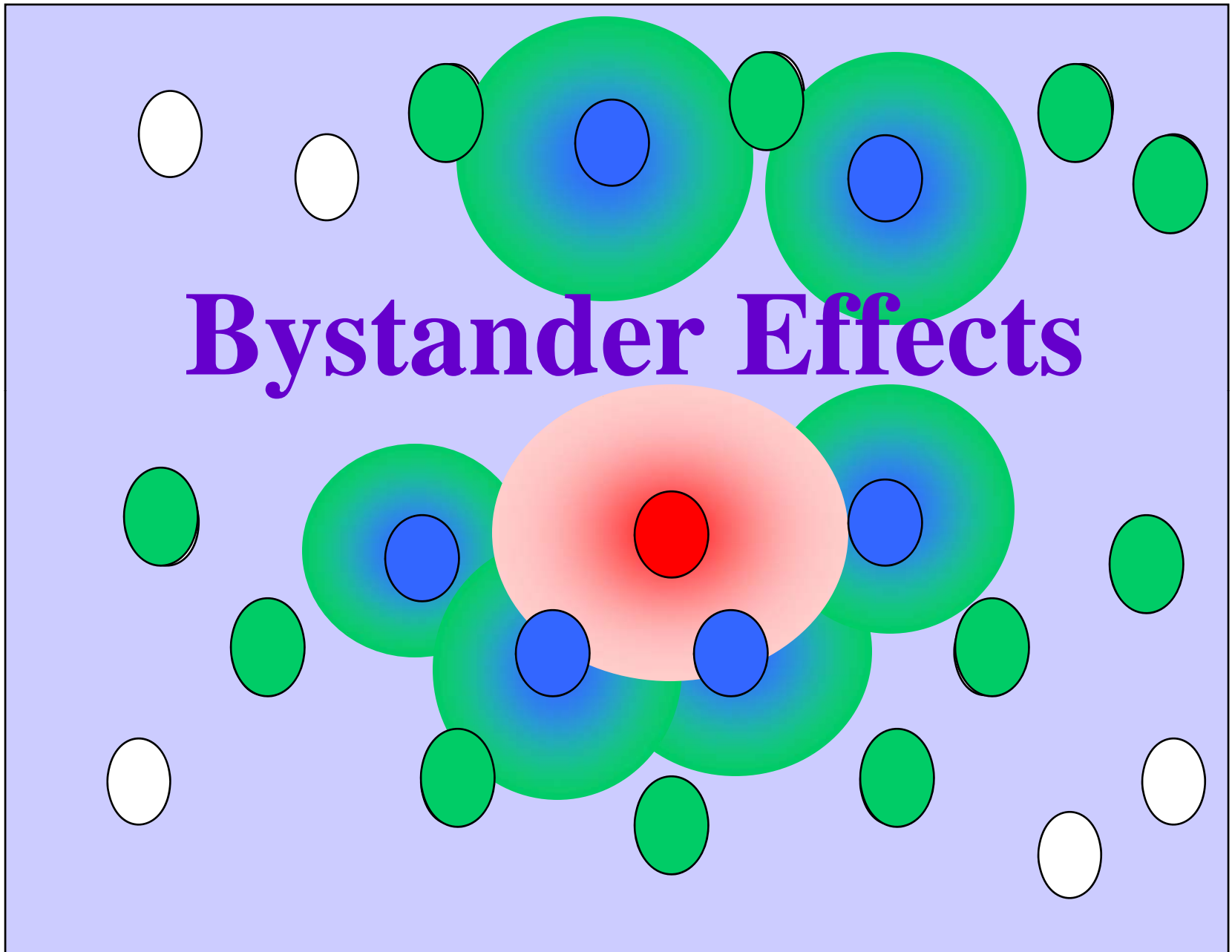
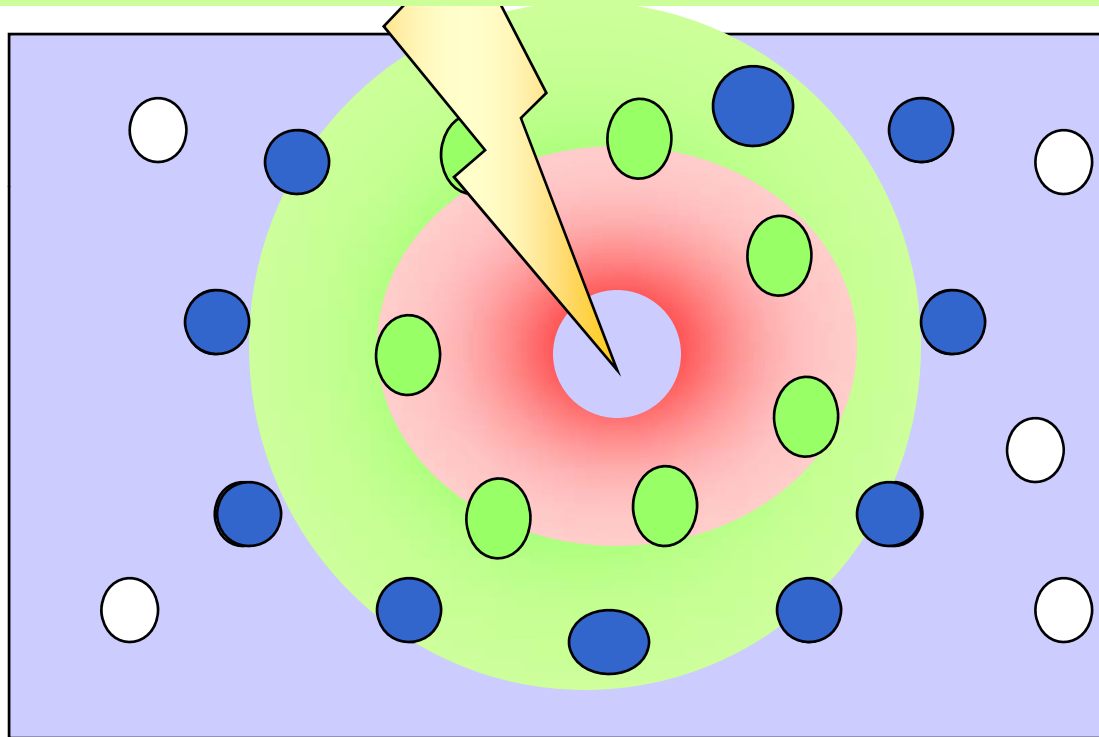


# Bystander Effects



# Bystander Effects

The signals sent by the bystander cells may help repair the damaged cell, or it may trigger the cell to commit cell suicide.



The signals sent by the damaged cell may disrupt the normal function of its neighboring cells, or it may stimulate them to respond with additional signals back to the damaged cell or to other nearby cells.

# How does radiation interact with cells?

## Past Theory

### Hit theory

Radiation causes free radicals to damage only the cell that is “hit” by direct ionization

## Present Theories

### Bystander effects

Radiation causes free radicals to trigger cell-cell communication and cell-matrix communication to cells other than those which are “hit” by the direct ionization.

# How do cells communicate to each other?

## *Direct* Cell-Cell Communication

- Direct cell contact
- Gap junctions

## *Indirect* Chemical Factors

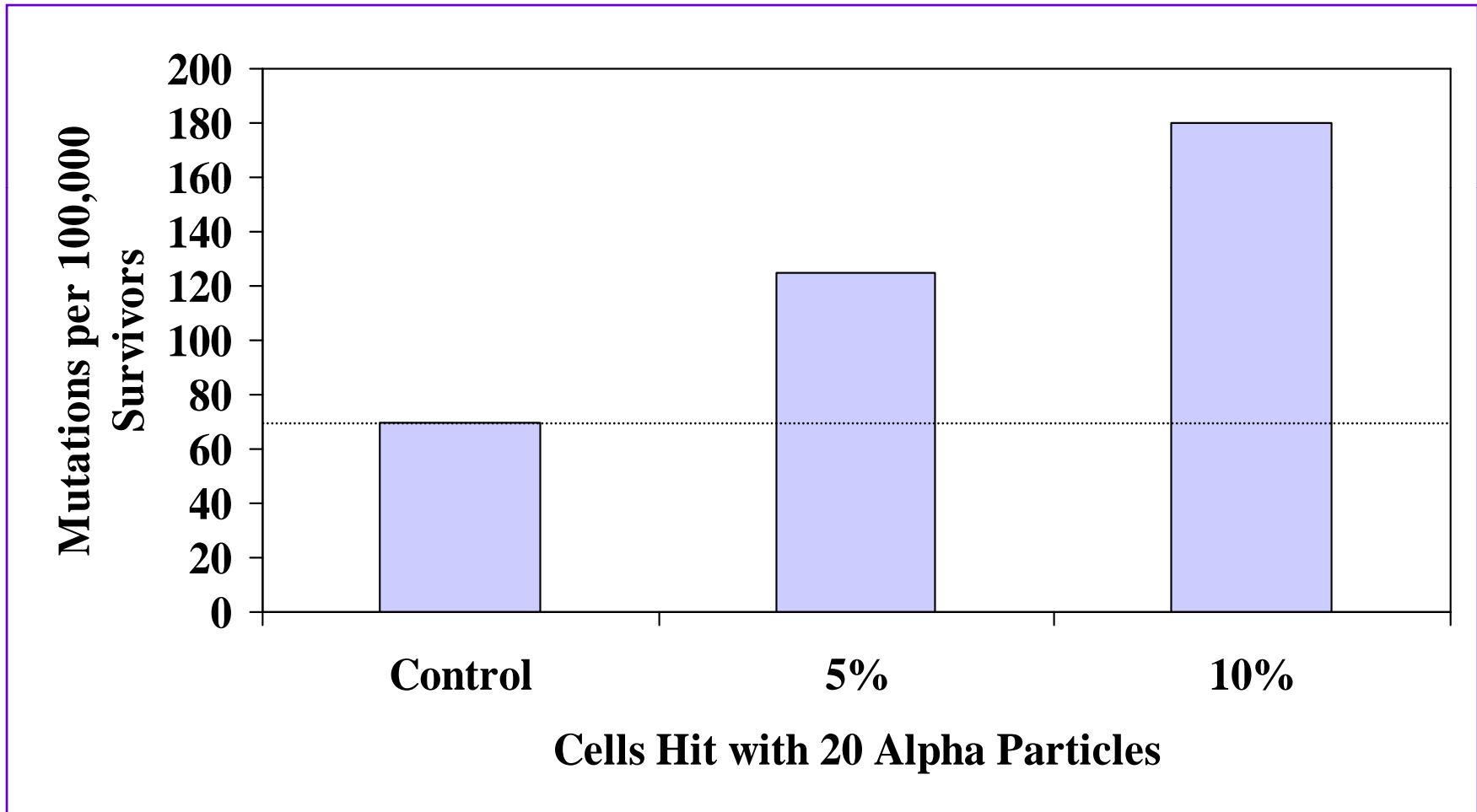
- Death Inducing Factor
- Clastogenic Factors

# Examples of bystander effects in cells, tissues, and organs

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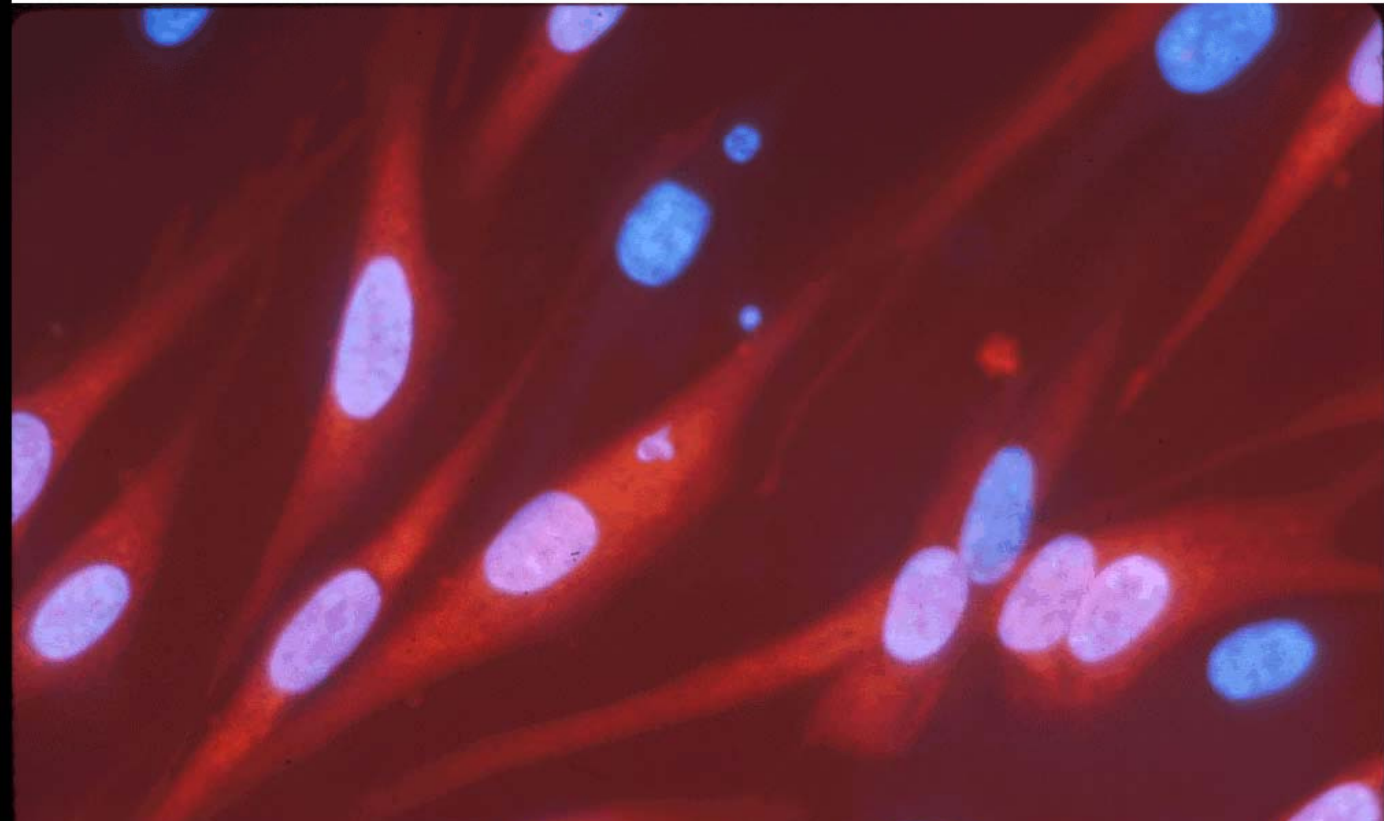
- Change in gene expression
- Mutations
- Apoptosis
- Chromosome aberrations
- Cell transformation
- Cancer
- Changes in sister chromatid exchanges

# Mutation Frequency



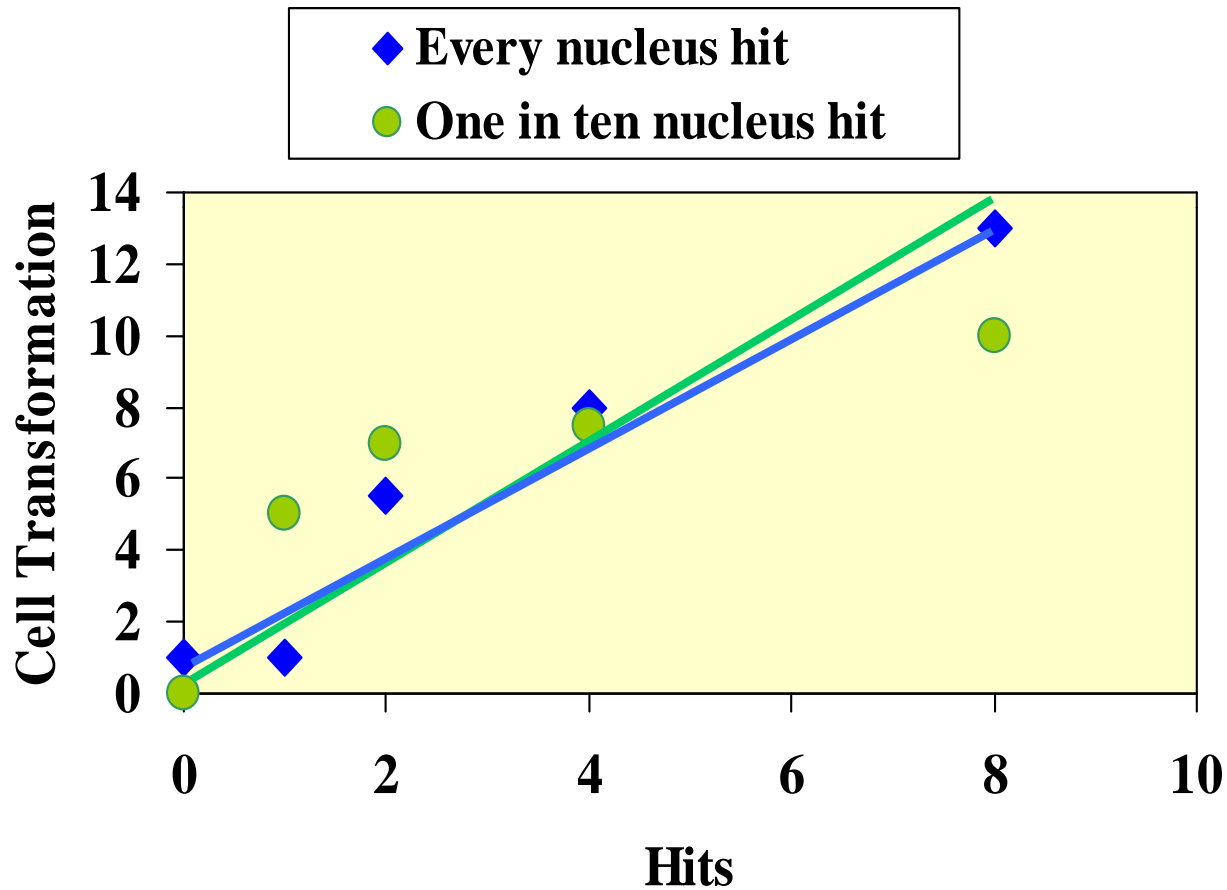
# Micronuclei

Geard



Cells were stained with two different dyes. Only the nuclei of the cells stained with pink dye were hit by alpha particles from a microbeam. The figures show the presence of broken chromosomes in the form of micronuclei (the smaller fragments of pink and blue). These micronuclei are present not only in the pink “hit” cells, but also in the blue non-exposed cells. Such studies provide direct evidence for bystander effects.

# Cell Transformation



# No bystander between organs exposed at low dose-rates

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The site of deposition of the radioactive material is the site of cancer induction

- $^{90}\text{Sr}$  - bone cancer
- $^{144}\text{Ce}$  – liver/bone cancer
- $^{239}\text{PuO}_2$  (inhaled)- lung cancer

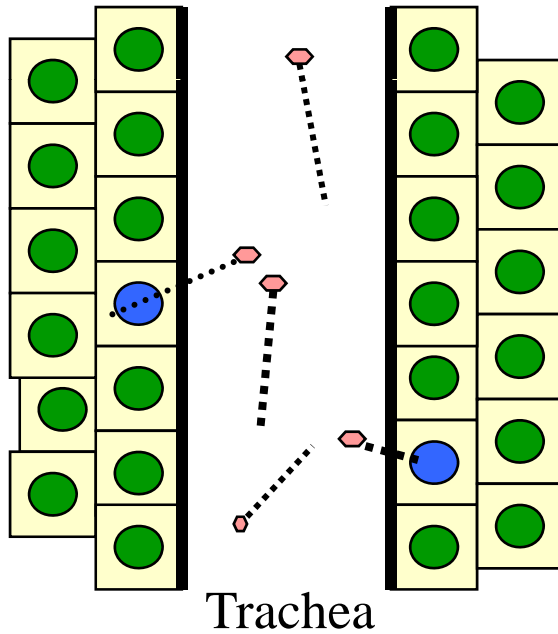
# Does the bystander effect occur in animals as well as cell culture?

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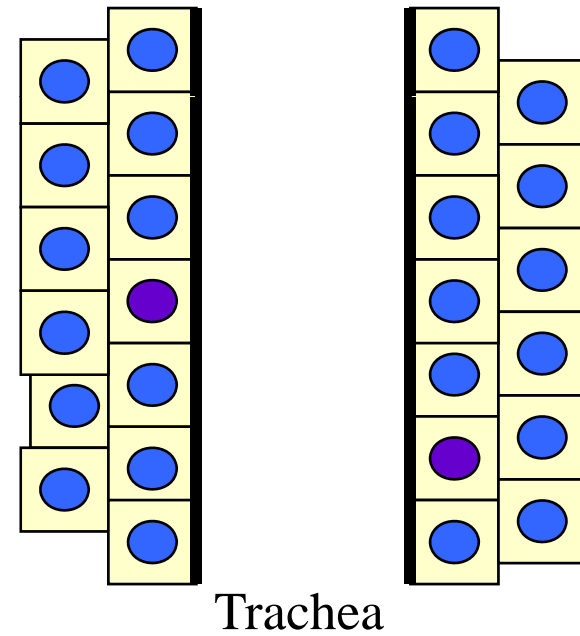
- The bystander effect occurs in animal systems
- The bystander effect is limited to specific organs or tissues
- The bystander effect
- No bystander effects seen between organs at low dose rates

# Induction of p53 in Rat Tracheal Epithelium by Radon

Few Cells Hit

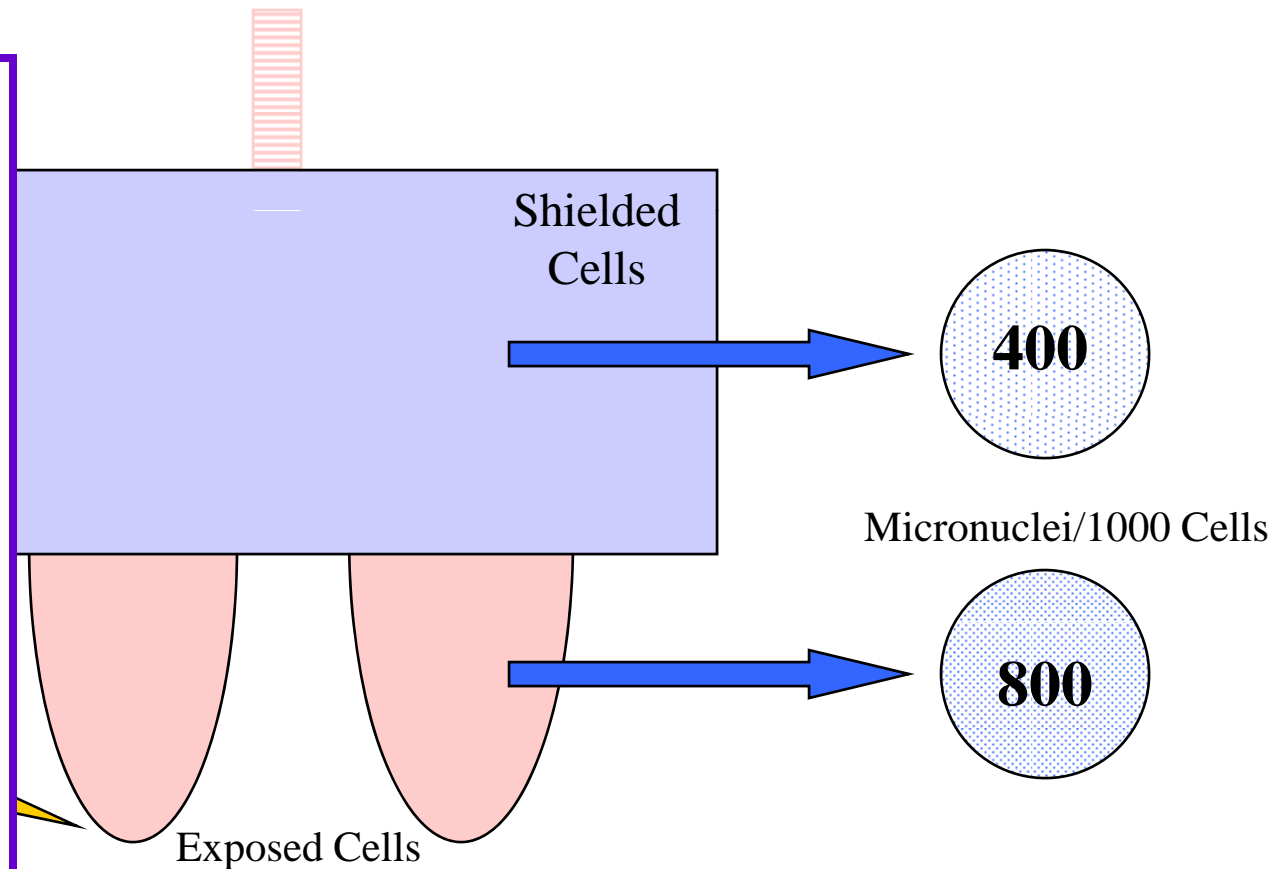


p53 Up-regulated in All Cells



# The influence of communication on radiation-induced micronuclei in lung

Lung cells shielded from direct radiation showed a major increase in the production of micronuclei (one indicator of chromosome damage) when other cells in the lung tissue were irradiated, indicating some type of communication between cells.



Khan et al 1998

# Conclusions

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- Radiation exposure to cells can induce bystander effects, or changes in cells not directly “hit” by any radiation.
- Bystanders result from communication due to direct cell contact or release of material
- At low dose rates, bystander effects for cancer induction are present *in vivo* and limited to the tissue exposed.
- Initial radiation-induced changes to bystander cells are very frequent events, suggesting total tissue involvement.
- Bystander effects indicate that radiation-induced cancer is not a single cell event, but a tissue and organ response.
- Bystander responses have resulted in a major paradigm shift related to the action of radiation.
- Bystander effects may either increase or decrease radiation cancer risk.

For More Information on  
**Bystander Effects**



[http://lowdose.tricity.wsu.edu/pub\\_topic/about\\_bystander.htm](http://lowdose.tricity.wsu.edu/pub_topic/about_bystander.htm)