Lecture 4, Part 2

RADIATION-INDUCED CANCER

Radiation and cancer

Nuclear fallout

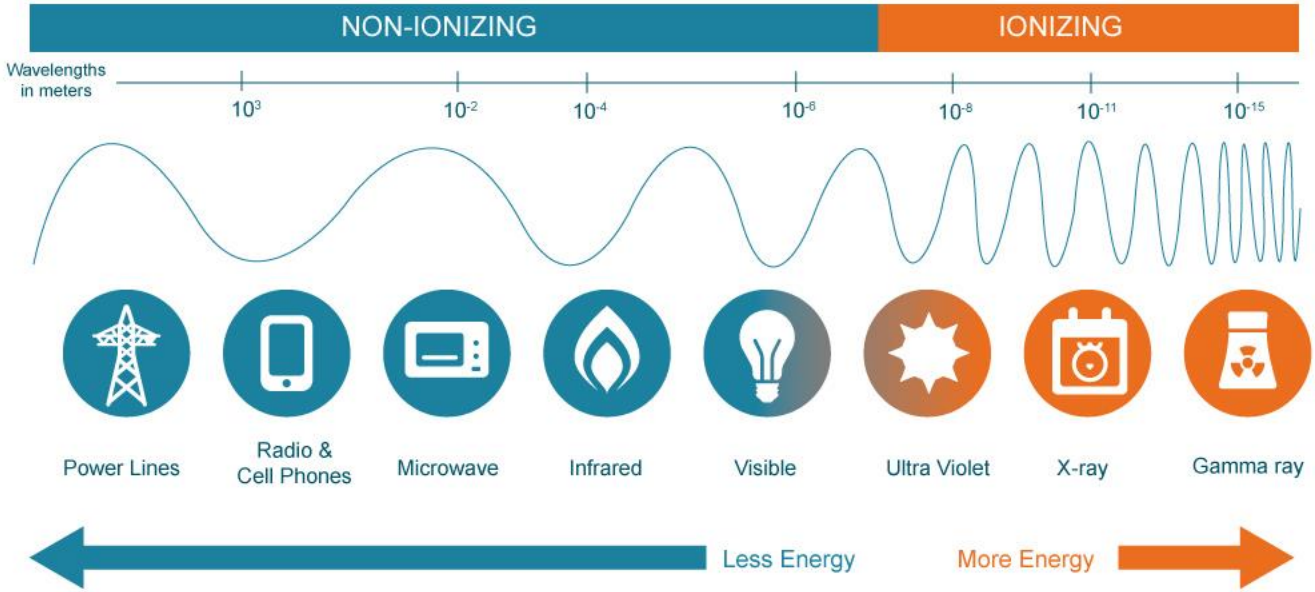
residual radioactive material in the upper atmosphere after a nuclear blast

UV

Ionizing and Non-ionizing radiation

- Radiation that does not have enough energy to break chemical bonds but can vibrate atom is referred to as '**Non-ionizing Radiation'**
  - e.g. radiowaves, microwaves, infrared, visible light etc.

- Radiation that has enough energy to break chemical bonds is referred to as **'Ionizing Radiation'**
  - e.g. alpha particles, beta particles, gamma rays etc.



Ultraviolet radiation

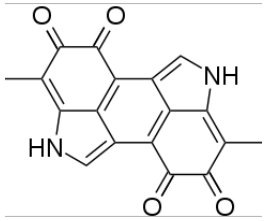
Sun exposure causally linked to skin cancer

- The UV portion of the solar spectrum is divided into three wavelengths:
  - UVA (320 to 480 nm) – (95% of sun) production of reactive oxygen species
  - UVB (280 to 320 nm) - most correlated with cutaneous cancer
  - UVC (200 to 280 nm) – most dangerous (e.g. those working with welding torches)

Sun exposure

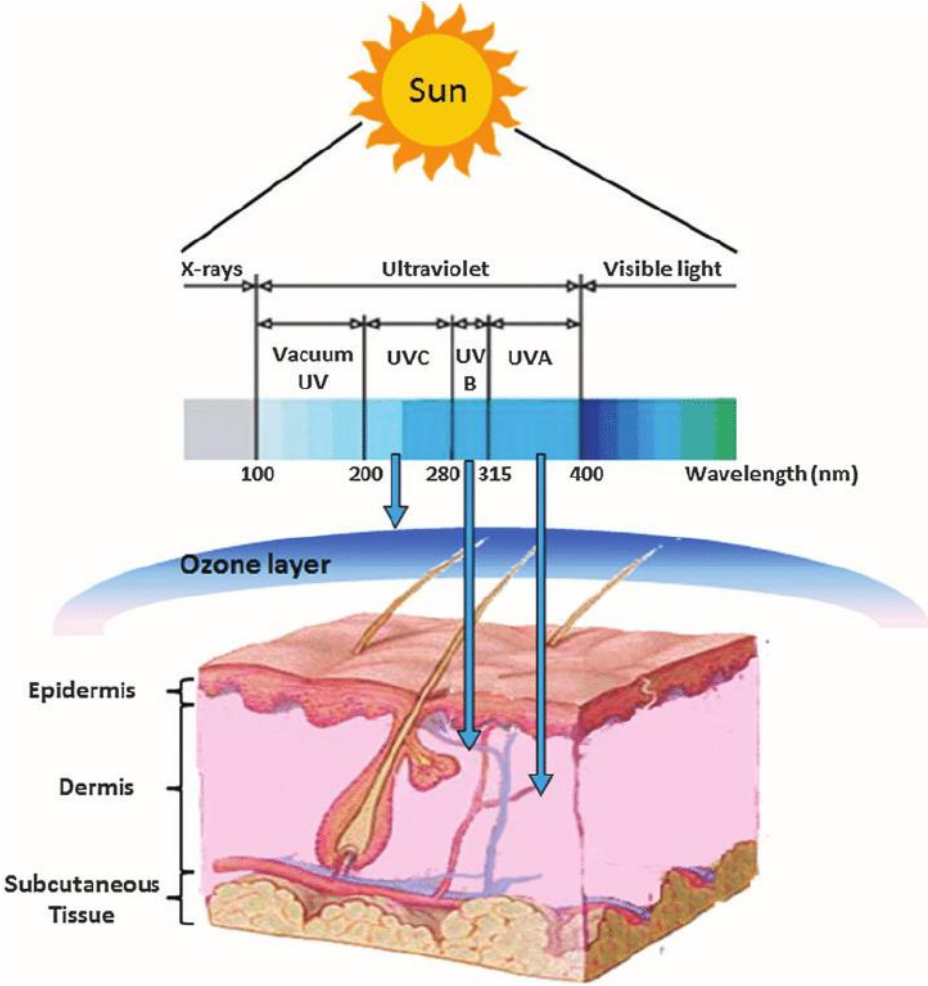
The ozone layer shields us from much of the effects of UV radiation

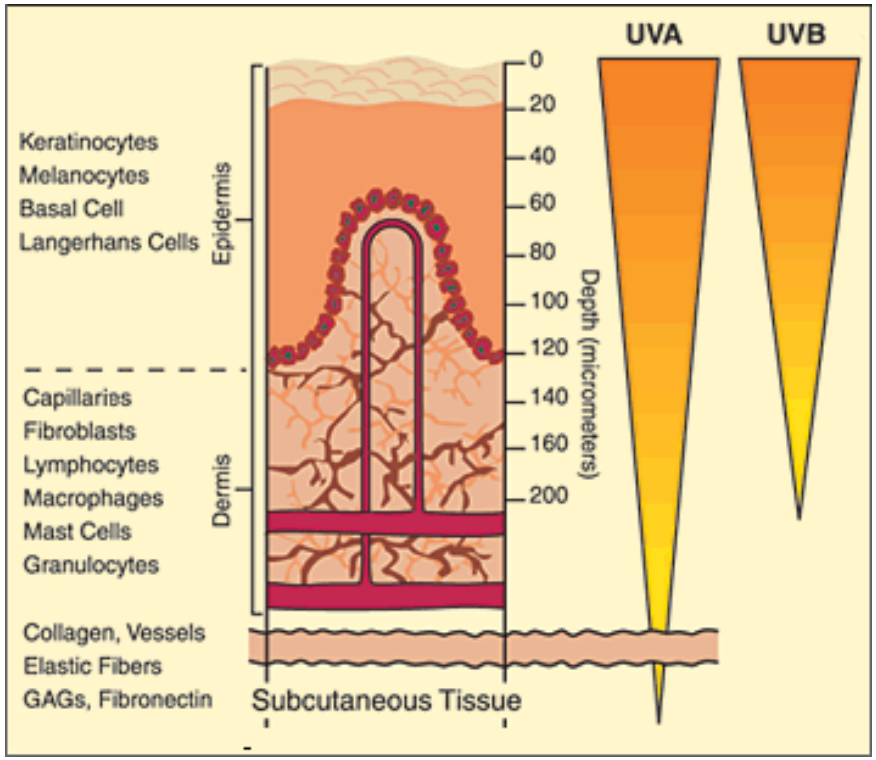
- Persons of European origin with fair skin that get sunburned repeatedly have higher incidence of skin cancer
- Persons of darker skin are protected by the pigment melanin that absorbs ultraviolet radiation



Melanin – derived from tyrosine

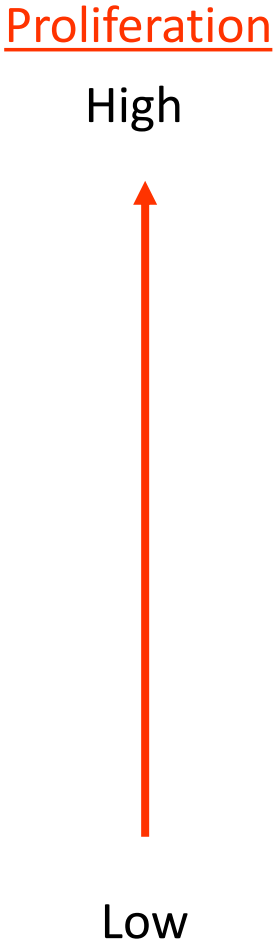
UV depth penetration in skin



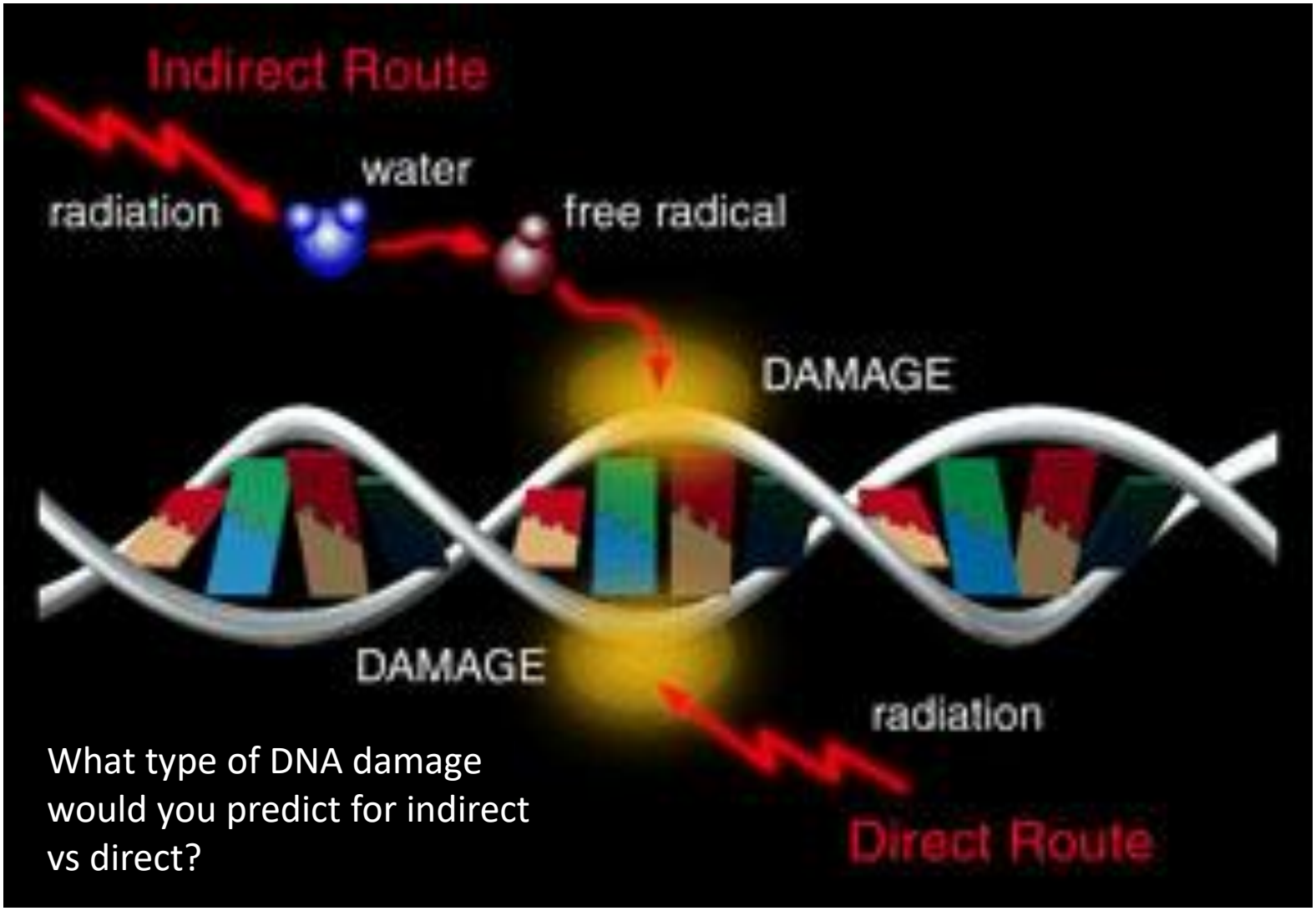


CANCER SITES AND TISSUE RADIOSENSITIVITY

- LYMPHATIC TISSUE, ESPECIALLY LYMPHOCYTES
- WHITE BLOOD CELLS AND IMMATURE RED CELLS OF MARROW
- CELLS LINING GASTRO-INTESTINAL TRACT
- GONADIC CELLS
- SKIN, ESPECIALLY THE PROLIFERATING LAYER
- BLOOD VESSALS AND BODY CAVITY LININGS
- TISSUES OF GLANDSA ND LIVER
- CONNECTIVE TISSUE
- MUSCLE
- NERVES

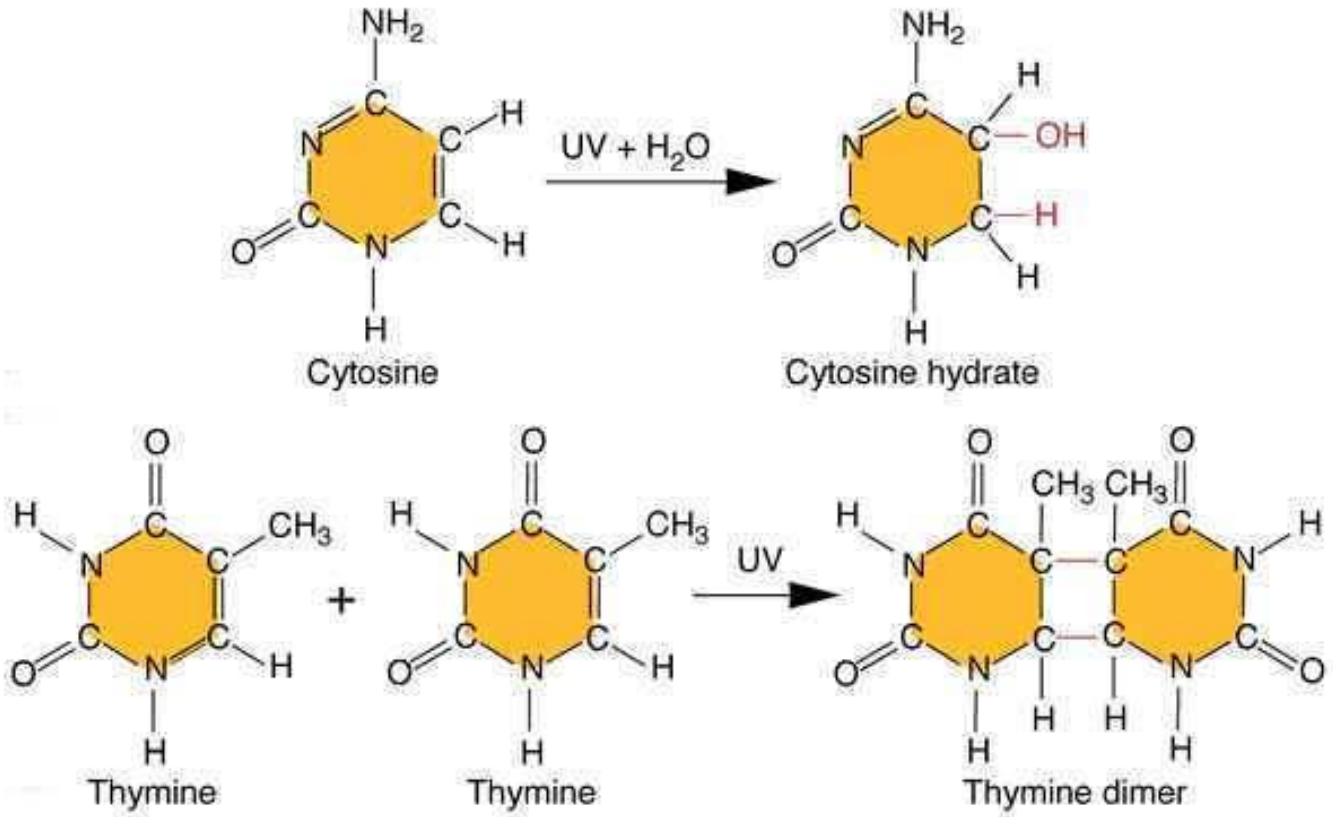


Radiation interacting with DNA

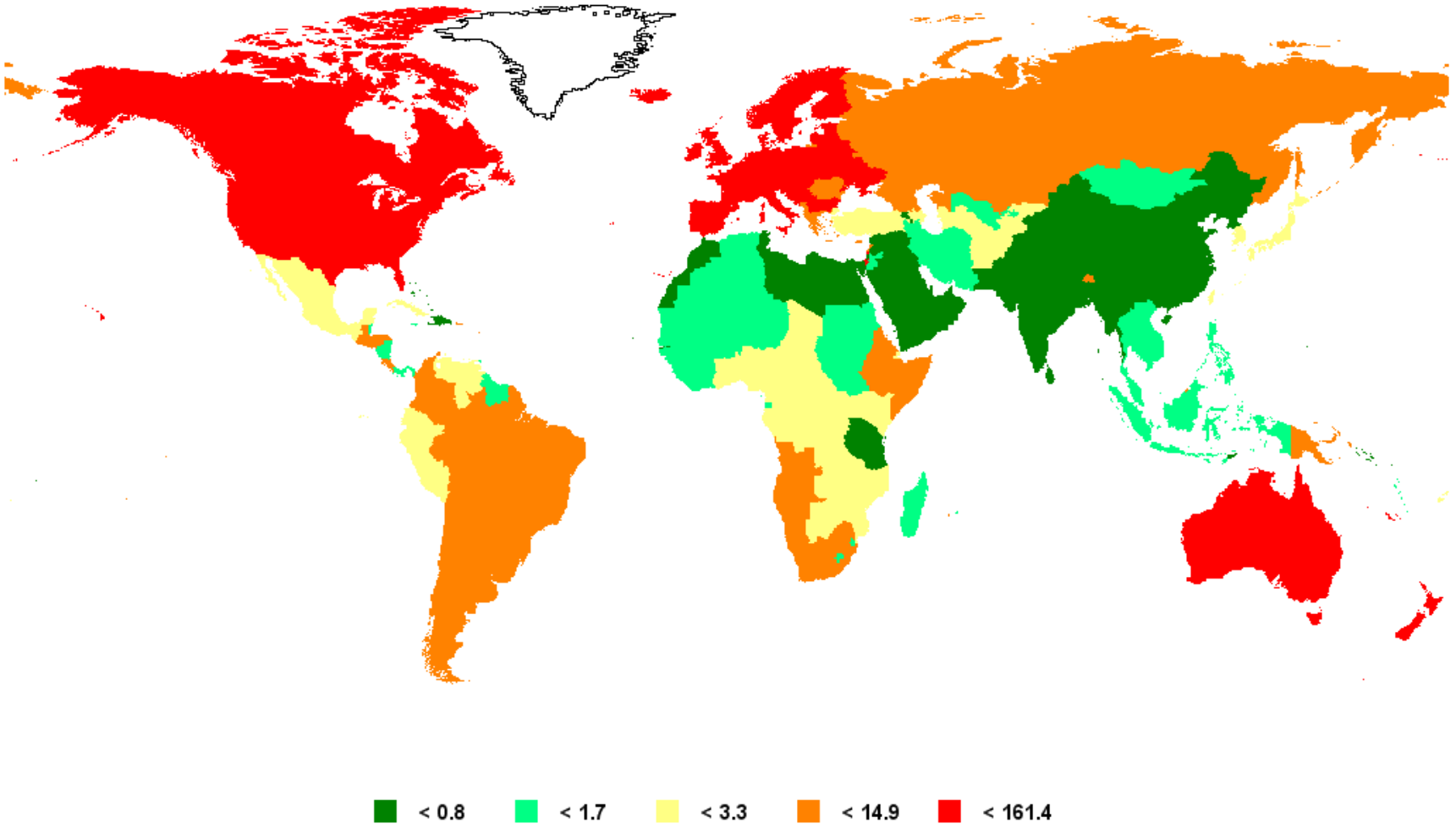


What type of DNA damage would you predict for indirect vs direct?

Direct and indirect DNA damage



Estimated 3-year prevalence proportions per 100,000
Melanoma of skin: both sexes, adult population

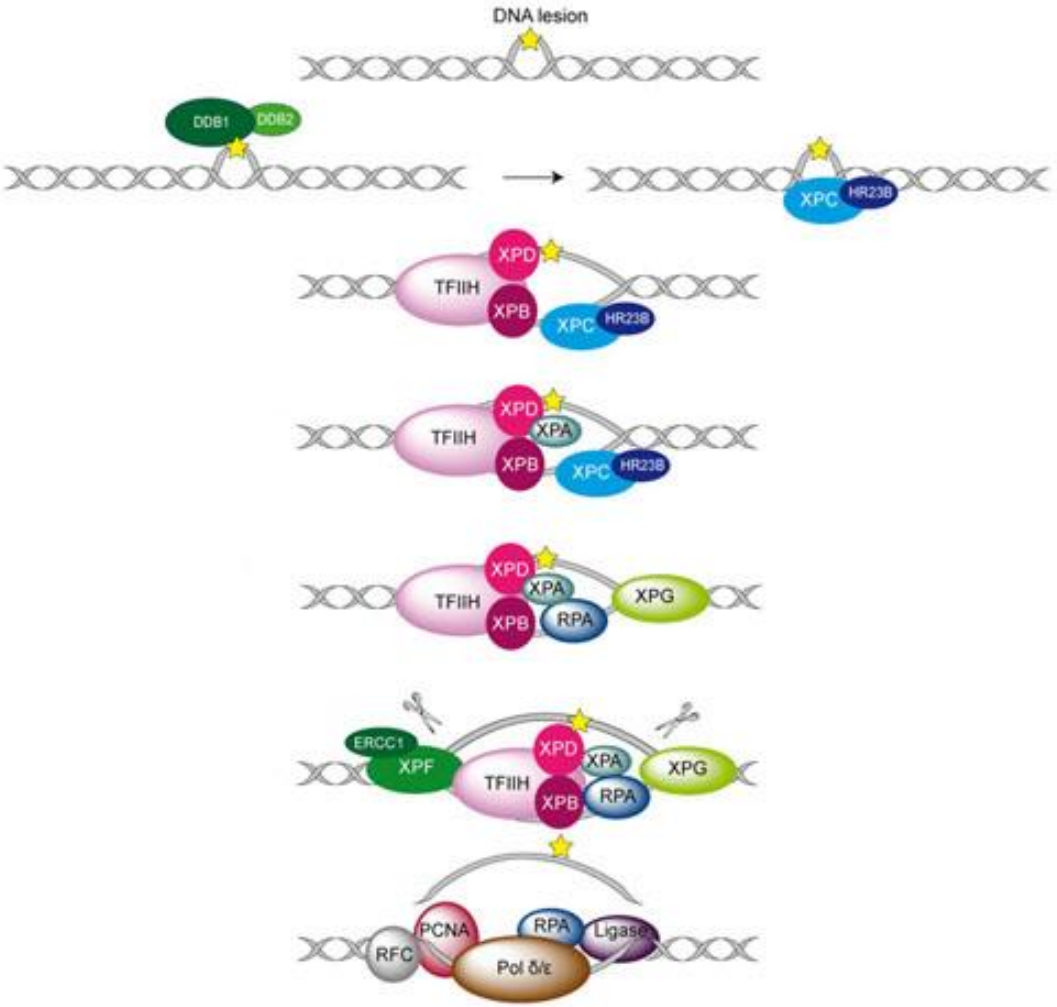


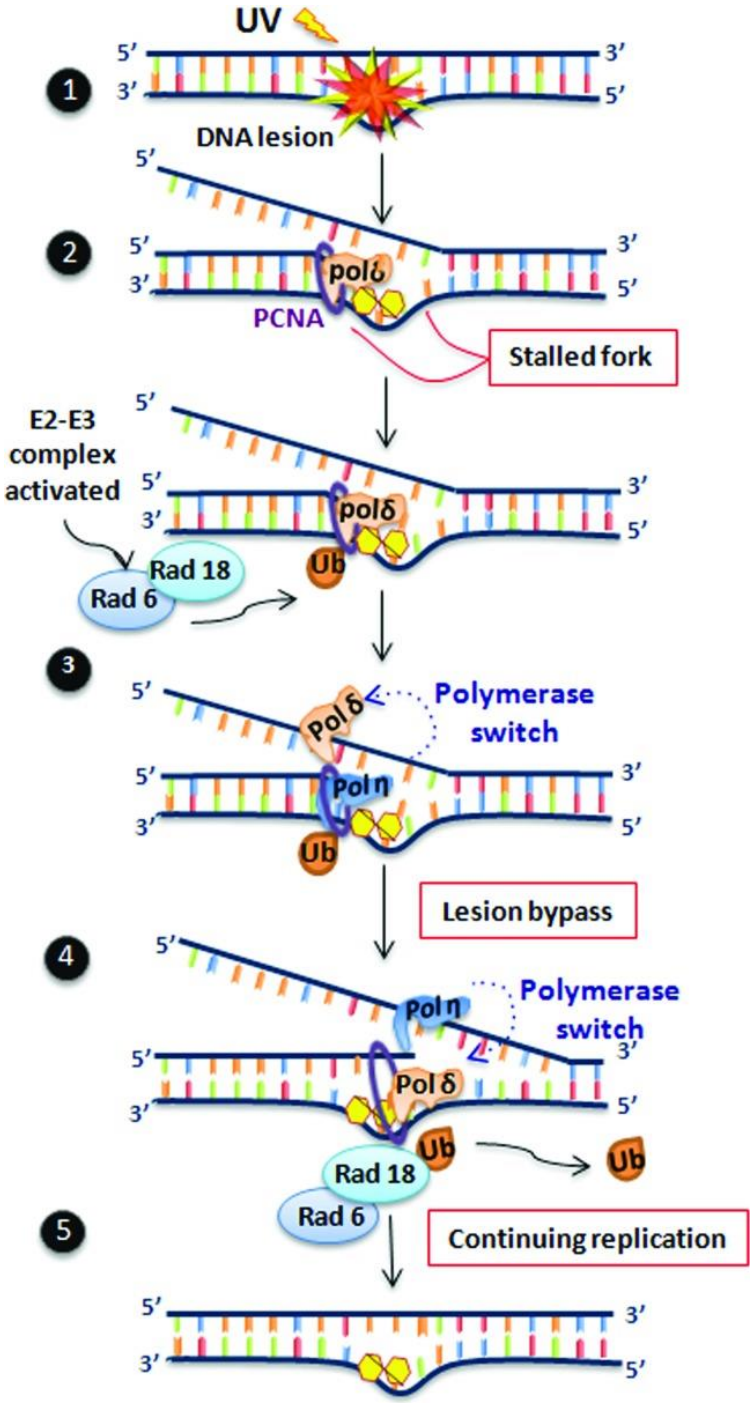
GLOBOCAN 2008 (IARC) - 21.2.2012

DNA repair defects and UV-induced cancer

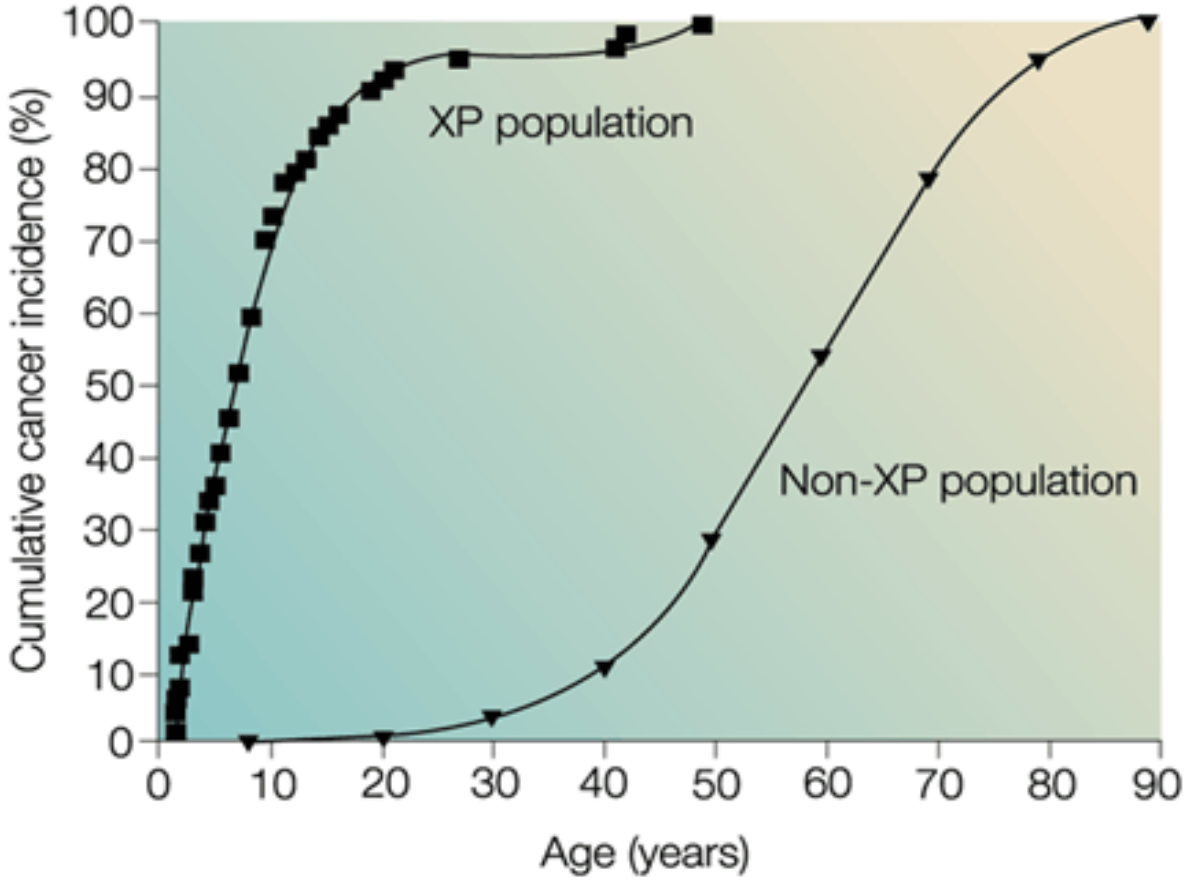
- Xeroderma Pigmentosum (XP) rare genetic disorder
- Increase in skin cancer risk 1000-2000 fold
- Defects in DNA repair (TT dimers)
- Defective XP proteins in NER
  - 7 variants (XPA most common type)
  - (plus one variant, XPV, defective in TLS by DNA polymerase η)

XP patients have defects in NER or TLS





Incidence of skin cancer in patients with Xeroderma pigmentosum



Nature Reviews | Cancer

Nuclear fallout radiation

Analysis of Chromosome Aberrations in Atomic Bomb Survivors for Dose Assessment: Studies at the Radiation Effects Research Foundation from 1968 to 1993

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Radiation Effects Research Foundation, Hiroshima, Japan

Key Words. *Chromosome · Radiation · Dicentric · Translocation · Atomic bomb*

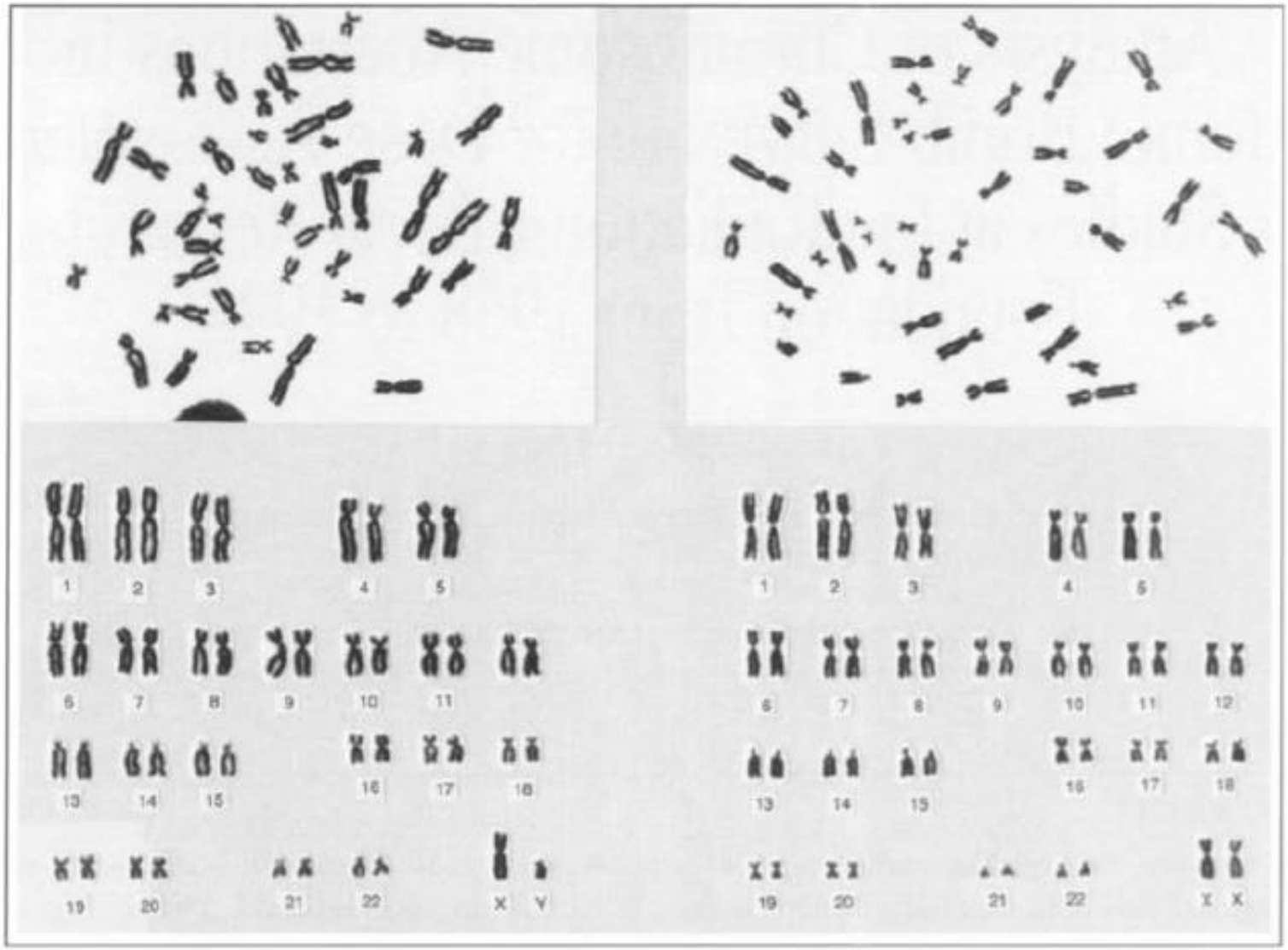
ABSTRACT

Exposure to ionizing radiation causes damage to living cells, especially to DNA in the cell nucleus. The degree of this cellular damage depends on the amount of radiation administered. This review discusses current findings concerning radiation-induced chromosome aberrations that were produced in 1945 and that can still be observed in the somatic cells of atomic bomb survivors in Hiroshima and Nagasaki. The scoring methods of G-banding and fluorescence in situ hybridization are compared. In addition, some findings concerning chromosomal aberrations in citizens of the former Soviet Union affected by the Chernobyl accident are presented.

Stem Cells 1997;15(suppl 2):163-173

Hiroshima Atomic Bomb Dome

Normal male and female karyotype



Chromosomal aberrations from radiation exposure

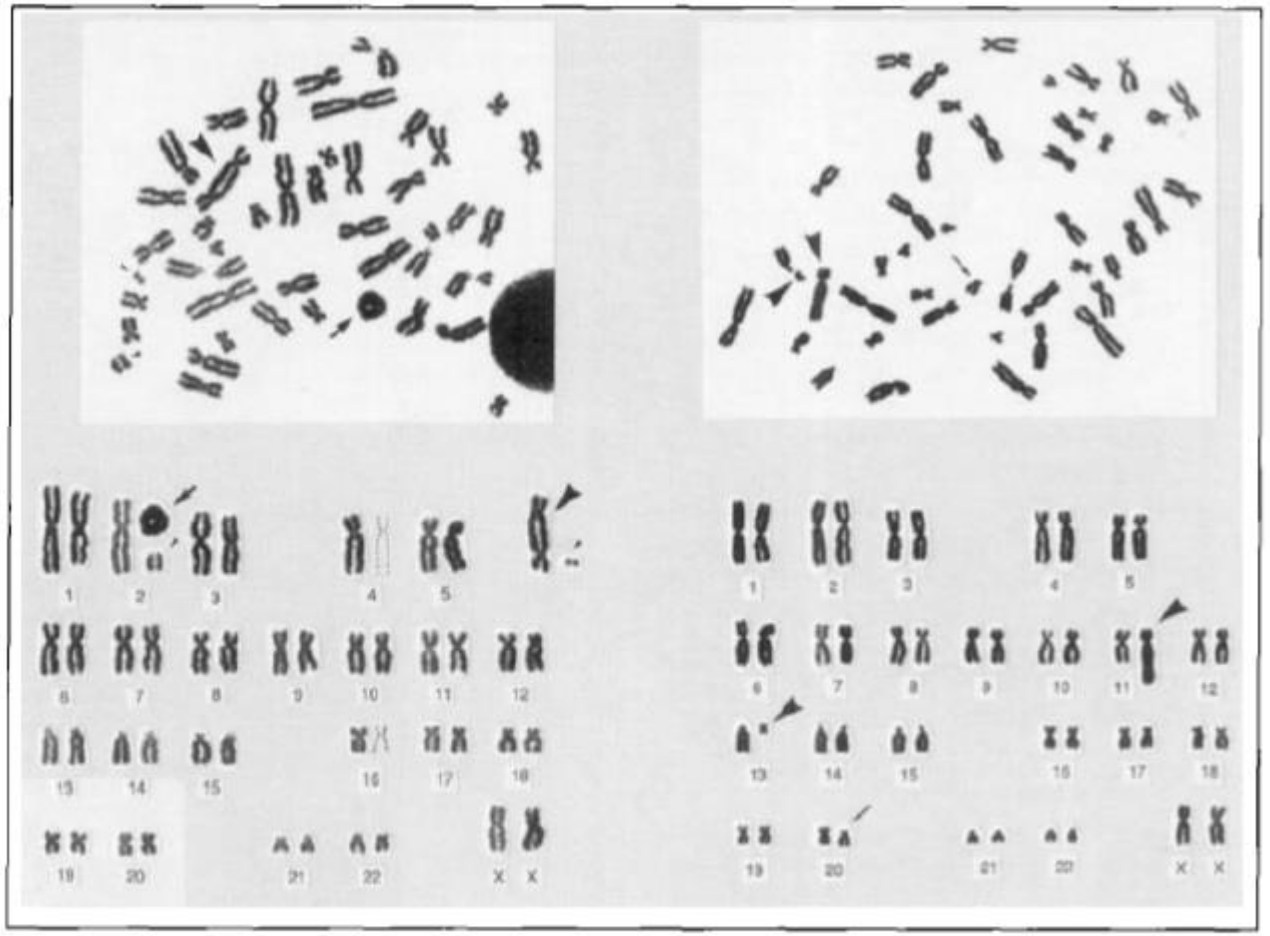


Figure 4. Examples of radiation-induced chromosomal aberrations. *The left panel shows a cell with a ring chromosome derived from chromosome 2 (→) and a dicentric derived from chromosomes 4 and 16 (▾). The right panel shows a cell with a reciprocal translocation between chromosomes 11 and 13 (▾), and a pericentric inversion involving chromosome 20(→).*

What are agents that can cause cancer?

chemicals

infectious agents

radiation