

Radiobiology A to Z

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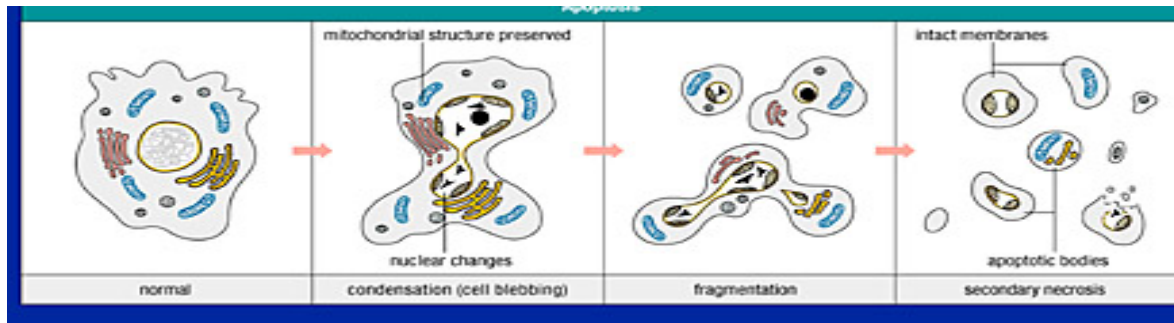
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Lawrence Berkeley National Laboratory

Apoptosis



- **Programmed cell death**
 - Changes cell nucleus
 - Condenses and fragments cell structures
 - Sends “eat me” signals
- **Normal: Radiation-damaged cells die**
- **Too much: Alzheimer’s, Parkinson’s**
- **Too little: cancer, autoimmune disease, ATM**

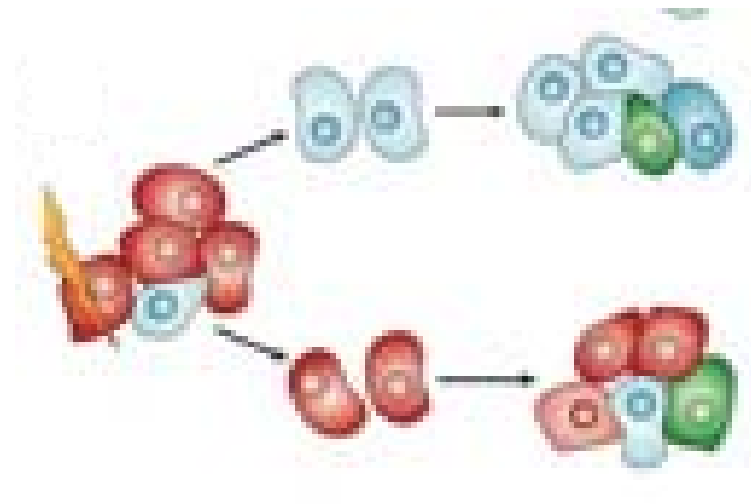
Bystander Effect

- **Irradiated cells send signals that affect nearby unirradiated cells**
 - Damage signal
 - Protection signal
- **Effect depends on cell type, genetic makeup**
 - Limited to cells in same organ
- **Chemical signal: free radicals?**
- **5 to 50 rad: maximum bystander effect**



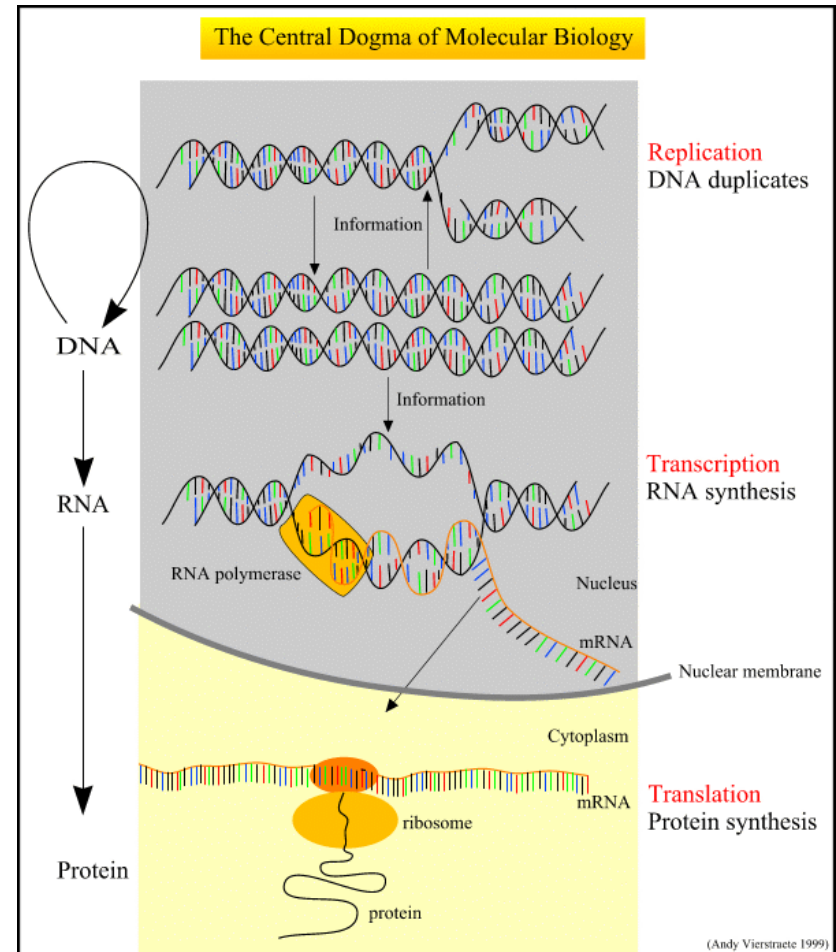
Cancer: Genomic Instability

- **Changes in progeny of irradiated & bystander cells**
 - Mutations
 - Chromosome rearrangements
 - Apoptosis
- **Caused by**
 - Faulty DNA repair proteins
 - Increased free radicals
 - Epigenetic changes



Dogma, Central

- Information flows one way from genes to proteins
- DNA to RNA to protein
- Flows by
 - Replication
 - Transcription
 - Splicing
 - Translation
- Challenged by epigenetics



Epigenetics

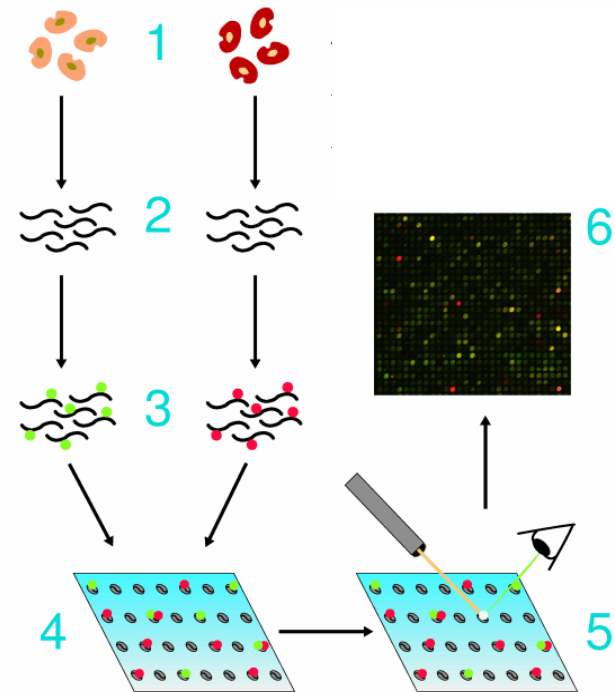
- **Heritable changes in gene function that occur without a change in DNA sequence**
- **Controls how, where, when genes are used**
- **Changes in response to**
 - Radiation
 - Hormones
 - Reactive oxygen species
- **Changes are misdirected in cancer**



Gene Expression Microarrays

Compare genes in two cells

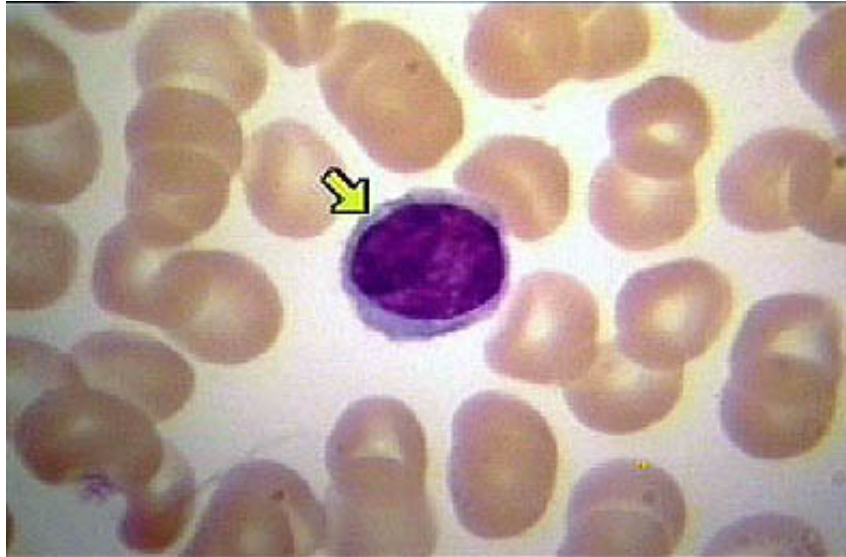
1. Isolate mRNA from cell
2. Transcribe it into cDNA
3. Label with fluorescent dye
= Probe
4. Add probes to array
= Hybridize
5. Stimulate array with laser
6. Quantify ratios of light



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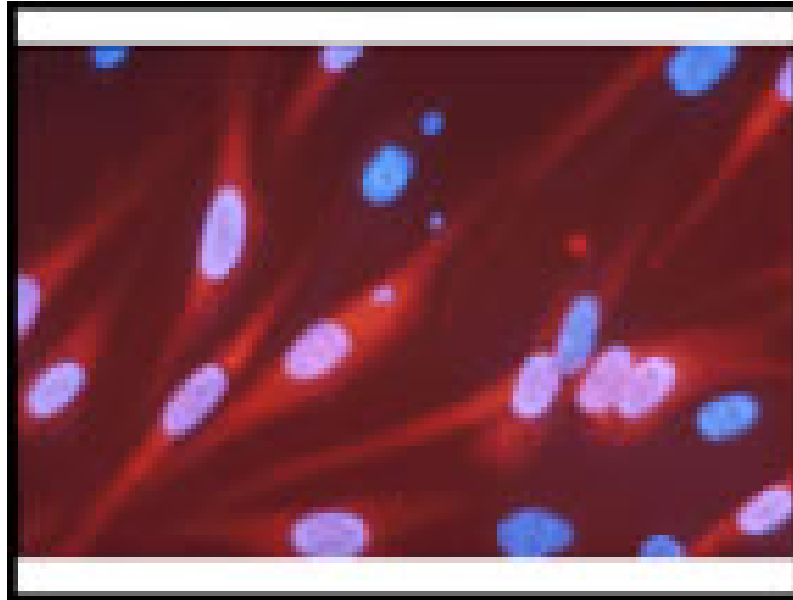


Lymphoblastoid Cell



- **Cells start as normal circulating lymphocytes**
- **Mononucleosis virus added to lymphocytes**
- **Virus transforms lymphocytes into lymphoblastoids: immortal, continuously dividing cells**

Micronucleation Assay



- Chromosomes break from radiation or chemical damage
- Broken bits get left behind when cell divides
- Form small, separate nucleus = micronucleus
- Count to quantify radiation damage
- Shown here outside nucleus of epithelial cells

Polymerase Chain Reaction

- **Technique multiplies DNA by repeated replication and strand separation**
- **Steps**
 - **Unwind double strand using heat**
 - **Match new nucleic acids to old using polymerase**
 - **Repeat**
- **Exponentially amplifies small amount a million times**



Zinc Finger

- Finger-shaped fold in a protein that permits interaction with DNA and RNA
- Regulates gene expression
- Common in radiation response proteins
 - Induce apoptosis
 - Repair broken DNA

