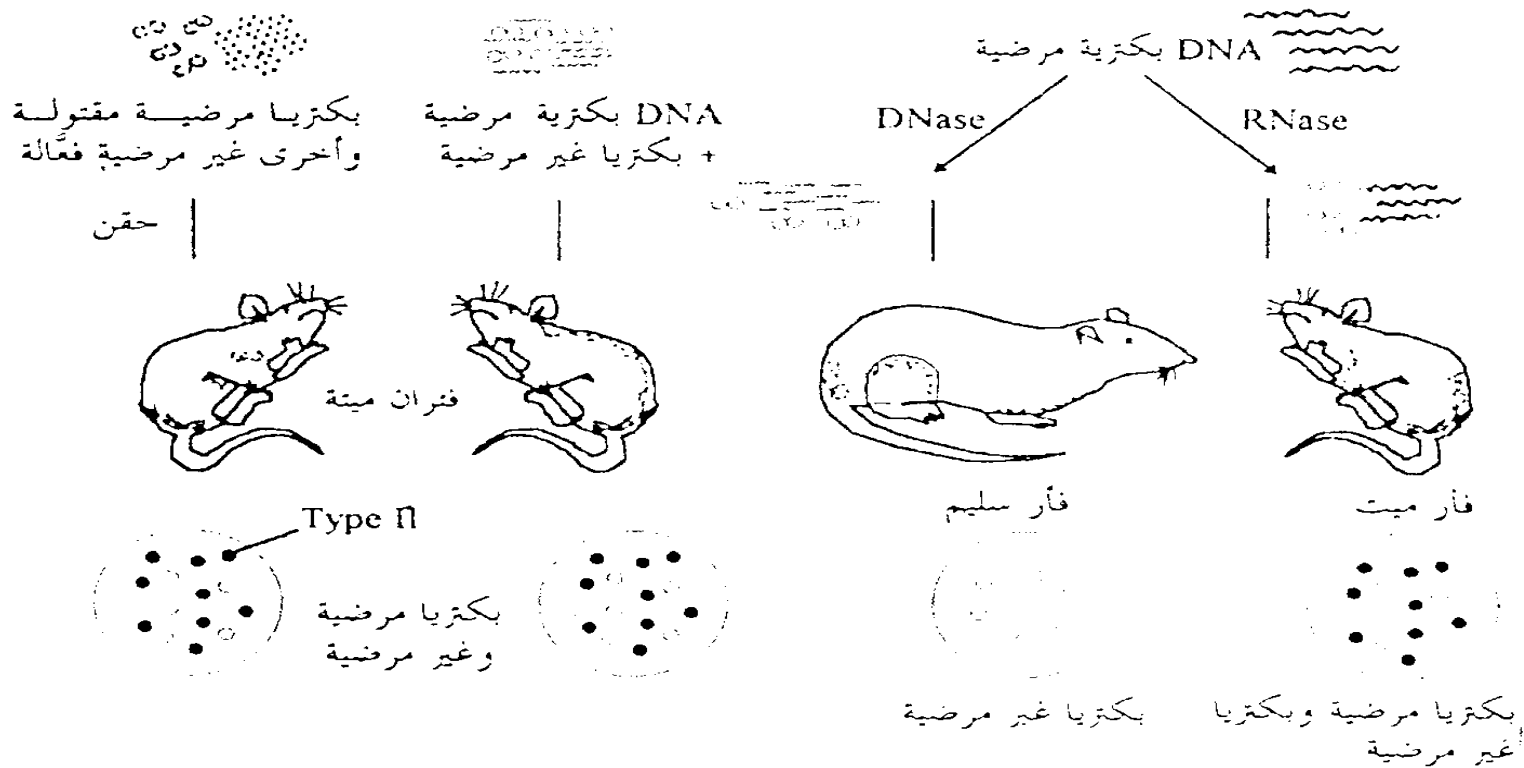# Oncogenes and Tumor suppressor genes

Prof . Dr. Abdul Hussein Moyet AlFaisal

Ph.D. in Cancer Molecular Genetics

Wales University – UK

Genetic Changes in cancer cells ◉
1. Boveri et al.,1944 theory ◉

شـكـل (2 - 2) : تجربة أفيري وجماعته التي أثبتت أن الحامض النووي منقوص الأكسجين هو المسؤول عن ظهور الصفات الجديدة وتحول البكتيريا إلى سلالة مرضية .

2. Boveri et al., theory and Cancer

-- Cancer arise from genetic errors

…… Evidence……

1.Cancer or risk of cancer could be inherited.

2. Tumors are monoclonal in origin.

3. Cancer development & alterations accumulations

- Proto-Oncogenes or Cellular Oncogenes

- Tumor Suppressor Genes

- DNA Repair Genes

    ... Xeroderma pigmentosum

    ... Ataxia telangiectasia

    … Fanconis anemia

    ... Blooms syndrome

- Other genes encoding proteins and enzymes.

- Genomic Imprinting.

- Combination of changes.

Chromosomes & Cancer

- Normal chromosomes number

- Stability of genome and chromosomes

- Primary and Secondary chromosomes abnormality

- Random and non random abnormality-

Table 1.2: Examples of primary chromosomal aberrations in hematological malignancies

Tumor	Abnormality	Tumor	Abnormality
AML	t(1;7)(p11;p11)	ALL	t(1;11)(p32;q23)
	Trisomy 4		t(1;19)(q23;p13)
	Monosomy 5		t(4;11)(q21;q23)
	t(6;11)(q27;q23)		t(8;14)(q24;q32)
	Monsomy 7		t(8;22)(q24;q11)
	Trisomy 8		t(2;8)(p12;q24)
	t(9;11)(p21;q23)		t(9;22)(q34;q11)
	t(10;11)(p14;q13)		t(10;14)(q24;q11)
	Trisomy 11		t(11;19)(q23;p13)
	del/t(12p)		del(12)(p11p13)
	t(15;17)(q22;q11)		t(11;14)(p13;q11)
	inv(16)(p13q22)		t(1;19)(q23;p13)
	del(16)(q22;q24)		Trisomy 21
	i(17q)	CML	t(9;22)(q34;q11)
	del(20)(q11q13)	CLL	Trisomy 12
	Trisomy 21	Lymphoma	t(8;14)(q24;q32)
	Trisomy 22		t(8;22)(q24;q11)
			t(2;8)(p12;q24)

Derived from ref.13. (This list shows examples of some of the rearrangements found in hematological malignancies.) AML, acute myeloid leukemia; ALL, acute lymphocytic leukemia; CML, chronic myeloid leukemia; t, translocation; inv, inversion; del, deletion; i, isochromosome.

**Table 1.3:** Examples of primary chromosomal aberrations in solid tumors

Tumor	Abnormality
Lipoma	t(3;12)(q27–28;q14–15)
Ewing's sarcoma	t(11;22)(q24;q12)
Renal carcinoma	t or del(3)(p11–21)
Wilms' tumor	t or del(11)(p13)
Bladder carcinoma	Changes of chromosome 1, i(5p)
Breast cancer	Changes of chromosome 1, t or del(16q)
Ovarian cancer	Changes of chromosome 1
Germ cell tumors of testis	i(12p)
Meningioma	Monosomy 22, del(22q)
Neuroblastoma	del(1)(p13–32)
Retinoblastoma	del(13)(q14)
Malignant melanoma	t or del(6q)/i(6p)
	t or del(1)(p12–22)
Uterine carcinoma	Changes of chromosome 1

Derived from ref.13. t, translocation; inv, inversion; del, deletion; i, isochromosome.

Apoptosis and Cancer

- Aim of apoptosis.

- Normal Function

- Apoptosis & Tumorigenesis.

Cell Cycle
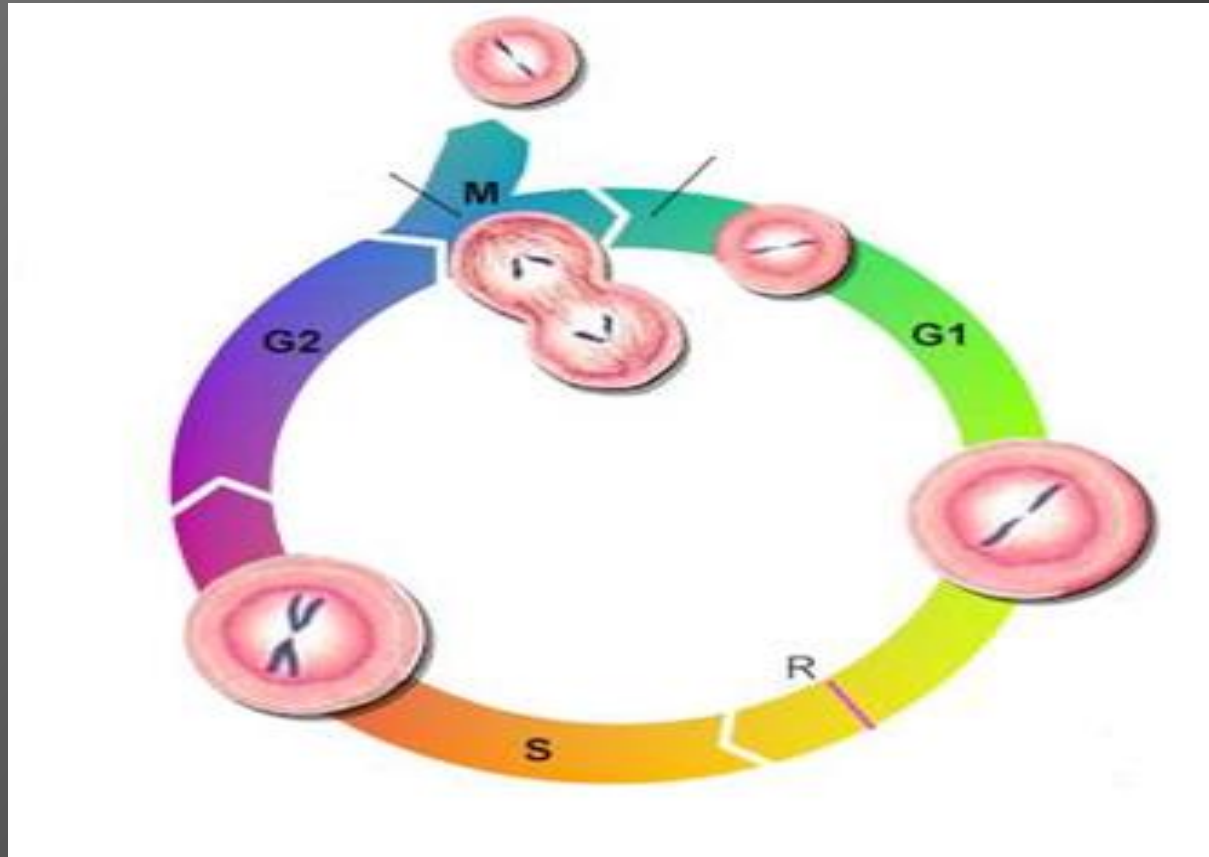
- Start –R
- Cyclin-dependent kinases –CDKs
- Cyclin-dependent Kinases Inhibitors-CDKIs

What is Cancer?

Cancer is a tissue or cells arisen from genetically defected normal cell with uncontrolled division and imbalance functions.

Normal vas Cancer cell

. Controlled proliferation vas Uncontrolled proliferation

. Differentiation vas Un differentiation?

. Normal apoptosis vas Lose of apoptosis

. Balanced functions vas Imbalanced function
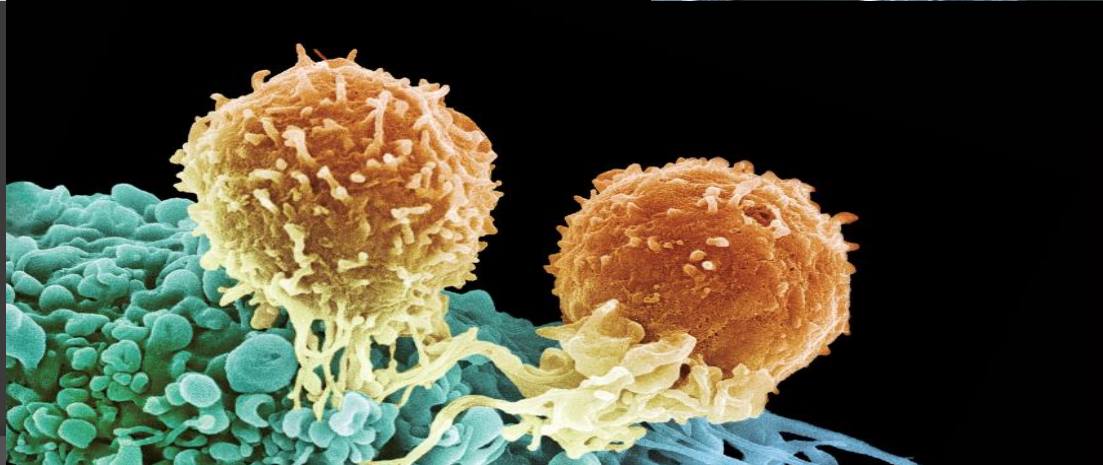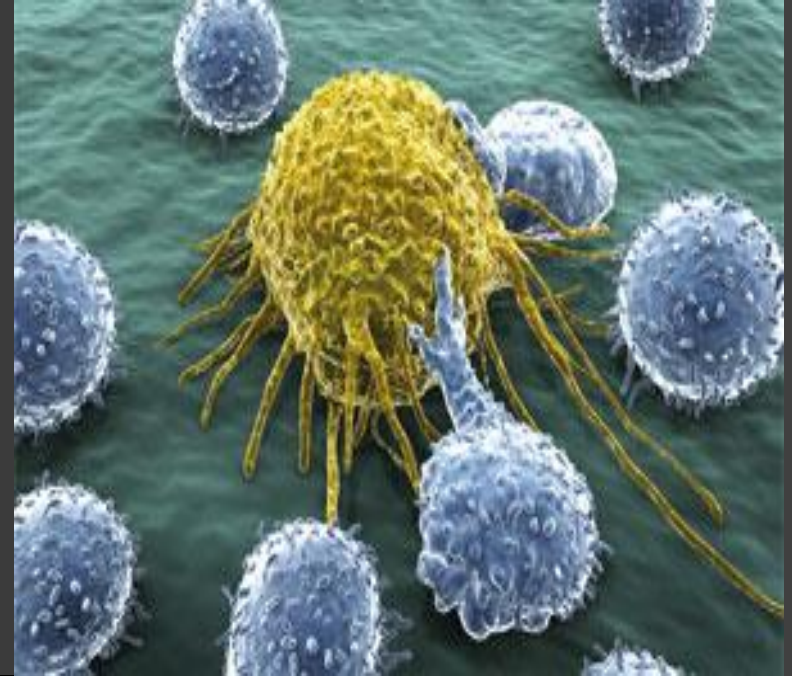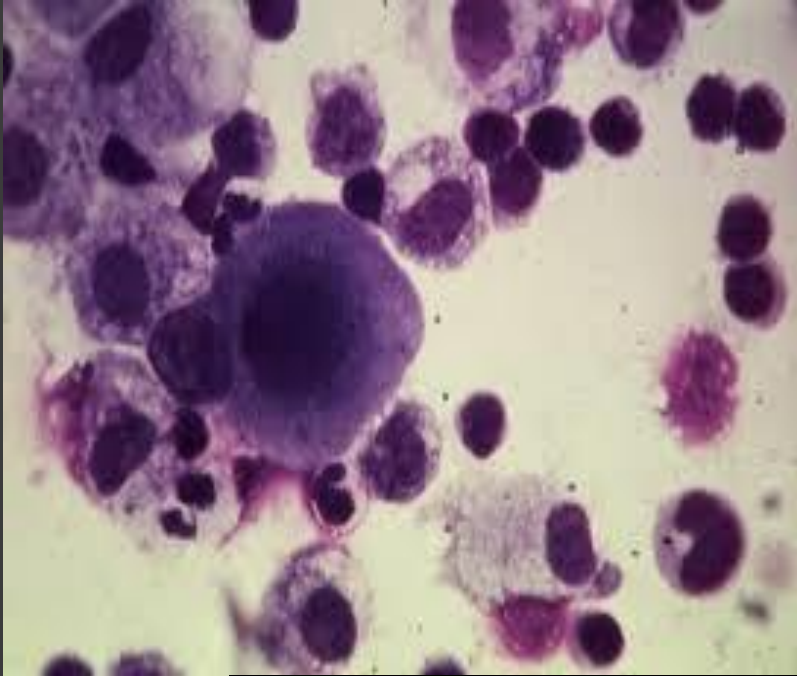
. Stable genome vas Genome instability

Cancer is a monoclonal origin
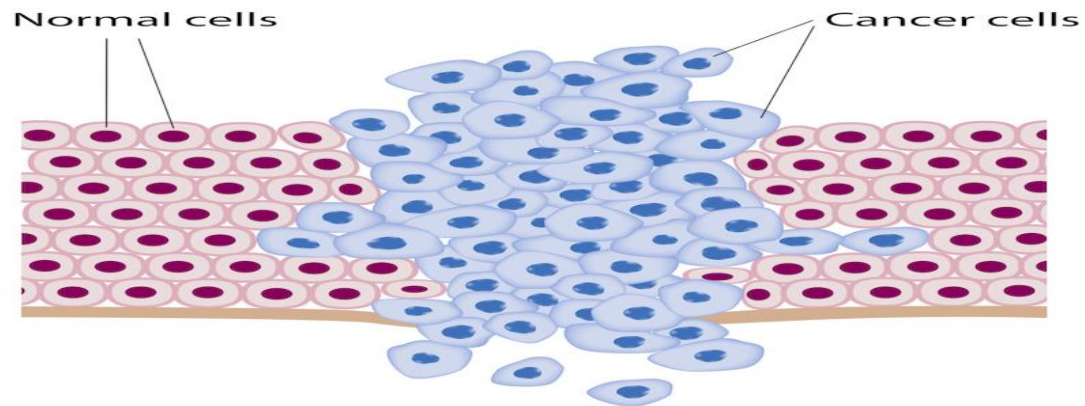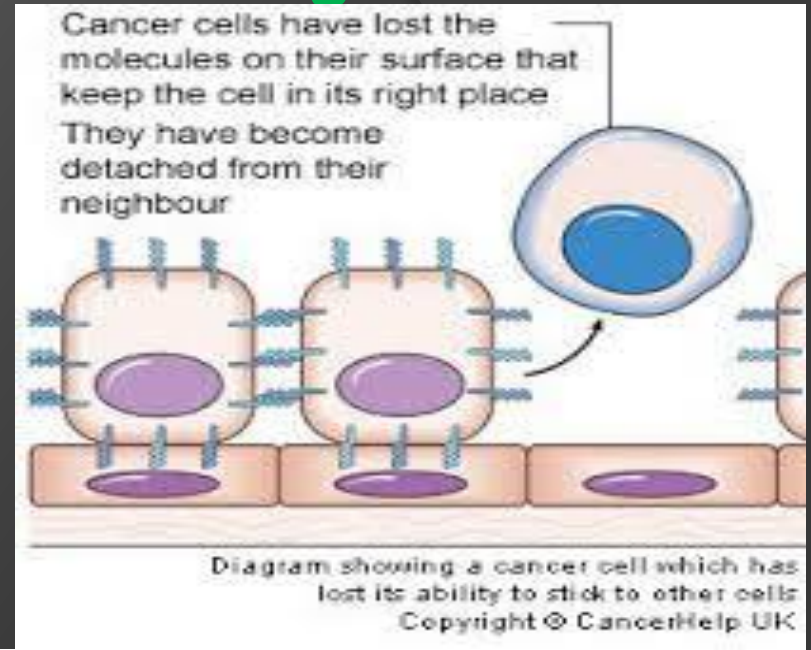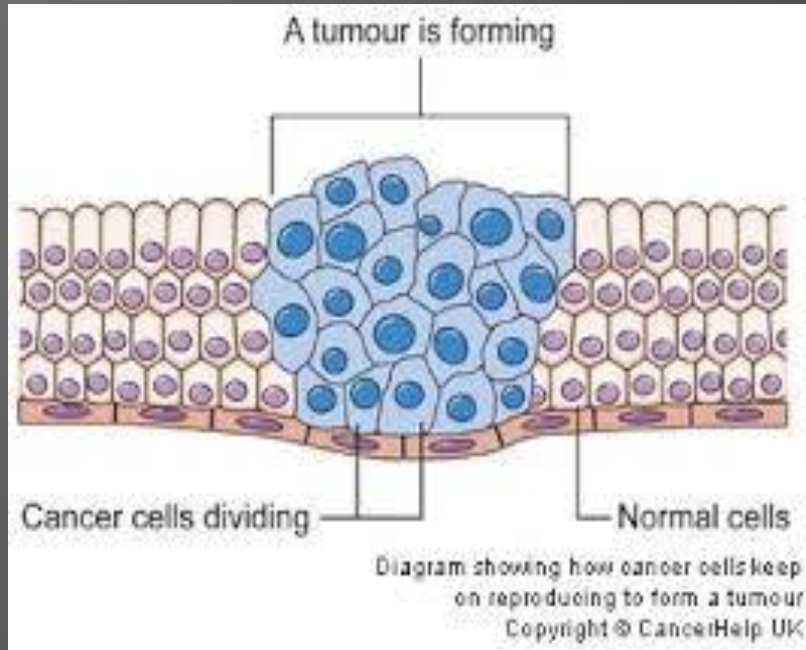
Features of Cancer Cell

1. No longer as dependent on growth factors.

2. Anchorage independent , no require to contact with the surface.

3. Lack the contact inhibition .

4. Less adhesive .

5. Growth with no certain density .

Morphological changes in cancer cells

Classification of Cancer

A- Sporadic and inherited cancer

4 groups

1. Acquired or sporadic cancer caused by environmental factors.

2. Cancer clustering in families with un recognizable genetic base.

a. earlier age of onset

b. individuals with multiple cancers

c. segregation of cancer in Mendelian manner

3. Cancer with clearly defined genetic cause.

4. Some syndromes related to chromosomes abnormalities have a increased risk of cancer.

B. Benign & Malignant cancer

C. Hematological & Solid cancer

D. According to the origin of cancer
a. carcinoma b. sarcoma c. leukemia d. myeloma

Cancer development stages

. Hyperplasia

- Cells lose of their division and growth control with normal shape.

. Dysplasia

- Cells with more genetic damages, rapid division and lose the normal shape and physiology.

. Anaplasia

- Cells with more genetic damages and able to invade the surrounding tissue.

. Metastasize

- Cells can invade other tissues far a way from the original cancer.

Cancer Theories

1. Chemical & Physical theory

         Chemicals, rays

2. Germinal theory

      Bacteria, Parasites, Viruses

3. Retardation theory

     Stem cells, c-oncogenes
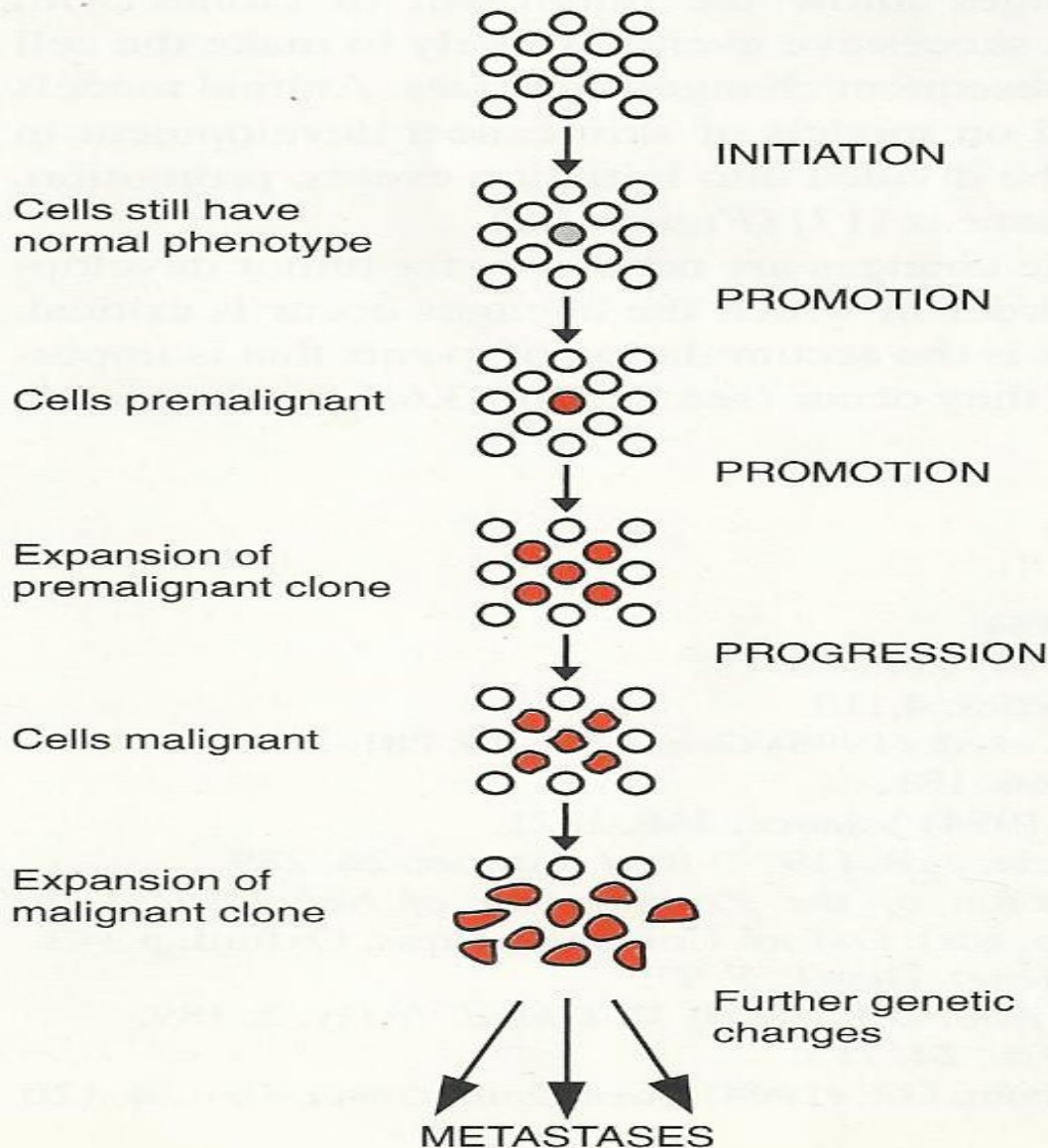
Multistage nature of cancer development

Figure 1.2: Multistage progression to malignancy.

Thank you for listening