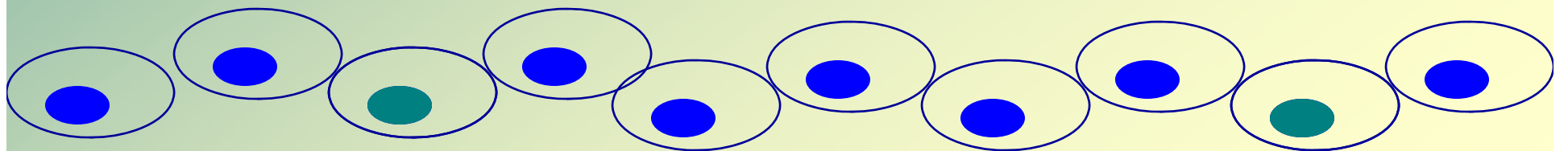


# Genetic Susceptibility



# Genetic Susceptibility

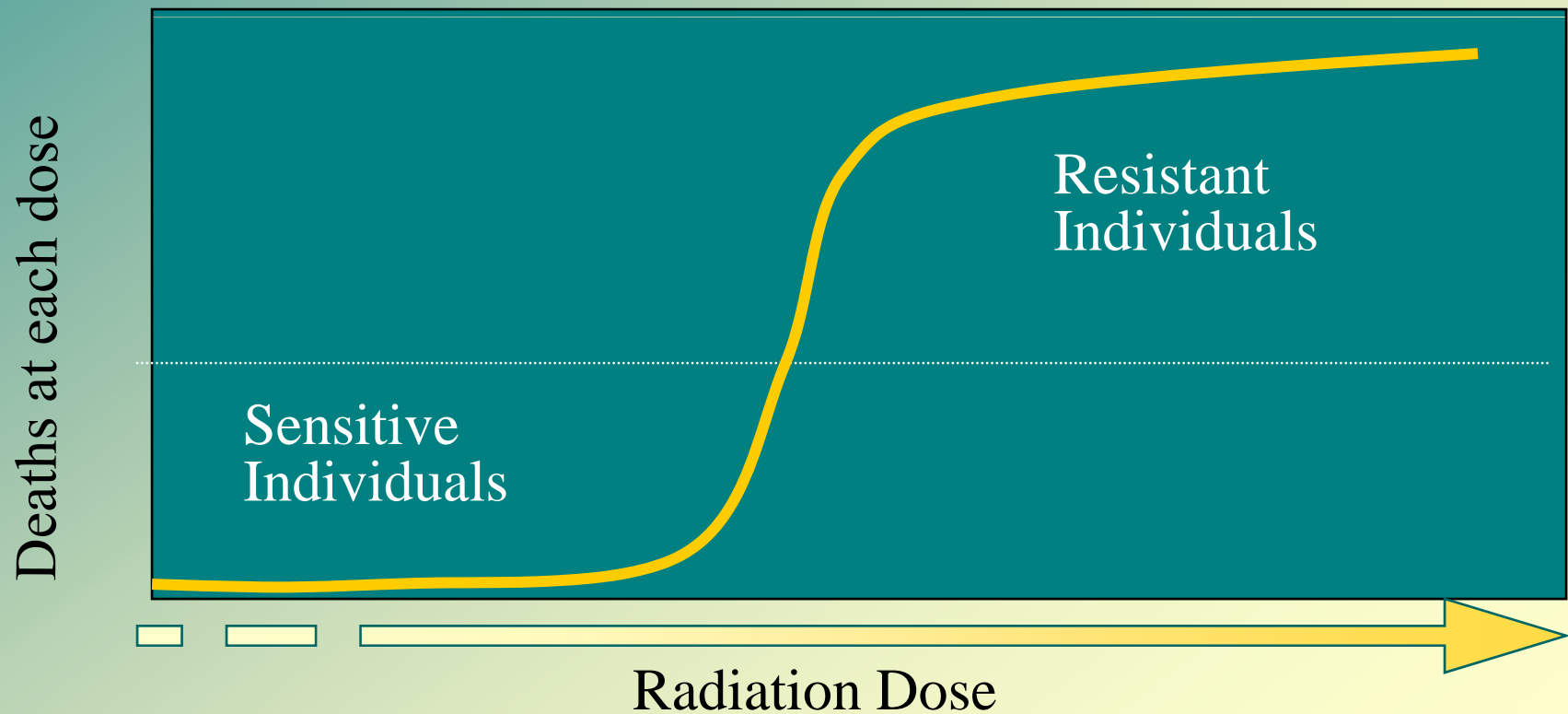
Can we identify cells, individuals or subpopulations that are genetically susceptible to radiation?



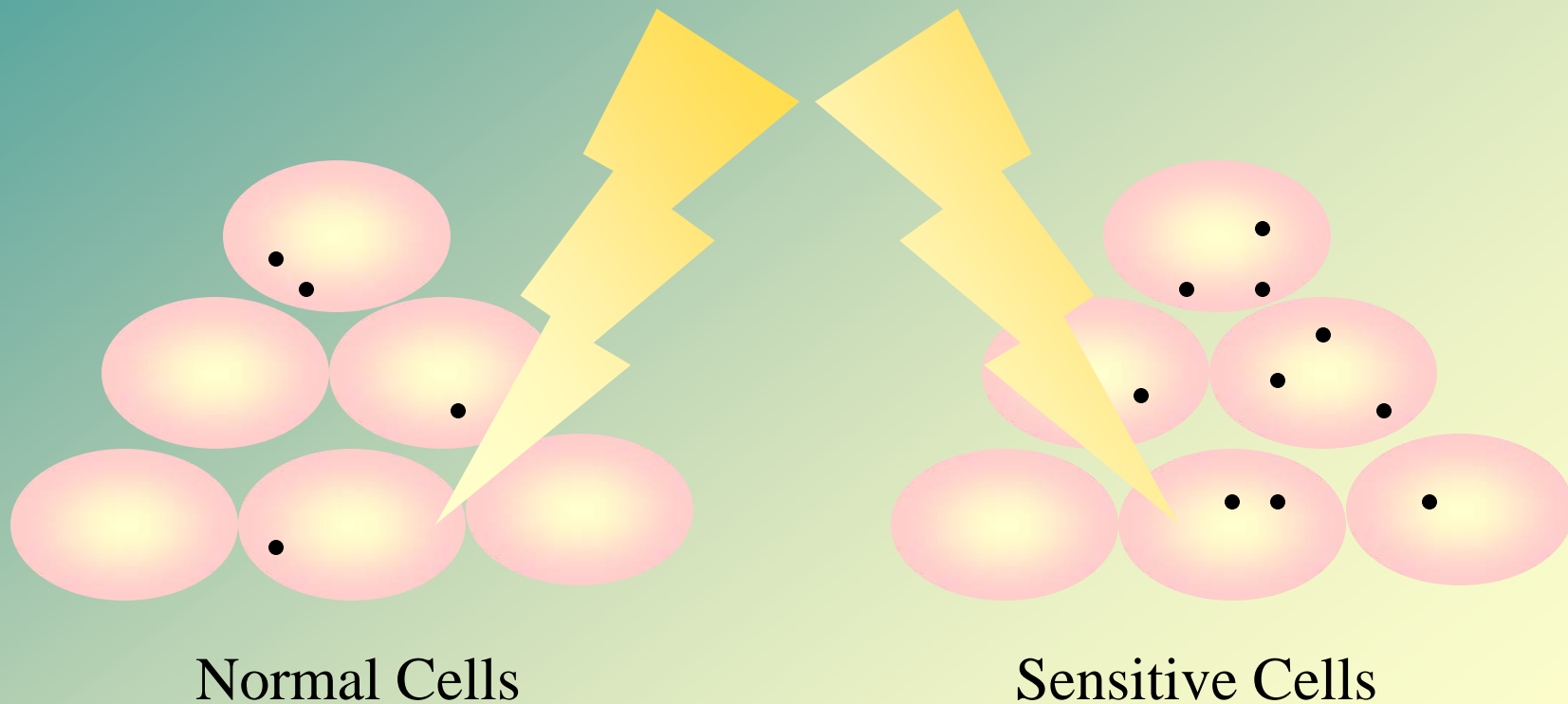
# Some individuals are more sensitive than others to a variety of things

- Dust
- Animal hair
- Chemicals
- Sun
- Drugs, medicines
- Foods
- Radiation

**We know that radiation is one of the things that has a wide range of sensitivities**



**Radiosensitive cells have been developed. After the same amount of radiation, they have more changes than normal cells.**



# Sensitive and Insensitive Mice



## Hybrid Mouse Models



Some strains of mice such as BALB/c are more sensitive to radiation than others. For example, C57BL/6 mice are particularly resistance to radiation-induced mammary cancer.

**Survivors** of radiation exposure have demonstrated that some people are less sensitive to radiation exposure than others.

LD<sub>50</sub> for radiation for humans is about 300,000 mrem. This means that at this high dose, half of all people will die- but half of all people will still survive.



## **A-BOMB**

Some survivors received more than 300,000 mrem, 60 years after the exposure, 40% of the population of A-bomb survivors are still alive.



## **CHORNOBYL**

One survivor in control room received 550,000 mrem

Why are these people apparently unaffected by the effects of radiation?

**Genetic susceptibility can be passed on from one generation to the next, therefore it probably involves genes.**

- Strains of mice have been developed that are more sensitive to radiation than others.
- Cell lines have been developed that are more sensitive to radiation than others.
- People with some genetic diseases, such as Ataxia, are radiation sensitive.

# Multiple genes contribute to radiosensitivity

- Different genes respond to high radiation and low radiation. The types of genes vary.
- Most biological systems have back ups or require homologous chromosomes, so that one mutation or irregularity does not automatically cause a problem.
- Most sensitivity to radiation involves disruptions of multiple genes.



# Genes which may effect Genetic Susceptibility

- **Radiation-induced genes**

- Some genes are activated or deactivated by radiation- these genes may make people more sensitive or more resistant to radiation damage.

- **Stress response genes**

- If these genes cannot deal appropriately with oxidative stress caused by radiation, the function of the cell can be disrupted.

- **DNA repair genes**

- Most radiation damage to DNA is repaired. If DNA repair genes are defective then cells cannot fix even minor damage caused by radiation.

- **Apoptosis genes**

- Genes which trigger the normal death of cells may malfunction, resulting in inappropriate death or survival of altered cells.

# Researchers have developed methods to identify radiation sensitive and resistant individuals

- Changes in gene expression are being used to predict sensitivity in individuals.
- It has been found that people with increased radiation-induced aberrations at the G2 stage of the cell cycle are more sensitive to radiation therapy.
- Dose response for cells taken from patients can help predict their radiation sensitivity.



# The impact of genetic susceptibility

- Identification of sensitive subpopulations may suggest an increased risk at low doses for that unique subpopulation.
- It might then be possible to control environmental exposure to these sensitive subpopulations.
- Resistant individuals would have lower than average risk.



# Summary

- Radiation does not effect individuals to the same degree.
- Some people may be radiosensitive, while others may be more resistant to the effects of radiation.
- Scientists are trying to find better ways to determine if someone is particularly sensitive to radiation.
- Understanding genetic susceptibility will help predict and control risk in clinical and occupational settings.