Introduction To Cancer Diagnosis & Treatment

By

Prof Ahmed Abd El-Warith

April 2022

Objectives

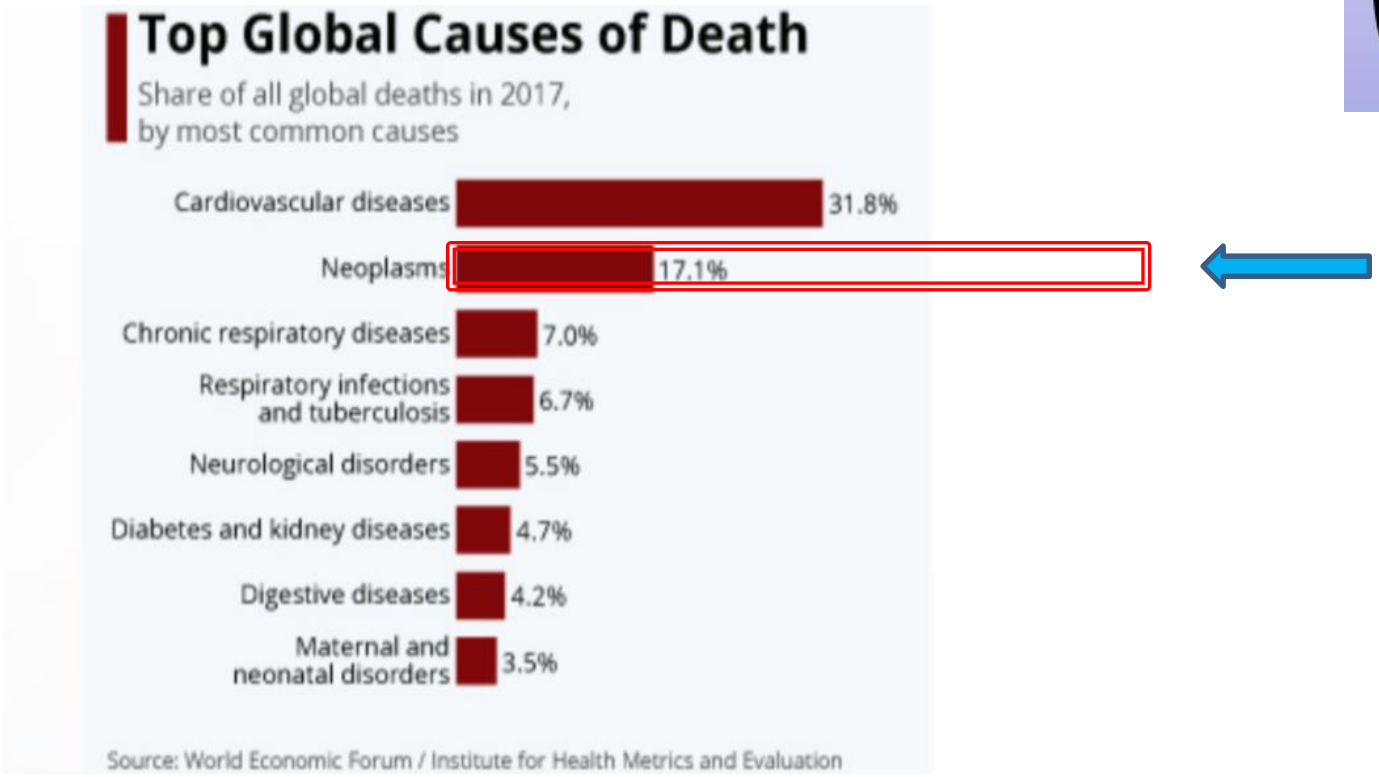
- 1- definition of cancer
- 2- etiology of cancer
- 3- staging of malignant diseases
- 4- principals of pathological classification of malignant diseases
- 5- general symptoms and signs of malignancy
- 6- principals of cancer management

  (curative Vs palliative concept)

  7- Principals of immuno- oncology

What is behind the Oncology Sad face?

The second common cause of death



Cancer is the second global cause of death (17.1%)
Coming after cardiovascular diseases (31.8%)

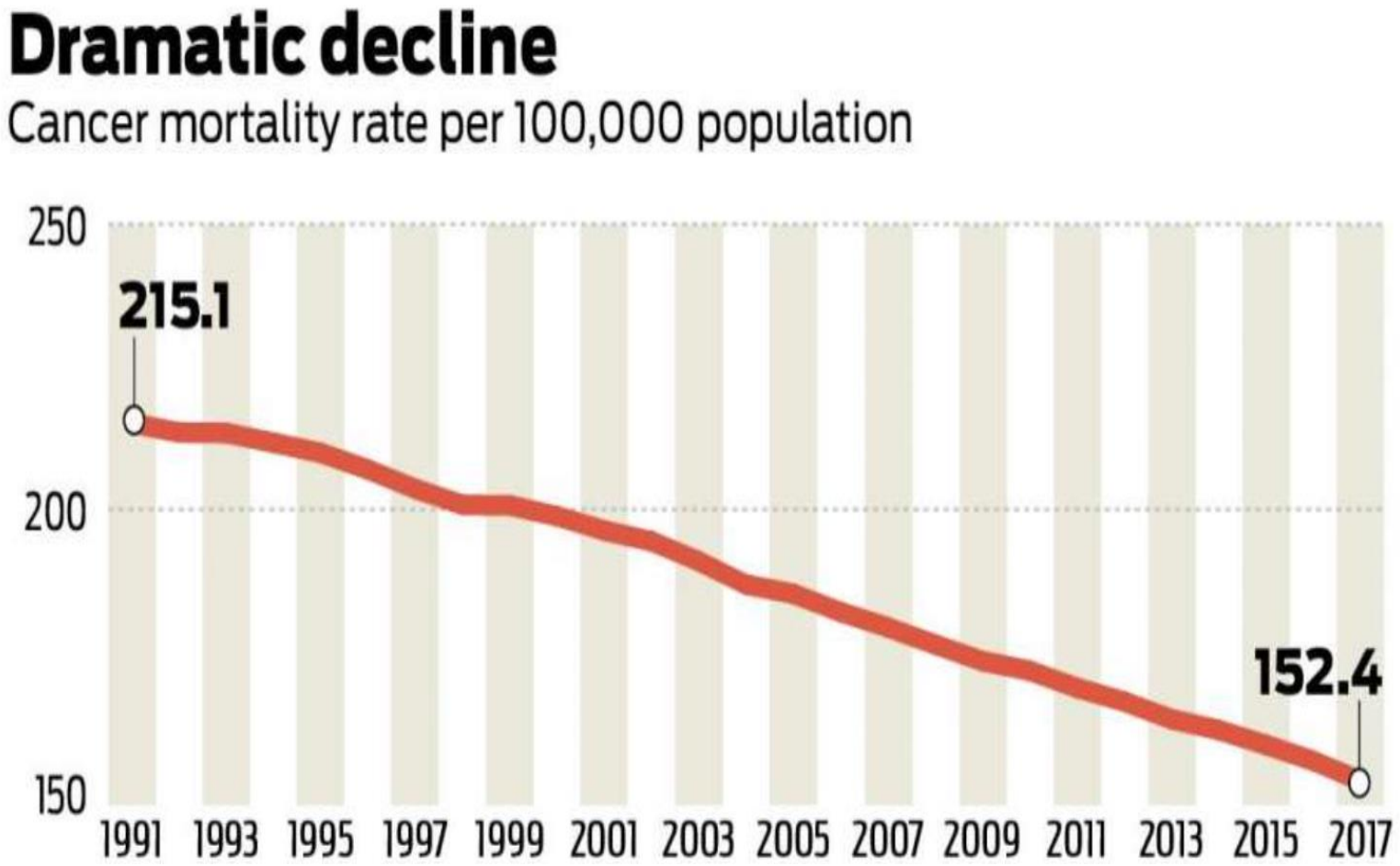
However dying from cancer always caries a dramatic story

Cardiovascular diseases	Cancer
Old ages (> 65y)	Wide age spectrum (infants , children , adolescents etc…)
Blamed to known avoidable factors (habits ,diet, stress)	Developed mostly due unknown factors
Usually acute onset	Long chronic history
Less impact on the families	Huge impact on the families

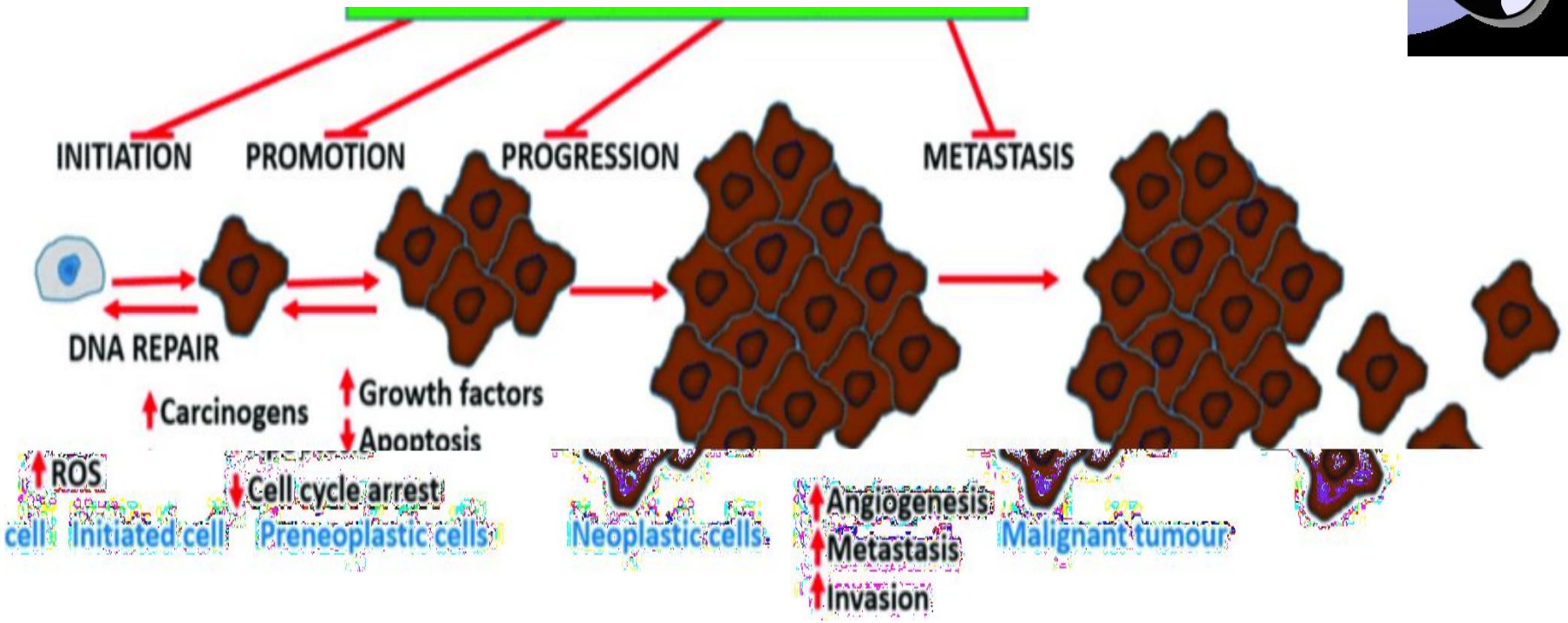
What is behind the Oncology Sad face?

- **Can we cure cancer???**

Currently We Are Witnessing



WHAT DID CHANGE THE FACE OF ONCOLOGY ?



Prevention

Screening

Early detection

Therapeutic Strategies

WHAT DID CHANGE THE FACE OF ONCOLOGY?

- **The change in our understanding of the ways of cancer development and dissemination.**

scienceblog.cancerresearchuk.org

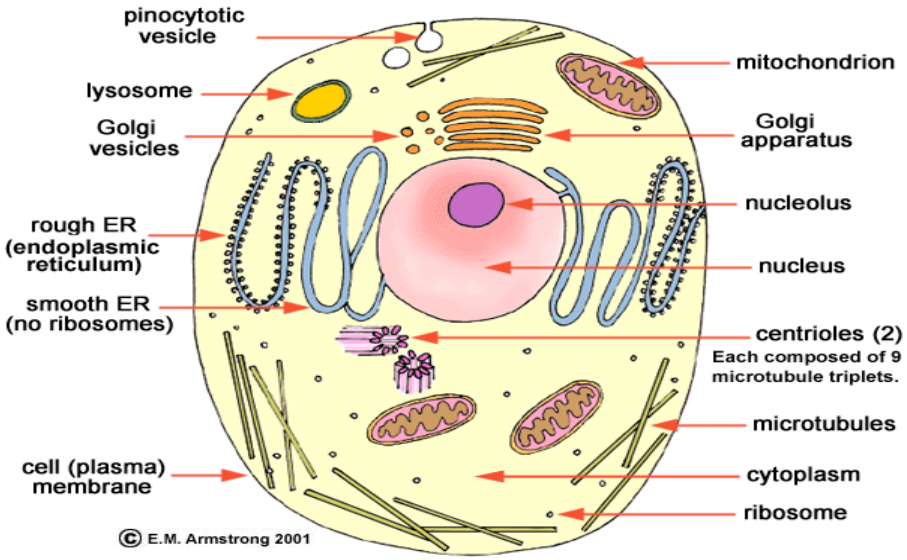
Posted on October 14, 2010 by Kat Arney

Claims that cancer is only a 'modern, man-made disease' are false and misleading

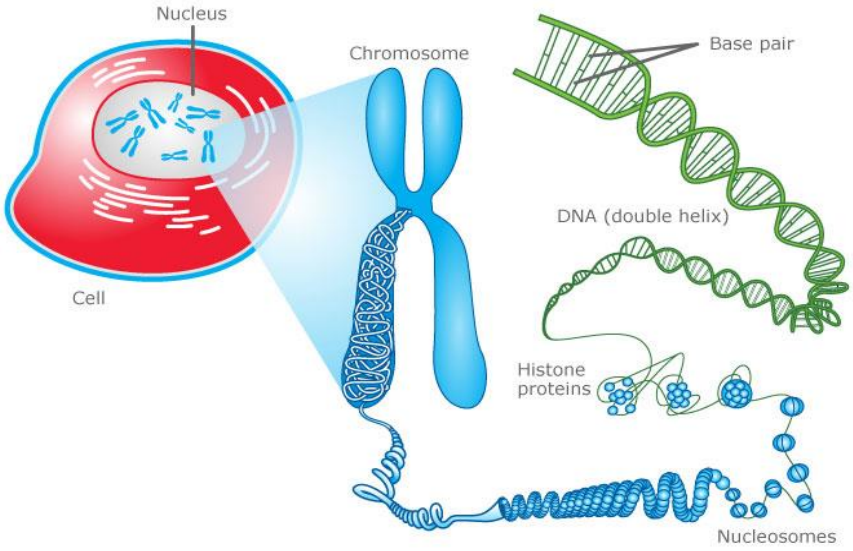
This is not only scientifically incorrect, but misleading

Cancer has always been with us, from ancient civilizations to today.

What causes cancer?



The nucluls is having chromosomes which are carrying the gens which made made of DNA

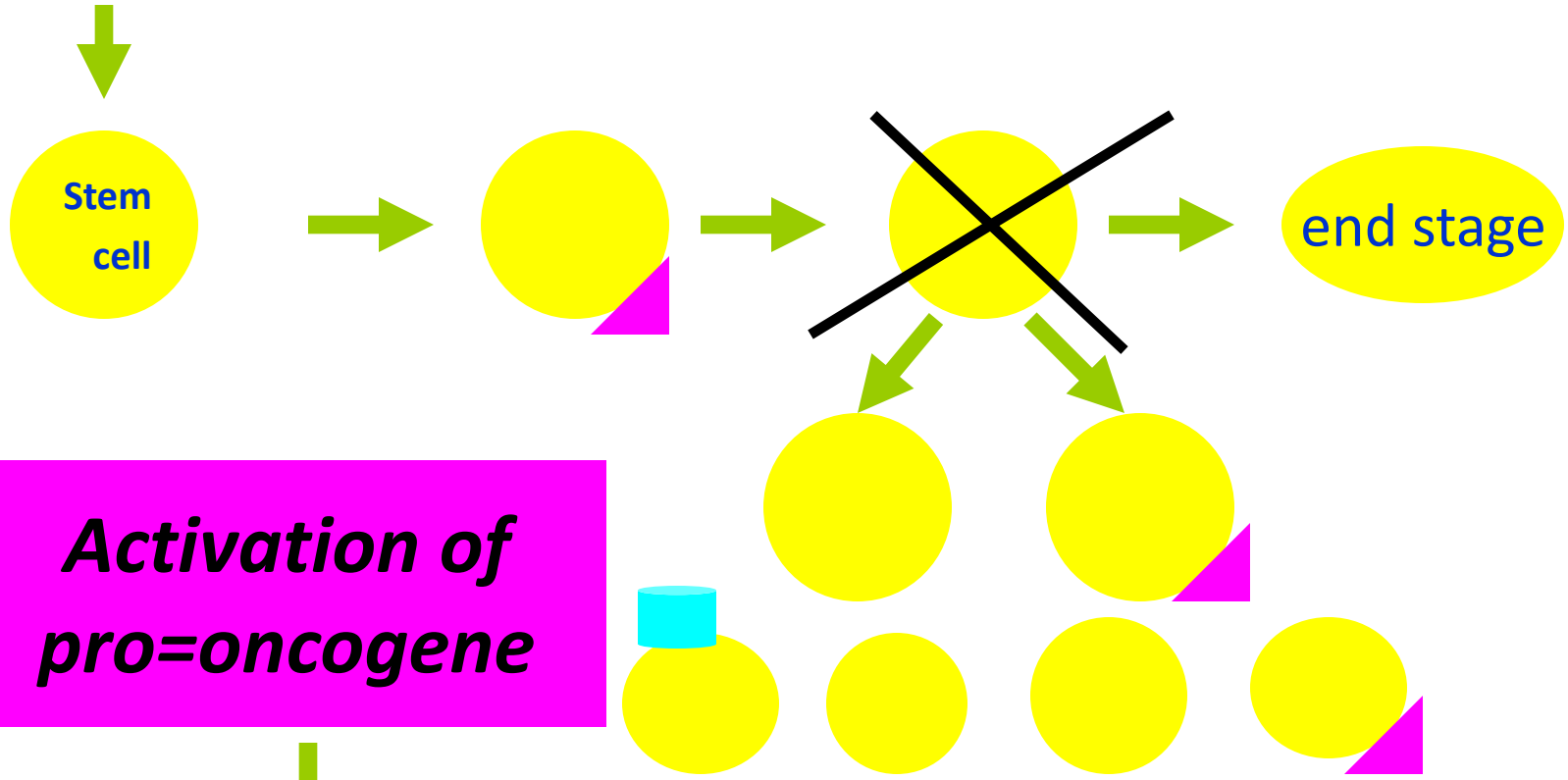


DNA controls cell functions

↓

Cell division

Development of Malignant Disease

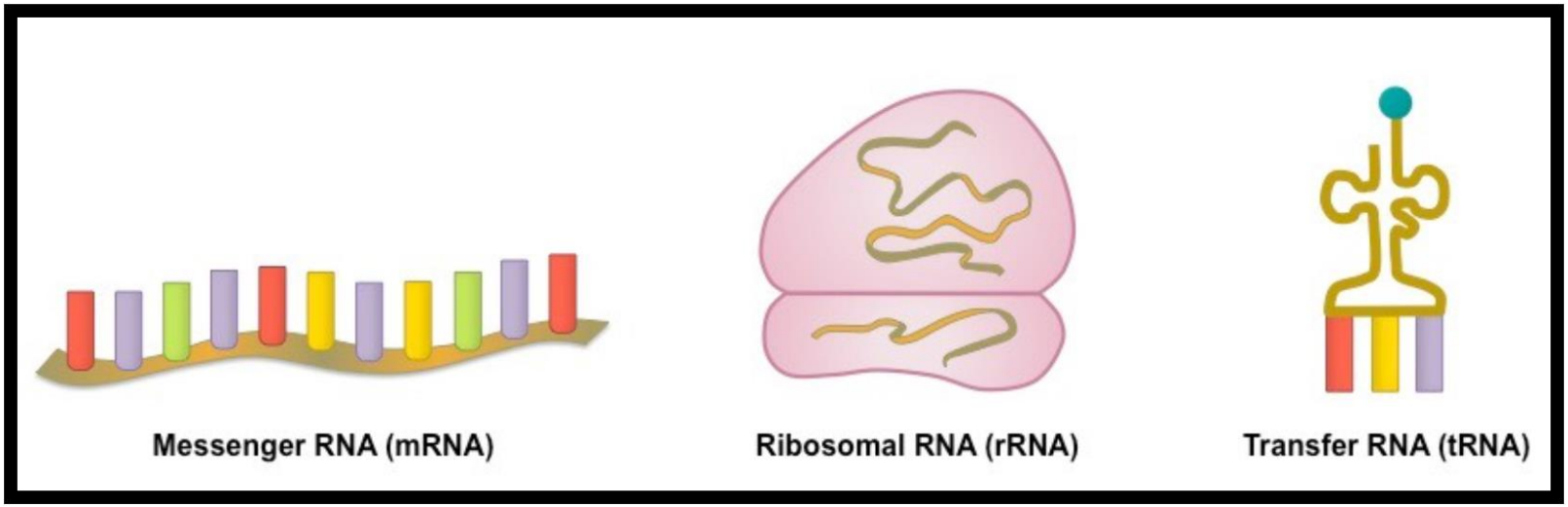


Activation of pro=oncogene

Genetic mutation

Cell Arrest & clonal expansion

TYPES & FUNCTIONS OF RNA



What causes cancer?

Cancer arises from the mutation of a normal gene.

Mutated genes that cause cancer are called oncogenes.

THIS PROCESS SHOULD BE COMPLETED BY COMPETENT RNA SYSTEM

Causes of Cancer

- • **DNA Mutations**
- – Radiation – and other environmental factors (Tobacco, Alcohol, Radon, Asbestos, etc)
- – Random somatic mutations
- – Inherited germ line mutations
- • **Infectious agents**
- – **Viral**
- • HPV – cervical cancer
- • Hepatitis – liver cancer
- –**Bacterial**
- • *H. pylori – stomach cancer*
- *EBV - Lymphoma*

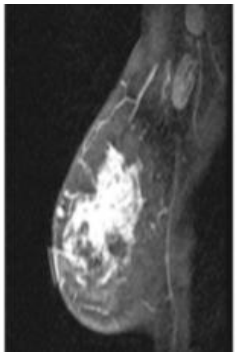
WHAT DID CHANGE THE FACE OF ONCOLOGY?

- **The change in our understanding of the ways of cancer**

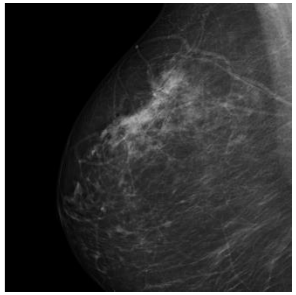
Dissemination.

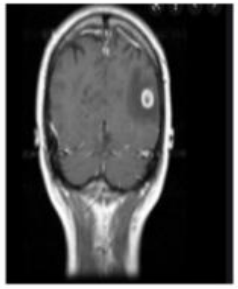
THE DIVERSE BIOLOGICAL BEHAVIOUR OF MALIGNANT TUMORS

51 y/o lady with:
- DX left breast cancer 2009
RT BREAST CA 2018
LOCAL REC 2021
TREATED BY Sx , RTH & Adj systemic therapy
NO DISTANT SPREAD

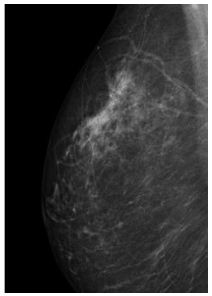


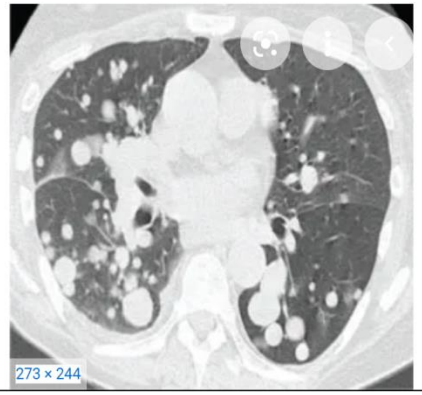
40 y/o lady with:
-2012 DX left breast cancer
S/P SX AND ADJUVANT TTT
2018 = BRAIN METS
TREATED BY SX & RTH
2021 = Alive with no evidence of disease





40 y/o lady with:
- DX T1 left breast cancer
S/P SX AND ADJUVANT TTT
One year later
Massive pulm mets





Explaining The Behavioral Diversity of Malignant Tumors

1889,
Stephen Paget
Seeding Theory

1894,
Halstead
Orderly Theory.

1980
Fisher
Systemic theory

ALL OF THESE THEORIES FAILED TO EXPLAINE HOW PATIENTS RECEIVING ONLY LOCAL TREATMEN BE CURED ?

1994 Hellman Spectrum theory

Cancer at initial presentation fell into a spectrum ranging from indolent disease to wide metastatic,

This is proportion to the tumor ability to metastasize

Irrespective to its size .

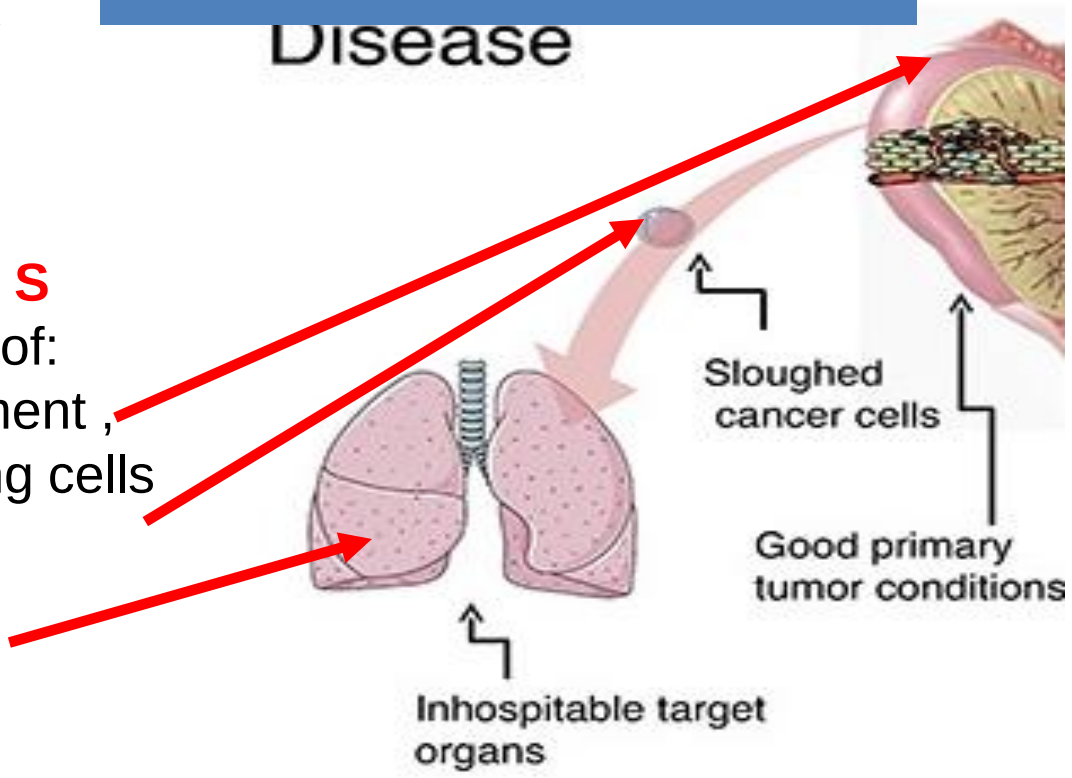
New theory for cancer dissemination

1994 ,

Hellman

Spectrum theory

1-HOMEY TUMOR STATE



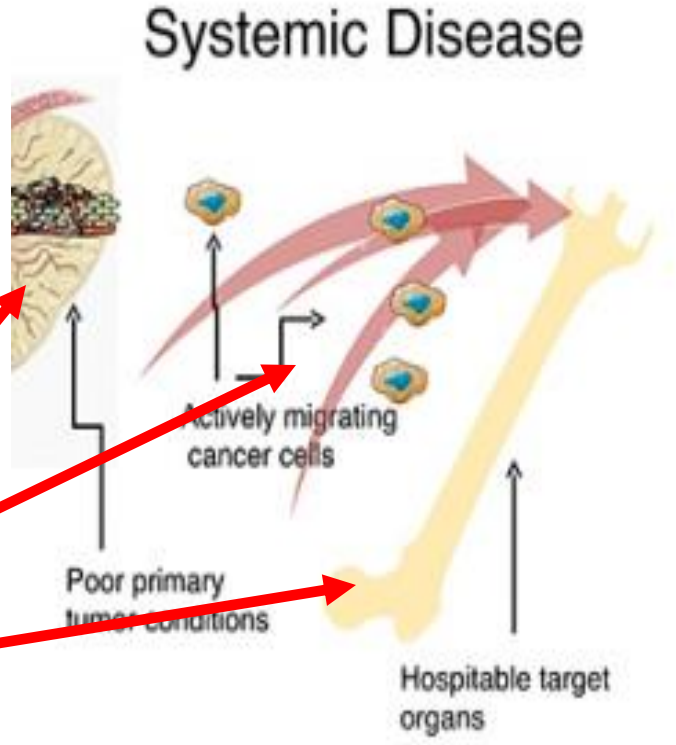
In the Homey state: **3 F S**
There is a combination of:
1- **Fine** micro environment ,
2- **Rare** **F**alling migrating cells
3- **F**ailure recipient soil

New theory for cancer dissemination

1994 ,

Hellman

Spectrum theory



In the systemic disease type :

There is a combination of **3 As**

1- **A**ggressive micro environment ,

2- **A**ctively migrating cells

3- **A**ccepting recipient soil

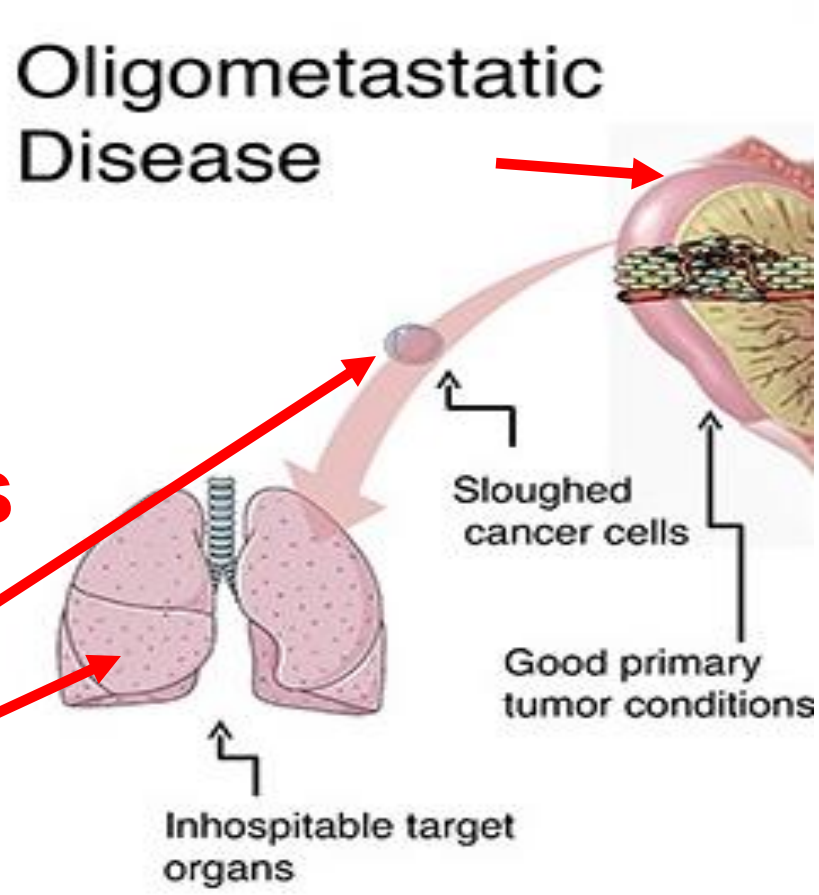
Oncotarget, Reyes et al 2015 Apr 20; 6(11): 8491–8524

New theory for cancer dissemination

1994 ,

Hellman

Spectrum theory



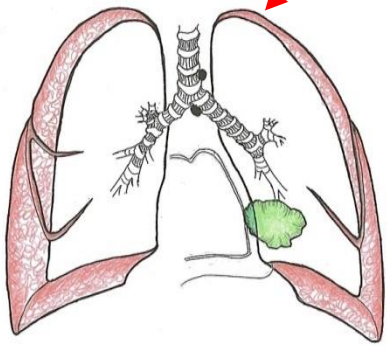
In the Oligometastatic state:

There is a combination of **3 Fs**

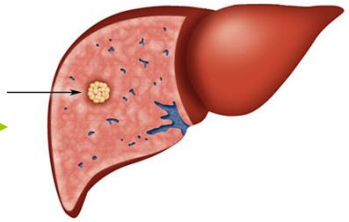
1- **F**ine micro environment ,
2- **F**alling migrating cells
3- **F**ailure recipient soil

BIOLOGICAL DEVELOPMENT OF MALIGNANT TUMORS

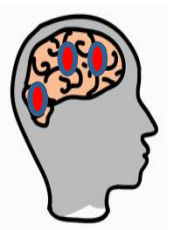
Behavioral diversity of malignant tumors?

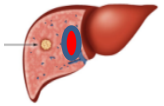


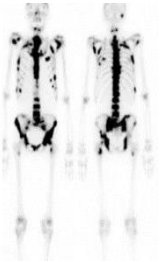
Type I
Homey



Type II
OLIGO



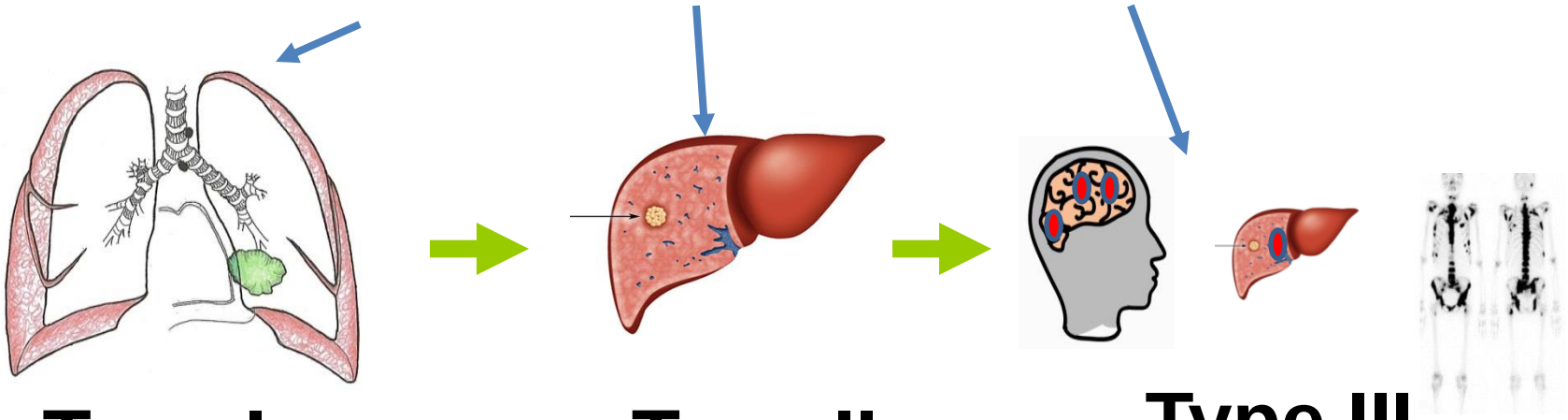




Type III
DISIMINATED

THE GOOD BAD AND UGLY ARE LIKE THAT SINCE THEY HAVE BEEN BORN

The tumor behavior is not related to its size



Type I
Homey

Type II
OLIGO

Type III
DISIMINATED

Different Treatment Modalities

- **Local therapy** = Surgery & RTH

- **Systemic therapy** = Cth
  Hormones
  Biologicals
  Immune therapy

General Staging of solid malignancies

Early

local
+/- Systemic

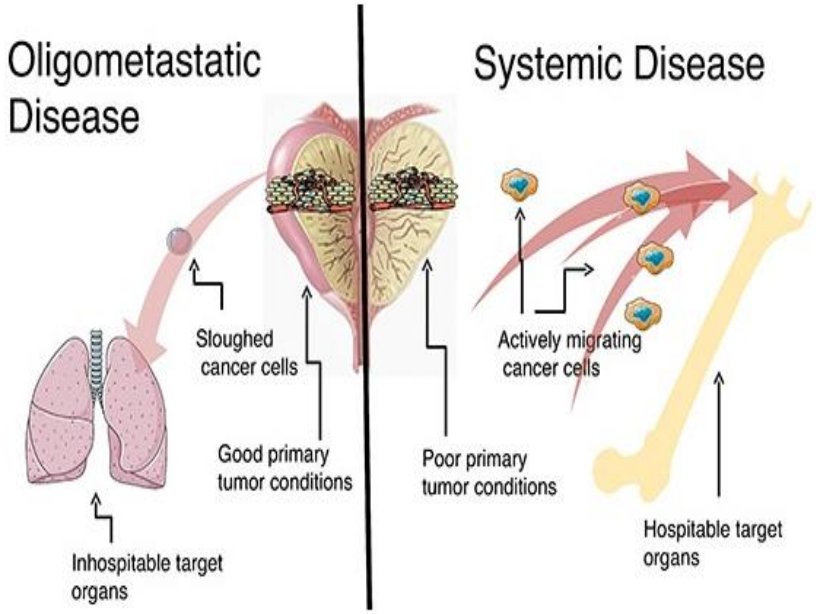
Locally Advanced

local
& Systemic

Metastatic

Systemic

1994 ,
Spectrum theory
By Hellman



Effective local ablative therapy

Effective systemic therapy

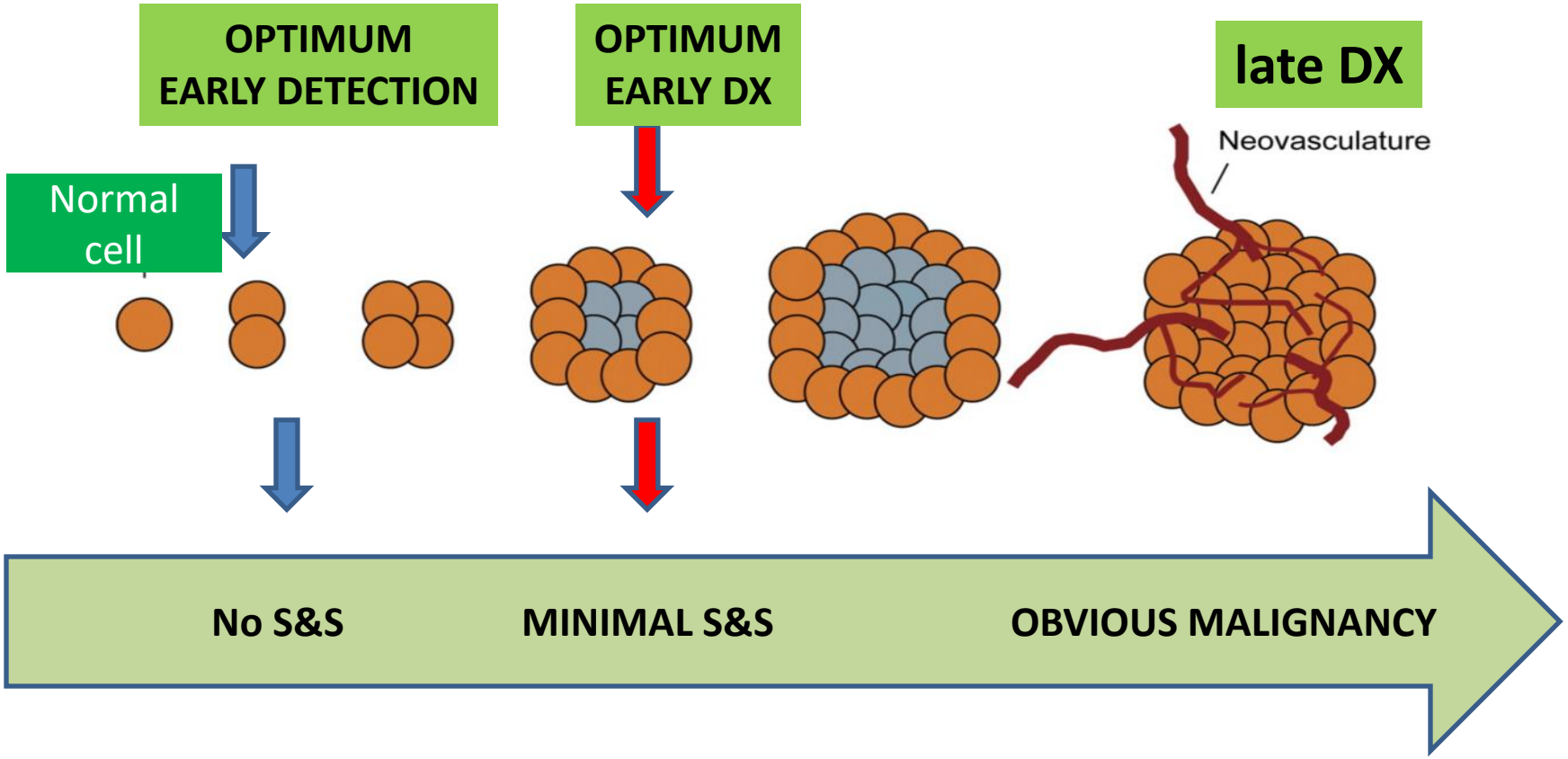
WHAT DID CHANGE THE FACE OF ONCOLOGY?

- The change in our understanding of the ways of cancer development and dissemination.
- **Improvement in:**

Screening & Early detection.

- The Change of the Therapeutic Strategies

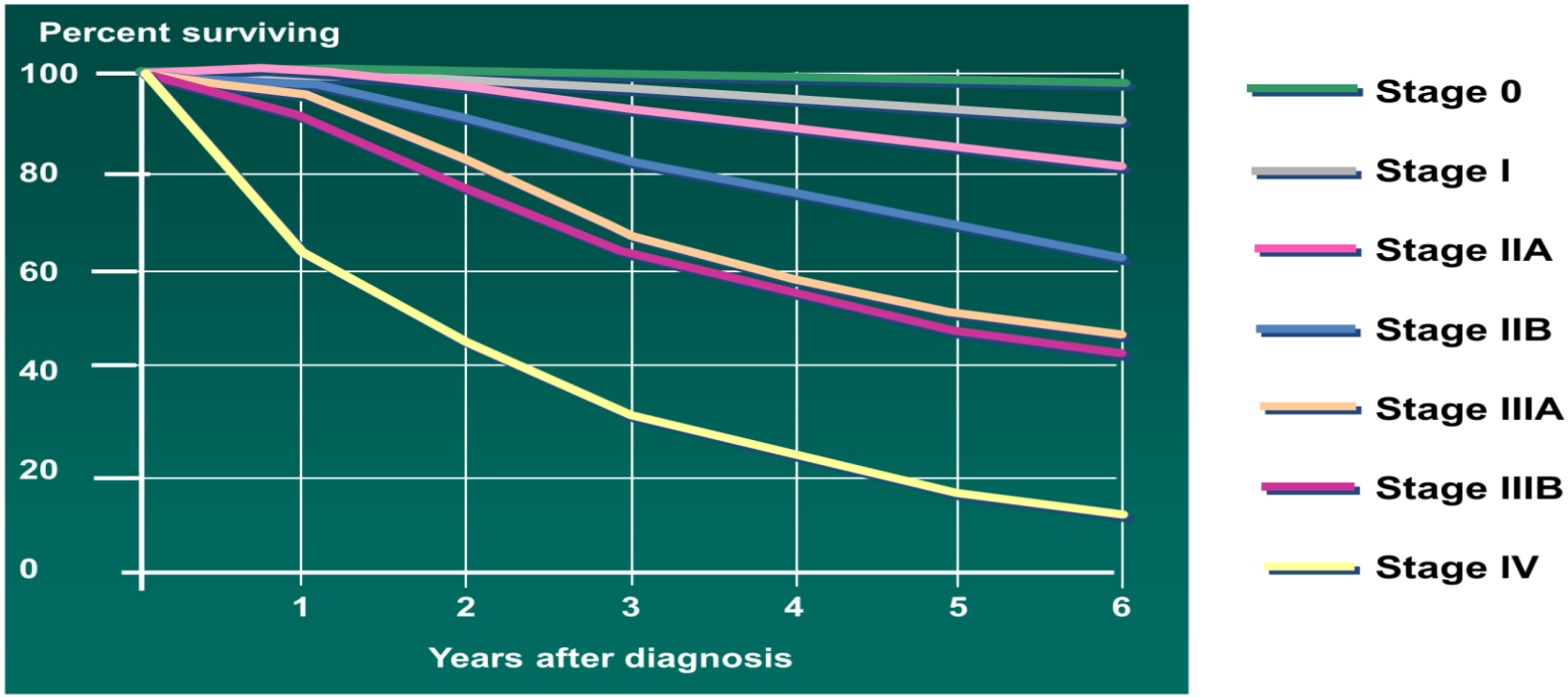
CANCER DEVELOMENT STAGES



Cancer Stage		
Early	Advanced	Late

Curable	Non-curable

To detect asymptomatic in the early-stage of the disease



EARLY DETECTION Vs EARLY DIAGNOSIS

	EARLY DETECTION	EARLY DIAGNOSIS
S& S	NON	MINIMAL
INVASIVE CANCER	+/-	YES
MASS SCREENING	YES	NO
FOCUS ON HIGH RISK GROUP	ESSENTIAL	NEEDED
IMPACT ON SURVIVAL	MAY BE	MORE DEFINTE
WHAT IS NEEDED?	PUBLIC & HEALTH CARE GIVERS AWARENESS	PHYSICIAN AWERENESS

Questions?

- **Is early detection an easy job?**

& What are the needed requirements for effective screening?

Perfect Screening Test

Is not found yet !

- Simple
- Cheap
- Accurate (Highly sensitive & Highly specific)
- Cost effective
- Widely accepted
- Non invasive and Non Morbid

So far ,,,, we have screening programs for only 6 />100 cancer types

Where are we standing?

Screening program are approved for:

-Breast Ca

-Colon Ca

-Lung cancer

-Prostate cancer

-Cervical cancer

WHAT DID CHANGE THE FACE OF ONCOLOGY?

- The change in our understanding of the ways of cancer development and dissemination.
  - **Improvement in: prevention, screening &**
    - **early detection.**
- The Change of the Therapeutic Strategies

Cancer early detection , is it easy?

Cancer Signs and Symptoms

-Cancer gives most people **no** symptoms or signs that **exclusively** indicate the disease.

-Unfortunately, every complaint or symptom of cancer can be explained by a harmless condition as well.

1- When to suspect cancer?

Cancer Signs and Symptoms

What are the clues???????

-Persistent

-Progressive

-Disabling

Cancer Signs and Symptoms

Do not forget the constitutional symptoms:

-Fatigue

-Fever

-Sweating

-Wt loss

Cancer Signs and Symptoms

What are the clues???????

- Symptoms & Signs changes according to the site of origin

Defining Cancer

Cancer is a group of diseases in which abnormal cells divide and escape the body control.

These cells are able to:

1-Invade surrounding tissues

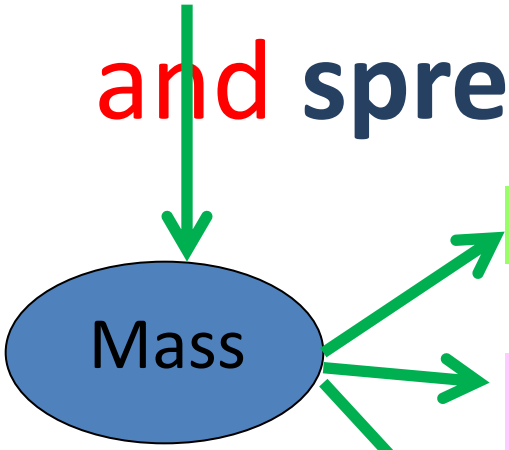
2-Send distant metastases.

3- Lost their functions

Cancer Signs and Symptoms

Think about the pathology and site:

- Mass that is able to invade locally and **spread** distantly



lump

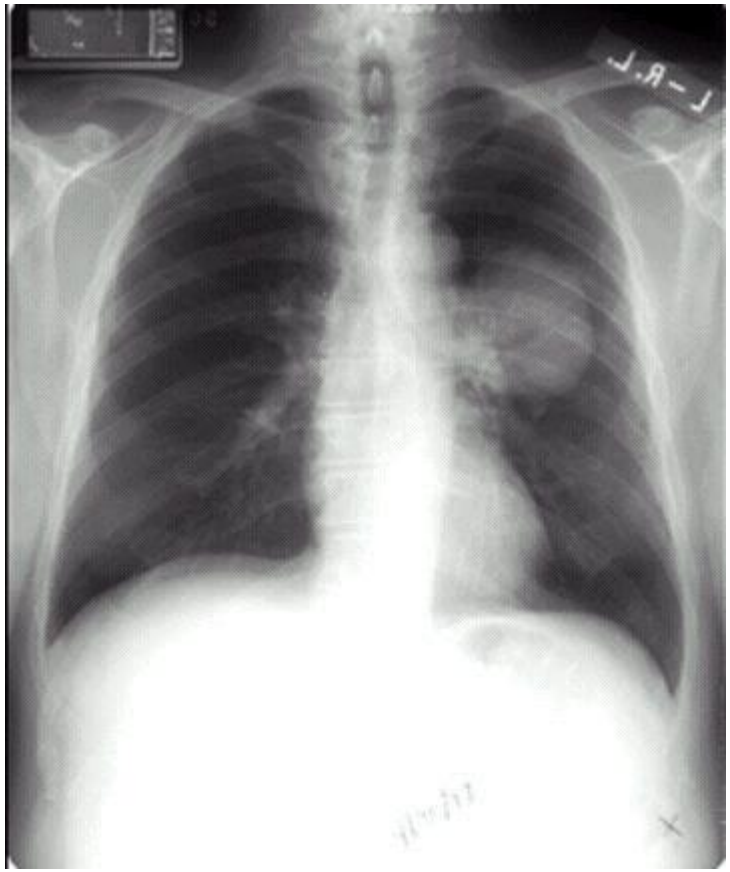
Pressure =on vital organs

Obstruction =of lumens

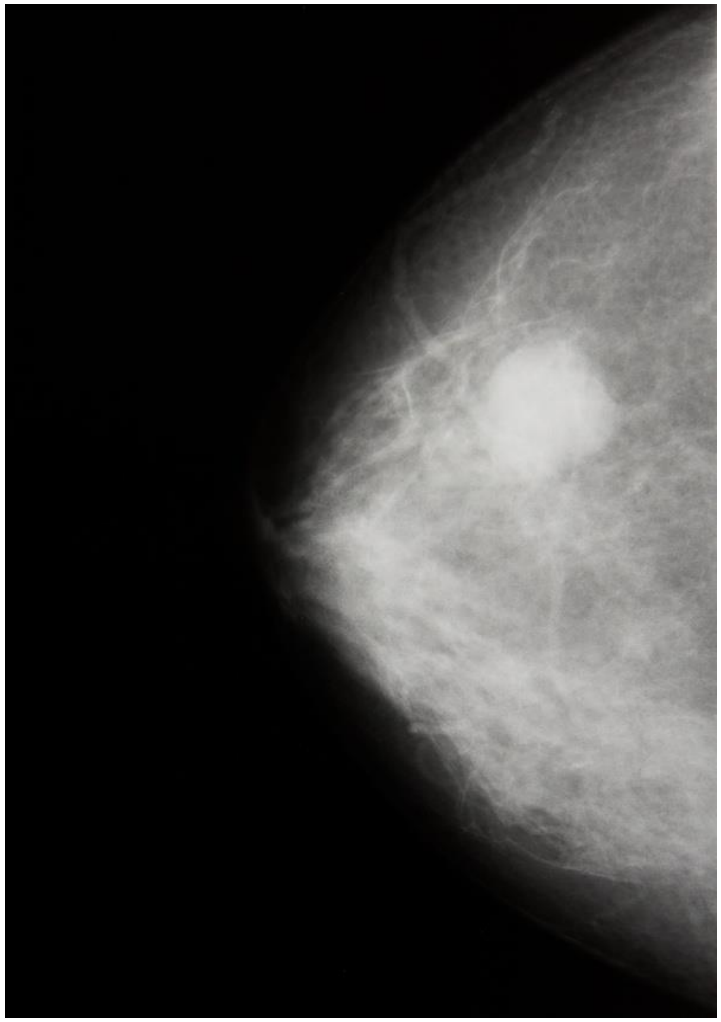
Blood vessels = bleeding
Nerves = pain

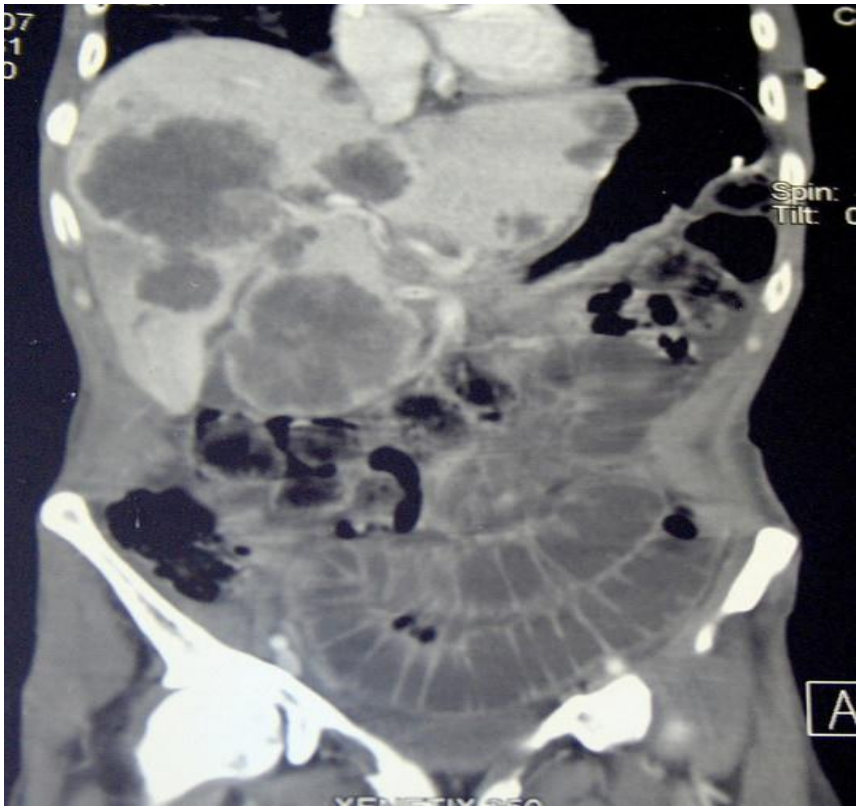
To bone, brain, lung, liver

2- How to diagnose cancer?



2- How to diagnose cancer?

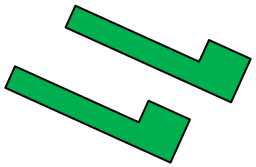




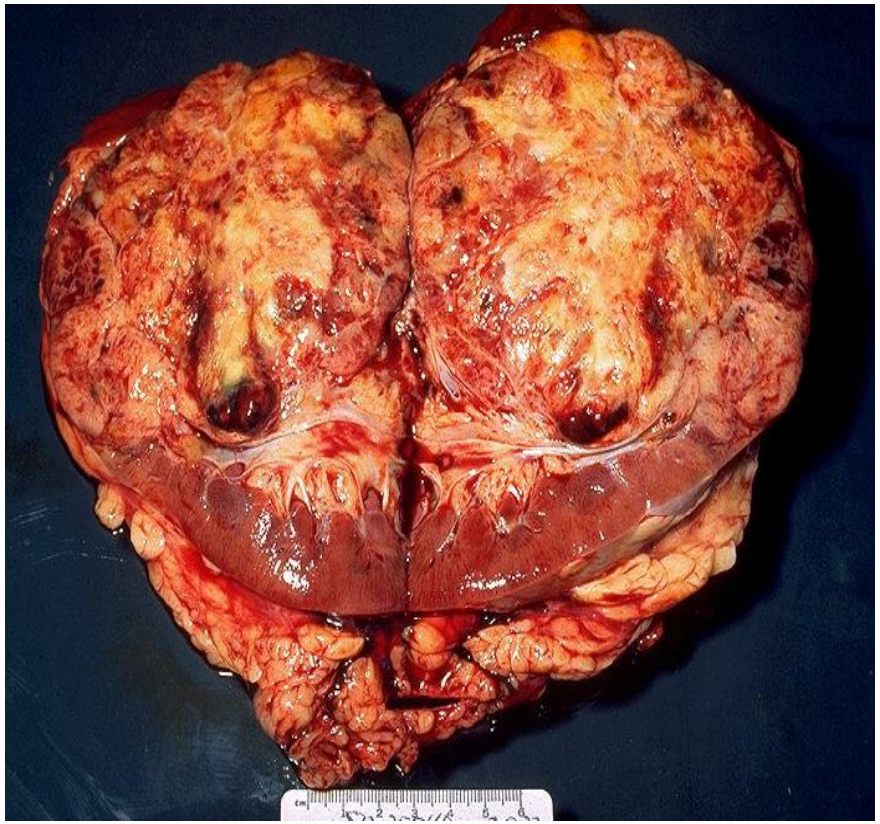
2- How to diagnose cancer?

CANCER DIAGNOSIS

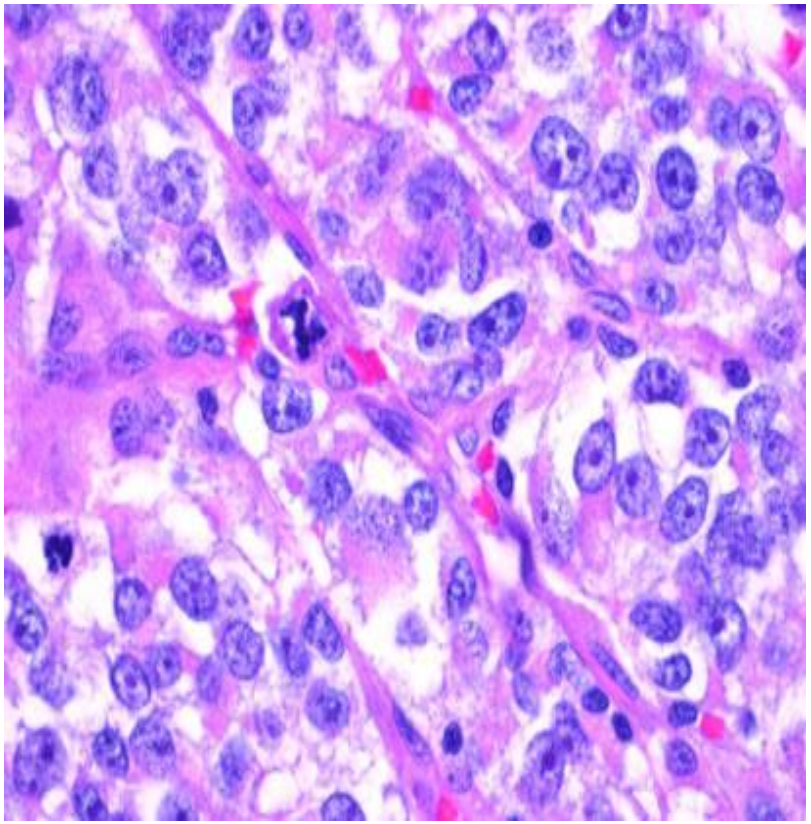
- IS **NOT** A CLINCAL DIAGNOSIS **X**
- IT IS **NOT** A RADIOLOLOGICAL DIAGNOSIS **X**
- IT IS **NOT** SEROLOGICAL DGNOSIS **X**
- IT IS A **PATHOLOGICAL** DIAGNOSI
- IT IS A **TISSUE** DIAGNOSIS-



GROSS AND MICROSCOPIC PICTURE OF RCC



Gross



Microscopic

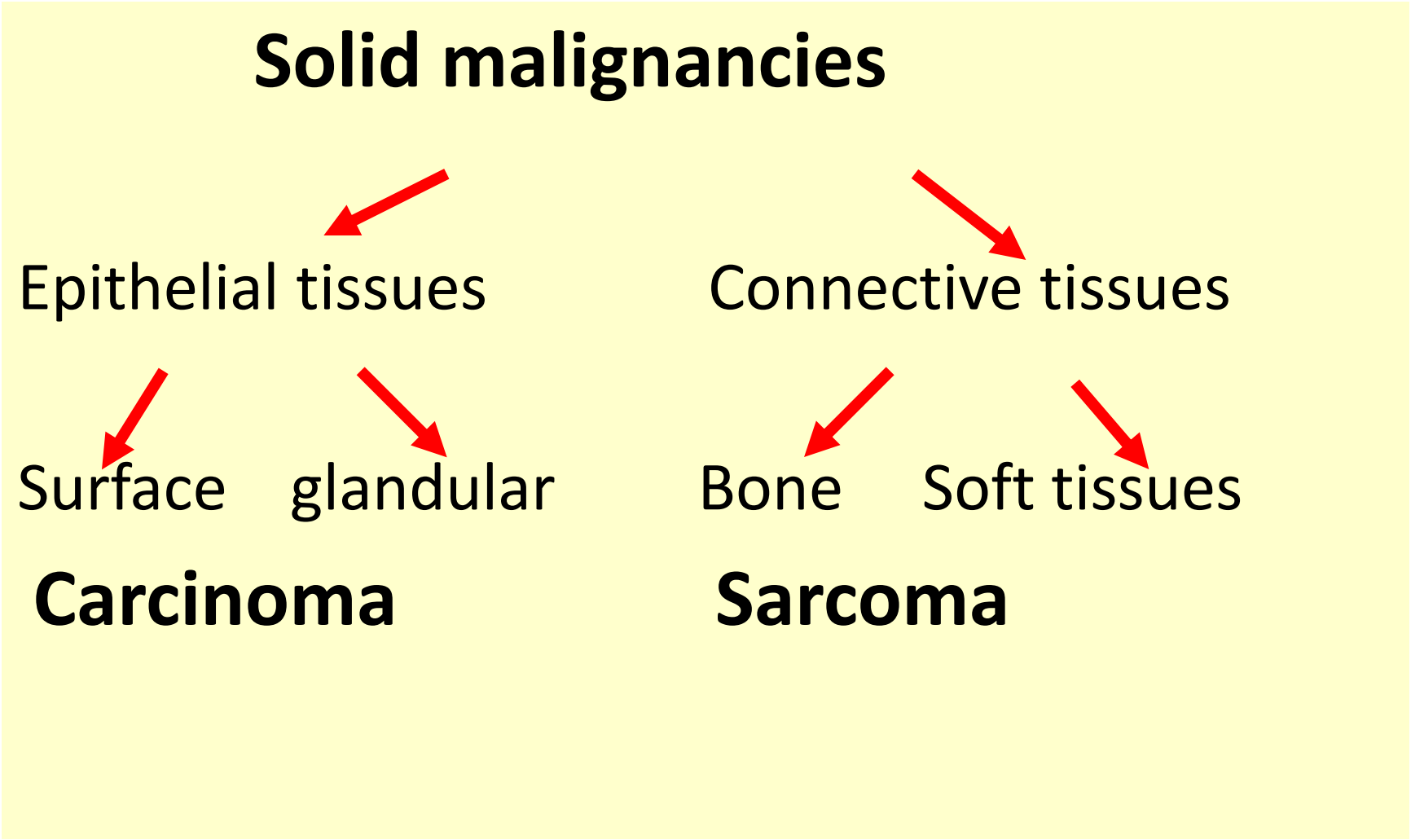
Categories of malignant disorders

- Liquid malignancies

  1-Myeloproliferative disorders= leukemia

  2-lymphopoliferative disorders= leukemia
- Solid malignancies

Categories of malignant disorders



3- What the essential work up for staging?

T= tumor
N= Node
M= Metastases

Clinical TNM
Radiological TNM
Pathological TNM

- RADIOLOGY:
XRAY
MRI
CT
US

SURGICAL STAGING

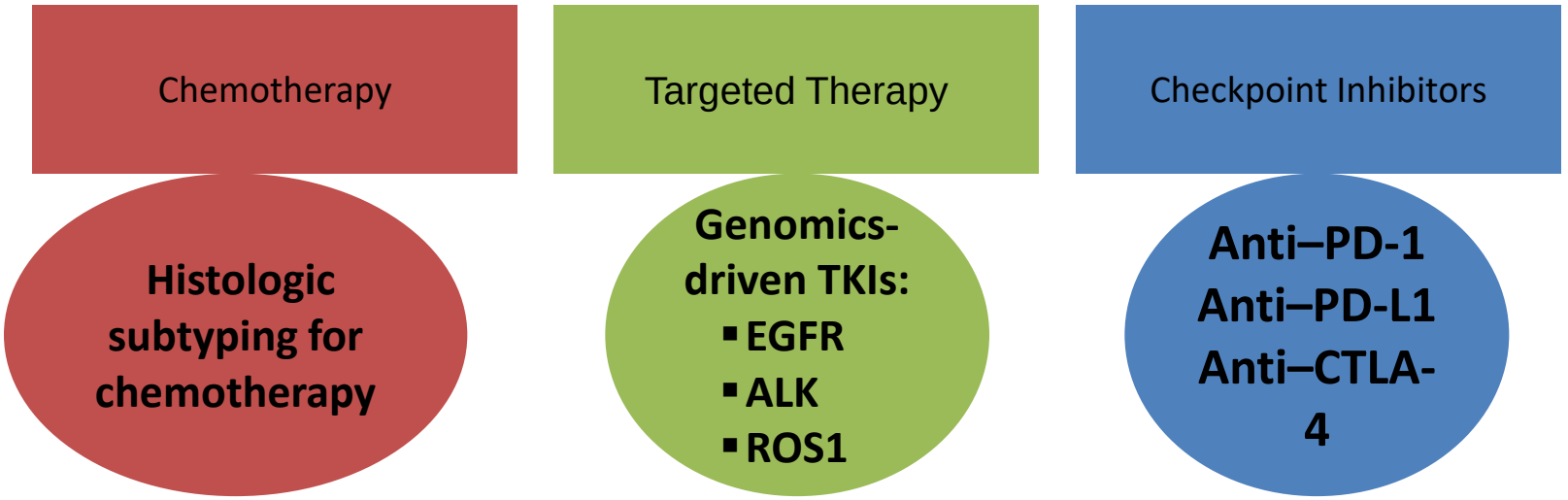
WHAT DID CHANGE THE FACE OF ONCOLOGY?

- **The Change of the Therapeutic Strategies**

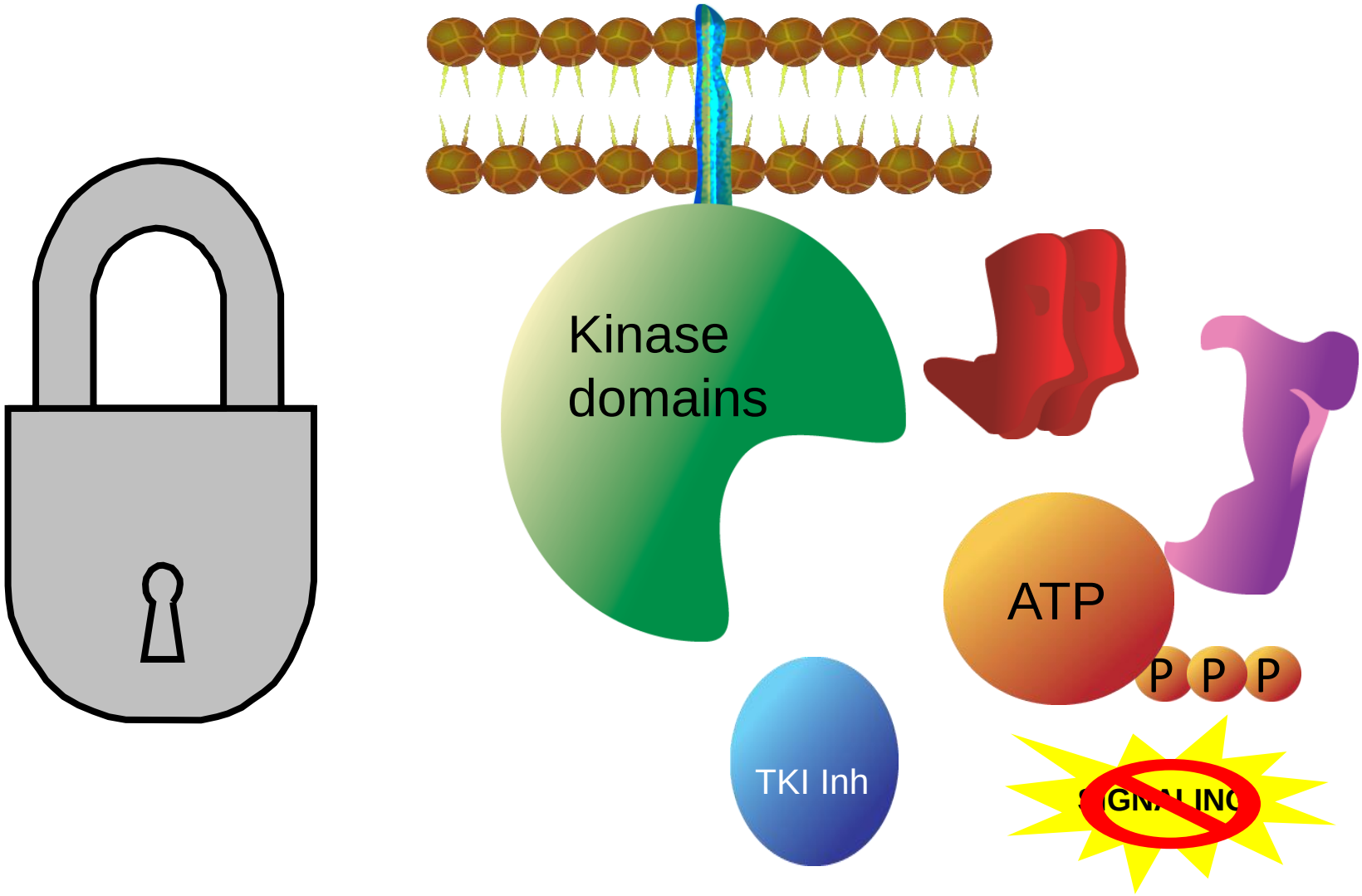
Change the paradigm of discovering, developing and disseminating new anticancer therapies

Try something	Identify the molecular target
See if it works	Prove that it works
GUESS → DRUG	MECHANISM → DRUG

Moving towards more of Personalized Therapy

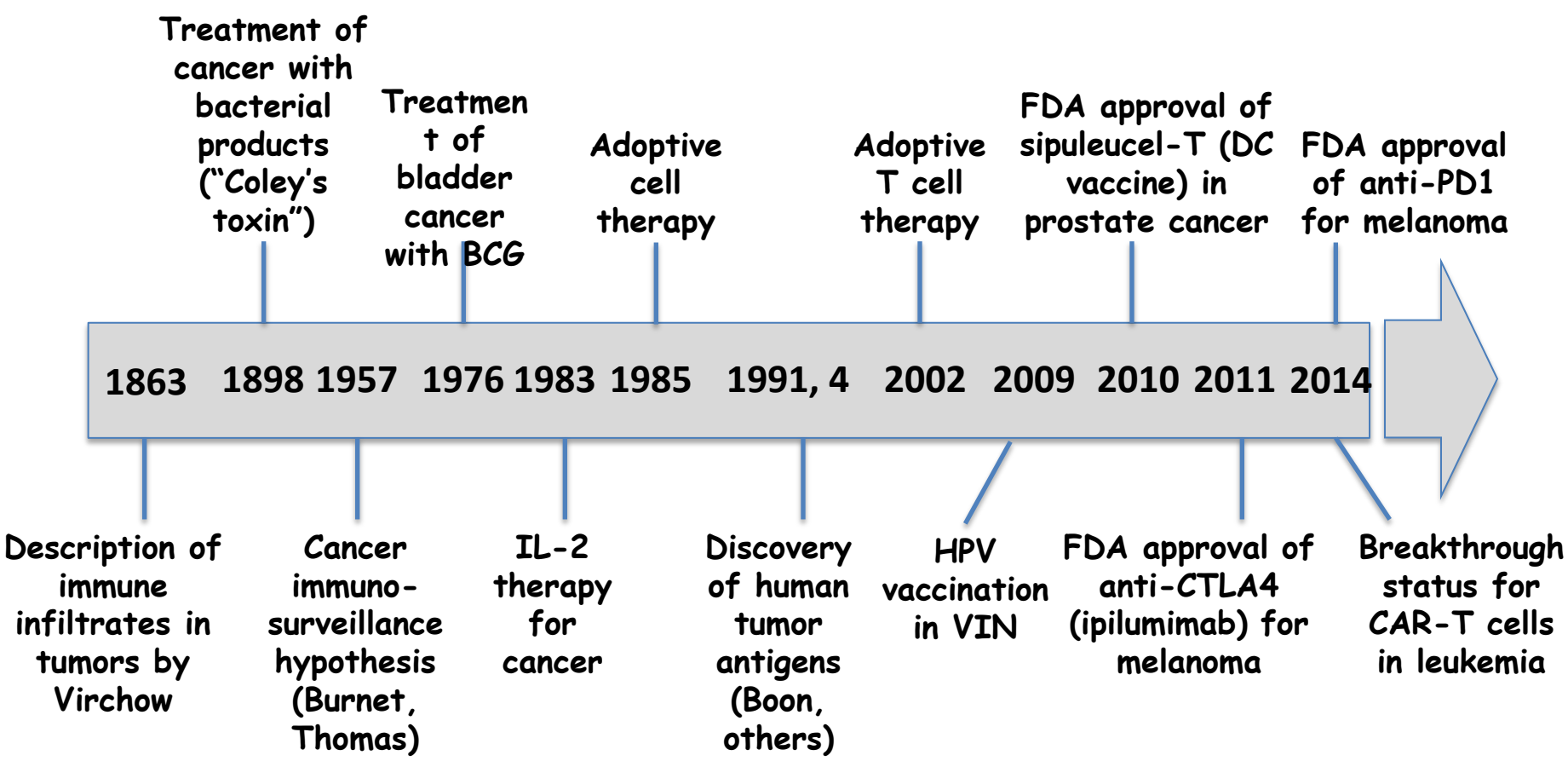


TKI inhibitors
Mechanism of Action

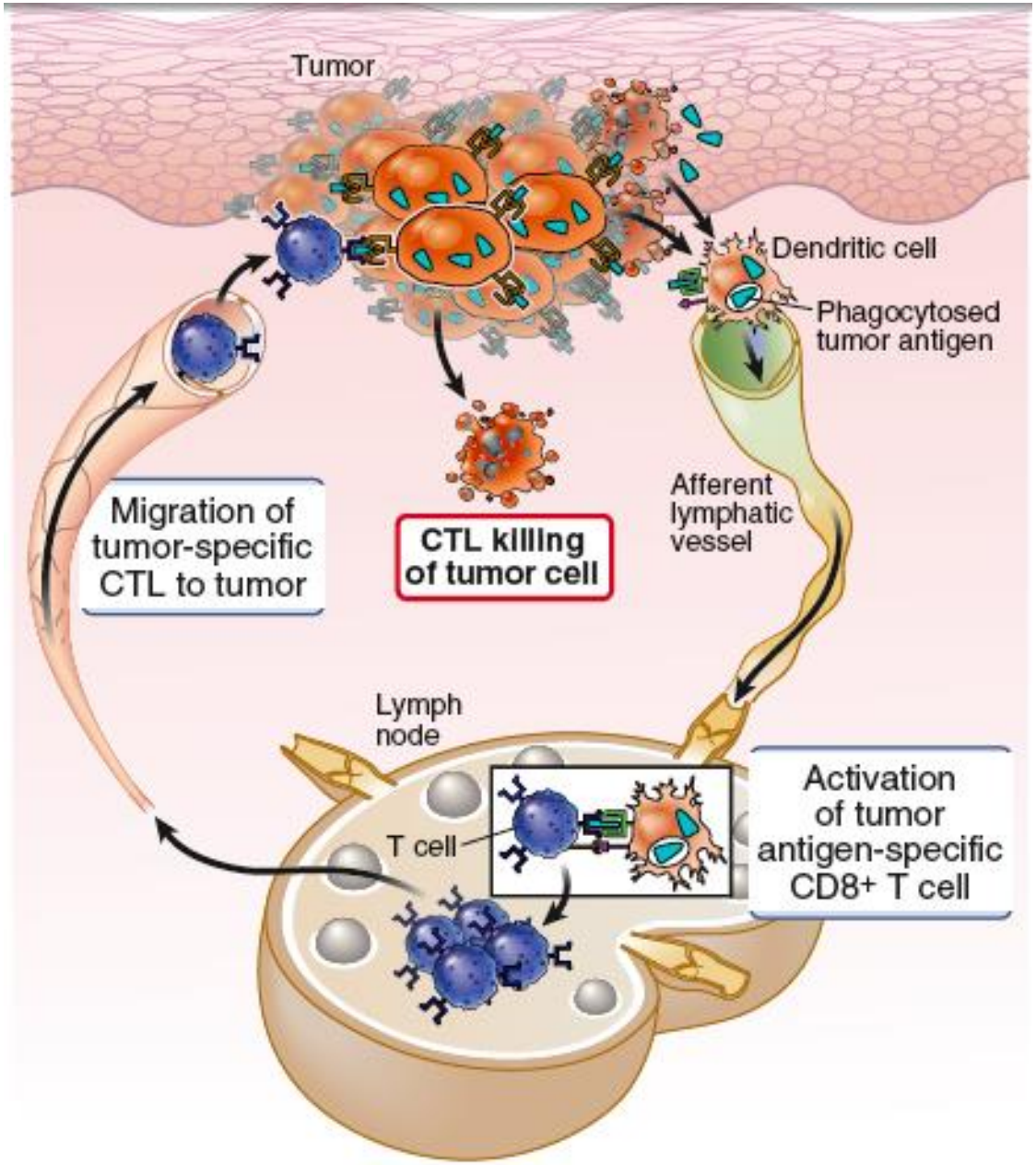


IMMUNO THERAPY

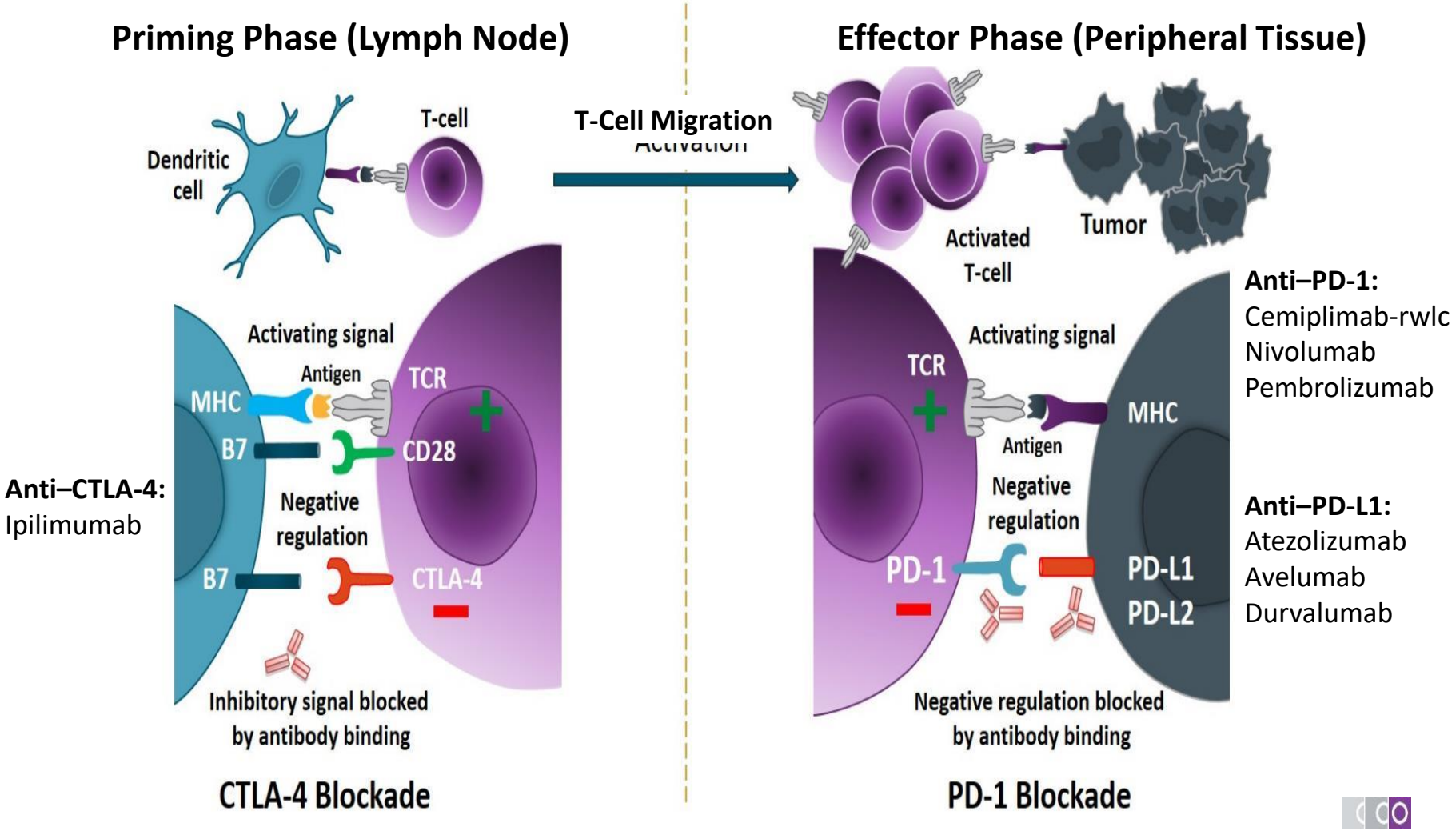
The history of cancer immunotherapy: from empirical approaches to rational, science-based therapies



T cell responses to tumors



CTLA-4 and PD-1/PD-L1 Checkpoint Blockade for Cancer Treatment



Ribas. NEJM. 2012;366:2517.

Slide credit: clinicaloptions.com

Where are we standing?

1- Tumors that can be cured:

lymphomas, leukemia, early solid tumors

2- Tumors that can have prolonged survival:

Locally advanced and some of
the metastatic tumors

3- Tumors that can be palliated:

Metastatic solid tumors

We need to change the Sad face of Oncology?

- **Are we going to cure cancer???**

THE ANSWER IS YES AND WE WILL?

- The change in our understanding of the ways of cancer development and dissemination.
- **Improvement in: prevention, screening & early detection.**
- The Change of the Therapeutic Strategies

THANK YOU

Prof A Abd el Warith