Most environmental causes of cancer are mutagens: mutagenic compounds, X-rays, uv

Enzymatic conversion to reactive epoxide

Spontaneous reaction with N7 of guanosine

Aflatoxin B

3,4-benzpyrene

DNA
Cancer tends to arise in actively dividing cells

- Epithelial cells (lining of intestine, lungs etc.) = carcinoma
- Blood and lymphatic cells = leukemia, meyloma, lymphoma
- Connective tissue (bones, tendons muscle) = sarcoma
Cancer is a genetic disease of somatic cells

The underlying cause is mutations that release cells from the normal constraints that exist in well organized tissues allowing uncontrolled growth

Which are the key genes that are mutated?
Incidence of stomach cancer as a function of age

Figures by MIT OCW.
Major complications in understanding the genetic basis of cancer

- Multiple mutations are necessary to produce a tumor cell
- Different types of tumor have different genes mutated
  - Early initiating events occur rarely in complex tissues and are therefore extremely difficult to detect
- The key initiating event often leads to an increase in mutation rate thus tumor cells often bear many fortuitous mutations

Important aspects of the disease we won't discuss relate to the spread of cancer cells and the formation of large tumors (metastasis and angiogenesis)
3T3 cells in culture

Transformed 3T3 cells

Images removed due to copyright reasons.
Isolation of the Ras oncogene from human tumor cells

DNA from human tumor cells

Transfect mouse 3T3 cells

Culture for 2 weeks

Focus of transformed 3T3 cells growing among untransformed cells

Extract DNA, transform new mouse cells

Second cycle

Extract genomic DNA

Surviving human DNA

Introduce into phage vector

Phage library

Plate phage on E. coli

Alu probe

Replica on filter paper

Oncogene

Figure by MIT OCW.
Synergistic effect of oncogenic forms of myc and ras