Introduction to Oncology Pharmacy

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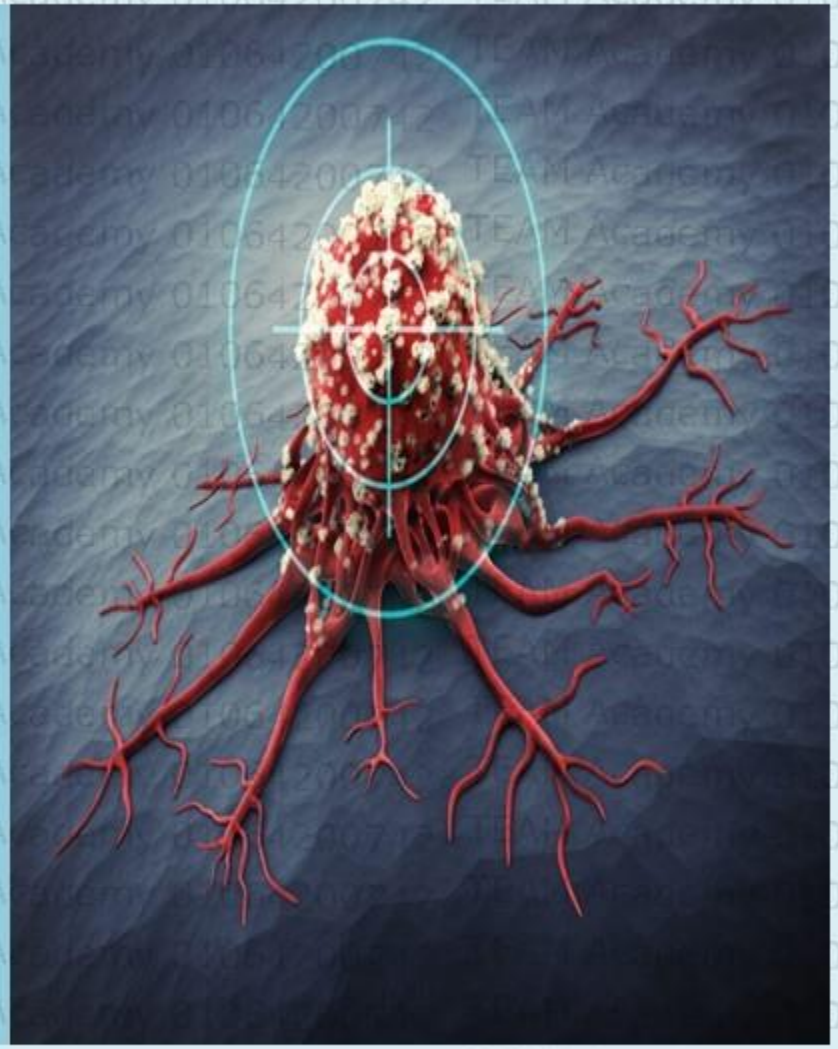

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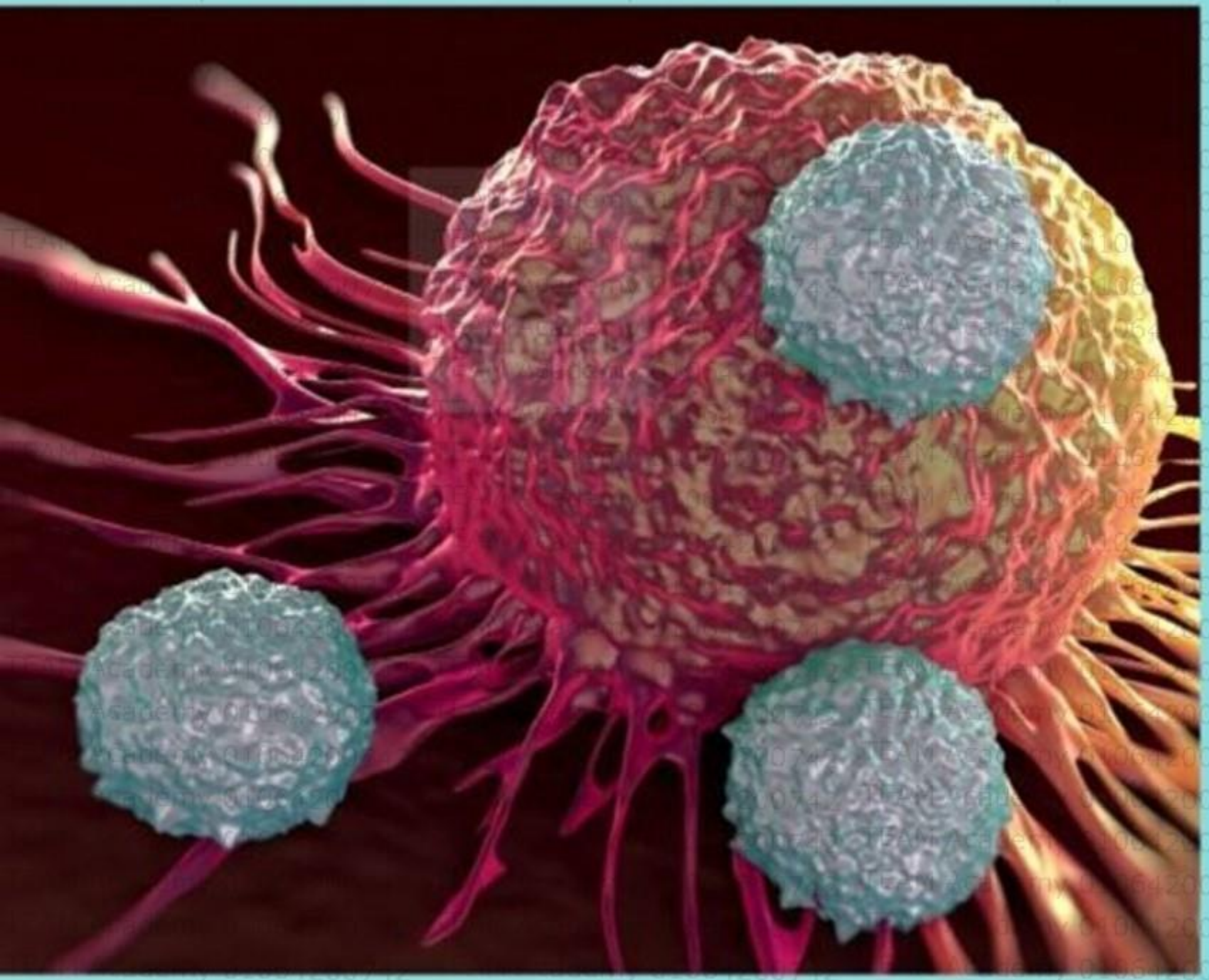


What is CANCER?

What is Cancer?

A malignant **growth** characterised by a **continuing, purposeless, unwanted, uncontrolled and damaging growth of cells** that **differ** structurally and functionally **from the normal cells** from which they developed

cancer is Latin for crab

because an advanced cancer was thought to resemble a crab, with "**claws**" **reaching out into surrounding** tissues.

-The process of **cell proliferation** (cell division and cell growth) is **controlled by genes**

-A cancer forms when this **genetic control is damaged** or lost in one or more cells, which then continue to divide and divide again producing more abnormal cells

Genes involved in Cancer

Proto-oncogenes

-respond to growth signals and are **positive regulators of cell growth**.

-Some of the **proto-oncogenes** have now acquired **mutations(changes in genes structure)** that mean they promote cell growth **even in the absence of growth signals**, i.e. **become oncogenes** (cancer promoting genes) and

e.g :
HER2

Tumour suppressor genes

-**negative regulators of cell growth** and **suppress or check the unregulated growth of cells**

-**In** the case of a **malignancy** there is **no "switching off"** mechanism. i.e **tumour suppressor genes are inactivated**

e.g:
BRCA1
BRCA2
p53 gene

What Causes Cancer?

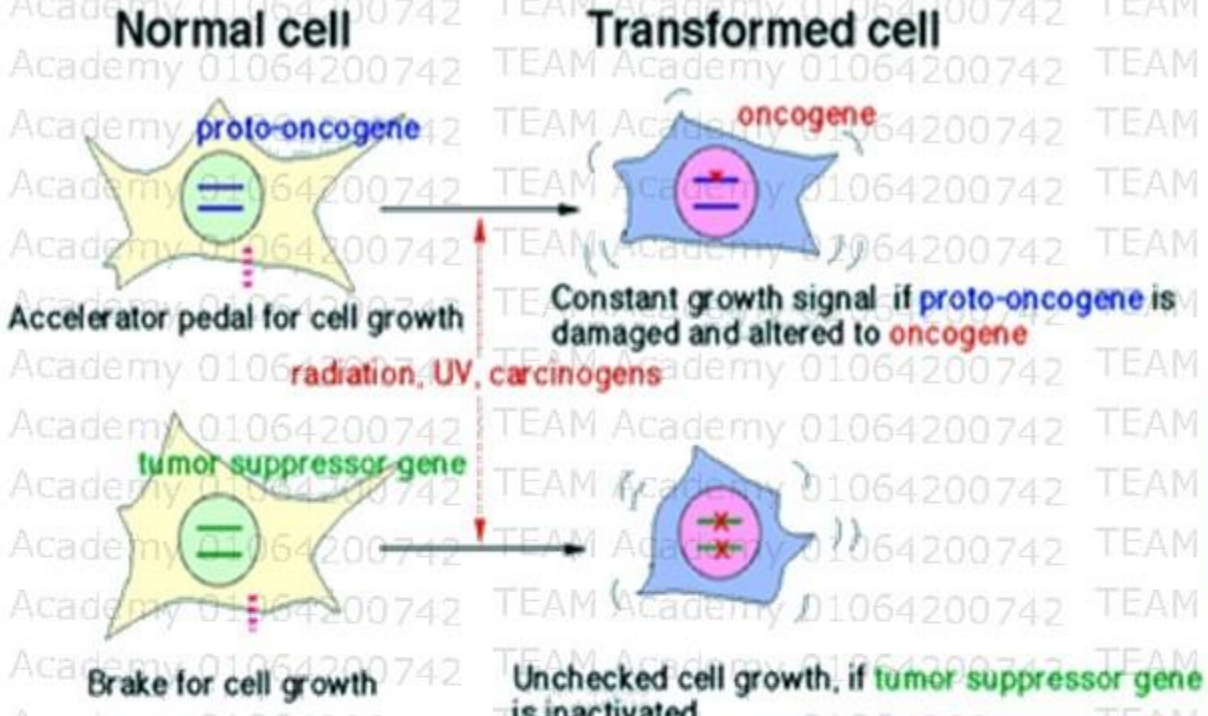
-Cells that have extensive **genetic damage(due to cancer causing agent)** often spontaneously undergo **apoptosis "commit suicide"** for the greater good of the host

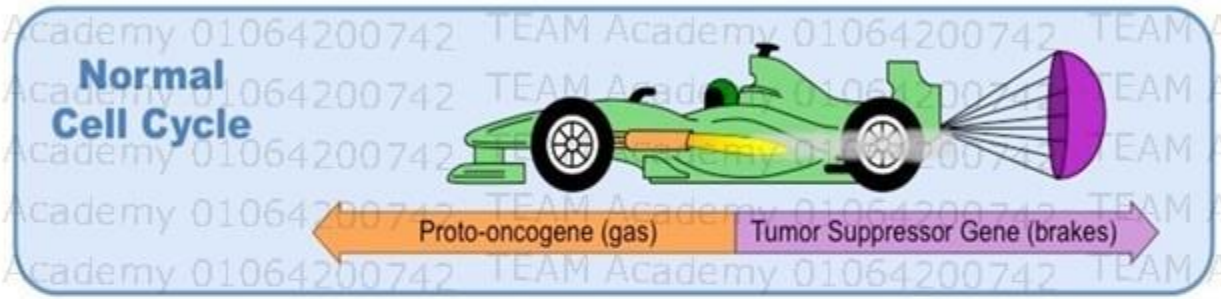
-Cells that **escape,** or evade, this **apoptotic** process **form tumours** that are more resistant to chemotherapy and radiotherapy, and are associated with **poor prognosis.**

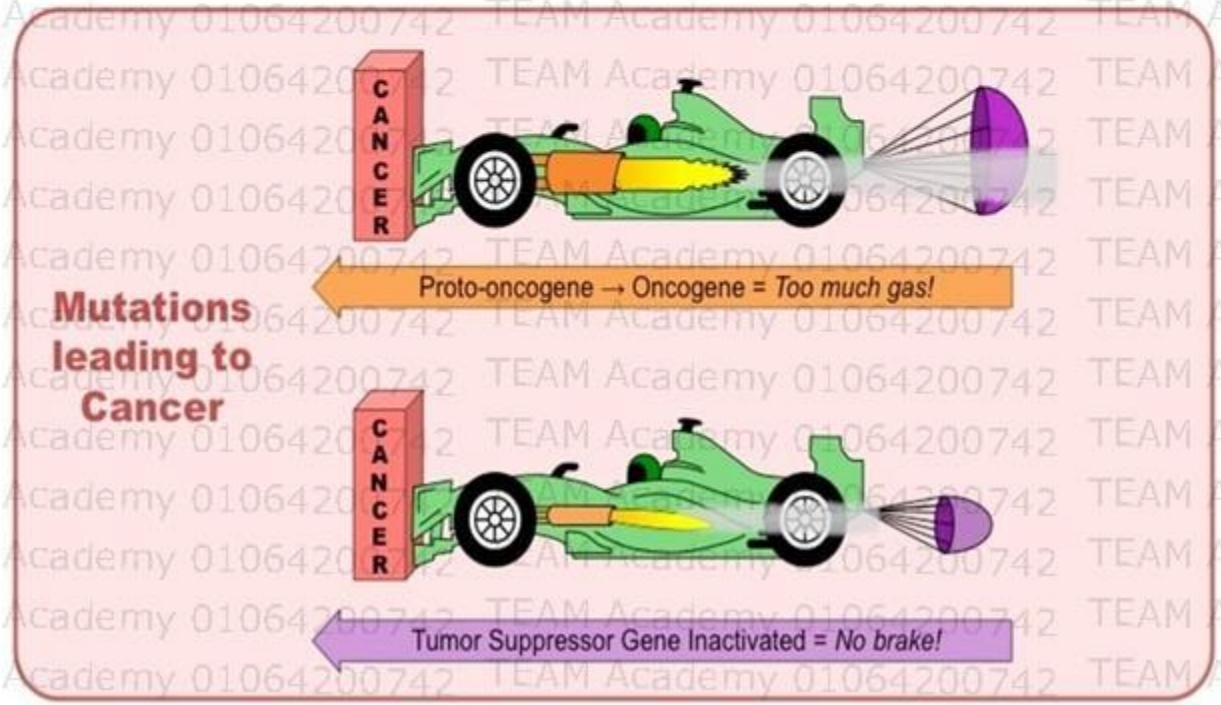
Carcinogens
cancer causing agents

Tobacco Smoking	Alcohol	Sunshine	X-rays and Atomic Irradiation	Pre-Existing Abnormalities Or genetic syndroms
lung, mouth, throat and larynx oesophagus, stomach, pancreas, kidney, bladder, cervix uteri &even the breast Cancer.	both heavy drinkers and heavy smokers in cancers from pharynx to colon and pancreas. There is a secondary association between alcohol and primary liver cancer	UV light causes skin cancer	thyroid cancer and leukaemias	e,.g familial adenomatous polyposis in Colon Cancer &Xeroderma pigmentosum in skin cancer
Industrial Irritants and Carcinogens	**Chemical Carcinogens**	**Hormones**	**Viruses & bacteria**	
osteosarcoma Bladder Cancer	Bladder Cancer	breast & prostate cancer	HPV:anal,cervix & oral cancer EBV:oral Cancer & burkitt lymphoma H.Pylori:gastric cancer	

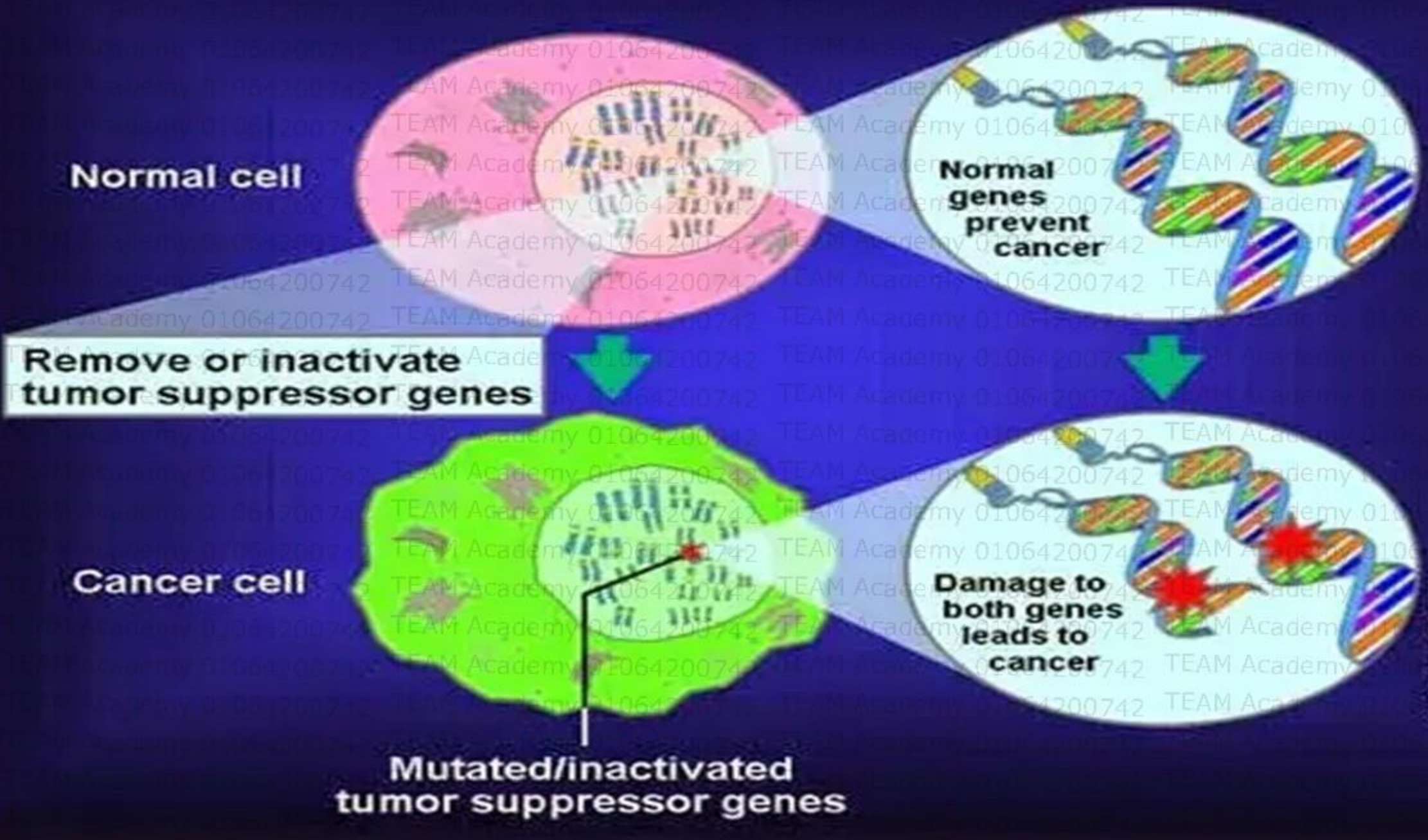
What are oncogenes and tumor suppressor genes?



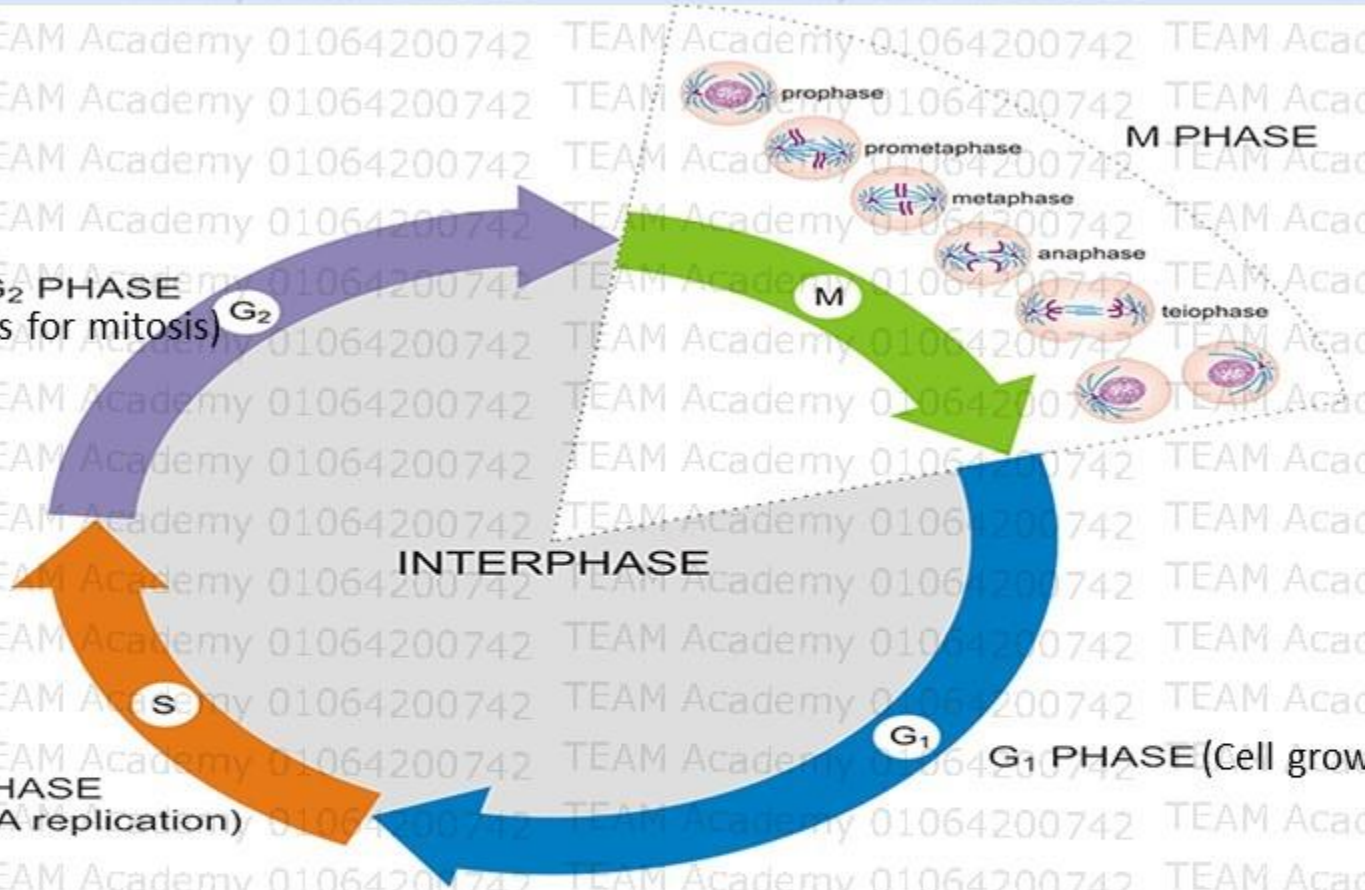




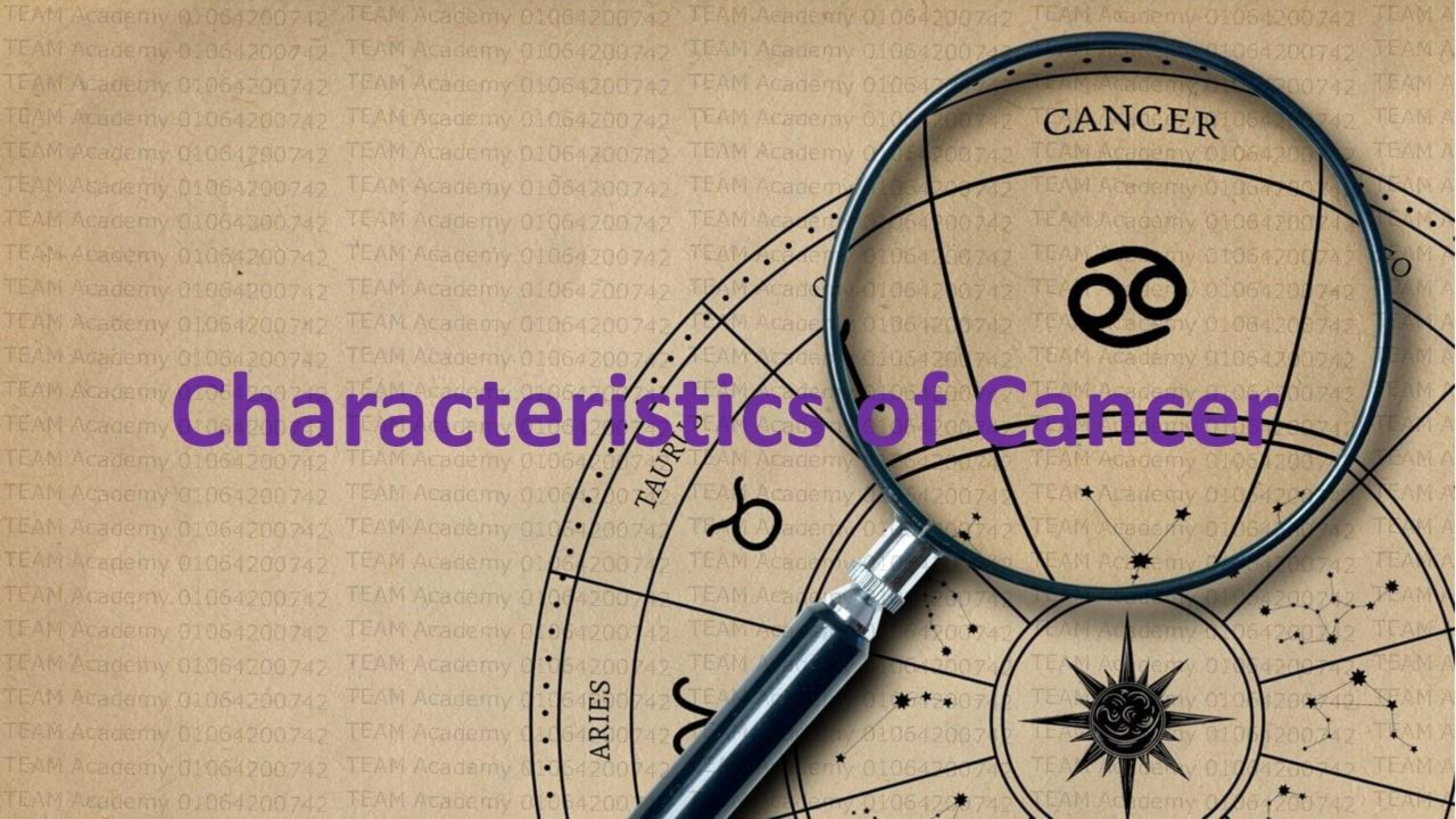
Tumor Suppressor Genes



Cell Cycle & Checkpoints



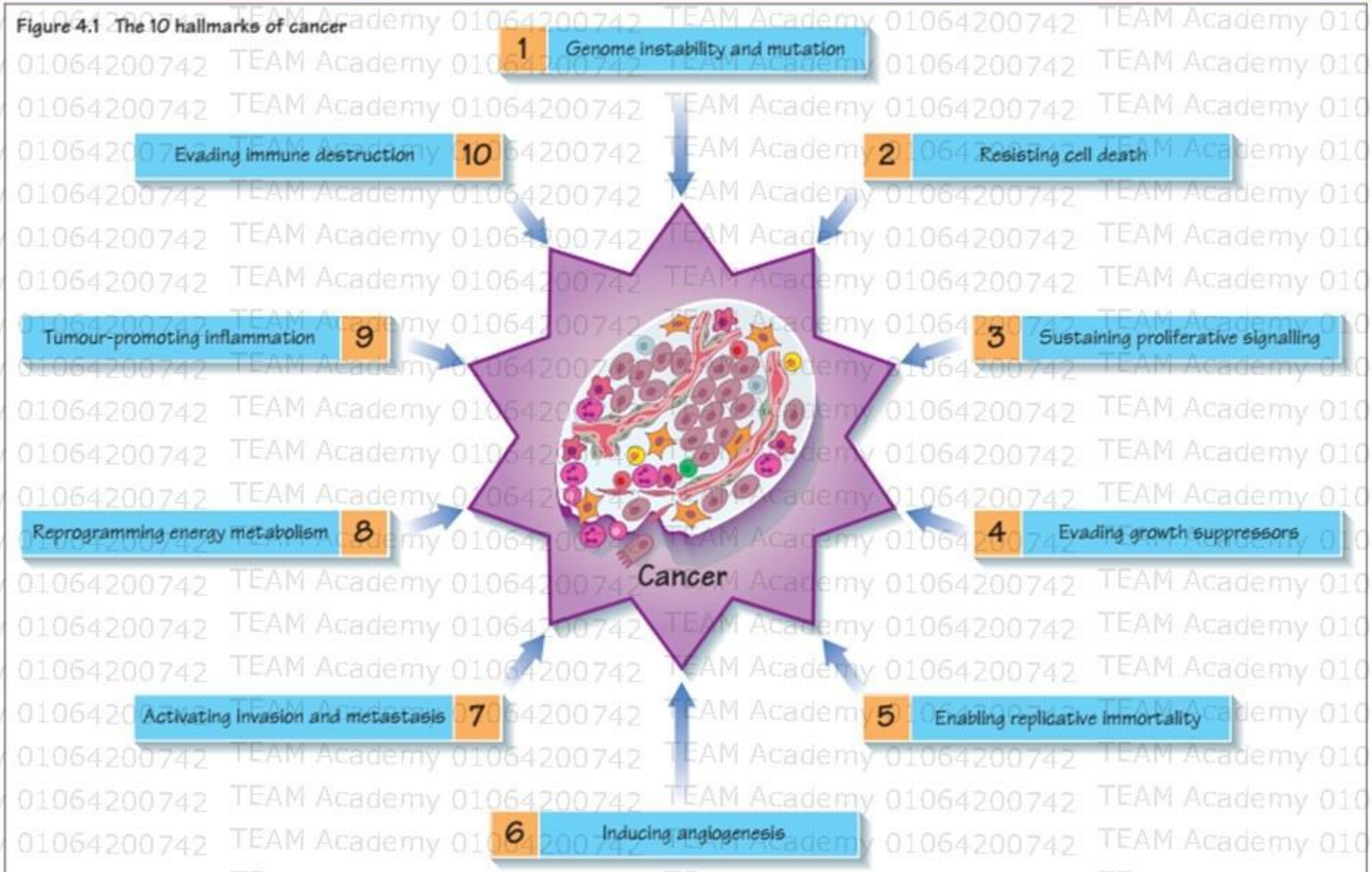
notable checkpoints occur at the G1-S and G2-M transition points. The G1-S checkpoint allows the cell to repair any DNA damage before it is copied in the S-phase, to prevent mutations becoming fixed in the genetic material. The second, G2-M checkpoint allows the cell to ensure that the chromosomes are arranged correctly prior to segregation to the daughter cells .



Characteristics of Cancer

Hallmarks of Cancer

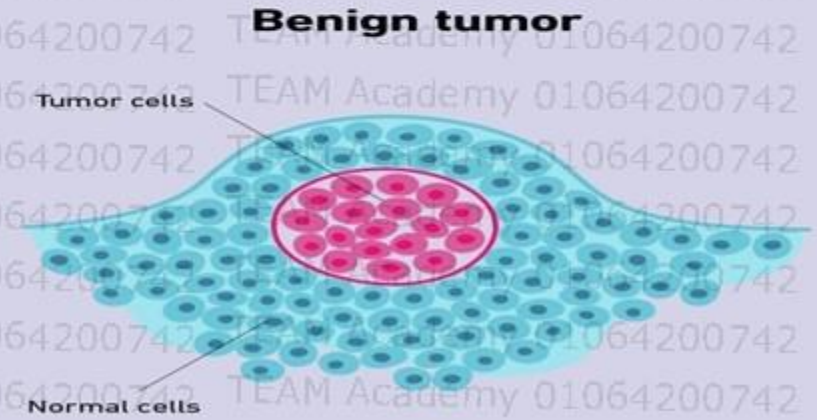
Figure 4.1 The 10 hallmarks of cancer

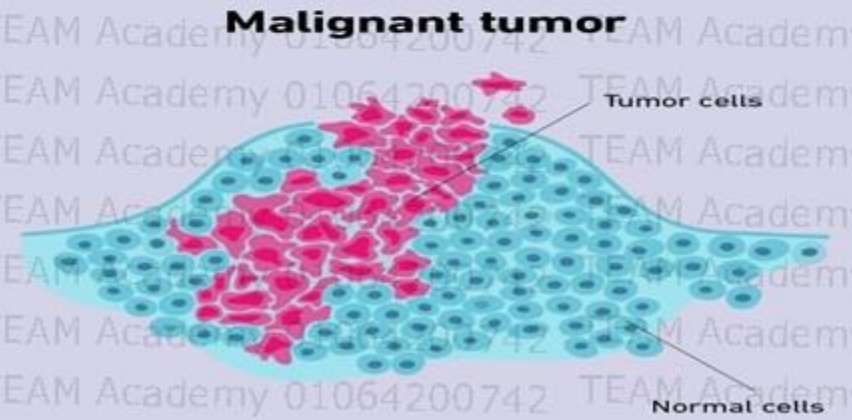


Different between Benign tumor & Malignant tumor (Cancer)

Benign Tumors	**Malignant** Tumors

• Small
• Slow-growing
• Non-invasive
• Well-differentiated
• Stay localized
  • Stay where they are.
  • Can't invade or metastasize.
	• Large
	• Fast-growing
	• Invasive
	• Poorly-differentiated
	• Metastasize
	  • Infiltrate, invade, destroy surrounding tissue.
	  • Then metastasize to other parts of body.





Nomenclature of different types of tumors

Originating tissue	Benign tumour	Malignant tumour
Blood vessel	Angioma	Angiosarcoma
Bone	Osteoma	Osteosarcoma
Cartilage	Chondroma	Chondrosarcoma
Fat	Lipoma	Liposarcoma
Fibrous tissue	Fibroma	Fibrosarcoma
Germ cell	Mature teratoma/dermoid cyst	Immature teratoma Seminoma/dysgerminoma
Glandular epithelium	Adenoma	Adenocarcinoma
Granulocyte		Myeloid leukaemia
Liver	Hepatic adenoma	Hepatocellular carcinoma
Marrow lymphocyte		Lymphocytic leukaemia
Node lymphocyte		Lymphoma
Plasma cell		Malignant myeloma
Skin	Papilloma	Squamous cell carcinoma Basal cell carcinoma
Skin melanocyte	Naevus	Malignant melanoma
Smooth muscle	Leiomyoma	Leiomyosarcoma
Squamous epithelium	Squamous papilloma	Squamous cell carcinoma
Striated muscle	Rhabdomyoma	Rhabdomyosarcoma
Transitional epithelium	Transitional papilloma	Transitional cell carcinoma

EARLY DETECTION SAVES LIFE

Early Detection Of Cancer(Screening) & Diagnosis

Cancer screening describes the **systematic testing of a population in order to detect a cancer before it causes symptoms.**

Screening differ according type of cancer you are screening involves using methods like:

1)**imaging** of organs

2)**Cytology** (looking for cancer cells or other organisms that causes cancer)

3)Testing for **genes** that causes cancer

4)Testing for some proteins that increase in some types of cancer(**tumor markers**)

-These tests are also used for diagnosis of cancer but of course we do them after some symptoms(signs) appear

-we confirm the presence of cancer by taking biopsy(sample) from part of organ we suspect cancer in

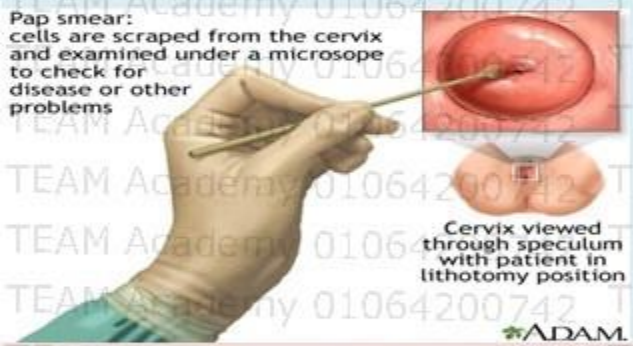
-some of these tests are also used in evaluation of response to treatment & follow up of cancer

Screening Programs

Screening :programs are **simple, non-invasive and relatively inexpensive methods of detecting early cancers in people in high-risk categories**. Early detection before symptoms or signs of cancer have become evident results in significantly better prospects of cure. When certain cancers are known to have a high incidence in a community, governments and health authorities have established on-going screening programs in many countries.

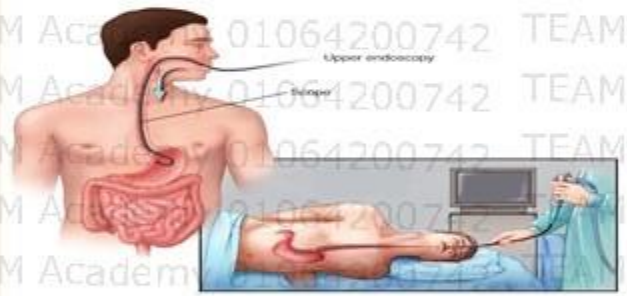
Example of Screening Tests

The Cervical Smear or "Pap" (Papanicolaou) Test
for cervix cancer



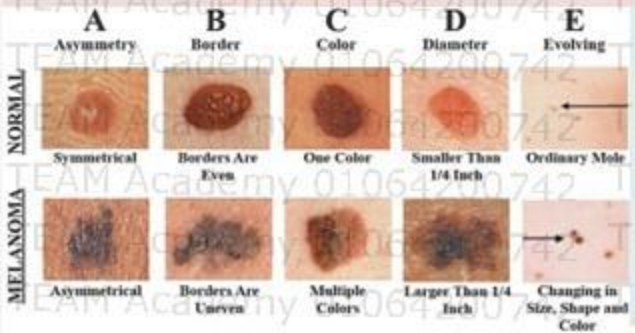
Occult Blood Tests
For bowel cancer

Upper GIT endoscopy
for esophageal cancer

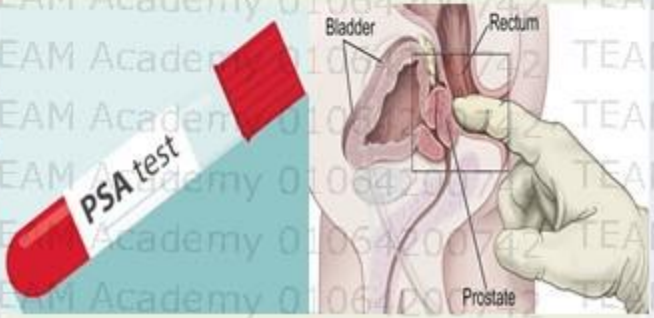


Breast Screenings: Mammography
for breast cancer

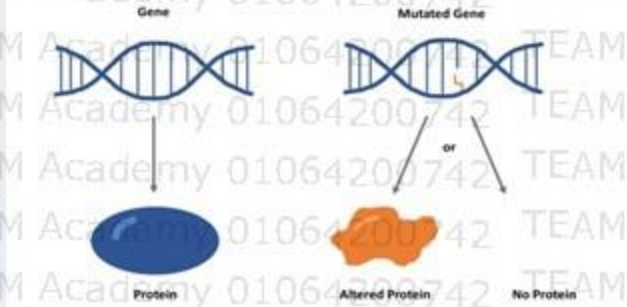
Skin Cancer Screening: Especially the "Mole Check"
for skin cancer



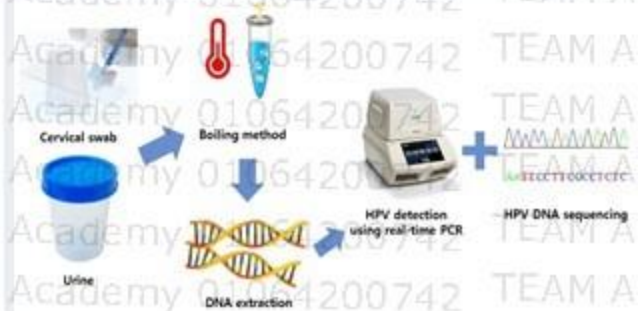
PSA/DRE Screening Test
for prostate cancer



Genetic Testing
some types of cancer



Virology Screening
HPV test for Cervix Cancer

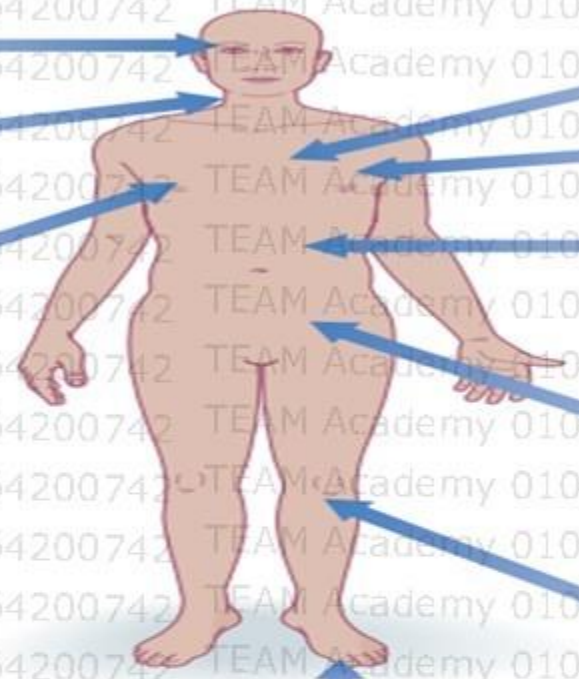


List Of Most Common Tumor Markers

Tumour marker	Related cancers
β2-microglobulin	Myeloma (60%) Non-Hodgkin's lymphoma (15%)
Alpha-fetoprotein (AFP)	Non-seminomatous germ cell tumours (80%) Hepatocellular carcinoma (50%)
CA125	Ovarian epithelial cancer (80%) Gastrointestinal cancer (10%) Breast cancer (5%) Lung cancer (5%)
CA15-3	Breast cancer
CA19-9	Pancreatic cancer (80%) Mucinous tumour of the ovary (65%) Gastric cancer (30%) Colon cancer (30%)
Calcitonin	Medullary cell carcinoma of the thyroid
Carcinoembryonic antigen (CEA)	Colorectal cancer (especially with liver metastasis) Gastric cancer Breast cancer Lung cancer
Human chorionic gonadotrophin (β-hCG)	Choriocarcinoma (100%) Non-seminomatous germ cell tumours (50–80%) Seminoma (15%)
Inhibin	Granulosa cell cancer of the ovary
Neurone-specific enolase	Neuroblastoma Small cell lung cancer
Paraproteins (monoclonal)	Myeloma (98%)
Placental alkaline phosphatase (PLAP)	Seminoma (50%) Ovarian dysgerminoma (50%)
Prostate-specific antigen (PSA)	Prostate cancer (95%)
SCC	Squamous cell cervical cancer Squamous head and neck cancer
Thyroglobulin	Papillary and follicular thyroid cancer

List Of Most Common Cancer Symptomps

Figure 10.1 Clinical examination of a patient suspected of having cancer



Face
- Conjunctival pallor
- Icterus, jaundice
- Horner's syndrome
- Cushingoid features
- Heliotrope rash

Lymph nodes
- Neck
- Supraclavicular
- Axillary
- Antecubital
- Inguinal
- Femoral
- Para-aortic

Breast examination
- Peau d'orange
- Puckering
- Erythema
- Nipple changes

Hands
- Clubbing
- HPOA
- Signs of smoking
- Pallor
- Tylosis of palms

Observation
- Skin changes
- Ascites
- Cushingoid appearance
- Cachexia
- Dehydration
- Temperature (Pel–Ebstein)

Other
- Haematuria
- PV examination
- PR examination
- Fundoscopy

Periphery
- Calf tenderness (DVT)
- Clubbing (if present in hands)
- Ankle tenderness (HOA)

Cardiovascular
- SVC obstruction
- Atrial fibrillation
- Pericardial effusion
- Hypo-, hypertension

Respiratory
- Stridor, obstruction
- Consolidation
- Pleural effusion

Abdomen
- Surgical scars
- Umbilical nodule
- Mass in epigastrium
- Visible peristalsis
- Abdominal distension
- Ascites
- Hepatomegaly
- Splenomegaly
- Renal mass
- Pelvic mass
- Adenexal mass

Neurological
- Focal neurological signs
- Sensory deficit
- Spinal cord compression
- Memory deficit
- Personality change
- Cerebellar signs
- Myasthenia gravis

Skeletal survey
- Focal bone tenderness (pelvis, spine, long bones)
- Wrist tenderness (HOA)

Table 10.1 Local features of malignant disease

Symptoms	Typical tumour primary site
Abdominal swelling (ascites)	Ovary, stomach, pancreas
Airway obstruction, stridor, cough, recurrent infection	Bronchus, thyroid
Bone pain or fracture	Bone (primary sarcoma, secondary metastasis from breast, prostate, bronchus, thyroid, kidney)
Change in bowel habit, abdominal discomfort or pain	Colon, rectum, ovary
Dysphagia	Oesophagus, bronchus, stomach
Haemorrhage	Stomach, colon, bronchus, endometrium, bladder, kidney
Jaundice	Hepatocellular carcinoma, lung, breast, colon, melanoma, stomach, oesophagus, endometrium, prostate, cervix, neuroendocrine tumours, renal
Lump	Breast, lymph node (any site), testis
Odynophagia, early satiety, vomiting	Bronchus, oesophagus, stomach, colon, rectum, ovary
Skin abnormality	Melanoma, basal cell carcinoma, all forms of skin cancer
Ulcer	Oesophagus, stomach, anus, skin

Organ Imaging That may help diagnosing ,Screening & follow up of Cancer

X-rays

tissues are of similar consistency and have similar penetration to X-rays as do tumours so that it is **not so easy to detect tumour shadows in soft tissues by simple X-rays**,

Barium (Baryum) and Iodine Contrast X-Rays

A barium meal is swallowed This outlines the shape of the stomach. If a cancer is present it may show as an abnormality in the shape or in the outline of the stomach. Similarly, a barium enema used in the lower bowel

Radiographic Screening

Air used to replace some of the fluid in the (ventricles) of the brain. This allows X-ray films to detect evidence of some brain lesions by the contrasting penetration of X-rays passing through air as compared to a tumour that might be distorting the shape of the brain ventricles.

Mammography

A mammogram is a special X-ray of the breast avoided in women who may be pregnant or wish to

Isotope Scans (Nuclear Scintigraphy)

technetium, is concentrated in bone Radioactive iodine, for example, is concentrated in the thyroid gland amount of uptake, size, shape, position, and consistency of tissue in the organ can be determined from such a test

CT Scan or CAT Scan (Computerised Axial Tomography)

small doses of X-rays were used to construct a picture of tissues in a cross-section of the trunk, head and neck, or limbs. Many cross-sectional pictures of the abdomen for example, are taken, thus allowing a three-dimensional image concept to be developed. The position, size and shape of all the organs, major blood vessels, bones and muscles in the abdomen can be seen and the position, size and density of any abnormal tumour can often be assessed with considerable accuracy.

Ultrasound Scans

ultrasound shows more information in the more dense breast tissue of younger women. It is also completely safe in studies during pregnancy or ovulation

Positron emission tomography (PET)

A radiopharmaceutical — a radioisotope attached to a drug—is injected into the body as a tracer. When the radiopharmaceutical undergoes beta plus decay, a positron is emitted, and when the positron interacts with an ordinary electron, the two particles annihilate and gamma rays are emitted.[2] These gamma rays are detected by gamma cameras to form a three-dimensional image, in a similar way that an X-ray image is captured

MRI (Magnetic Resonance Imaging)

MRI scanners use strong magnetic fields, magnetic field gradients, and radio waves to generate images of the organs in the body. MRI does not involve X-rays or the use of ionizing radiation, which distinguishes it from computed tomography (CT) and positron emission tomography (PET) scans

Fig. 7.3. A barium (baryum) meal X-ray showing a "filling defect" of the greater curvature of the stomach due to a gastric cancer

Fig. 7.4. A barium (baryum) meal X-ray showing a "filling defect" of the greater curvature of the stomach due to a gastric cancer

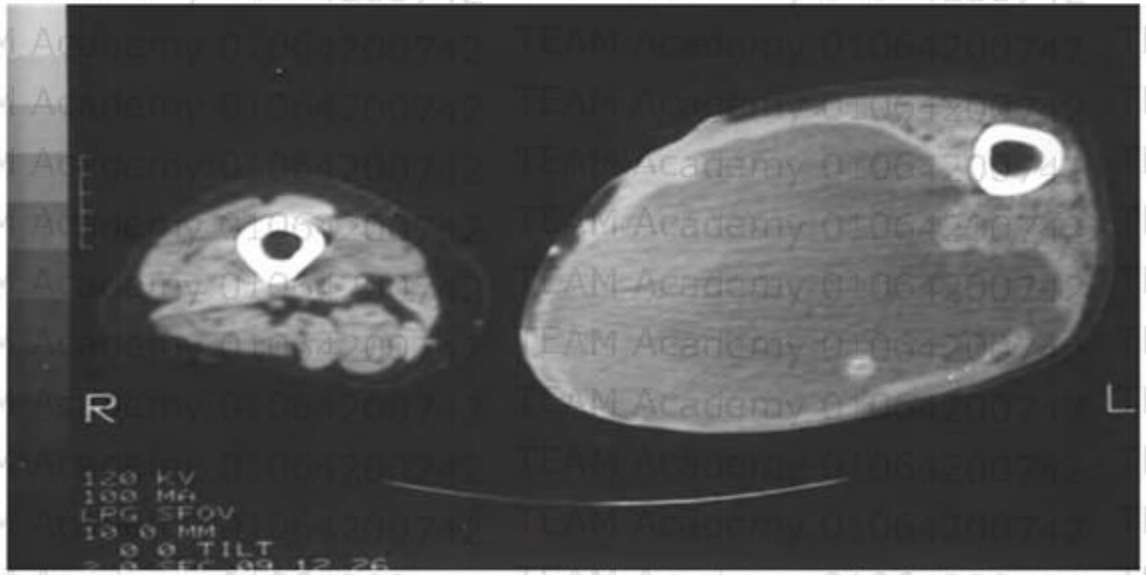


Fig. 7.7. CT scan showing a cross-section of both thighs with a large sarcoma in one thigh

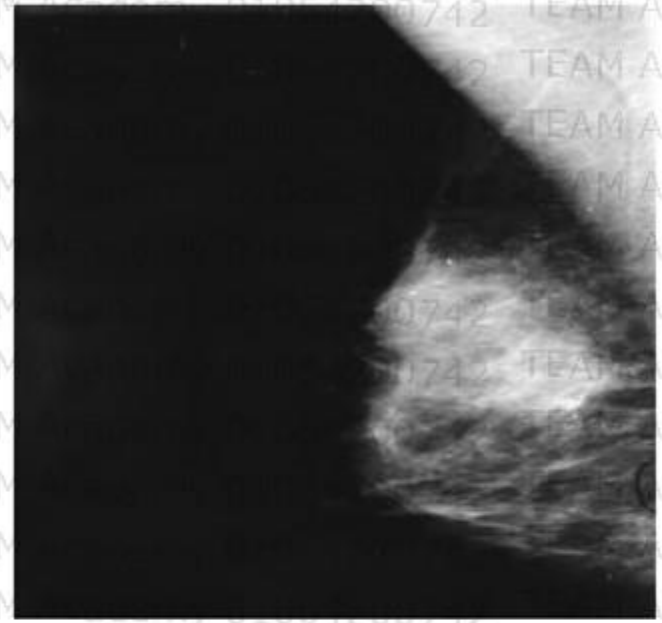


Fig. 7.2. Mammogram showing a rather dense area of breast with a cluster of spicules of calcification suggestive of breast cancer

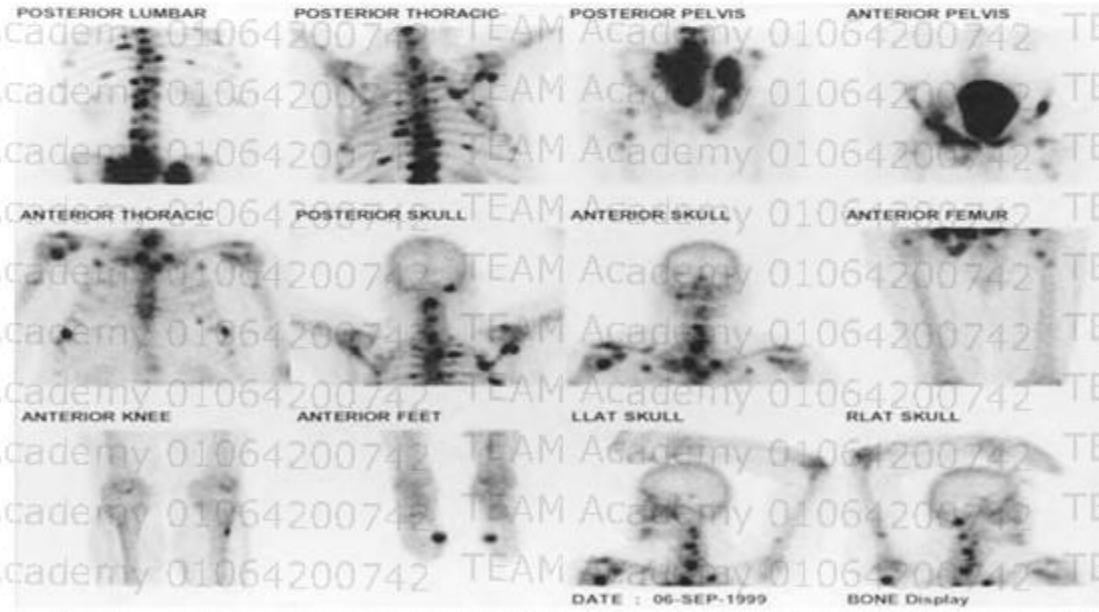
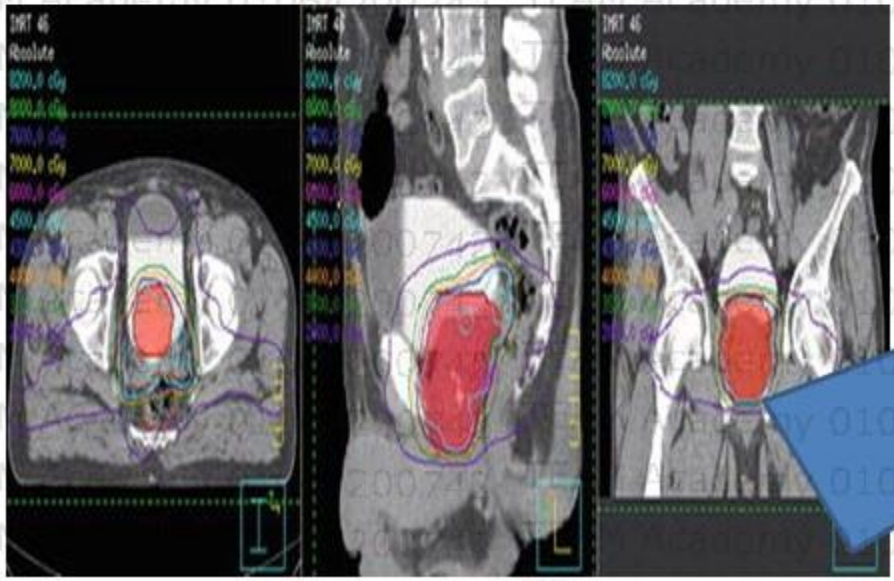
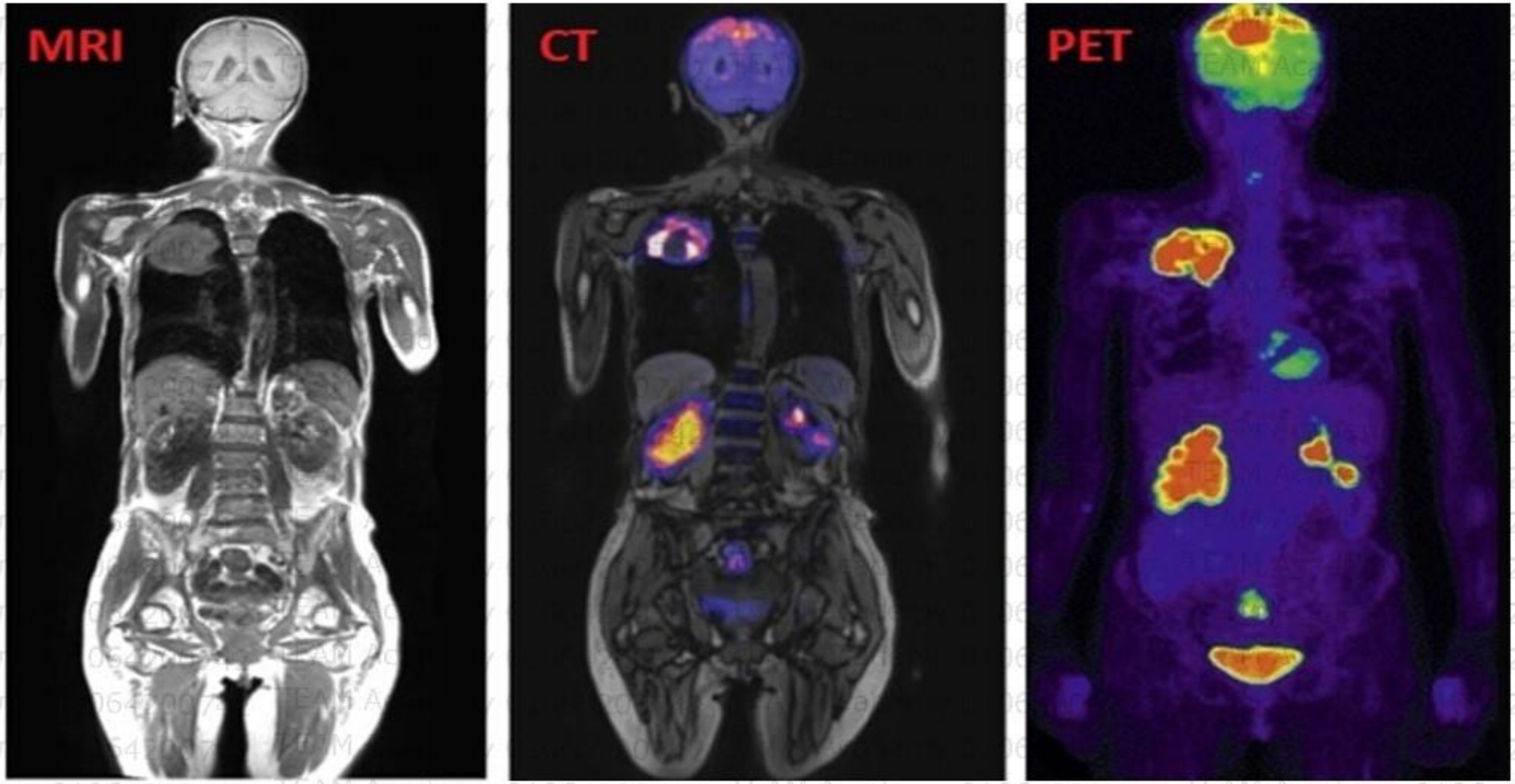


Fig. 7.6. Radio-isotope bone scans showing many metastatic cancer deposits in bones (*dark spots*). The patient had advanced metastatic prostate cancer

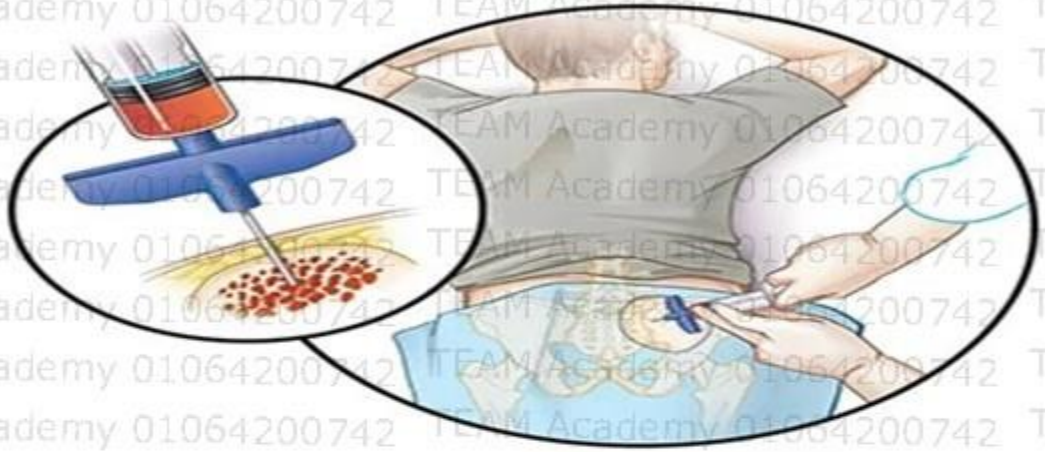
CT Scan

Computed Tomography

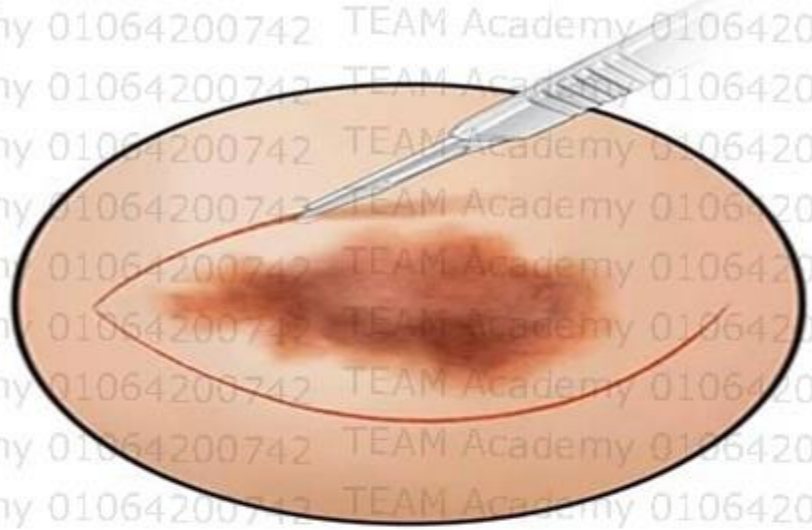



MRI
CT
PET

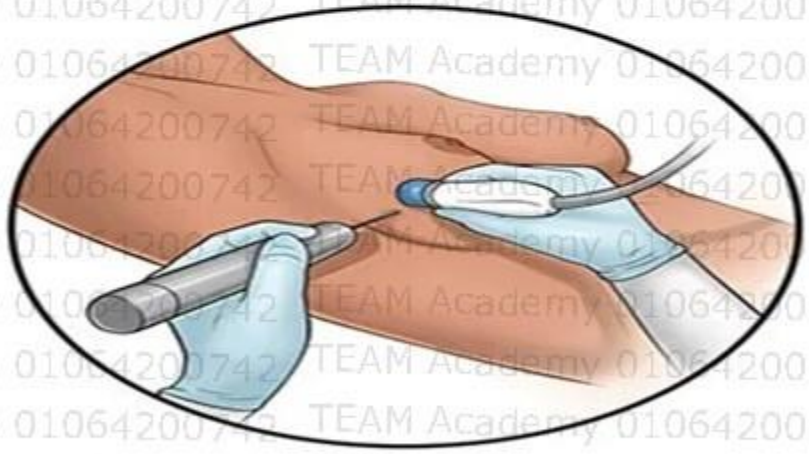
Biopsy



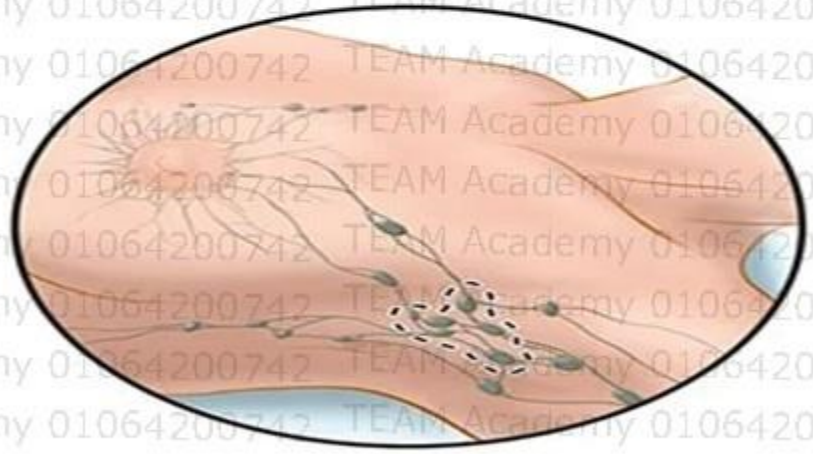
Bone marrow biopsy



Excisional biopsy



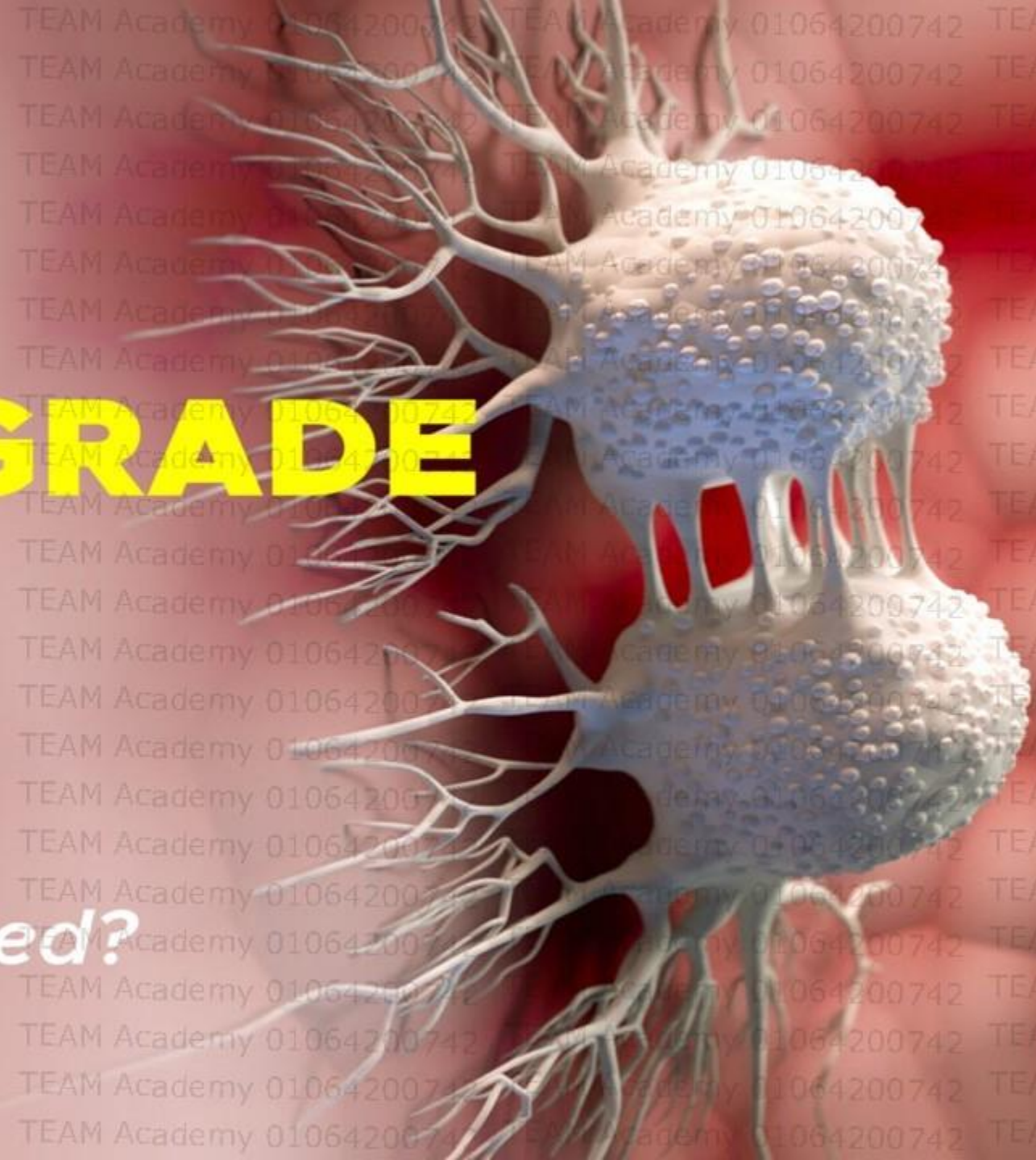
Needle biopsy



Sentinel node biopsy

CANCER STAGE & GRADE

Why is Cancer Staging and Grading Needed?



Typing, Grading and Staging of Cancer

Cancer Typing

The treatment team depends on the pathologist for confirmation of the presence of cancer, the cancer type and other features of the cancer.

All Cancers fall into 2 major categories

A)Solid tumors e.g:breast cancer

B)Hematological Cancers e.g:Lymphoma

Cancer Grading

, highly differentiated tumour cells(that closely resemble their cells of origin) may be either benign or may be very low-grade cancers with little tendency to grow rapidly or to metastasise early. Whereas poorly differentiated, anaplastic cancer cells that have often lost all special features of their tissue of origin are much more likely to behave in an **aggressive** fashion and invade nearby tissues as well as to metastasise to other sites.

Nuclear pleomorphism is the degree to which cell nuclei vary in size, shape and in staining patterns. The more pleomorphic the cell nuclei, the more aggressive the likely behaviour of the cancer.

Example:GI<GII<GIII

Staging of Cancer

TNM system for solid tumors

"T" :size of the tumour and the extent of its spread on scale of 1–4; T1 being a small localised cancer; T4 being an advanced cancer that is destroying surrounding tissues and unlikely to be curable.

"N":involvement of adjacent lymph nodes on scale of 0–3

N1 indicates only; N2 indicates that a further set of lymph nodes is involved; and N3 indicates distant involvement of lymph nodes.

"M":spread of cancer to distant organs(metastasis) on scale 0–1

The best prognosis cancers are T1, N0, M0 and the worst prognosis cancers are T4, N3, M1

according to above cancer staged from I-IV

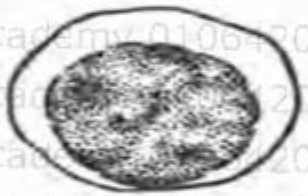
According to Cancer Type,Grade & Stage we decide :

1)prognosis of Cancer i.e higher grade and stage mean bad prognosis

2)What Type of Therapy patient needs e.g : early stage I requires surgery only in most cases while higher II-III requires chemotherapy with or without radiotherapy ,stage IV meanwhile derive no benefit of surgery or radiotherapy so chemotherapy and/or targeted therapy are the possible choices

Cancer Grades

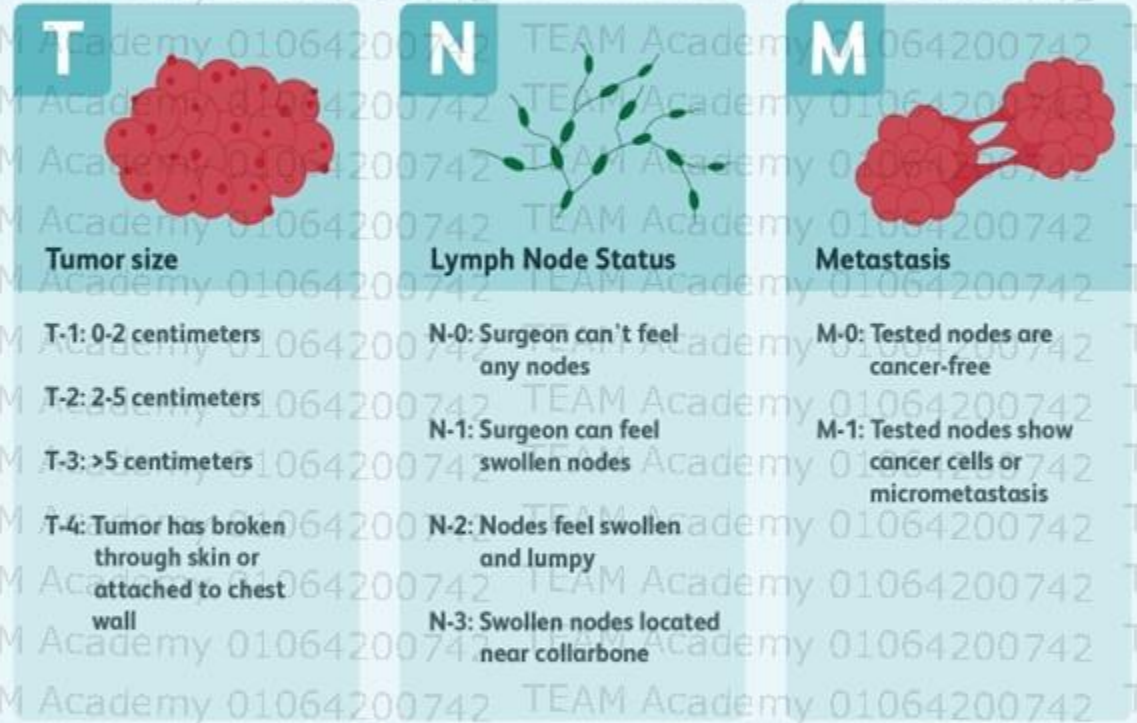
Normal Cell



Malignant Cell with little Anaplasia

Anaplastic Malignant Cell

TNM System for Staging Breast Cancer



How to measure Patient Performance to decide how much intensive the therapy will be?

ECOG/ Zubrod Scale		Karnofsky Scale	
0	Normal activity	100	Normal; no evidence of disease
		90	Able to perform normal activities with only minor symptoms
1	Symptomatic and ambulatory; cares for self	80	Normal activity with effort; some symptoms
		70	Able to care for self but unable to do normal activities
2	Ambulatory >50% of time; occasional assistance	60	Requires occasional assistance; cares for most needs
3	Ambulatory ≤50% of time; nursing care needed	50	Requires considerable assistance
		40	Disabled; requires special assistance
		30	Severely disabled
4	Bedridden	20	Very sick; requires active supportive treatment
		10	Moribund

Treating Cancer

Can Cancer Be Cured? An Outline of Prognosis

A small cancer detected early and before it has spread or involved other tissues may be eminently curable whereas the same cancer neglected, perhaps for some months, until it has enlarged and spread to other sites, may be quite incurable.

Many years ago a great American pathologist, Arthur Purdy Stout, said:
"The best chance of curing cancer lies in the hands of the therapist who makes the first attempt".

Nowadays this should be paraphrased as:
"The best chance of curing many advanced and aggressive cancers lies in the hands of the team of therapists that makes the first attempt".

That is, a cancer that has recurred after a failed attempt at treatment is more difficult to cure than it would have been at the first attempt

breast and bowel and cancers of the uterus curable now that methods of early detection

Cancers with the worst prognosis deep body tissues oesophagus, pancreas and lung

Types of Cancer Treatment

Surgery

Radiation Therapy

Chemo Therapy

ImmunoTherapy

Hormone Therapy

Targeted Therapy

Stem cell therapy

I)Surgery

-was the first effective form of cancer treatment. It is now used to establish a diagnosis, to effect a cure or in some advanced or incurable cases, to give good palliation and relief of symptoms. When possible the surgeon's primary objective is to excise the cancer in its entirety, together with all adjacent tissues (and lymph nodes)into which cancer cells may have spread

-surgeries can be followed by other types of cancer treatment like chemotherapy or radiotherapy to prevent tumor to come back again(recurrence)

-some times tumor is large so needs treatment like chemotherapy or radiotherapy to shrink tumor and make it easy to remove

Types of surgery according to extent of organ removal

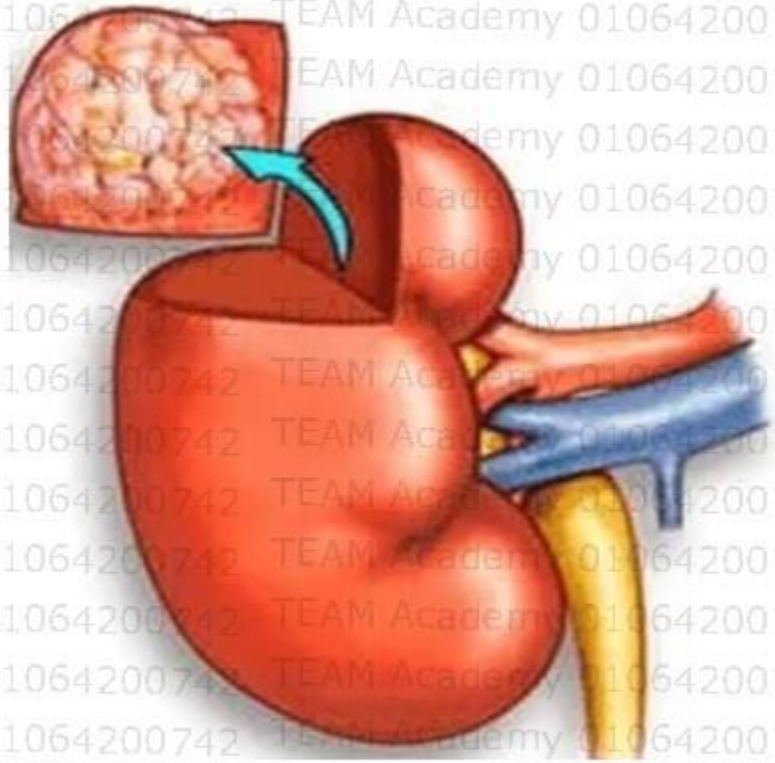
1)**Partial**:removal of tissue part that contains cancer

2)**Total/Radical**:removal of all organ

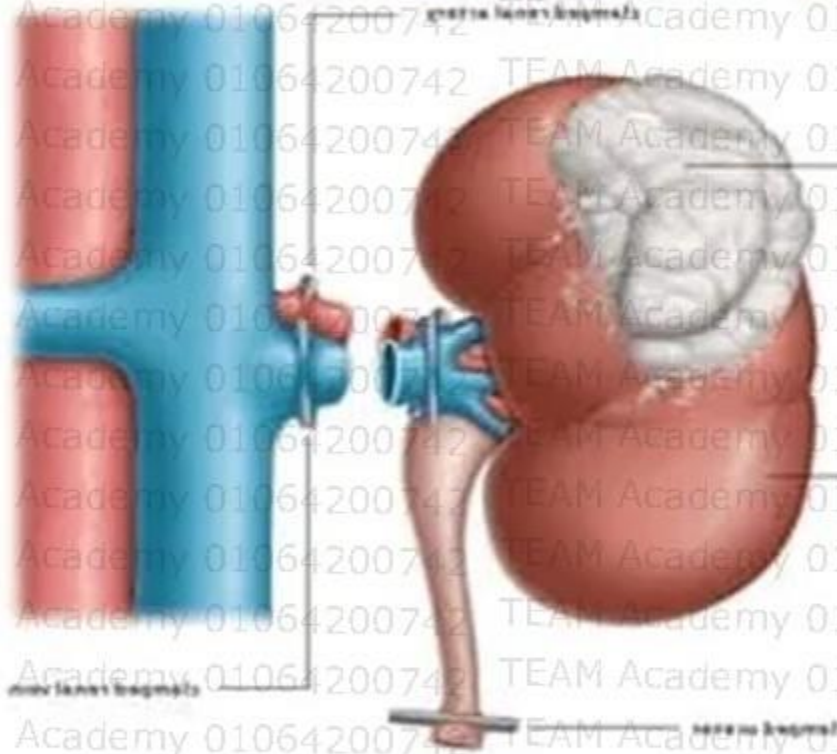
Naming of surgery

By adding ectomy to the name of organ e.g:gastrectomy is resection of stomach

Partial Nephrectomy



Radical Nephrectomy



II)Radiotherapy

Types of beams used in radiation therapy

Radiation beams used in external radiation therapy come from three types of particles:

- photons
- protons
- Electrons

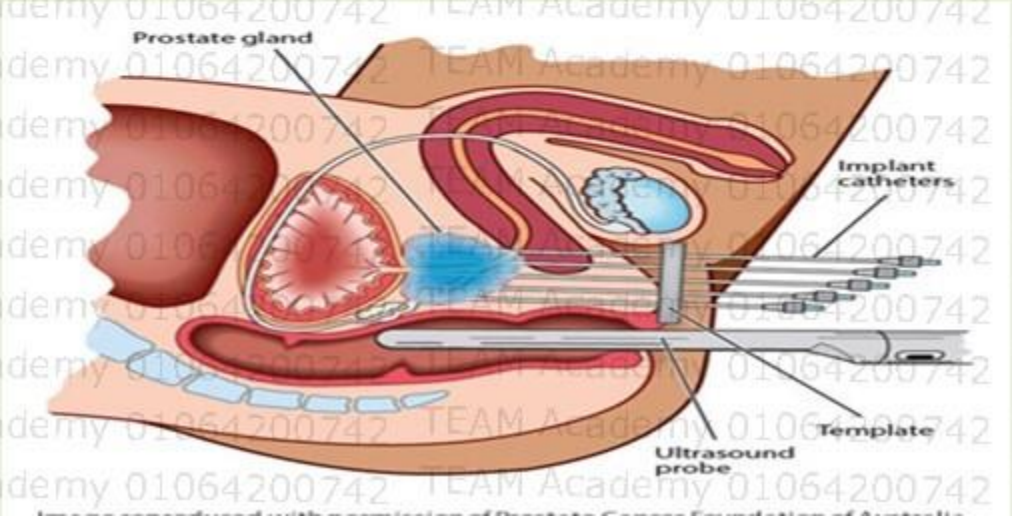
Radiotherapy Can Be delivered By 2 techniques

EBRT

Using a special X-ray machine called a linear accelerator, EBRT delivers high-energy rays to tumors. The machine delivers radiation from any angle and shapes radiation beams to the contour of the tumor. The machine moves around the body without touching the patient, aiming radiation at the cancer. Some types of focused EBRT target a tumor with higher, more precise doses of radiation, while reducing damage to healthy tissue and nearby organs. As a result, modern EBRT may help reduce the risk of side effects associated with traditional radiation treatment

Brachytherapy

Brachytherapy is a form of radiotherapy in which radio-active needles or "seeds" are inserted into a tumour to give a measured dose of irradiation directly to the cancer. The dose of irradiation given by such needles (withdrawn after the required dose has been administered) or "seeds" (left permanently in place in the cancer) is critical.



III)Chemotherapy (Cytotoxic Drug Treatment)

n 1945 it was first observed that a gas that had been used during World War I, destroyed dividing cells, and so nitrogen mustard was discovered as being a drug that could be used clinically against cancer cells in patients. This was the beginning of modern anti-cancer chemotherapy

The present anti-cancer drugs are grouped or classified according to how they affect dividing cells

See Figure

Using Combined Anti-Cancer Agents

(oncologist) selects drugs that are known to be effective against the type of cancer being treated with least possible damage to normal body cells. In general, appropriate combinations of effective drugs are more effective than large and increasingly toxic doses of

Time and Concentration of Anti-Cancer Cytotoxic Drugs on Different Cancer Cell Types

For example 5FU is generally more effective if given by continuous infusion over several days whereas melphalan seems to have a greater impact given in greater concentration over a shorter period, possibly an hour or so. Similarly cancers of different types respond differently to different periods of exposure and to different concentrations of agents. Gastrointestinal cancers and mouth and throat cancers seem to respond best to continuous prolonged drug exposure over days or weeks whereas melanoma responds best to a more intense concentration of agents that can only be given over a short period.

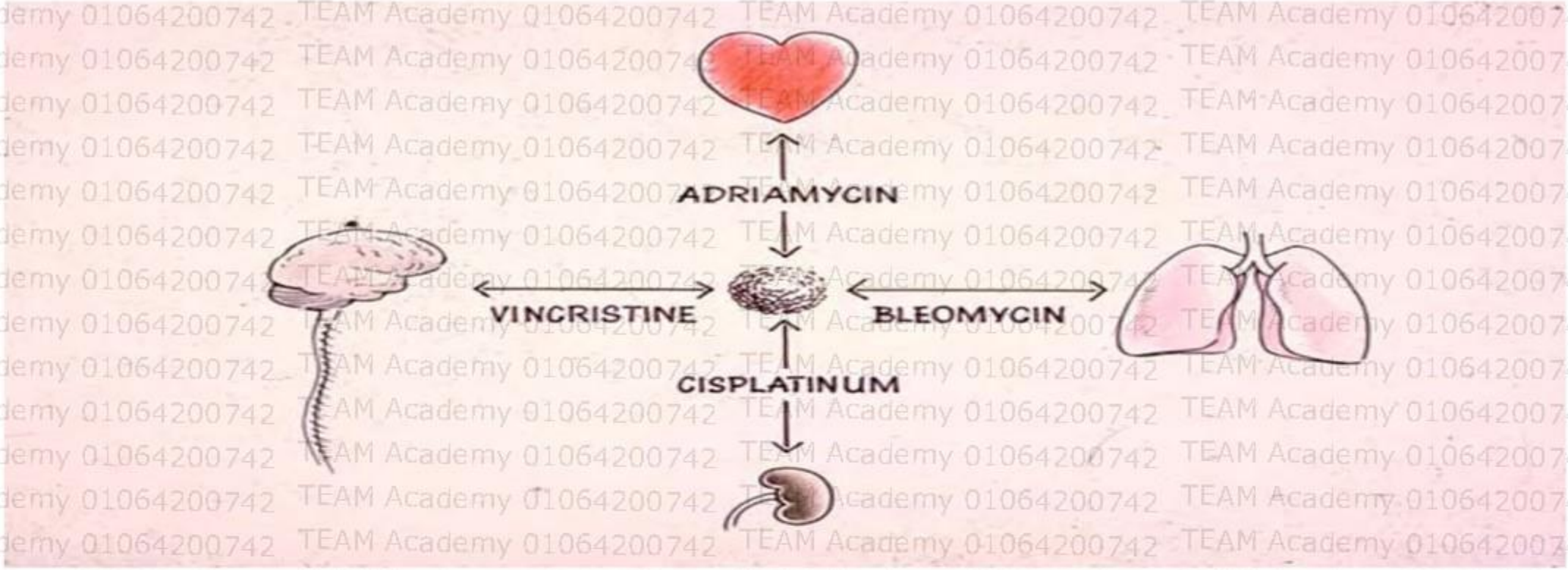


Fig. 8.4. Diagram indicating the principle of use of multiple agents in combination in treating a cancer rather than using larger and more toxic doses of just one agent. As illustrated, provided the drugs are known to be active against the type of cancer being treated, a selection of two or more agents should have increased activity against the target cancer cell. It is like hitting the cancer cell in two or more places at the same time. It is safer to avoid using drugs with the same side effects so that normal cells are less likely to be damaged by multiple agents

one drug only. Much research is constantly being carried out to discover the most effective and safest combinations and dose and timing schedules of drugs against different types of cancer with minimal damage to normal dividing cells (Fig. 8.4).

Class	Example agents	Mode of action
Alkylating agents	**Bifunctional alkylating agents** • Nitrogen mustard • Cyclophosphamide • Ifosfamide • Chlorambucil • Melphalan	Alkylating agents transfer an alkyl group to the purine bases of DNA, which are adenine and guanine. Bifunctional alkylating agents form covalent bonds between two different bases, resulting in interstrand or intrastrand cross-links. This inhibits DNA synthesis and therefore acts during S phase of the cell cycle. Bifunctional agents can act on more than one base and are more cytotoxic
	Monofunctional alkylating agents • Dacarbazine • Temozolomide • Nitrosureas	Monofunctional alkylating agents cannot form cross-links but cause adducts. This inhibits DNA synthesis and therefore acts during S phase of the cell cycle. Monofunctional agents are more mutagenic and carcinogenic than bifunctional agents
Intercalating agents	**Platinum compounds** • Cisplatin • Carboplatin • Oxaliplatin	Platinum agents intercalate and disrupt the steric integrity of the DNA double helix but also form intrastrand links similar to those formed by alkylating agents
	Anthracyclines • Doxorubicin • Daunorubicin • Epirubicin **Anthraquinones** • Mitoxantrone	Anthracyclines intercalate into the DNA major groove between base pairs of the DNA double helix. This action is non-covalent and therefore not base specific. This disrupts the steric integrity of the DNA double helix and blocks DNA replication. The main target for these agents is the enzyme topoisomerase II
Topoisomerase I/II inhibitors	**Topoisomerase I inhibitors** • Topotecan • Irinotecan **Topoisomerase II inhibitors** • Etoposide • Teniposide	Topoisomerase enzymes prevent DNA strands from becoming tangled by cutting DNA and allowing it to wind or unwind. Topoisomerase I breaks single-strand DNA and relieves torsion, and inhibitors act in S phase and prevent the re-ligation step of the nicking-closing reaction, trapping topoisomerase I in a covalent complex with DNA. Topoisomerase II breaks both strands of DNA and allows the other strand to pass through and re-ligate

Antimetabolites	**Antifolates** • Methotrexate • Raltitrexed **Pyrimidine analogues** • 5-fluorouracil • Gemcitabine • Cytosine arabinoside **Purine analogues** • 6-mercaptopurine • 6-thioguanine	Antimetabolites are structurally related to natural compounds and inhibit the metabolism of compounds necessary for DNA, RNA, or protein synthesis. Most of these agents have activity during S phase
Tubulin binders	**Vinca alkaloids** • Vincristine • Vinblastine • Vindesine • Vinorelbine **Taxanes** • Paclitaxel • Docetaxel	The vinca alkaloids bind to the tubulin dimer and prevent the assembly of microtubule filaments and therefore interfere with function of the mitotic spindle and prevent cell division during the M phase of the cell cycle. The taxanes bind to tubulin as a polymerised molecule and prevent disassembly back into the dimeric form. They act during the M phase of the cell cycle
Antibodies	Rituximab (CD20) Bevacizumab (VEGF) Trastuzamab (HER2 receptor)	Monoclonal antibodies bind to cell surface proteins expressed in the target tissue. High-affinity binding prevents the normal ligand from attaching and therefore inhibits the normal activation of the receptor. This diminishes the intracellular signal that drives cellular processes such as angiogenesis or cell growth
Kinase inhibitors	Imatinib (BcrAbl, C-Kit) Erlotinib (EGF receptor) Lapatinib (HER2 and EGF receptors)	Kinase inhibitors are small molecules that bind to intracellular domains of a cell-surface receptor and prevent activation of the intracellular signals that drive cellular processes

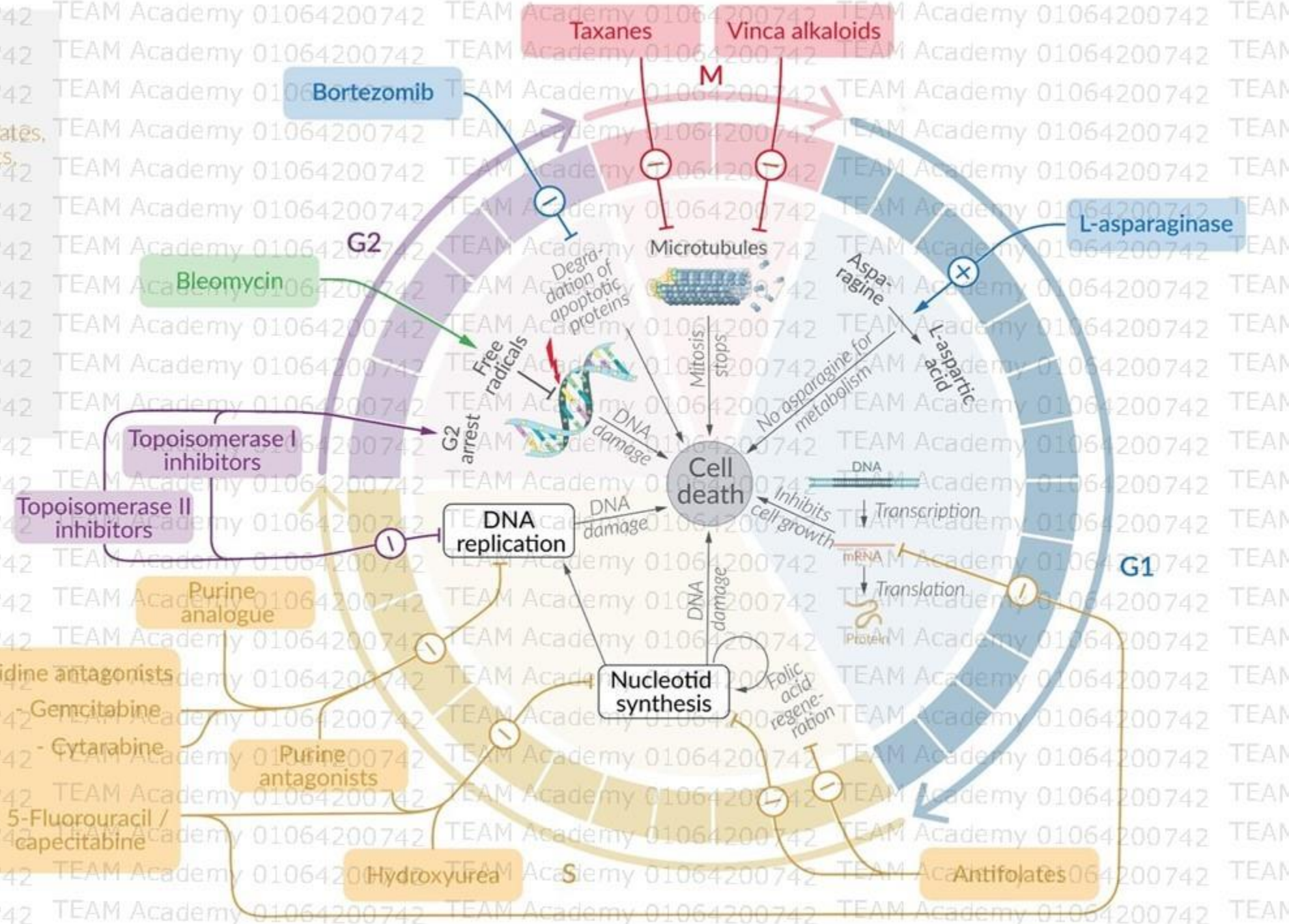
Mitotic inhibitors:
vinca alkaloids, taxanes

Antimetabolites:
pyrimidine antagonists, antifolates, hydroxyurea, purine antagonists, purine analogues

Topoisomerase inhibitors:
topoisomerase I inhibitors, topoisomerase II inhibitors

Antibiotics:
Bleomycin

Other:
L-asparaginase, bortezomib



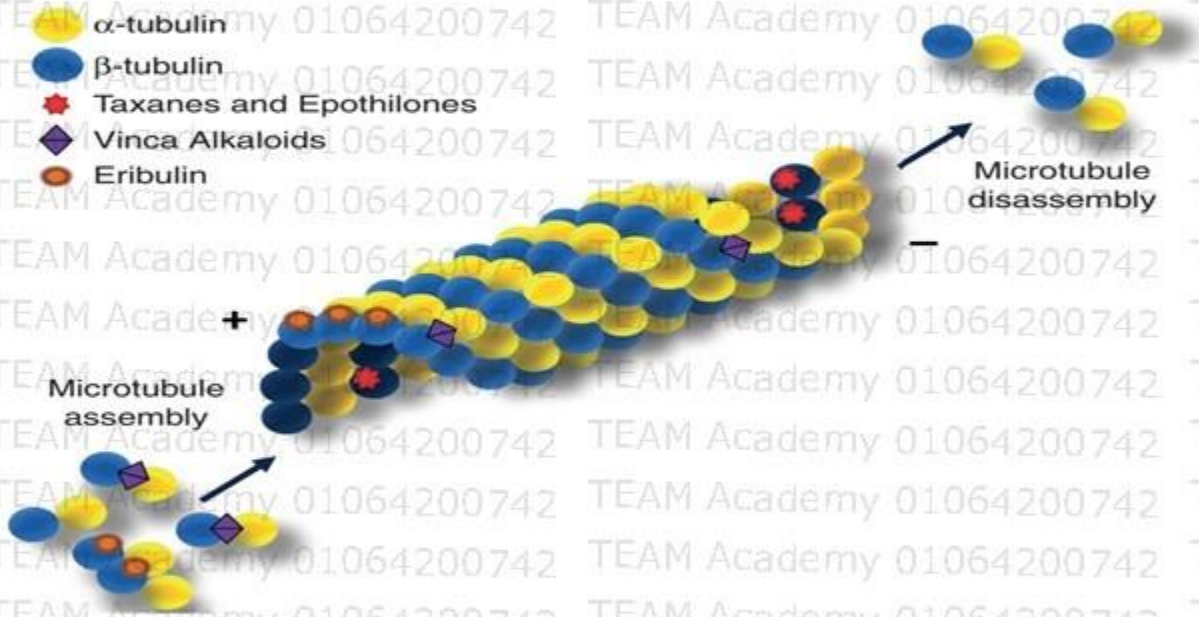


FIGURE 1.1. Mechanism of action of microtubule inhibitors: As a class, microtubule inhibitors interfere with microtubule dynamics and the formation of the mitotic spindle, thus preventing cell cycle progression from the G2→M phase, ultimately leading to apoptosis. Vinca alkaloids prevent microtubule assembly by binding β-tubulin and promoting depolymerization. Eribulin binds to a site near the vinca-binding site, preventing microtubule assembly and causing formation of nonproductive tubulin aggregates. Uniquely, eribulin binds only to the "plus" end of microtubules and does not affect microtubule shortening. Taxanes bind to β-tubulin on the interior surface of microtubules, promoting stabilization of the microtubule and preventing dissociation of tubulin. Epothilones have a similar mechanism of action to taxanes and occupy the same

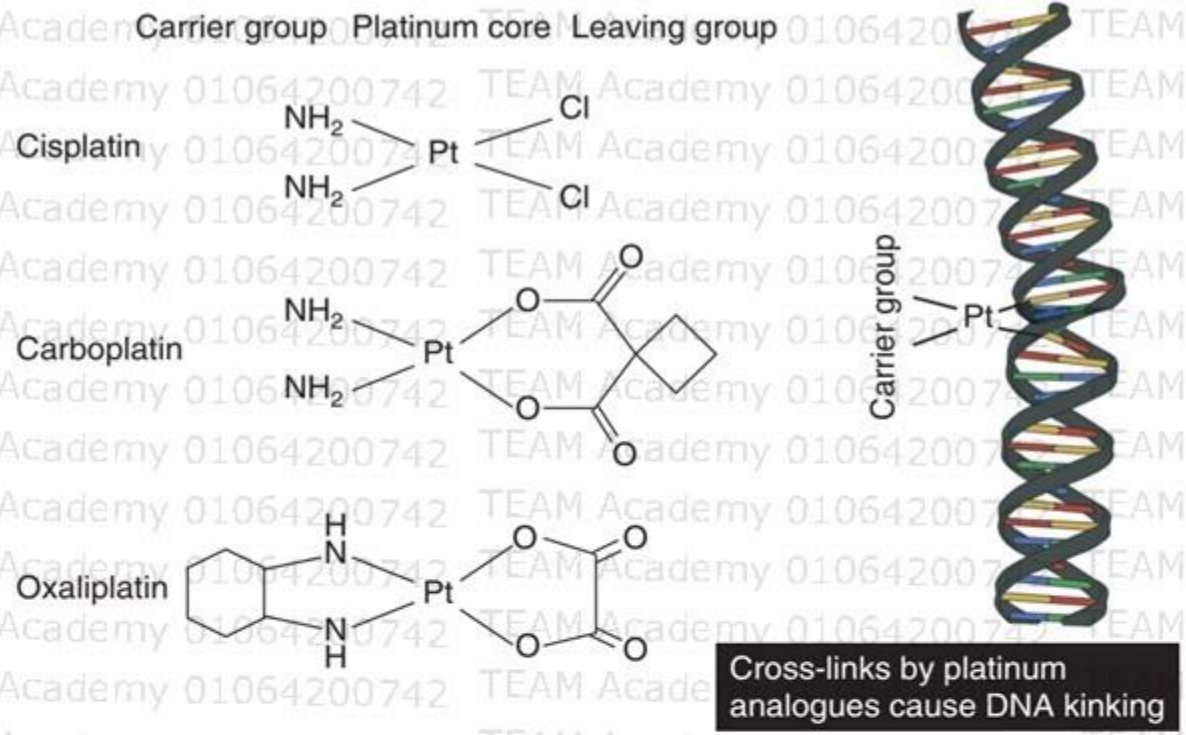


FIGURE 2.3. Platinum structure and mechanism of action.

13 SIDE EFFECTS OF CHEMOTHERAPY

Fatigue

Weaker immune system

Neuropathy

Nausea

More bruising and bleeding

Pain

Loss of hair

Difficulty breathing

Sores in the mouth

Increased number of rashes

Swelling

Heart issues

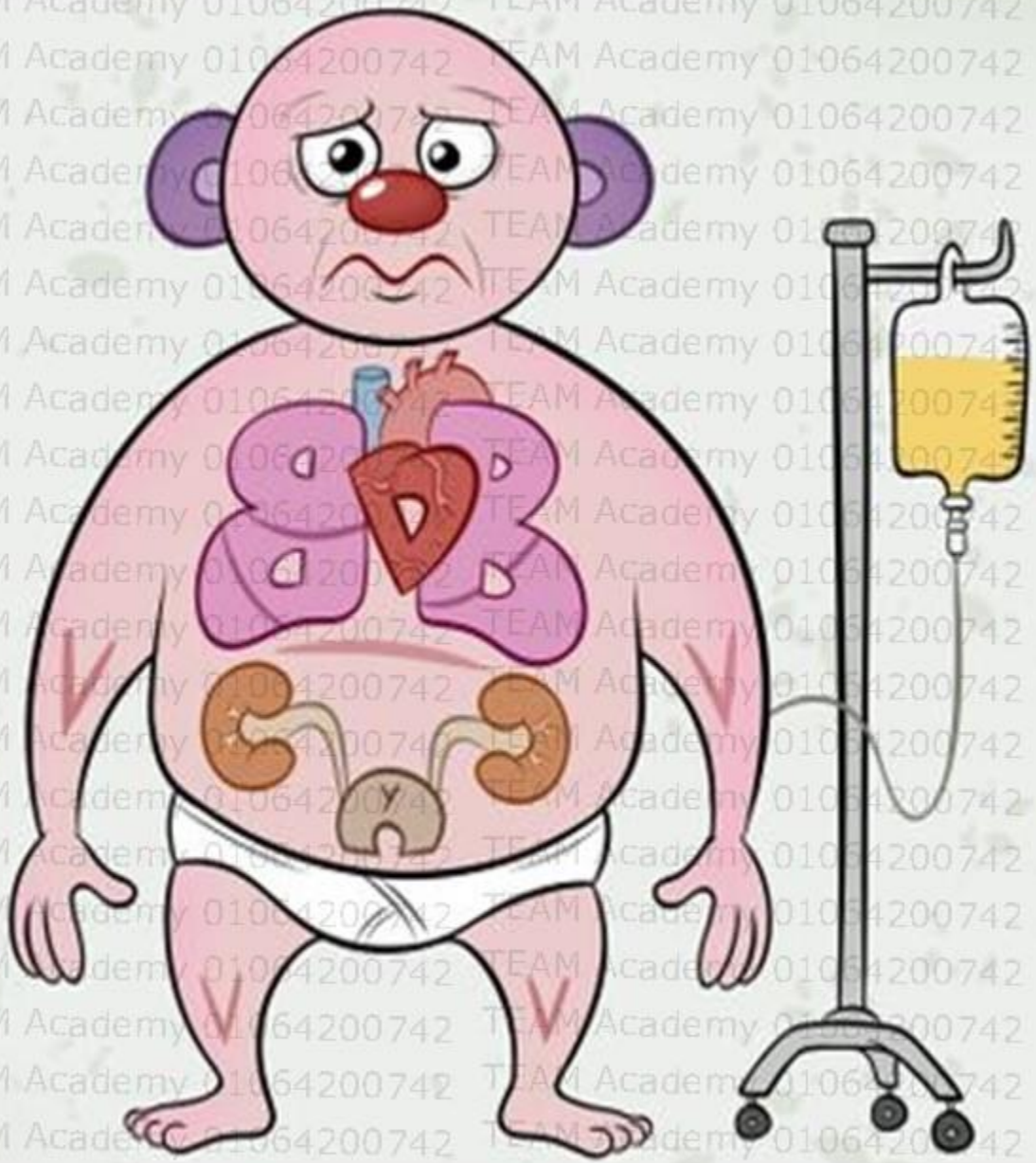
Changes in personality behaviour

DxD

Dr Ooi Wei Seong

Oncologist

CHEMOTHERAPY TOXICITIES



METHOTREXATE:
STOMATITIS

BLEOMYCIN:
PULMONARY FIBROSIS

DOXORUBICIN:
CARDIAC TOXICITY

CISPLASTIN:
OTOTOXICITY & NEPHROTOXICITY

CYCLOPHOSPHAMIDE:
HEMMORRHAGIC CYSTITIS

VINCRISTINE/VINBLASTINE:
PERIPHERAL NEUROPATHY

Intent of treatment

Curative

Neoadjuvant=Preoperative=induction chemotherapy

If the tumor is large so we give Chemotherapy before surgery **to make it easier for removal**

Adjuvant=postoperative chemotherapy

To **prevent come back (relapse) of cancer** and to **eradicate any unseen disease**

some cancer cells will have already escaped from the local tissues and formed micro-metastases in other organs

palliative

to shrink tumor to increase survival and decrease symptomps

Systemic and Regional (Intra-Arterial) Chemotherapy

Regional

When cancers appear to be limited to one particular body region and that region is supplied with blood by one particular artery, it is sometimes possible to concentrate anti-cancer drugs to the cancer **by injecting or infusing the drugs directly into the artery supplying blood to the cancer**

Example:Sarcoma,melanoma & Liver Cancer

Systemic

Infused inside vein to reach all body parts but it will concentrate and affect more on rapidly dividing cells like caner cells

Concomitant Chemotherapy and Radiotherapy:The So Called "Sandwich Treatment"

Using chemotherapy and radiotherapy over the same treatment period, has been shown to be more effective than using the two treatment modalities separately.

Some chemotherapeutic agents e.g. cisplatinum, appear to sensitise cells to radiotherapy.

Combined Integrated Treatment

using surgery with radiotherapy then you may add chemotherapy for larger tumors i.e stage II-III achieve better control of disease and increase cure rate

IV)Hormone Treatment

-some cancers grow due to excessive amount of hormons that act on cancer cells and make them grow larger

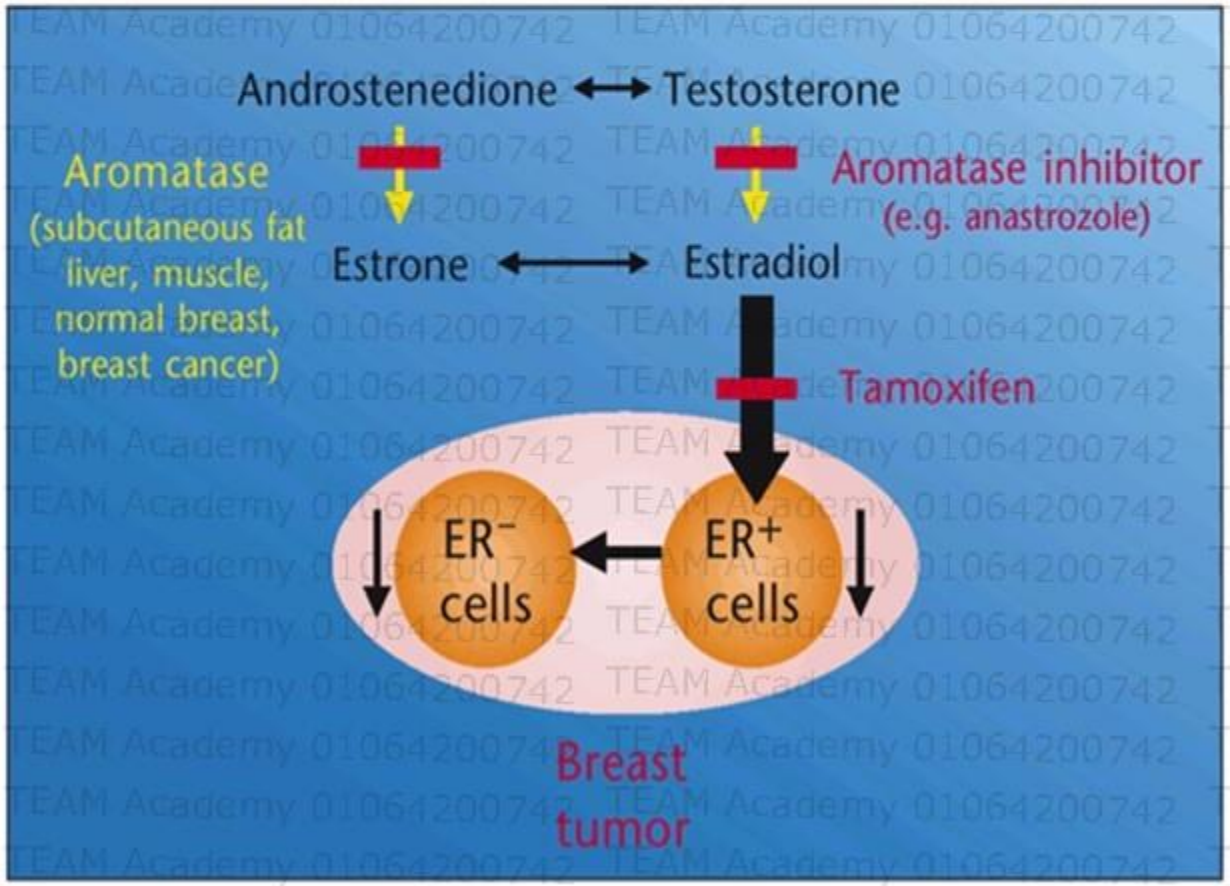
-examples are:breast & Prostate Cancer

-so we can use some drugs to prevent these hormons actions on cancer cells

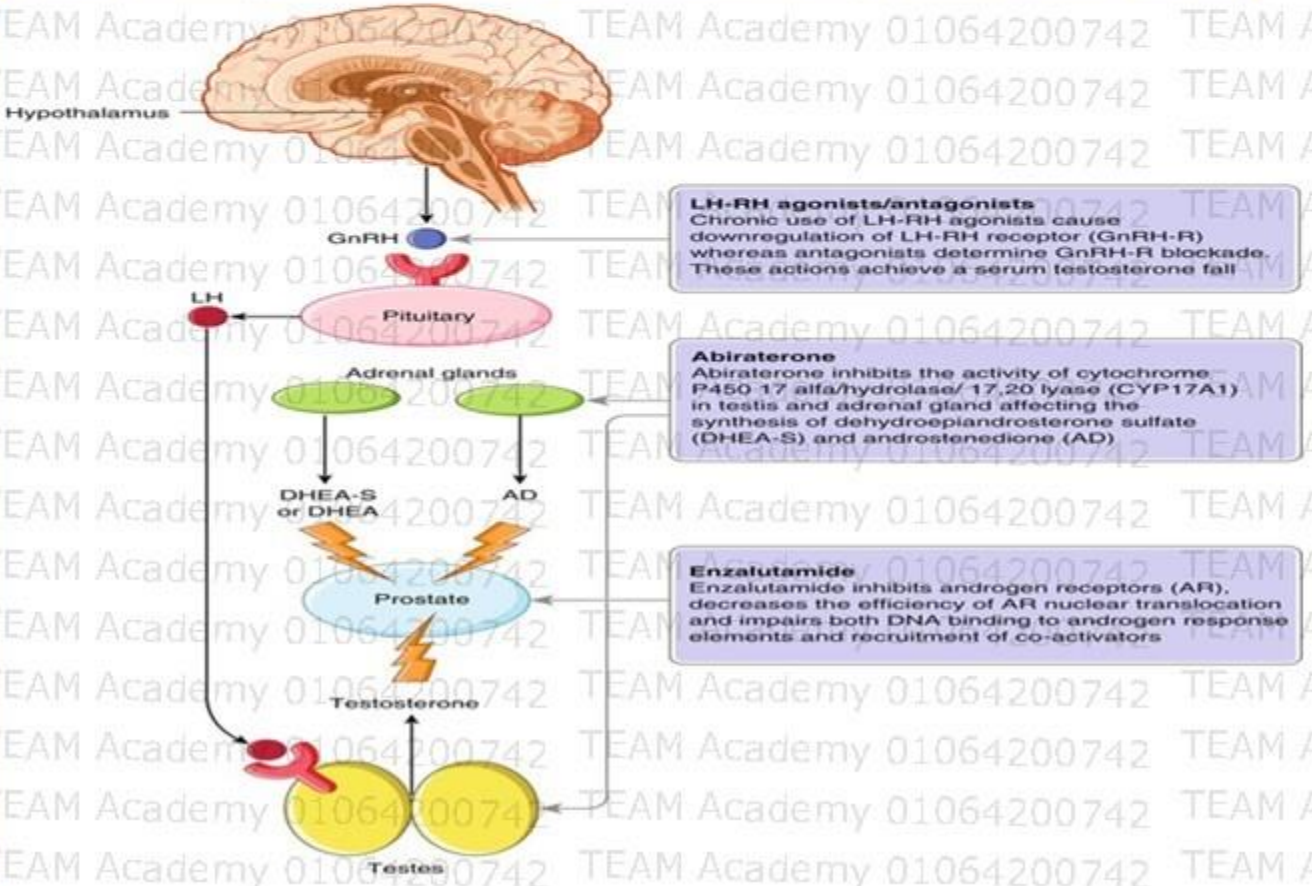
-some of these hormons are oral and others are Parenteral

Example: Tamoxifen tabs for breast cancer & Goserelin SC injection for Breast & Prostate Cancer

Mechanism of Action of Tamoxifen/A.Is



Mechanism of Action of Goserelin



V)Targeted therapy

Targeted therapy is a type of cancer treatment. It uses **drugs to target specific genes and proteins that help cancer cells survive and grow.** Targeted therapy can affect the tissue environment that cancer cells grow in or it can target cells related to cancer growth, like blood vessel cells.

Types

I)Tyrosin kinase inhibitors (TKIs)

The tyrosine kinase inhibitors are a family of **small molecules or peptides with the ability to inhibit enzymes inside cell called tyrosin kinase that give signal to reach nucleus DNA then this will activate the cell to grow and multiply**

It acts by inhibiting ATP binding site of these enzymes

e.g Imatinib inhibits BCR-ABL protein

Lapatinib inhibits HER1/HER2 protein

II)Monoclonal Antibodies (MABs)

"killer antibodies" that specifically act against a particular protein on surface of cancer cell so killing it.

-each one of thiese proteins has external domain(region) which blocked by MABs and internal domain which blocked by TKIs (so in some cancers we may use MAB with TKI to fully inhibit such proteins and inhibit signal transmission that tell cell to multiply e.g in breast cancer we may use trastuzumab with lapatinib to inhibit HER2

III)Immunotherapy

A)Immune checkpoints inhibitors ICPIs)

MABs that activate immune cells to attack cancer

Its work depends on the presence of protein called PD-L1 on the surface of cancer cells in enough quantity tumor cells that have this are called PD-l 1 positive cells and so its ok to use thiese drugs with

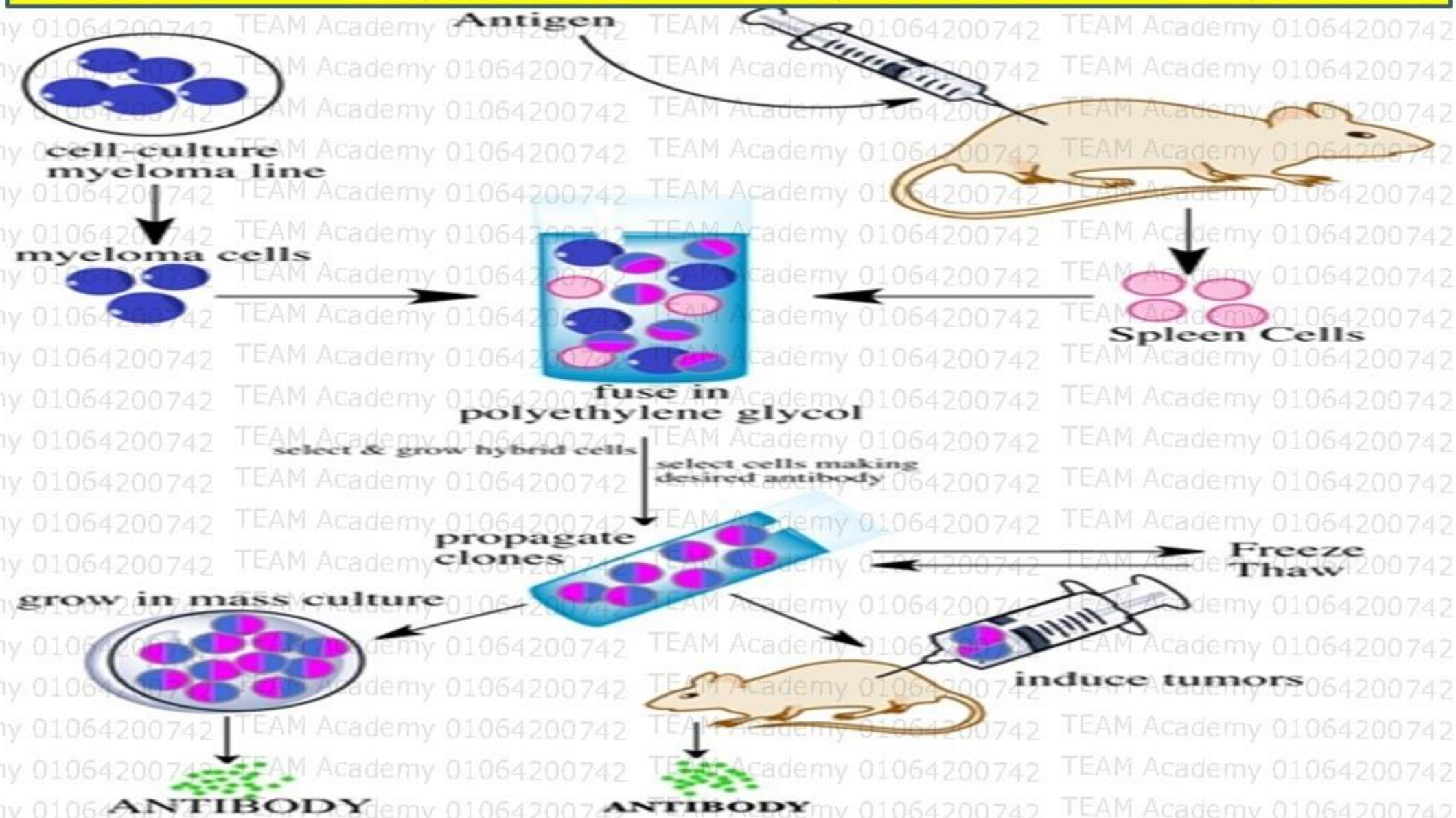
B)Cellular therapy e.g:CAR-T cell therapy

Patient s T-Cells is collected then modified genetically to have new type of receptors known as Chimeric(hybrid) antigen T-Cell Receptors which are able to attack cancer cells more efficiently

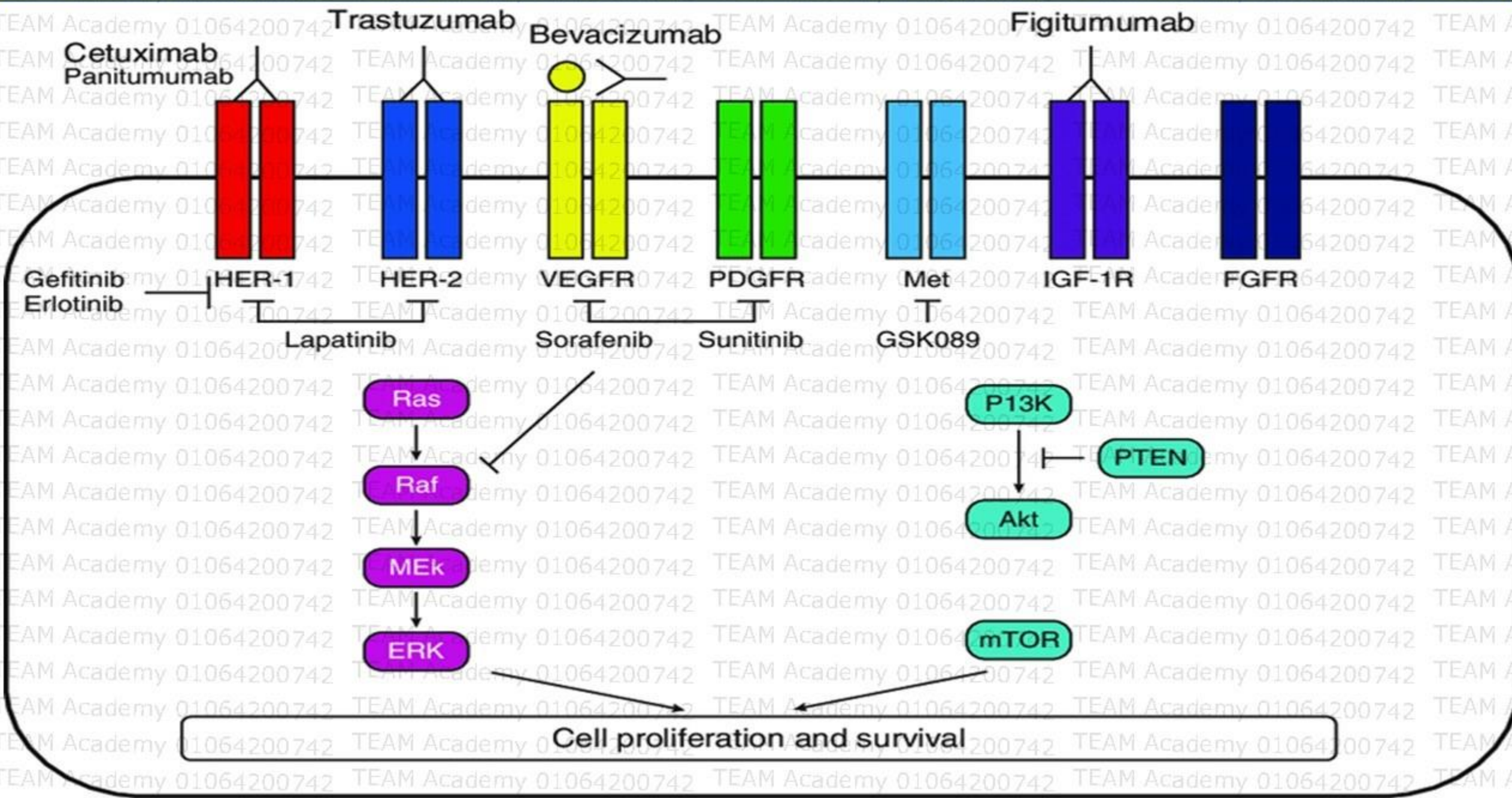
C)Inactivated bacteria or viruses e.g:BCG or (Corynebacterium parvum)

Injections of certain relatively harmless organisms to stimulate natural immune defence mechanisms.

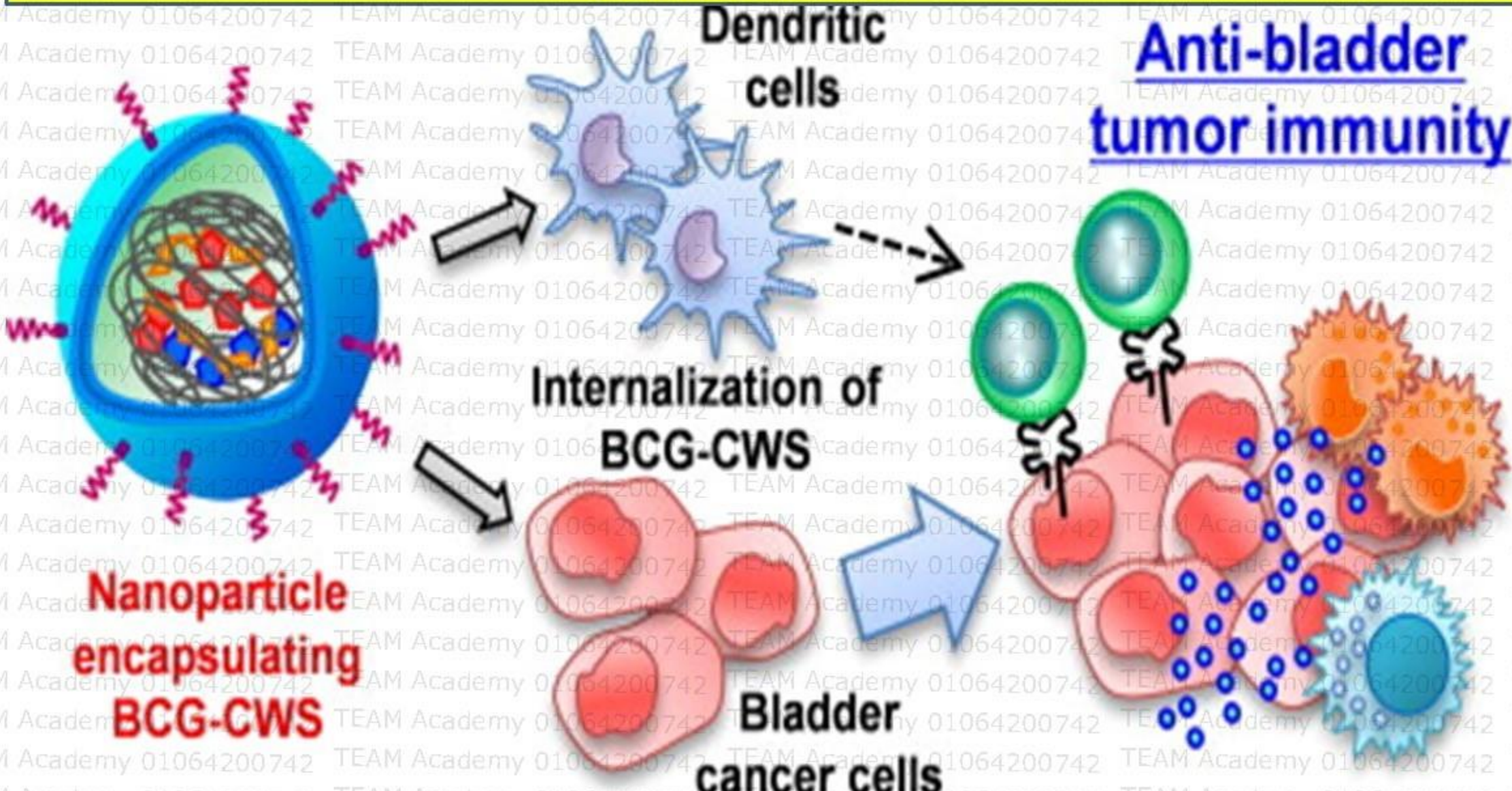
How Monoclonal Antibodies Are Produced?



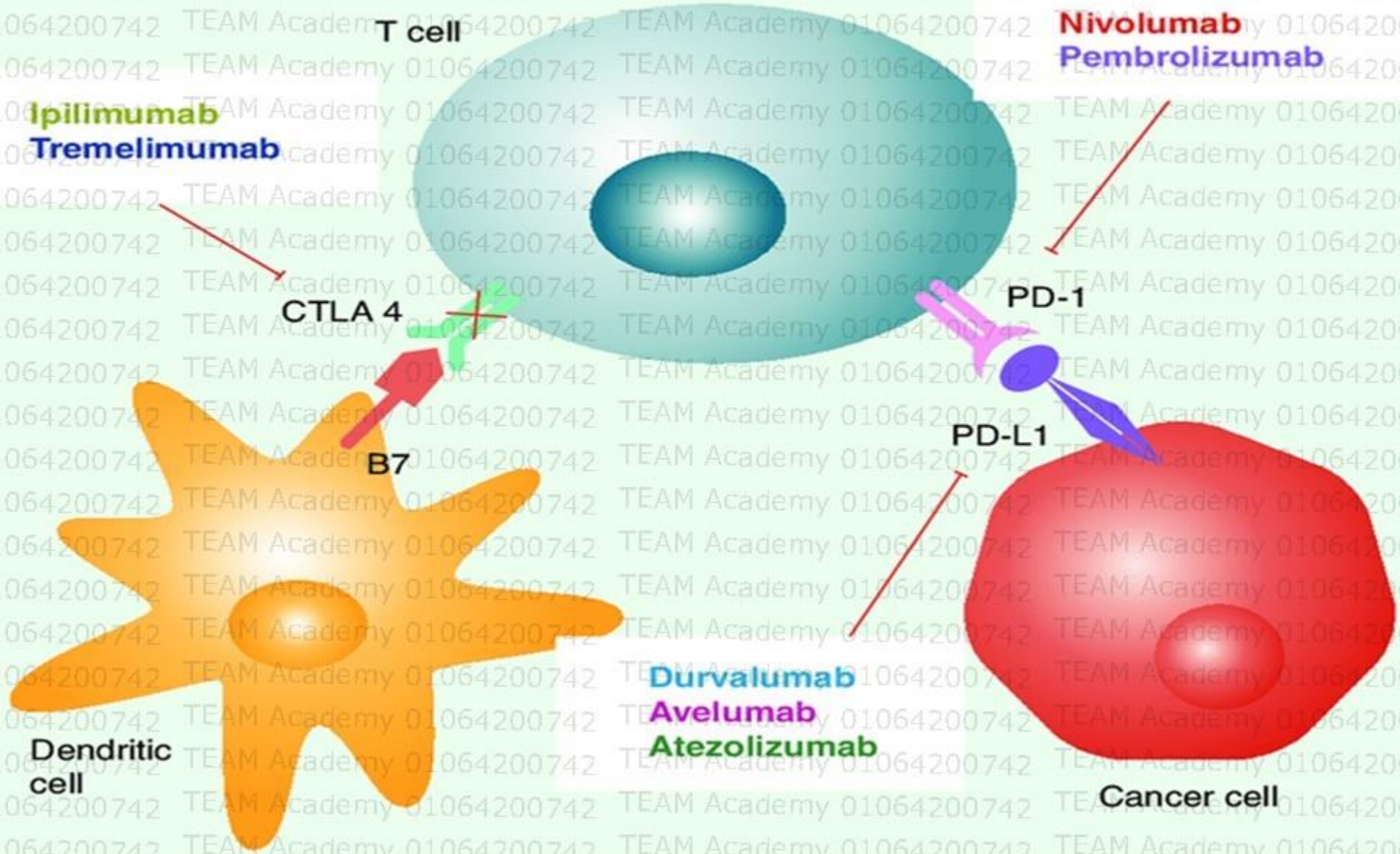
How monoclonal antibodies work outside and TKIs work inside Cell membrane?



How BCG works?



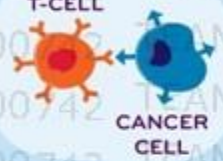
How Immune Check Point Inhibitors Work?



CAR T-Cell Cancer Therapy

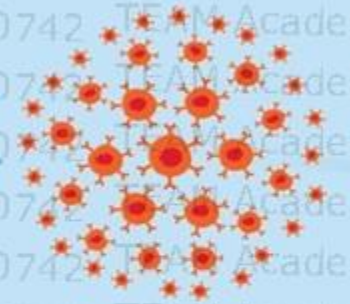
2 REPROGRAMMING

The T-cells are reprogrammed by introducing a genetic sequence through a lentiviral vector so the T-cells produce surface receptors (called CARs)



3 CAR T-CELL

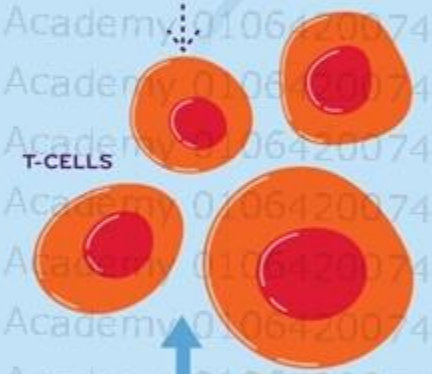
The CAR T-cells can now recognise and attach to specific marker proteins on the cancer cell surface - signalling its destruction



4 EXPANSION

The CAR T-cells are then 'expanded' in the lab to create millions of identical copies.

4-5 WEEKS



5 CONDITIONING

Before the CAR T-cells are reintroduced, the patient undergoes conditioning chemotherapy.

CAR-T CELLS

6 ADMINISTRATION

CAR T-cells are infused back into the patient.

7 MONITORING

After treatment, the patient is monitored to make sure any side effects are managed appropriately.

1 LEUKAPHERESIS

Blood is drawn from a patient and T-cells are separated out in a process known as 'leukapheresis'. The rest of the blood is returned to the body.

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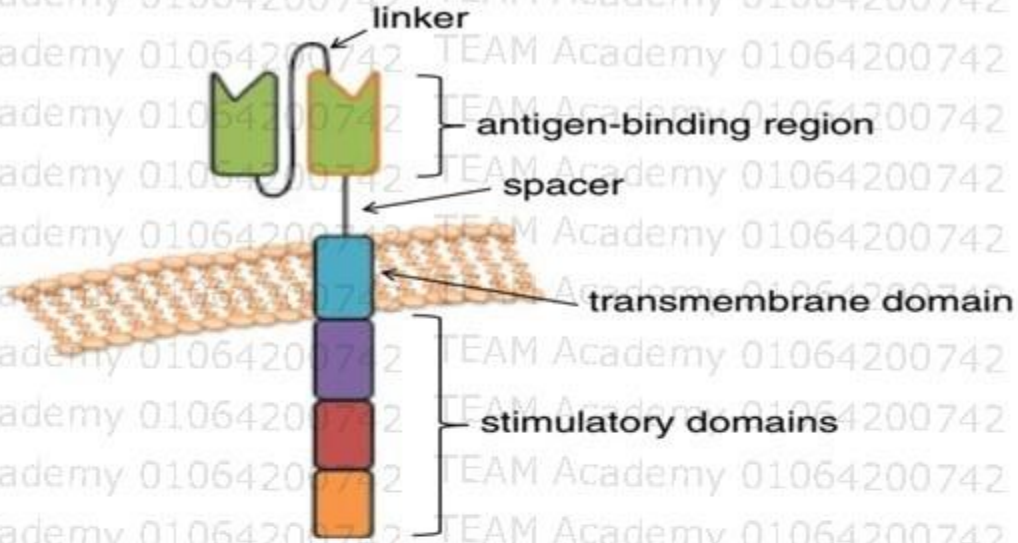


Figure 5.11 Structure of a CAR (chimeric antigen receptor) protein. CAR proteins are constructed from various pieces taken from a variety of different proteins. The extracellular, antigen-binding region is the variable region (also called the scFv) of an antibody, which is held together by a linker – a short string of amino acids. This is joined to a spacer, which provides flexibility. This in turn is connected to a protein segment known as the transmembrane domain that spans the cell membrane. Inside the cell are stimulatory domains taken from a number of proteins such as CD3, CD28, OX40, or CD247. These protein segments powerfully trigger the activity of T cells.
Abbreviations: CAR – chimeric antigen receptor

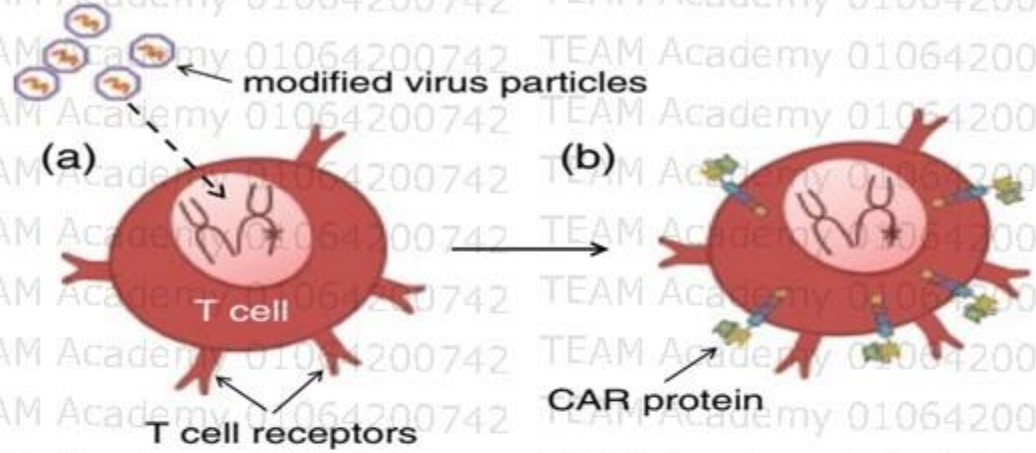


Figure 5.12 Viruses can be used to genetically modify T cells and force them to produce CAR proteins. (a) A modified virus containing the gene for a CAR protein is used to genetically modify T cells taken from the patient's blood. The CAR gene permanently integrates into the cells' chromosomes. **(b)** T cells use the instructions in the CAR gene to manufacture the desired CAR protein. They insert this protein into their outer membrane.
Abbreviation: CAR – chimeric antigen receptor


Evaluation of Response to treatment

Evaluation of Response of cancer to treatment

-First as we learnt we give patient therapy that composed of different treatment modalities(methods)
e.g: surgery then chemotherapy with or without radiotherapy
-we call that initial treatment first line therapy

-after end of this treatment duration we do tests that we discussed in the part detection & diagnosis of cancer (see slide 14) to know if tumor shrinks/disappear and respond to treatment or not

-the most important of these tests are imaging especially PET/CT Scan

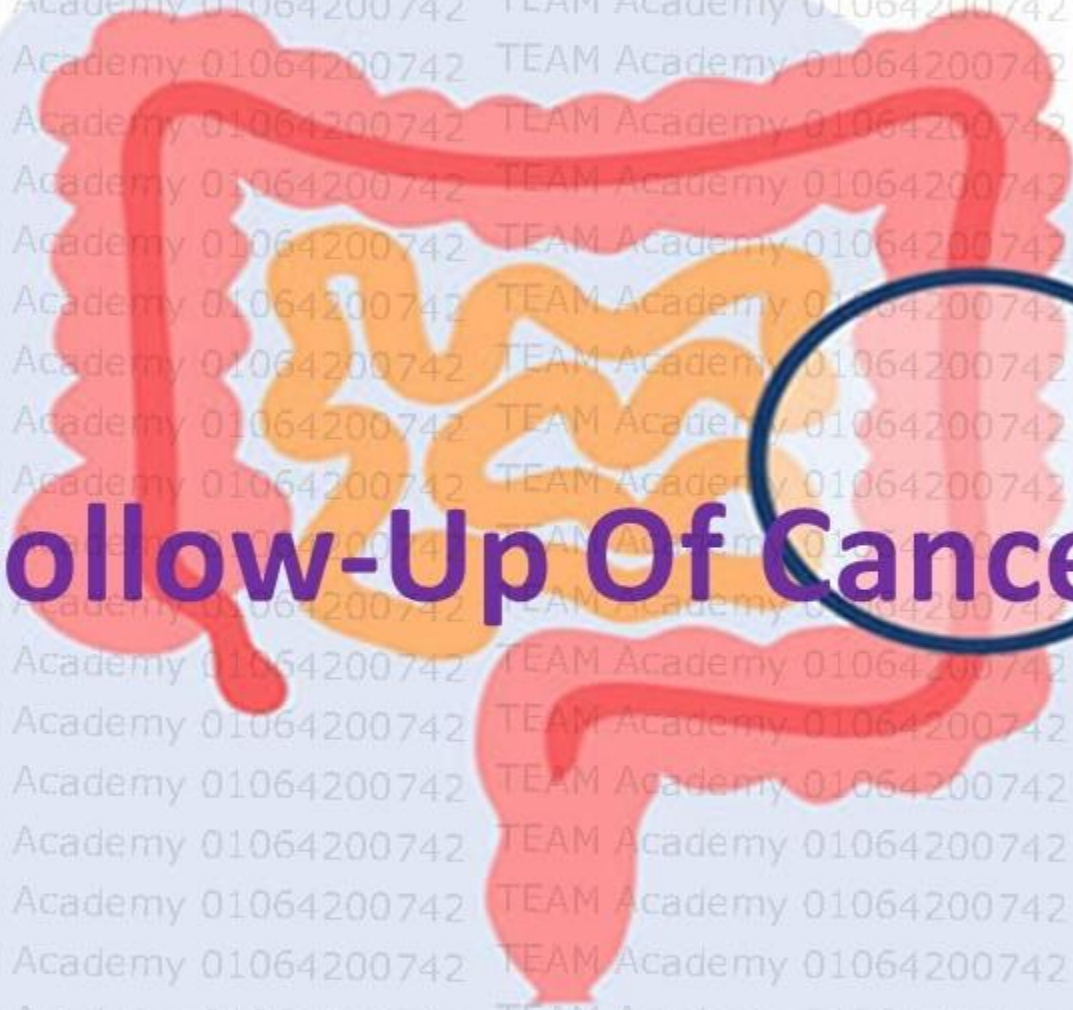
-we compare the size of tumor after treatment with these before treatment

Depending on this we classify tumor response into the following categories(RECIST Criteria):

Response	Criteria
Complete response (CR)	Disappearance of all target lesions
Partial response (PR)	At least a 30% decrease in the sum of the longest diameter (LD) of target lesions, taking as reference the baseline sum LD
Progressive disease (PD)	At least a 20% increase in the sum of the LD of target lesions, taking as reference the smallest sum LD recorded since the treatment started and at least 5 mm increase or the appearance of one or more new lesions
Stable disease (SD)	Neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD, taking as reference the smallest sum LD since the treatment started

-if cancer responded i.e achieved CR or PR and sometimes SD we continue treatment or end treatment if patient completed his course
-if cancer did NOT responded i.e achieved PD we stop current treatment and give patient different treatment
-we call this new treatment second line of therapy

Follow-Up Of Cancer



Follow-Up

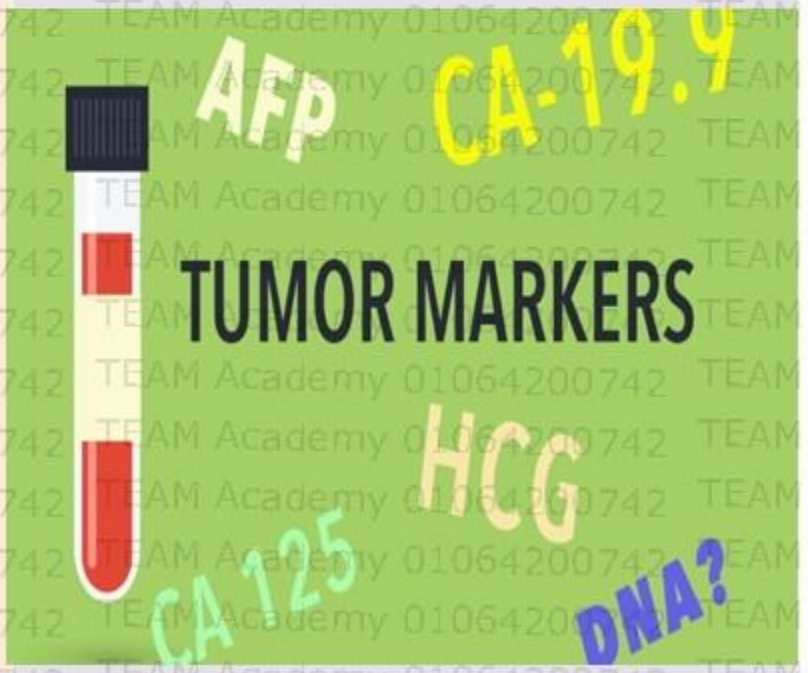
No matter what treatment is used in cancer management it is important that **all patients should undergo regular medical follow-up examinations. This is mainly to detect and treat, at an early stage, any problem that might arise but also gives most patients confidence that they are not being neglected** and that any new problem will be detected and treated early

for example some cancers need:

A) history taking & physical examination (H&P)

B)imaging e.g PET scan/CT every 6 months for the first 2 years following treatment then this will be done every 12 months in the next 5 years

C)Tumor Markers levels in some Cancers e.g CEA in CRC



Oncology Pharmacy

Oncology pharmacy services

Oncology pharmacist, is considered to be the front-line health caregiver for patients

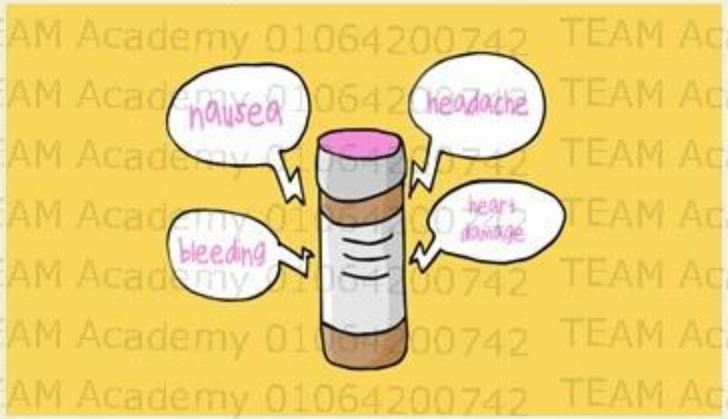
Role Of Oncology Pharmacist

1)Supply of Cancer/support drugs

2)monitoring their treatment protocols e.g:Protocol Schedueling, suitability of protocol for patient/disease,drugs doses,labs required,etc by reviewing patient file & Doctor s order

3)Follow up of patients for recording adherence to therapy & side effects also reporting side effects or medication errors

4) providing the suitable support to decrease SEs



5)Preparing Cancer therapy according to guidelines

6)Assuring application of most recent guidelines & education of their team

Requirements for oncology pharmacists

1. Legally certified pharmacist has taken the official license for pharmacy practice.
2. Must pass successfully the 3 levels of competency to be upgraded to Oncology pharmacy specialist.

these levels are:

1st, Entry Level, where training on:

- Centralized IV admixture Unit service.
- Dispensing & Patient counselling.
- Drug Information Centre.

This level is designed to be undertaken in maximum of 1 year.

2nd, Intermediate level:

Rotation in different patient-care settings and clinical practice for a minimum of 3 months in each department according to departments availability in the facility, i.e.:

1. Adult Medical oncology departments (inpatient &outpatient)
2. Pediatric Medical oncology departments (inpatient &outpatient)
3. Critical care unit.
4. Surgical & inside operation room.
5. Bone marrow transplant department
6. Radiotherapy and Nuclear medicine.
7. Clinical Research department.
8. Pharmacoeconomics.
9. Nutrition

This Level is designed to be undertaken in 2 years.

3rd, Advanced "Specialization & Certification" Level:

- Working in one of the oncology specialties mentioned in level 2 and available in the facility.
- This level is designed to be undertaken in maximum of 5 years to be upgraded officially to an oncology pharmacy specialist.
- Getting certification in this level is a must, whether internationally or nationally inoncology pharmacy practice.

Requirements for an oncology pharmacy specialist:

1. official license for pharmacy practice.
2. passed the three competency levels.
3. a board certification or relevant specialized certification to be upgraded further on to an Oncology Pharmacy Specialist.
4. In-depth knowledge of oncology disease states, with knowledge of evidence-based treatment, including standard-of-care treatment guidelines (e.g., those of the National Comprehensive Cancer Network [NCCN], American Society of Clinical Oncology [ASCO], and Multinational Association of Supportive Care in Cancer [MASCC], European Society for Medical Oncology [ESMO] etc.)
5. Specialized knowledge of anticancer therapy, administration, symptom management,and supportive care
6. Provision of effective patient education and medication counseling
7. Knowledge of storage, safe handling, administration, and disposal of hazardous medications.
8. Therapeutic drug monitoring.
9. Discharge and admission planning, transitions of care
10. Education of inter-professional team members and trainees
11. Familiarity with availability, structure, and design of clinical trials
12. Ability to communicate effectively with healthcare professionals, patients, and caregivers.

Oncology Pharmacy refrences you need in your work

Drug Informations

Lexicomp App/Genebrandex App/
Medscape App/Micromedix App

Chemotherapy Protocols

NCCN App/website
CTA App/St Luke website/BC cancer website

Patient education

BC cancer/Lexicomp App

Refrences of this presentation

- **Basics Of Oncology** Frederick O. Stephens · Karl R. Aigner
- **Oncology at a glance** Graham G. Dark
- **Cancer Pharmacology and Pharmacotherapy** Francis P. Worden, MD, RPh/Anthony J. Perissinotti, PharmD, BCOP
- **EDA Oncology Pharmacy Guide**

Thank You