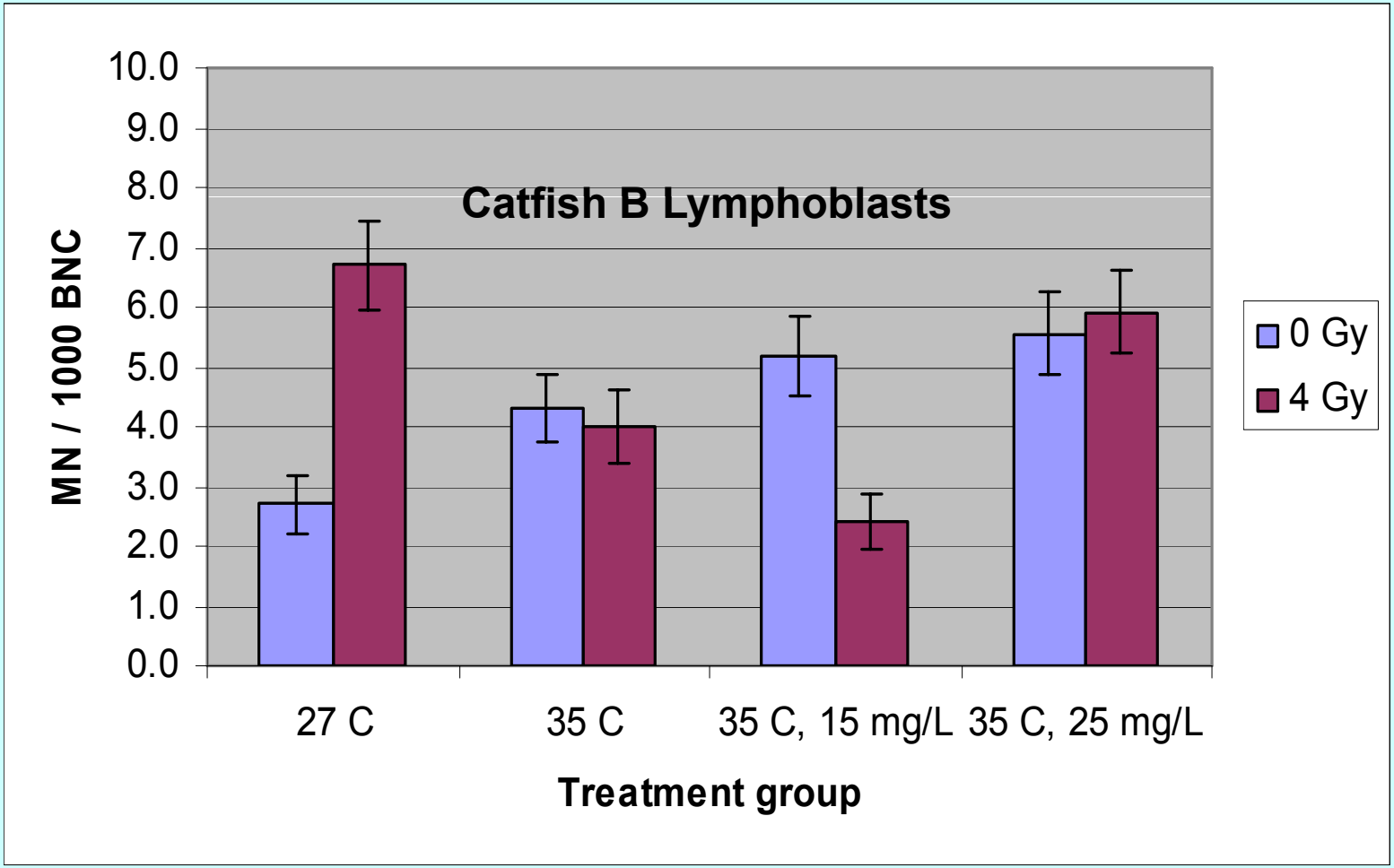
Effect of Low Thermal Stress
On Adaption to a High Dose of Radiation



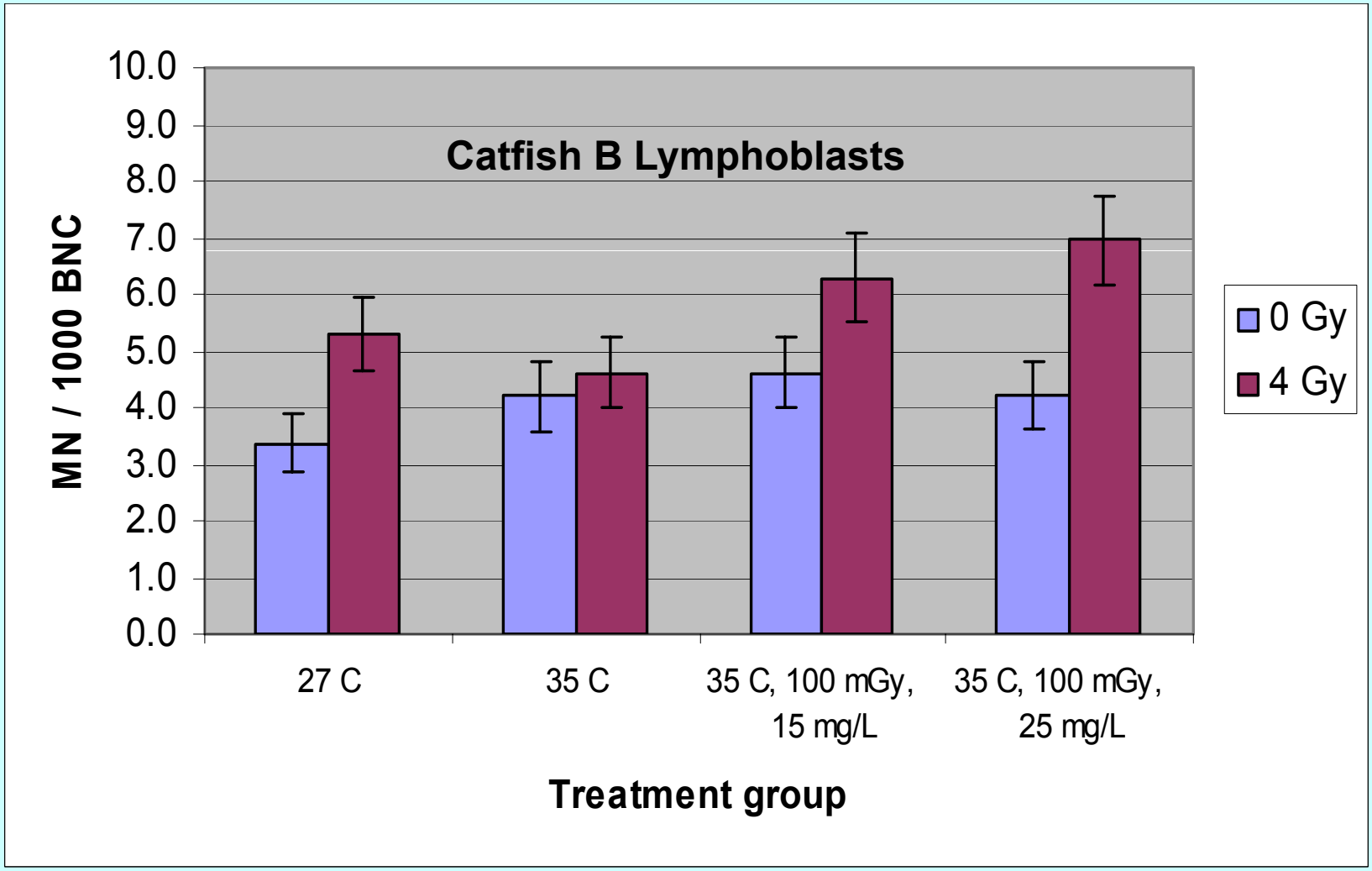
Effect of Sequential Exposure to Low Thermal Stress and Low Gamma Radiation on Adaption to a High Dose of Radiation



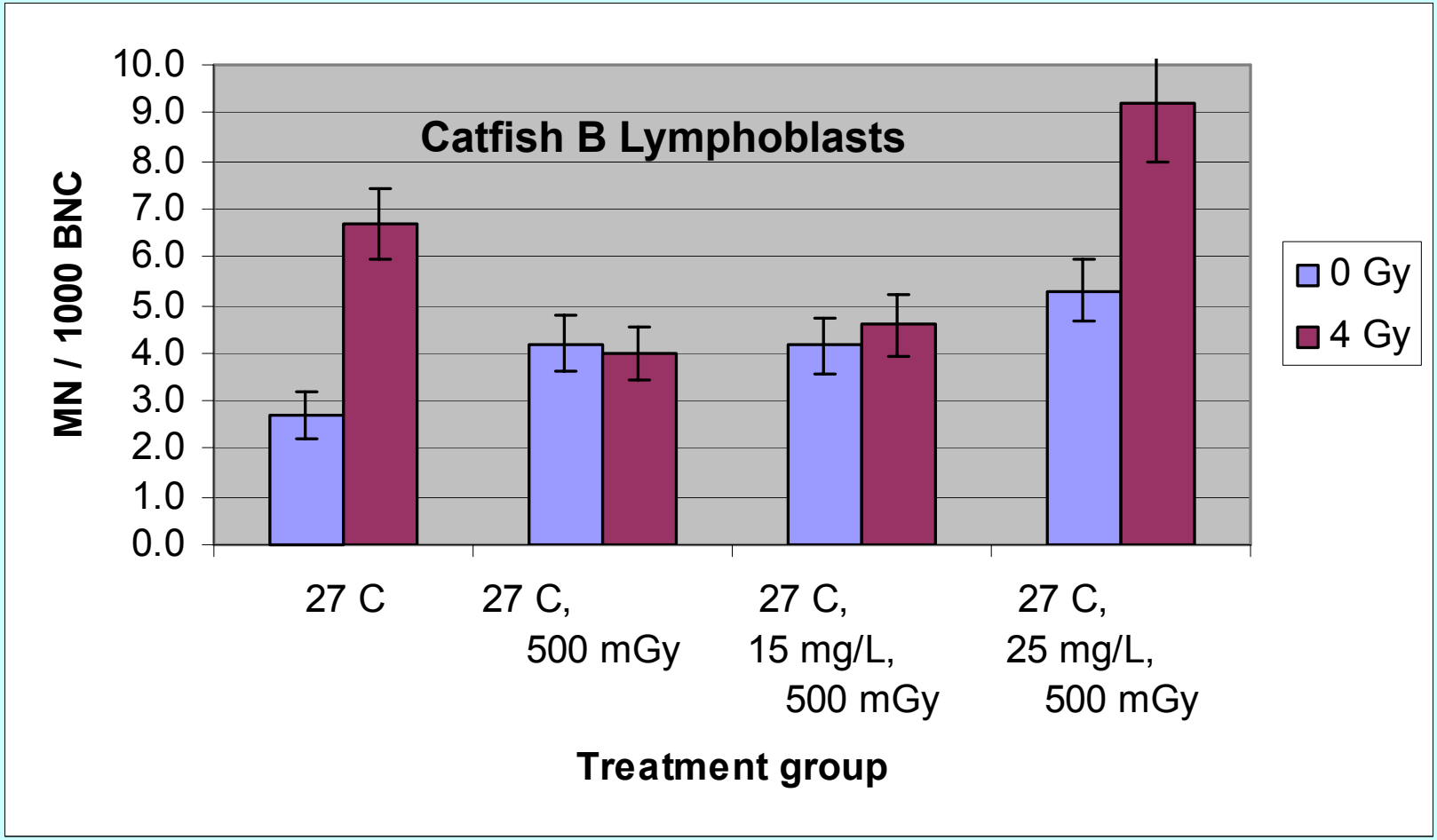
Effect of Sequential Exposure to Low Thermal Stress and Chlorine on Adaption to a High Dose of Radiation



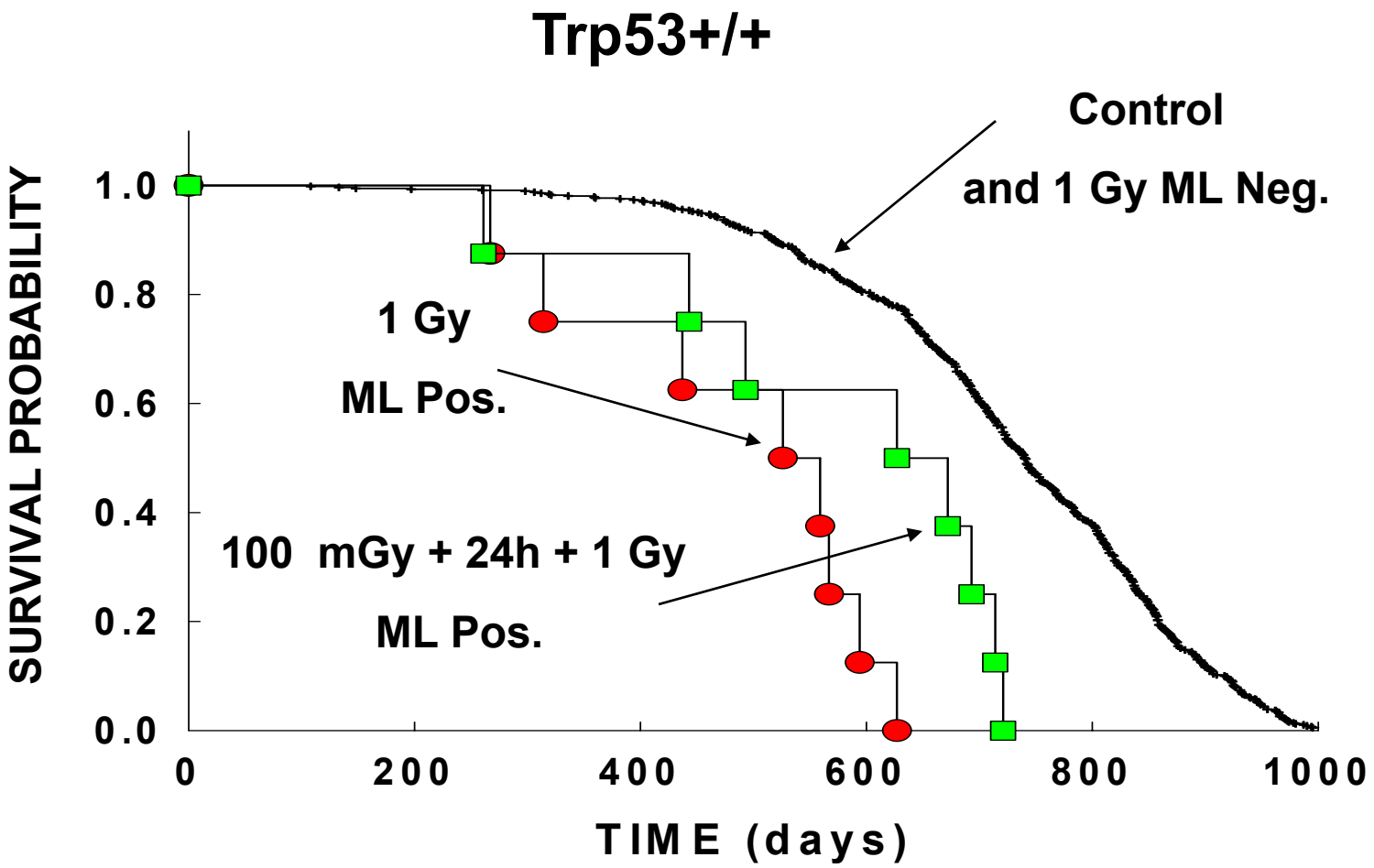
Effect of Sequential Exposure to Low Thermal Stress and Low Gamma Radiation and Chlorine on Adaption to a High Dose of Radiation



Effect of Sequential Exposure to Chlorine and Low Gamma Radiation on Adaption to a High Dose of Radiation

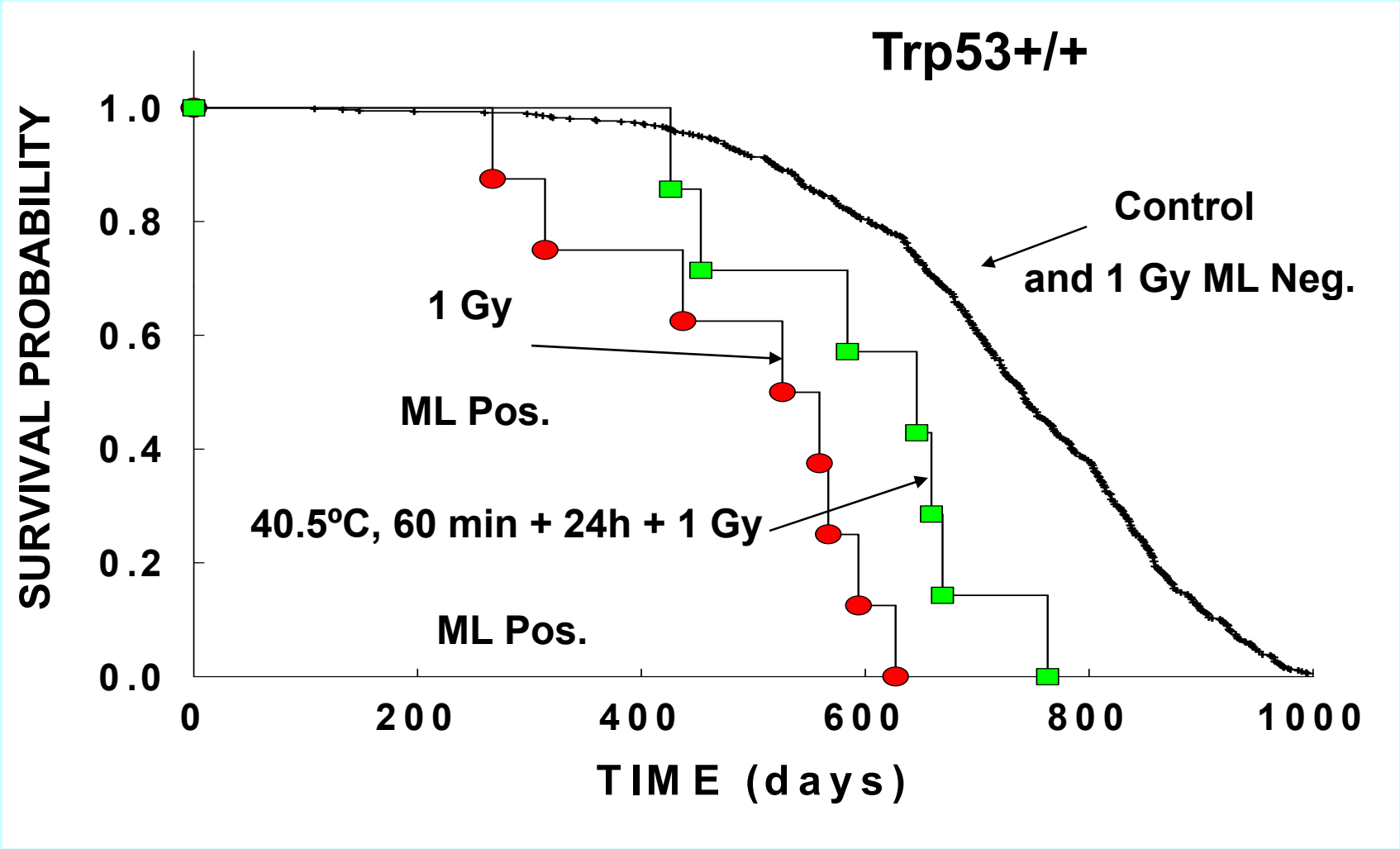


Low Doses and Myeloid Leukemia in Genetically Normal Mice



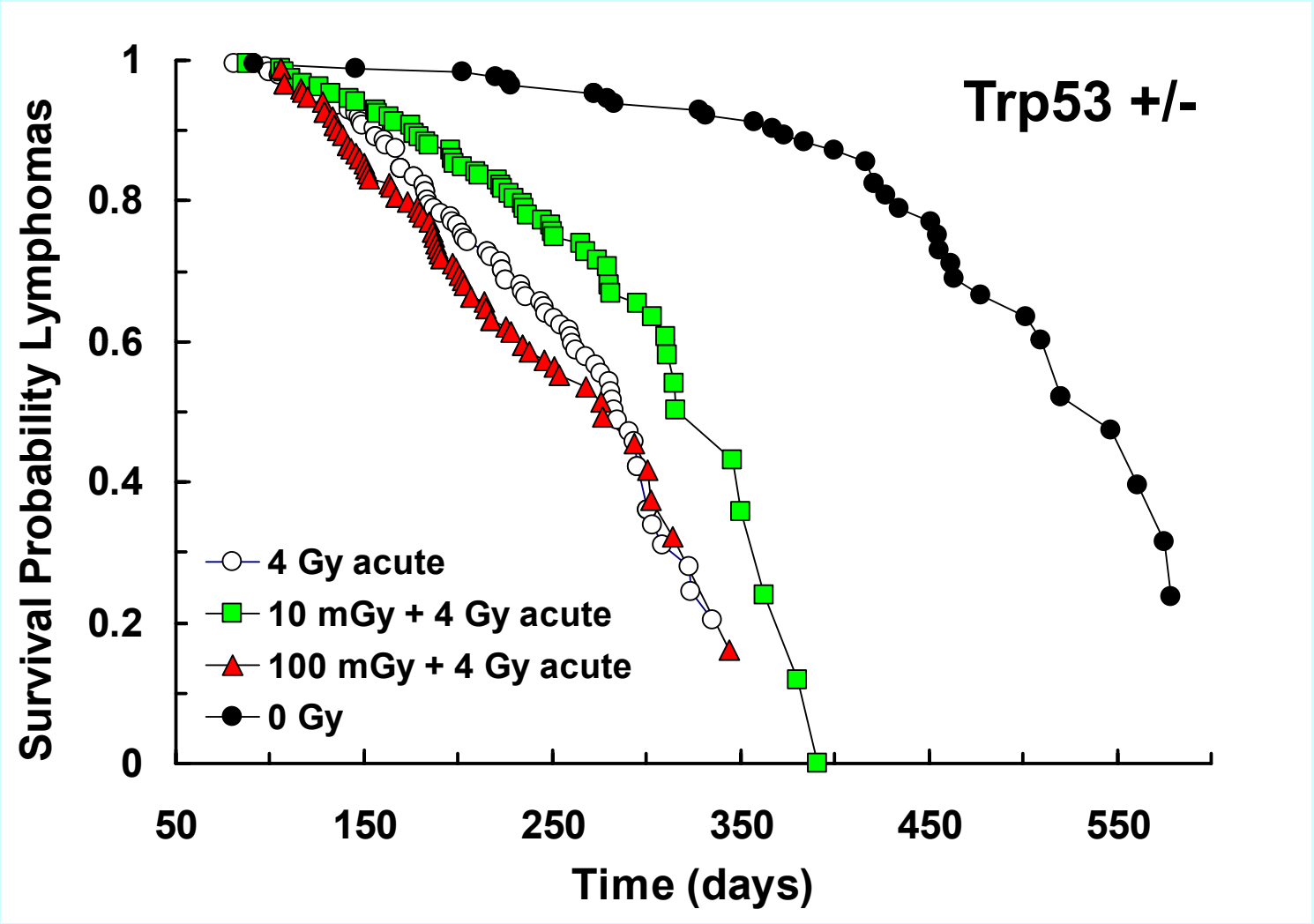
Mitchel, Jackson, McCann and Boreham, Radiat. Res. 152:273-279 (1999)

Mild Heat Stress and Myeloid Leukemia in Genetically Normal Mice



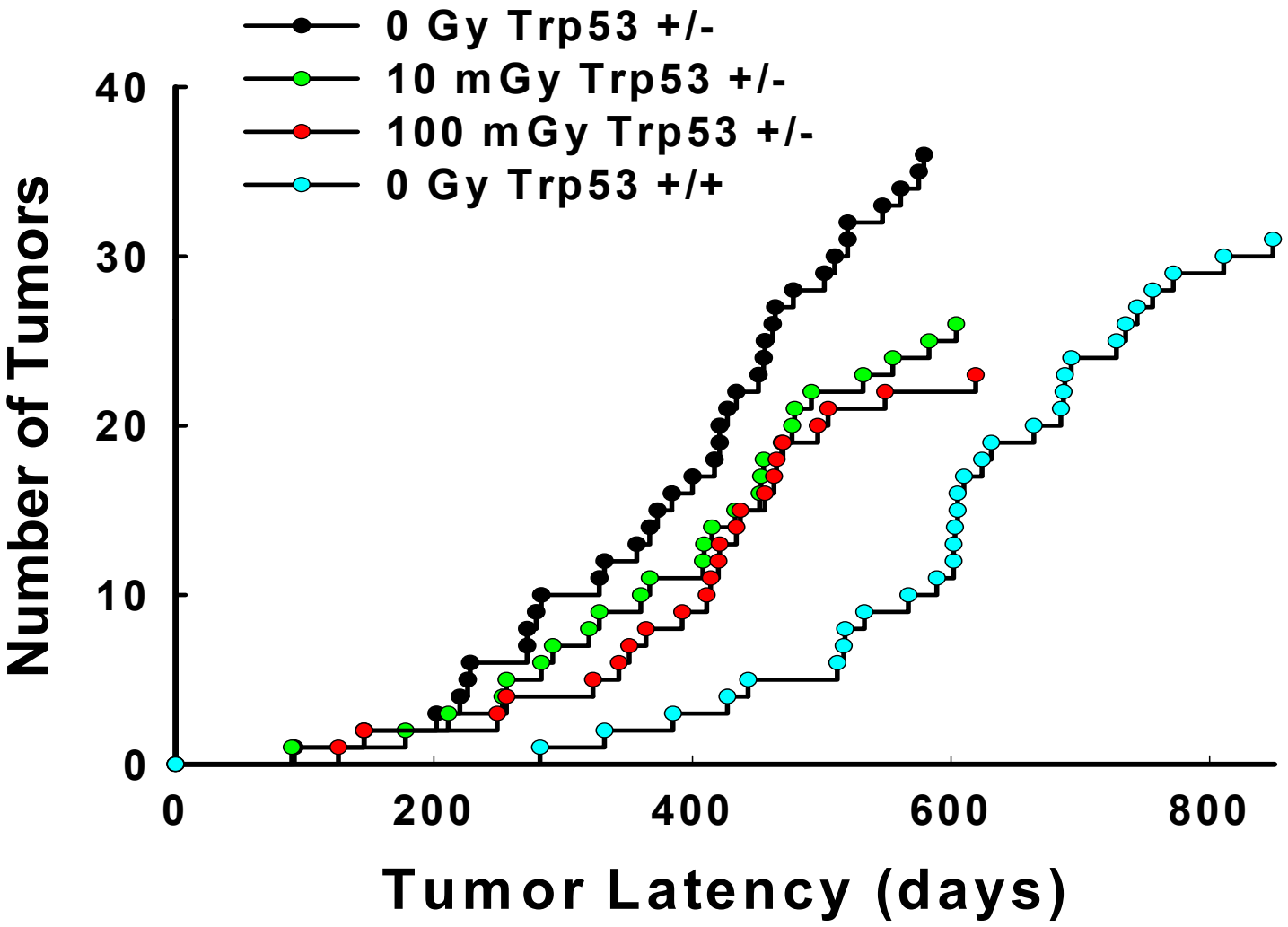
Mitchel, Jackson, McCann and Boreham, Radiat. Res. 152:273-279 (1999)

Lymphomas in Cancer-Prone Mice



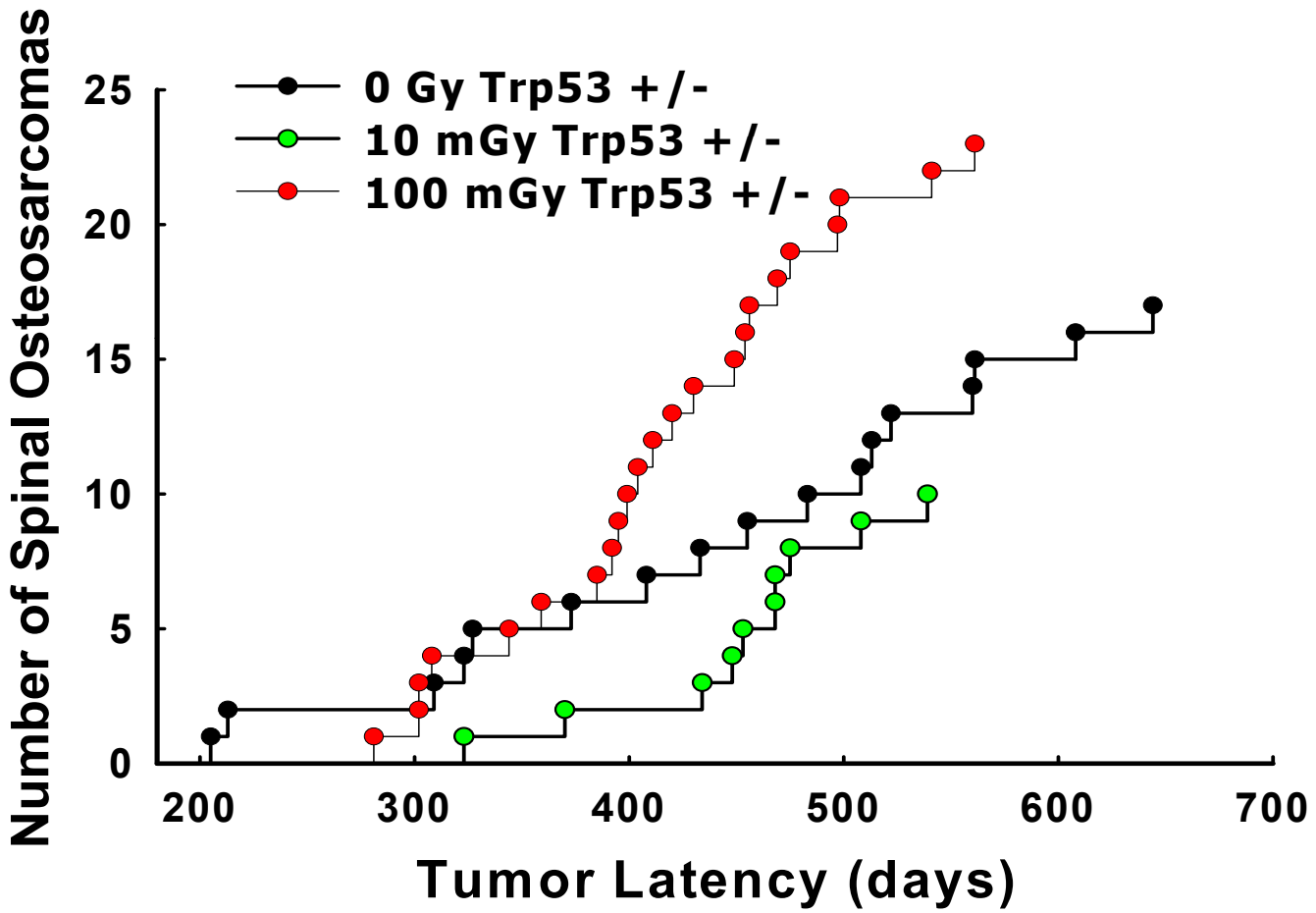
Mitchel, Jackson and Carlisle, Radiat. Res. 162:20-30 (2004)

Lymphoma Latency



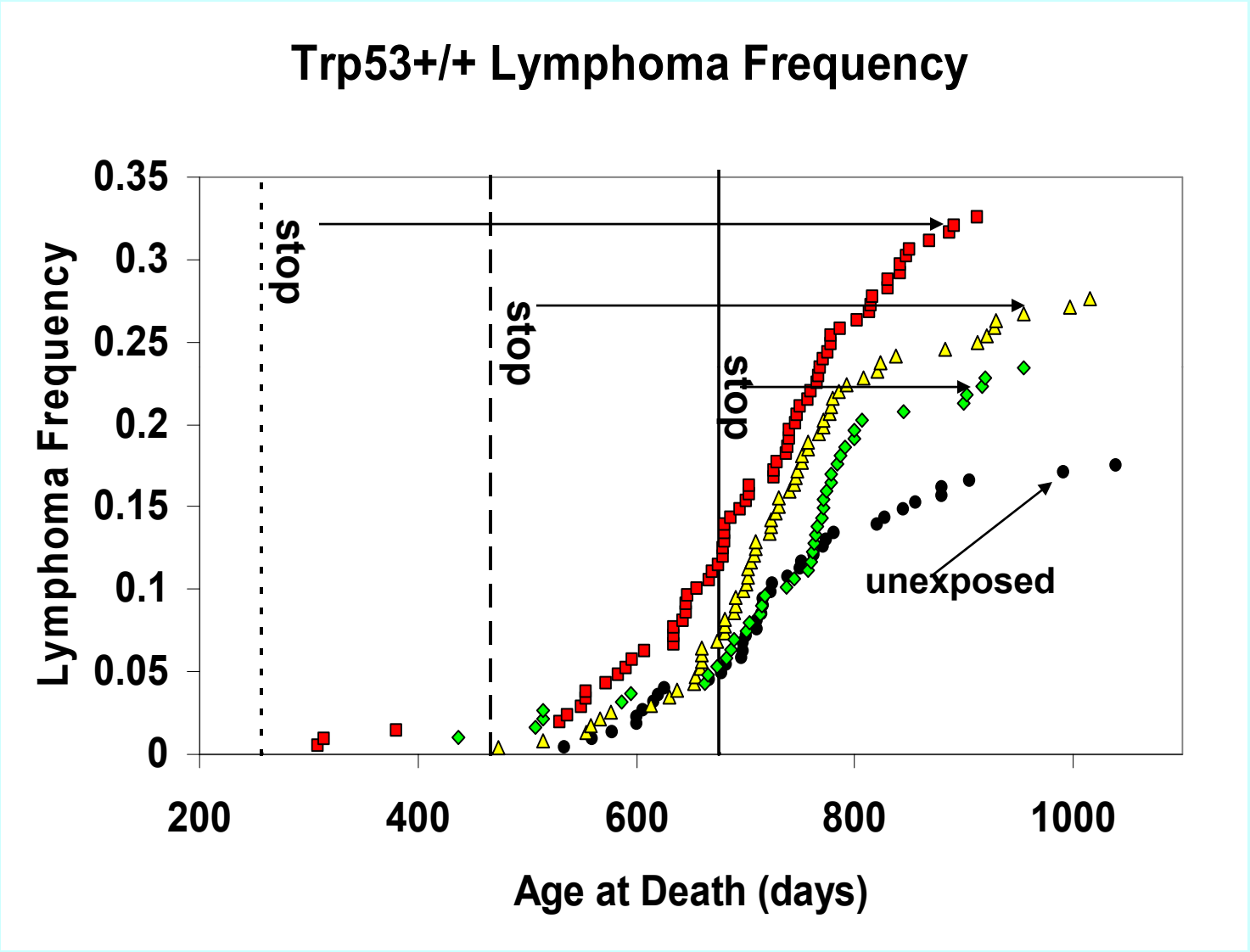
Mitchel, Jackson, Morrison and Carlisle, Radiat. Res. 159:320-327 (2003)

Spinal Osteosarcomas in Trp53+/- Mice



Mitchel, Jackson, Morrison and Carlisle, Radiat. Res. 159:320-327 (2003)

Cancer Increase by Sequential Low Dose Exposures



^{60}Co-γ
0.7 mGy/h
0.3 mGy/d
5d/wk

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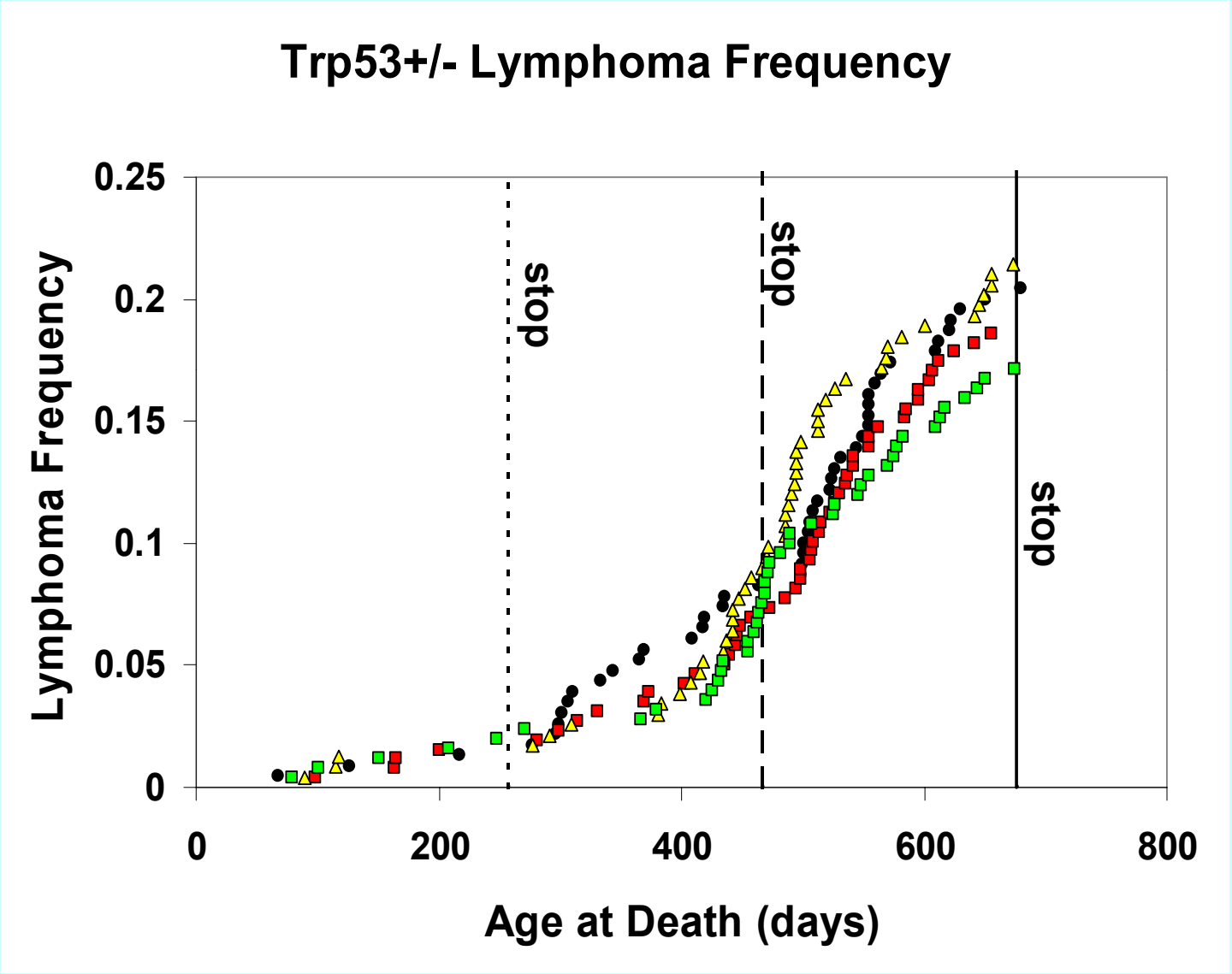
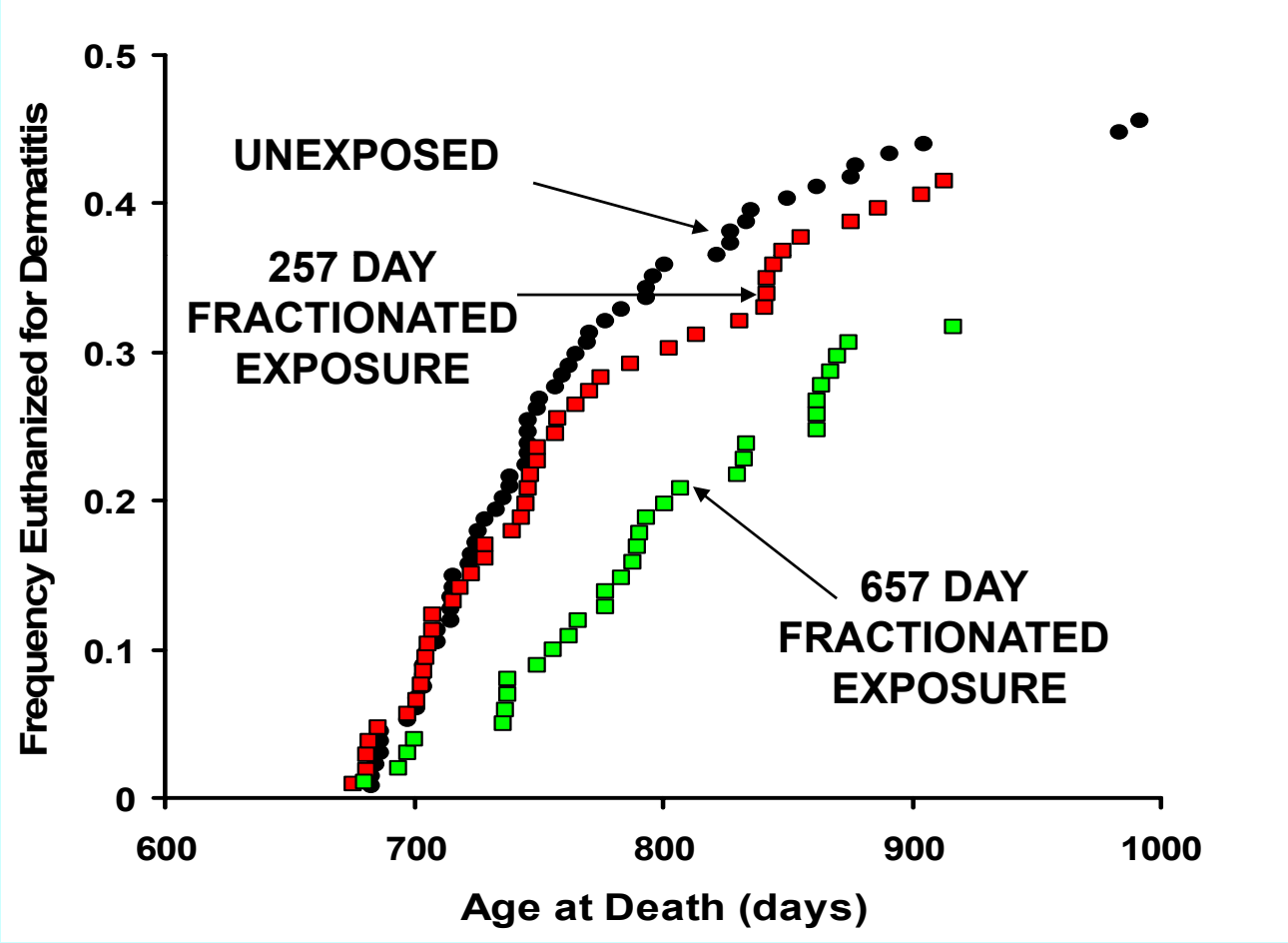
No Cancer Increase by Sequential Low Dose Exposures



^{60}Co-γ
0.7 mGy/h
0.3 mGy/d
5d/wk

MITCHEL, BURCHART AND WYATT, UNPUBLISHED

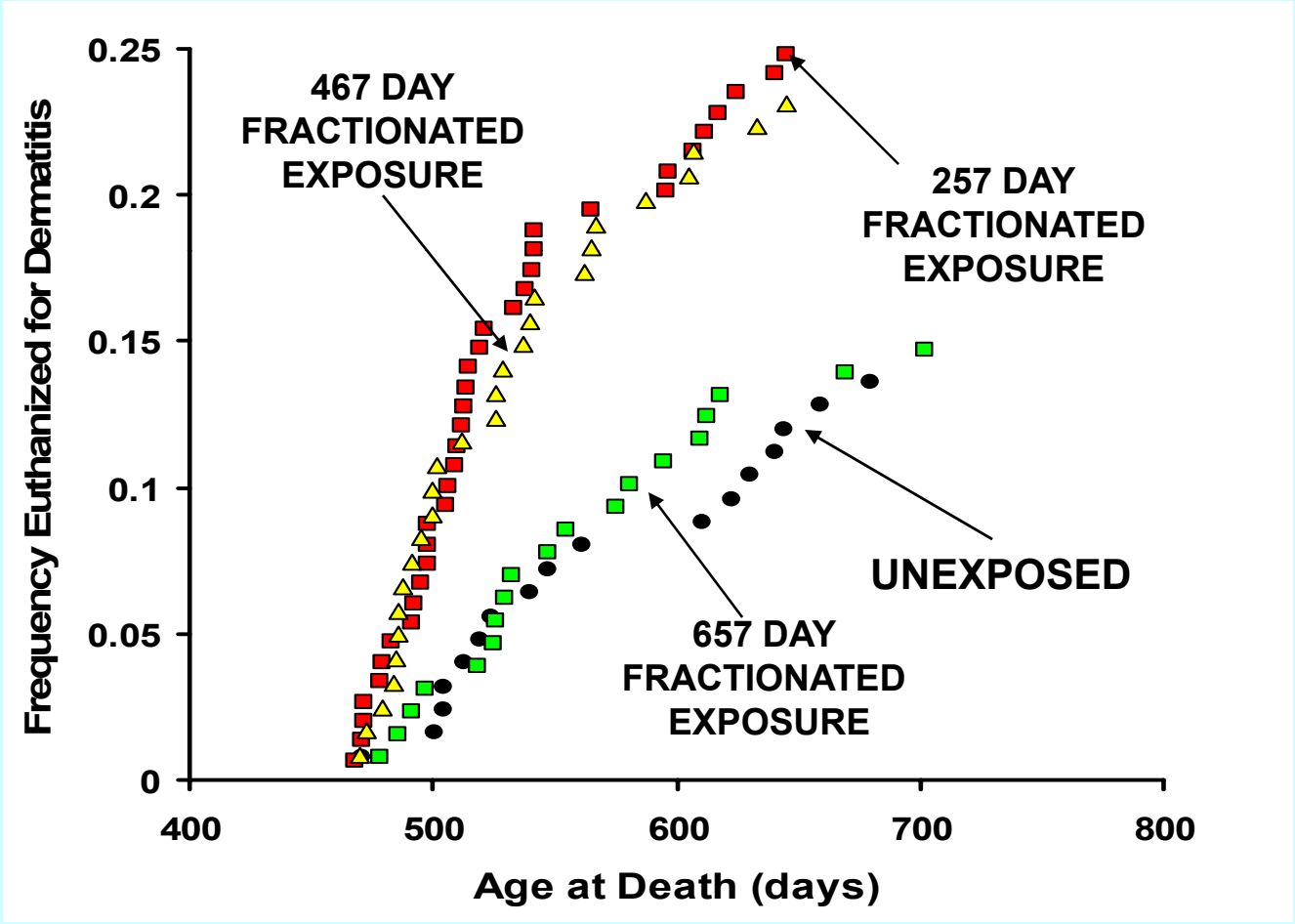
Sequential Low Dose Exposures and Acute Ulcerative Dermatitis in Old Mice with Normal p53 function (Trp53+/+)



^{60}Co-γ
0.7 mGy/h
0.3 mGy/d
5d/wk

MITCHEL, BURCHART AND WYATT, UNPUBLISHED

Sequential Low Dose Exposures And Acute Ulcerative Dermatitis In Old Mice with Low p53 Function (Trp53+/-)



^{60}Co-γ
0.7 mGy/h
0.3 mGy/d
5d/wk

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We Know:

Low levels of stress are generally cross protective (to a maximum)

However:

Continued or combinations of stress *above* or *below* normally protective levels may be detrimental

BE PREPARED FOR SURPRISES!!