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# Evaluation of Updated Research on the Health Effects and Risks Associated with Low Dose Ionizing Radiation

2009 ISOE North American ALARA Symposium  
EPRI Radiation Protection Conference

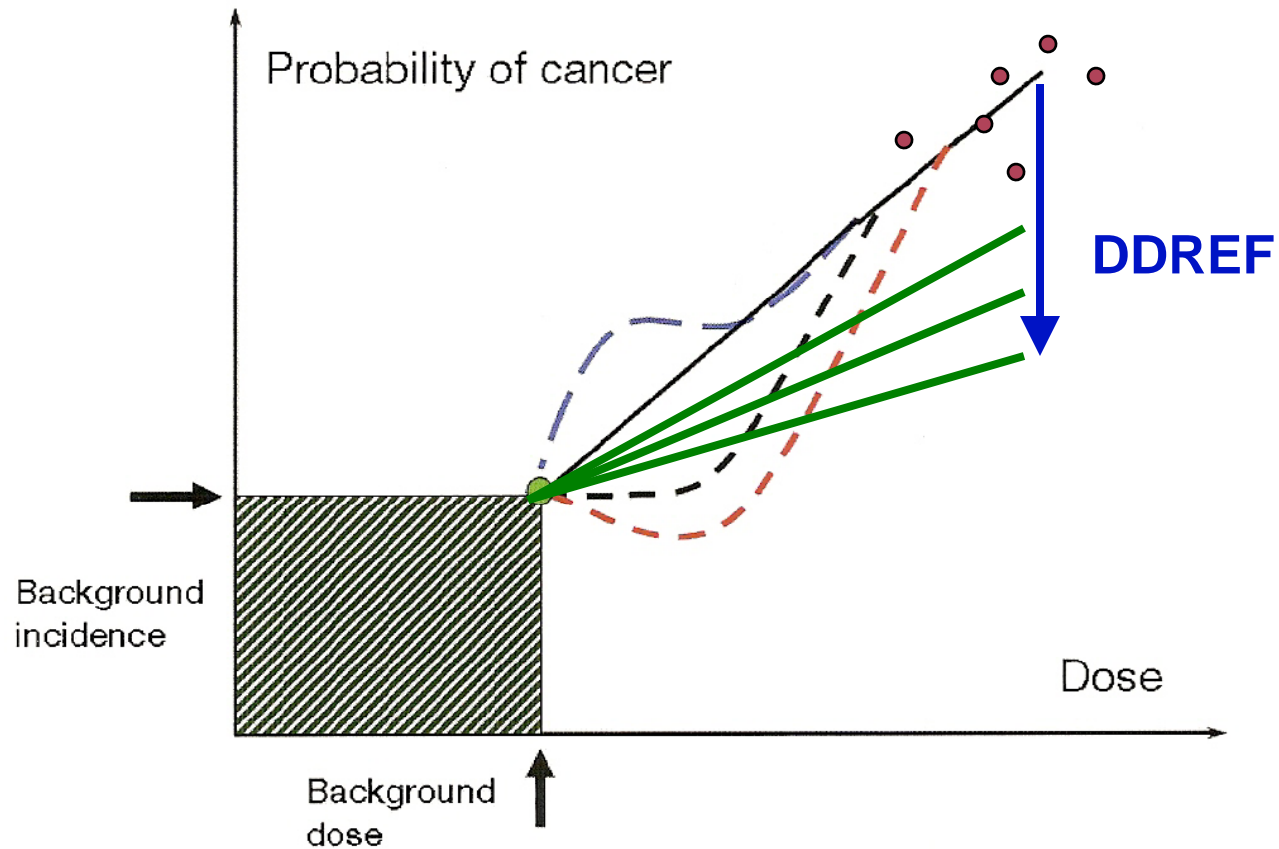


# EPRI Research Team

- Project Manager:
  - Phung K. Tran
- Principal Investigators:
  - Dr. Antone Brooks
  - Dr. David Hoel
  - Dr. William Morgan
  - Dr. Daniel Stram
- Technical Advisors:
  - Ralph Anderson
  - Dr. Sean Bushart
  - Dr. Lawrence Dauer
  - Richard McGrath
  - Dr. Christopher Wood

# The Quandry ...

## Dose-Response Relationships



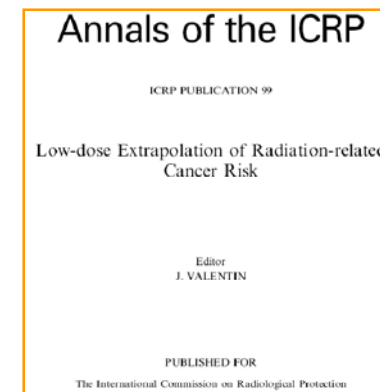
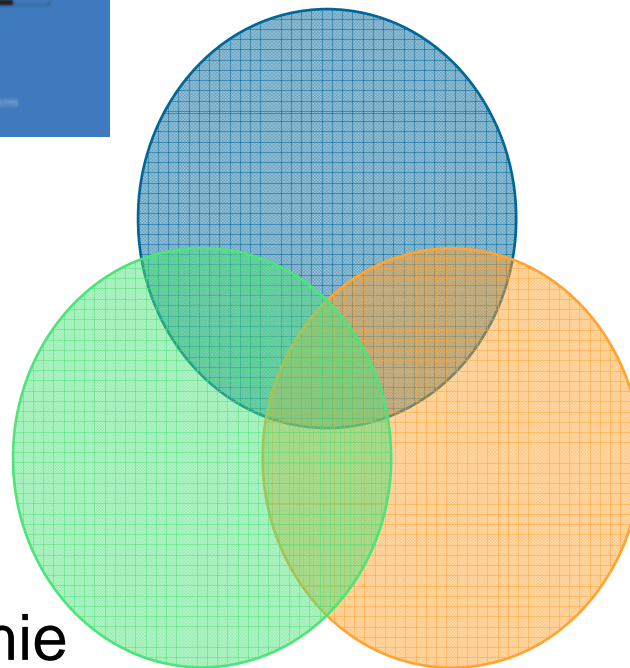
# Recent Past Attempts at Understanding ...



BEIR VII



French Academie



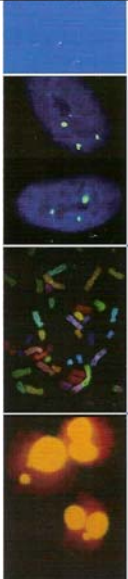

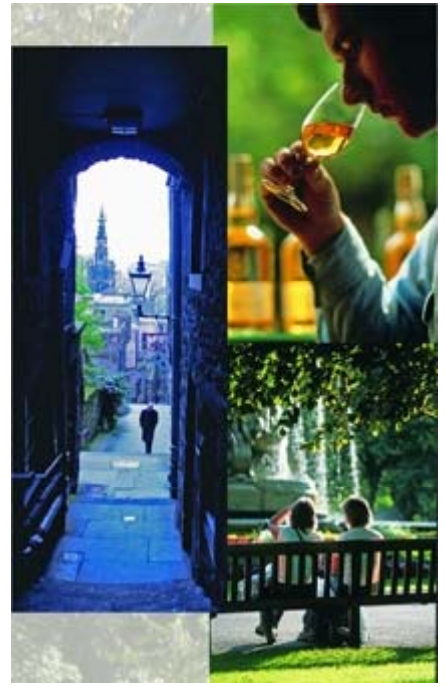
ICRP 99

## ... Conclusions Vary

- BEIR VII
  - Available biological and biophysical data supports a linear-no-threshold (LNT) risk model.
- ICRP 99
  - While existence of a low dose threshold may be likely for radiation related cancers in some tissues, the evidence does not support a universal threshold. DDREF-modified LNT suggested as prudent.
- French Academie
  - Radiobiology focus. Biological differences at high vs. low doses. LNT overestimates risk at low doses.



# ... and Discussion Continues...

 <p><b>Forty-Fourth Annual Meeting Program</b></p> <hr/> <p><b>Low Dose and Low Dose-Rate Radiation Effects and Models</b></p> <hr/> <p><b>April 14–15, 2008</b></p> <p>Bethesda North Marriott Hotel &amp; Conference Center 5701 Marinelli Road North Bethesda, MD 20852</p> <p><b>NCRP</b> National Council on Radiation Protection &amp; Measurements</p>	 <p>UNITED STATES NUCLEAR REGULATORY COMMISSION ADVISORY COMMITTEE ON NUCLEAR WASTE AND MATERIALS WASHINGTON, D.C. 20555-0001</p> <p><b>AGENDA</b> <b>188<sup>th</sup> ACNW&amp;M MEETING</b> <b>APRIL 8-10, 2008</b></p> <p><b>WORKING GROUP ON THE EFFECTS OF LOW RADIATION DOSES SCIENCE AND POLICY</b></p>	<p><b>The Society for Radiological Protection</b></p>  <p>June 2008</p>
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# EPRI Project Purpose

- Evaluate the published literature that was not included in these earlier reports
  - special emphasis on new information published since these reports were issued
- Determine if and how this new literature may impact our understanding of the health effects of low doses of radiation.
- Review >200 publications as part of this re-evaluation effort.
- Publish summary report addressing the state-of-science and noting gaps and research needs.

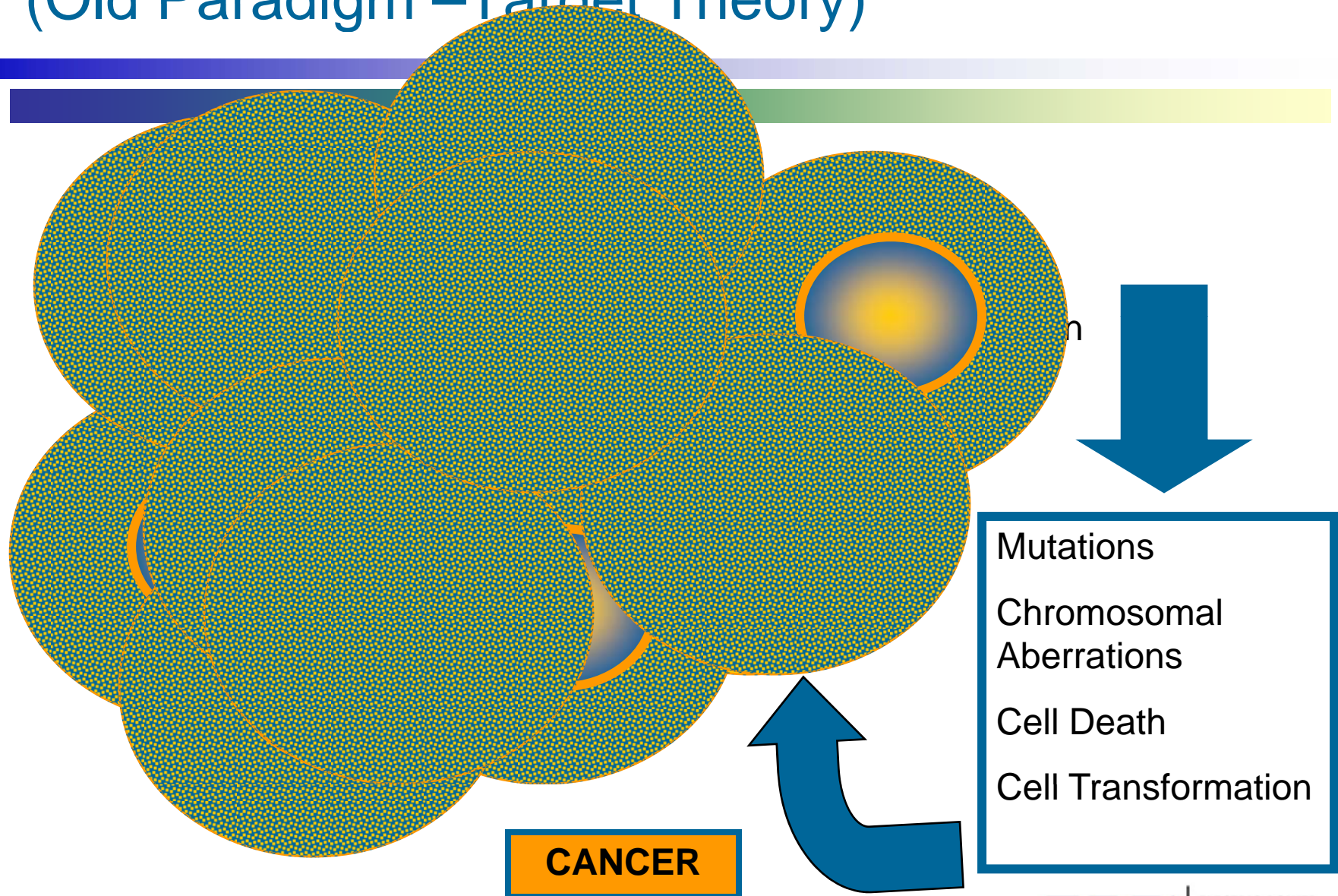
# The Recent Low Dose Research in Radiobiology and Epidemiology has ...

- Identified a need for expanding radiation paradigms and challenged the models used to extrapolate risks from high to low radiation and high dose rates to low dose rates.
- Provided integrated advances in biological and physical technology to study low dose <10rad (10cGy) radiation effects providing a strong scientific basis for radiation standards and adding to our understanding of the cellular and molecular mechanisms of action.
- Provided mechanistic data that support re-evaluating DDREF.
- Provided an incremental increase in available epidemiological data (including initial attempts at radiation-worker meta-analysis).



# Paradigm Shift Needed in Risk Models

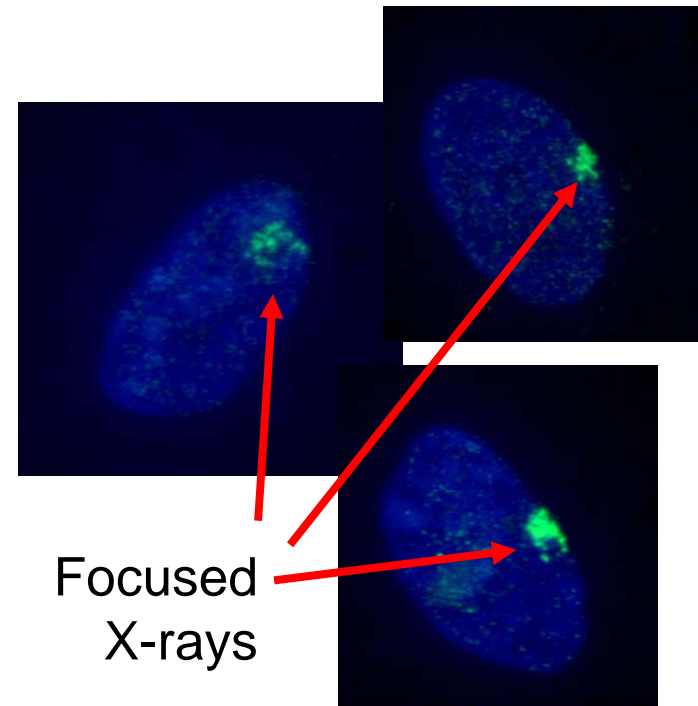
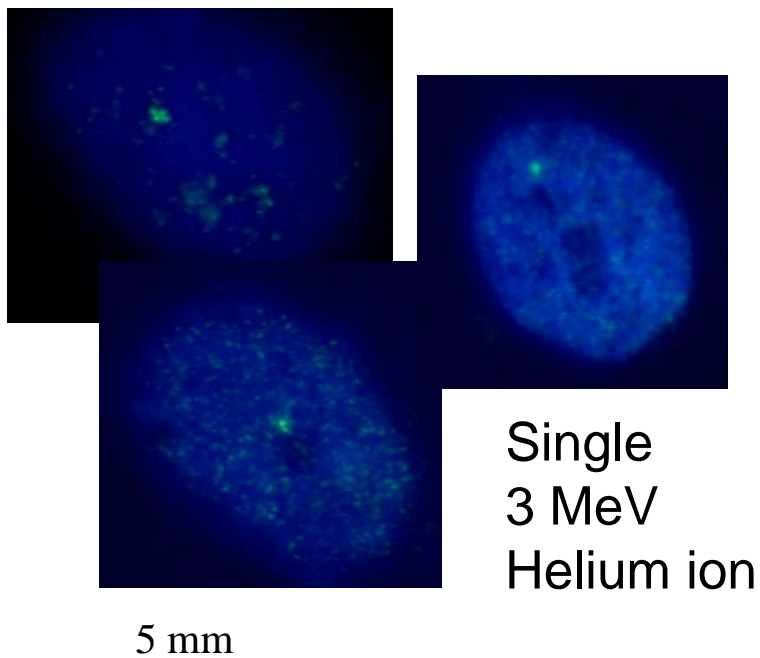
## (Old Paradigm –Target Theory)



# Paradigm Shift Needed in Risk Models

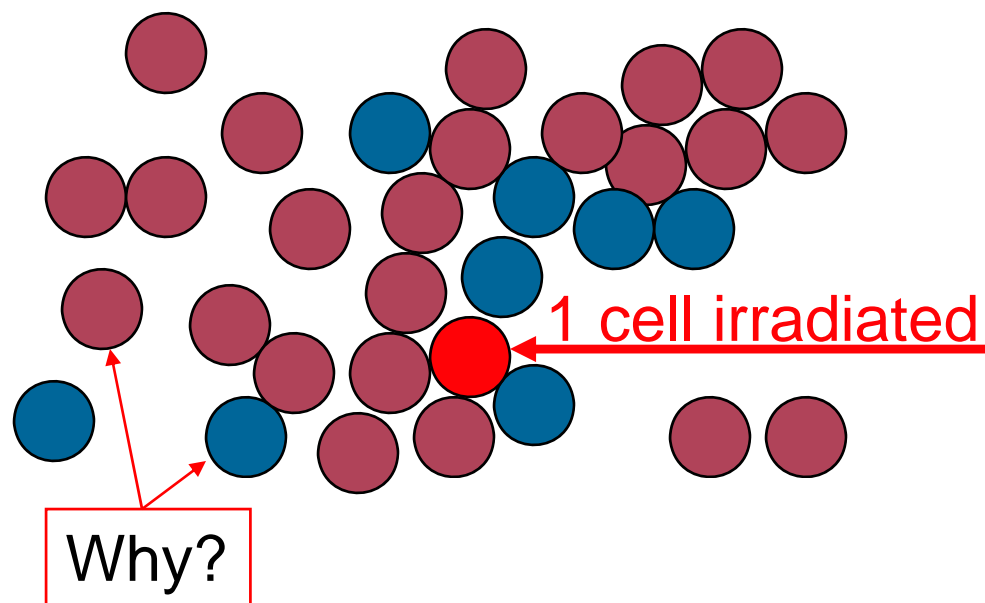
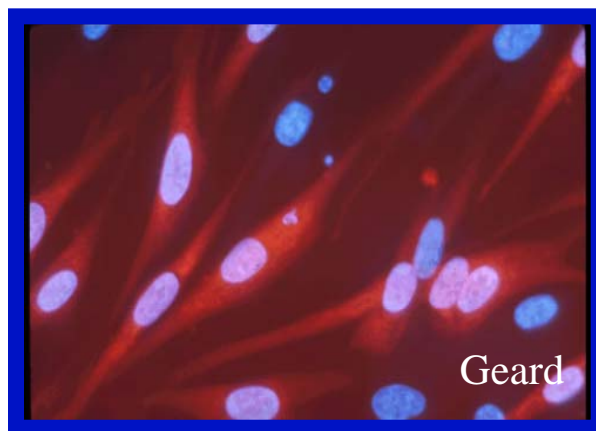
## Microbeams- Recent findings

Localized DNA damage observed after both microbeam soft X-ray production and charged particle induction.

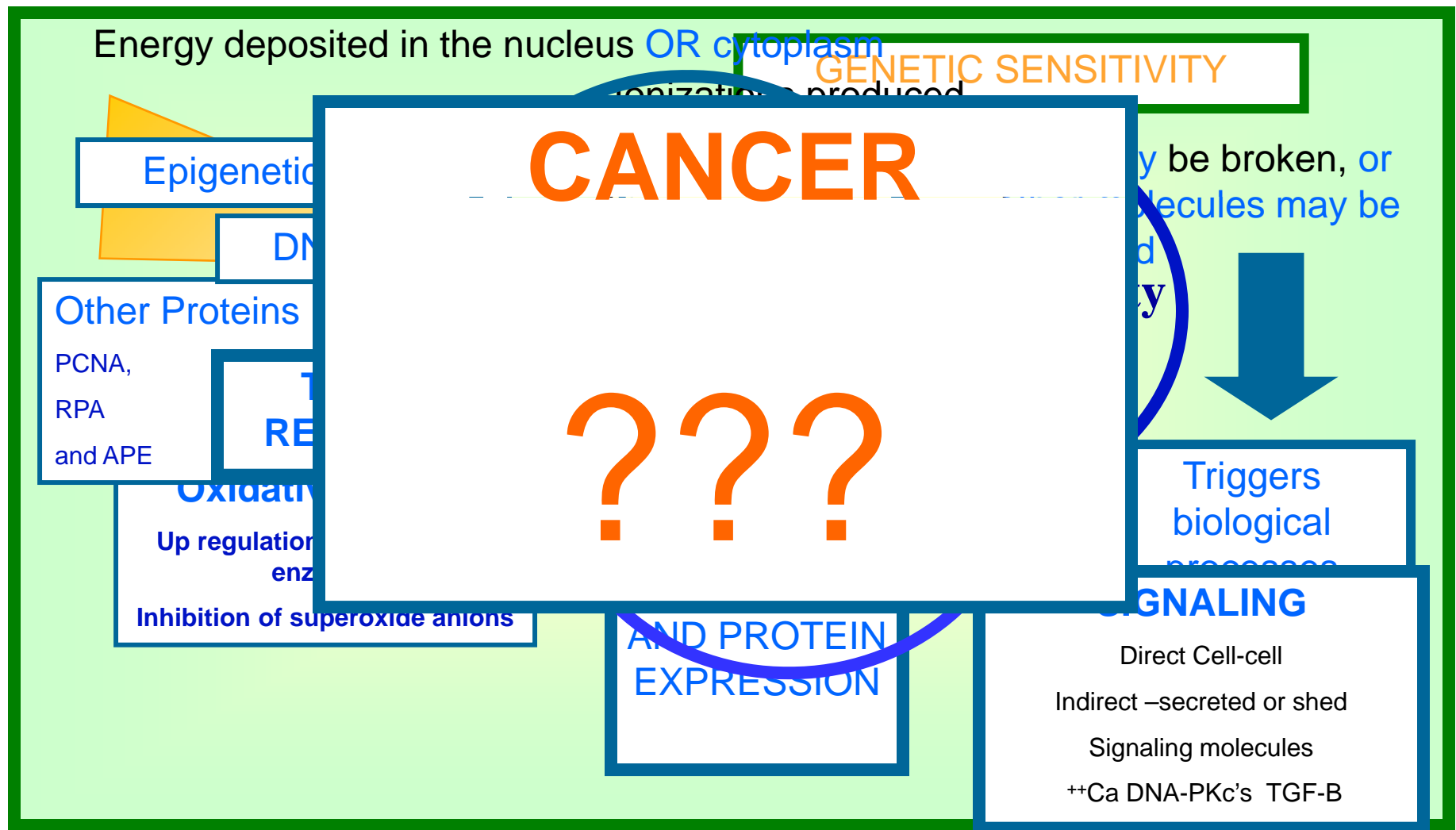


# Paradigm Shift Needed in Risk Models

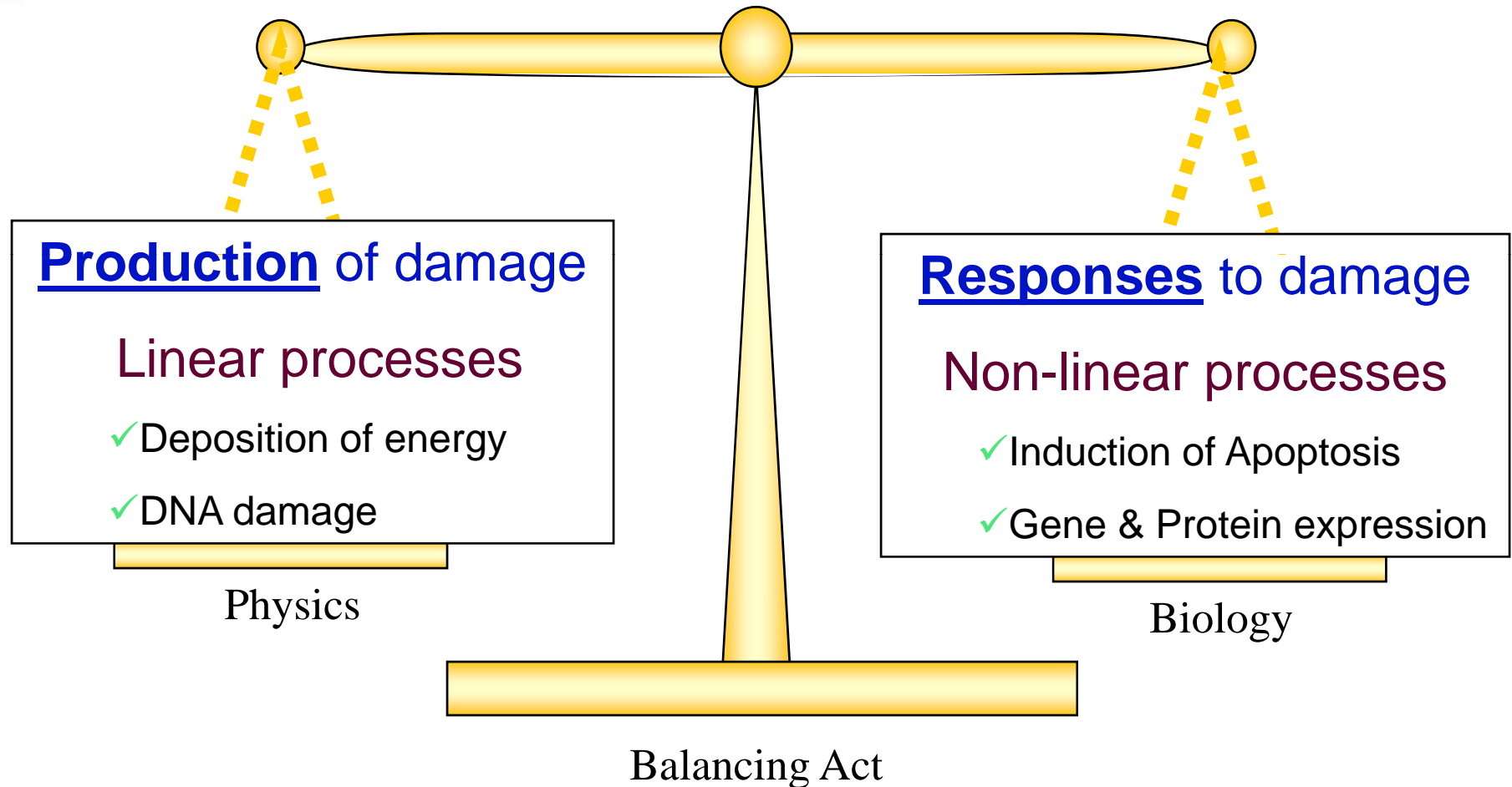
## ...Yet we see Micronuclei in Non-Exposed Cells



# Paradigm Shift Needed in Risk Models (Expansion of Existing Paradigm)

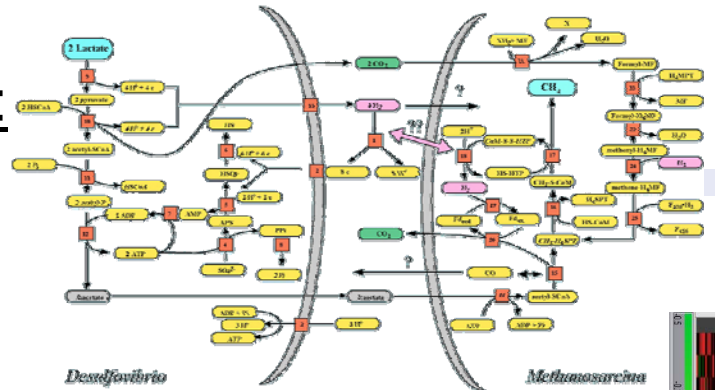


# Expanded Paradigm Impact on Dose-response

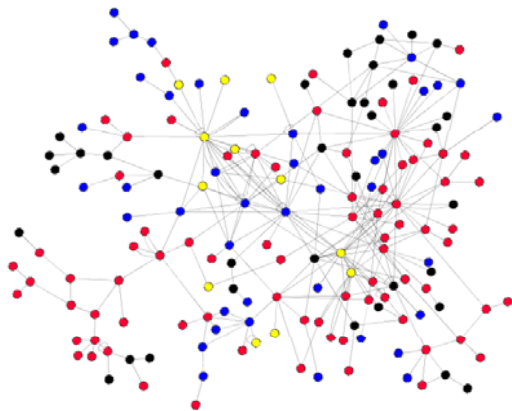


# System's Biology Approach

Systems Perspective:  
couple modeling,  
experiments and  
analysis in a  
recursive manner



Metabolic and  
regulatory models

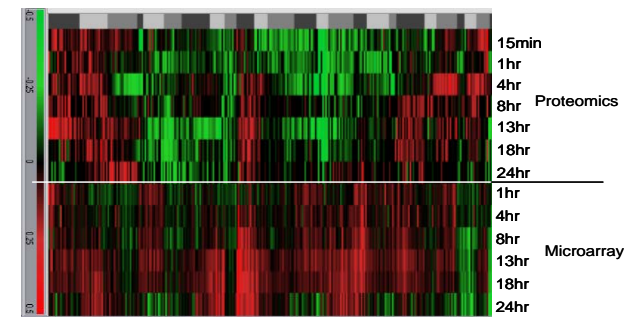


Advanced  
computation and  
information  
management

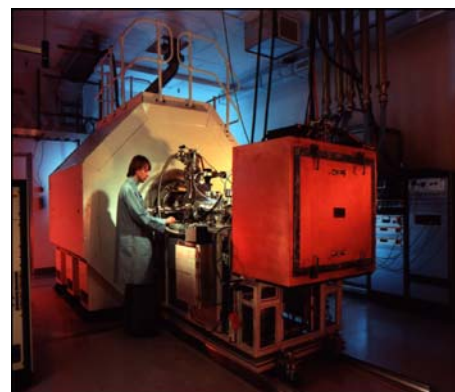
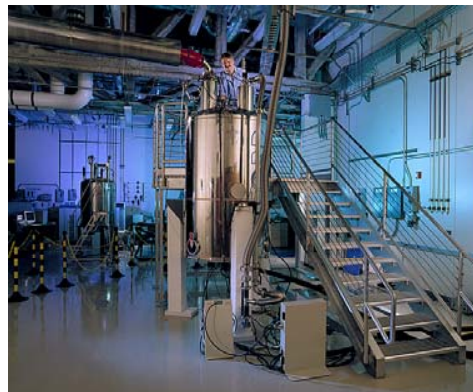
Hypothesis

Analysis

Experiment

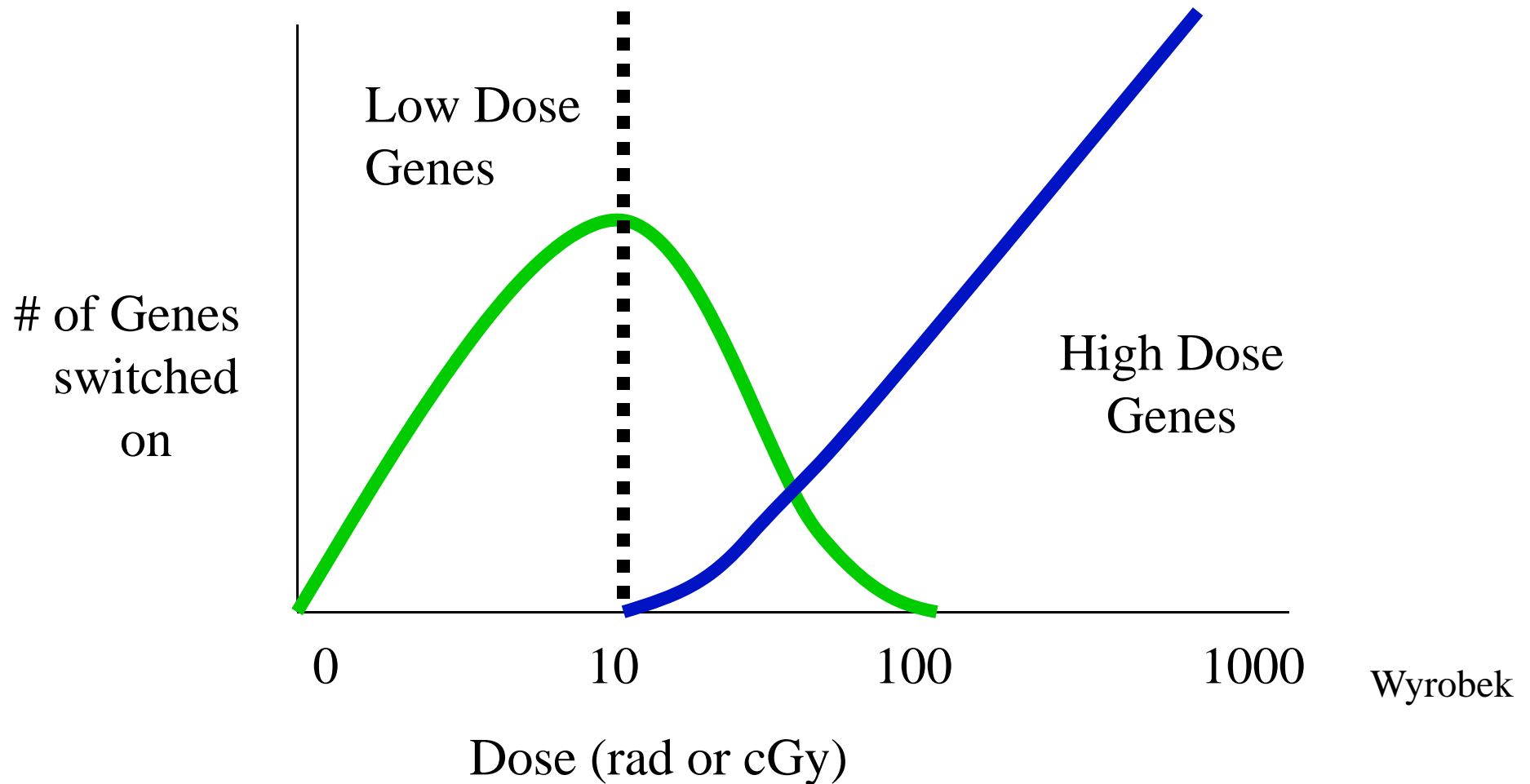


Advanced  
high-throughput  
technologies





# Non-Linear Radiation-induced Changes in Gene Expression Shown by Microarrays



# A-Bomb Survivor Studies Continue to Provide Relevant Information, however...

- Additions to the preponderance of epidemiological evidence has been mostly incremental in nature (since BEIR VII, ICRP99, and French Academie reports).
- Epidemiology evidence increases slowly in real time.
- Small incidence numbers.
- Need support of animal studies where total dose, dose rate, dose distribution, and disease outcome are well established.
- Still work to do:
  - Evaluate confounders and dosimetry with distance and dose
  - Examine more carefully the issue of neutrons and the RBE impact on low-dose gamma effects and DDREF
  - Consider medical exposures



# Multi-Country Nuclear Worker Studies Warrant Continued Evaluation

- There appears to be some evidence for excess risk for solid tumors at  $<10$  rem ( $<100$  mSv) lifetime cumulative dose. **However**, there are a number of significant and serious questions about these results.
- Clearly the studies will need updating in the future:
  - Much of the follow-up data used is already out of date from that which is available from the individual cohorts (especially for the US cohorts), and
  - Many of the non-US workers are still quite young with much more data expected in the future as the cohorts age
  - Need to re-examine outlier cohort results
  - Study confounders – smoking, occupational medical x-rays
  - Evaluate other recent US data (eg Naval Shipyard, Rocketdyne studies, etc.)

# Multi-Country Nuclear Worker Studies Warrant Continued Evaluation

## Cohorts

## All Cancers (excluding leukemia)

Canada

Sweden

UK

USA

USA – Hanford

USA – NPP

USA – ORNL

All Combined

This study is useful in that it provides specific direct information about the effects of dose rate and exposure protraction that complements the studies on which current risk estimates are based, in particular that of the atomic bomb survivors. Caution, however, should be exercised in the use of these risk estimates for radiation protection because of the potential overestimation of the risk due to possible confounding, particularly by smoking. Future studies, in particular a case-control study of lung cancer nested within the cohort, using detailed individual data on smoking and other potential occupational carcinogens, will be important to better quantify the effect of residual confounding on the radiation risk estimates.



Cardis et al. RR167,396-416(2007).

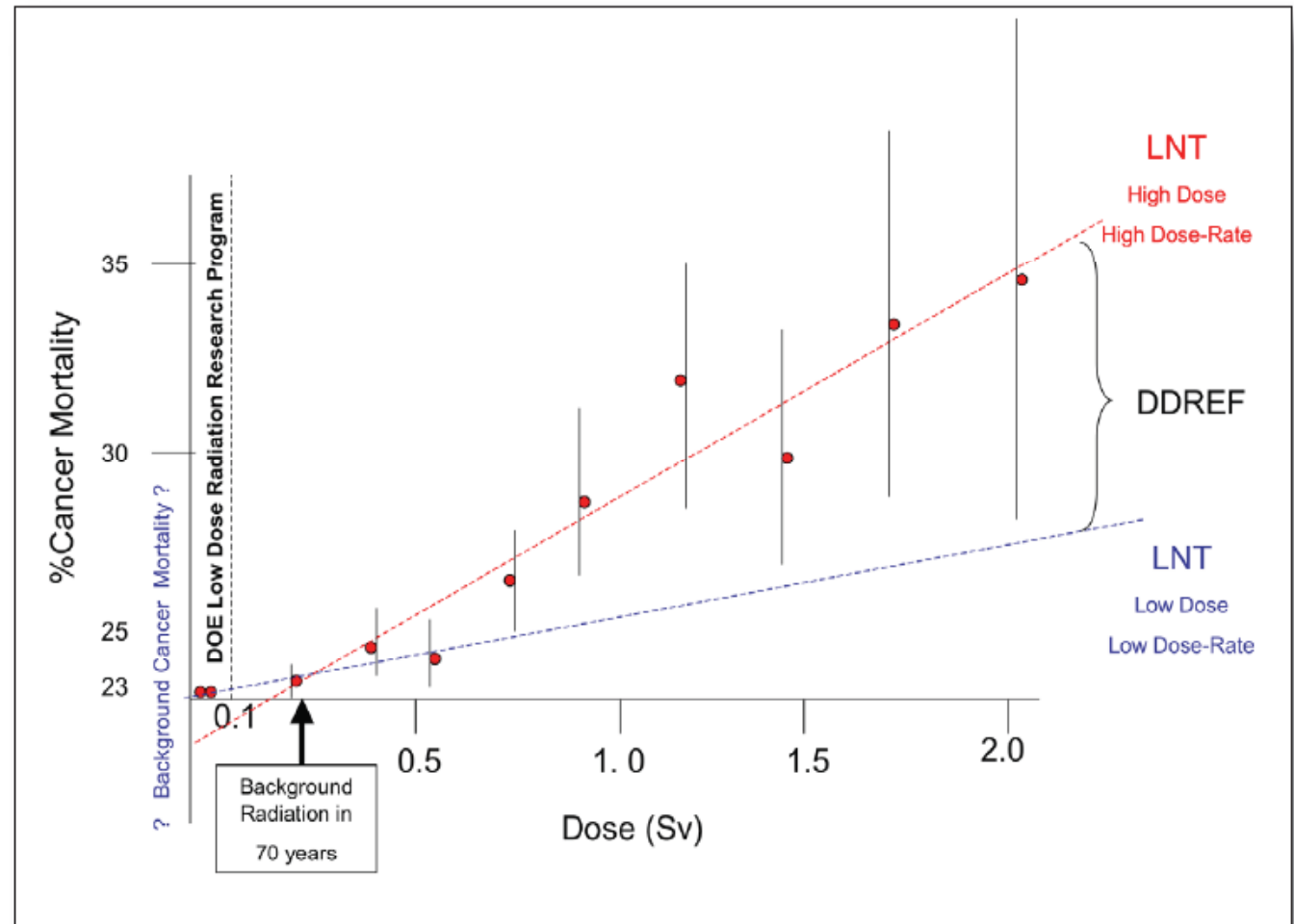
ERR/100rem or ERR/Sv (90% CI)

**EPR2**

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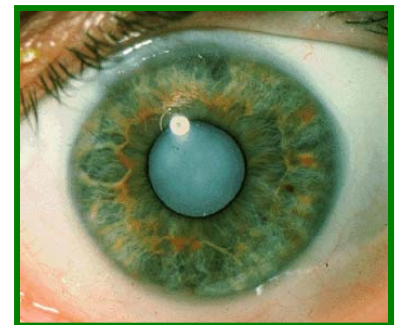
# Re-evaluating our understanding of DDREF is Needed

- Mechanistic data support a DDREF  $>1$ .
- Animal data support a DDREF of between 1-35.



# Non-Stochastic Effects Require Continued Epidemiology Clarification

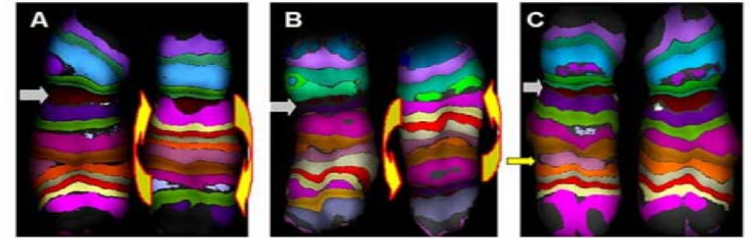
- The A-bomb survivor studies have shown effects on both coronary heart disease and stroke at doses above 0.5Sv. Other cohorts have shown mixed results.
- Without an understanding of possible biological mechanisms for the non-stochastic effects, it is difficult to interpret the mixed statistical associations that have been observed in epidemiological studies.
- Growing evidence that perhaps low doses  $< 1\text{Gy}$  could be associated with cataracts.  
(A-bomb, Chernobyl, Radiology, Astronauts, Pilots)





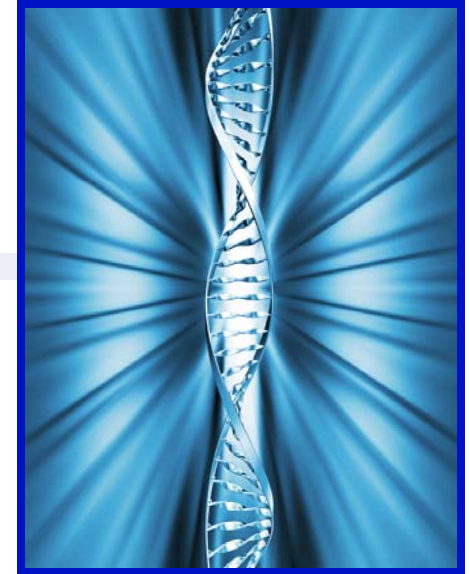
# Science Gaps & Research Needs

## Radiobiology



- Bystander effects, tissue, matrix effects, and adaptive responses.
- Cell/organ signaling and communications.
- DNA repair at very low doses.
- Genetic sensitivity and individual susceptibility.
- Develop biomarkers of risk.
- Epigenetic changes.
- Induction and shape of dose-response relationships for cancer and non-cancer.

# Science Gaps & Research Needs



## Epidemiology

- Continue A-bomb survivor studies.
- Re-analyze effects of neutron component.
- Update, expand, and further clarify the statistical analysis of 15 country study.
- Consider non-cancer outcomes.
- Develop models to join radiobiology findings with risk models.
- Incorporate genome-wide association studies.
- Prospectively study CT scan patients and high-background populations (direct study of low and fractionated doses in human population)

# Potential Implications of Latest Research

- Expanded paradigm for risk models fusing radiobiology and epidemiology results into a comprehensive understanding.
- Re-evaluation of understanding of DDREF is needed - perhaps may result in future regulatory implications.
- Cataract study results may suggest a reduction in limits on lens of eye doses, impacting nuclear workers, interventional radiologists and cardiologists.
- Communication is now more important in light of Nuclear Renaissance. Increasingly complex models require more efficient, effective, practical, and understandable vehicles to distribute relevant scientific information to those with the responsibility of setting radiation policies and standards for the workforce and the public.

# EPRI Project Team – Conclusions

- ***To be or not to be LNT...that is not the right question!***
  - Paradigm shift from target theory to a comprehensive model that addresses both damage (linear) and response (not linear).
  - At very low doses and dose rates does linear vs. non-linear have any real impact?
  - Final Evaluation Report to be issued in 2009.
- ***Understanding DDREF is most important. (EPRI 2009/10)***
- ***Low dose and low dose rate research needs to continue.***
  - The new paradigms and epidemiological evidence in the low dose and low dose rate region will prove to be useful and directly applicable in standard-setting and decision-making.

# EPRI Project Team – Future Actions

- Final Evaluation Report
  - Technical Summary Fact Sheets (eg. NCRP, HPS, NEI)
  - Final Evaluation Report - 2009
    - Executive Summary
    - Support NEI efforts
- DDREF Evaluation -2009/10
  - Understanding the State of Science
  - Implications if DDREF were to change
- Continue to monitor the progress of ongoing research studies during annual EPRI meetings