

Curable cancers: Progress in Oncology

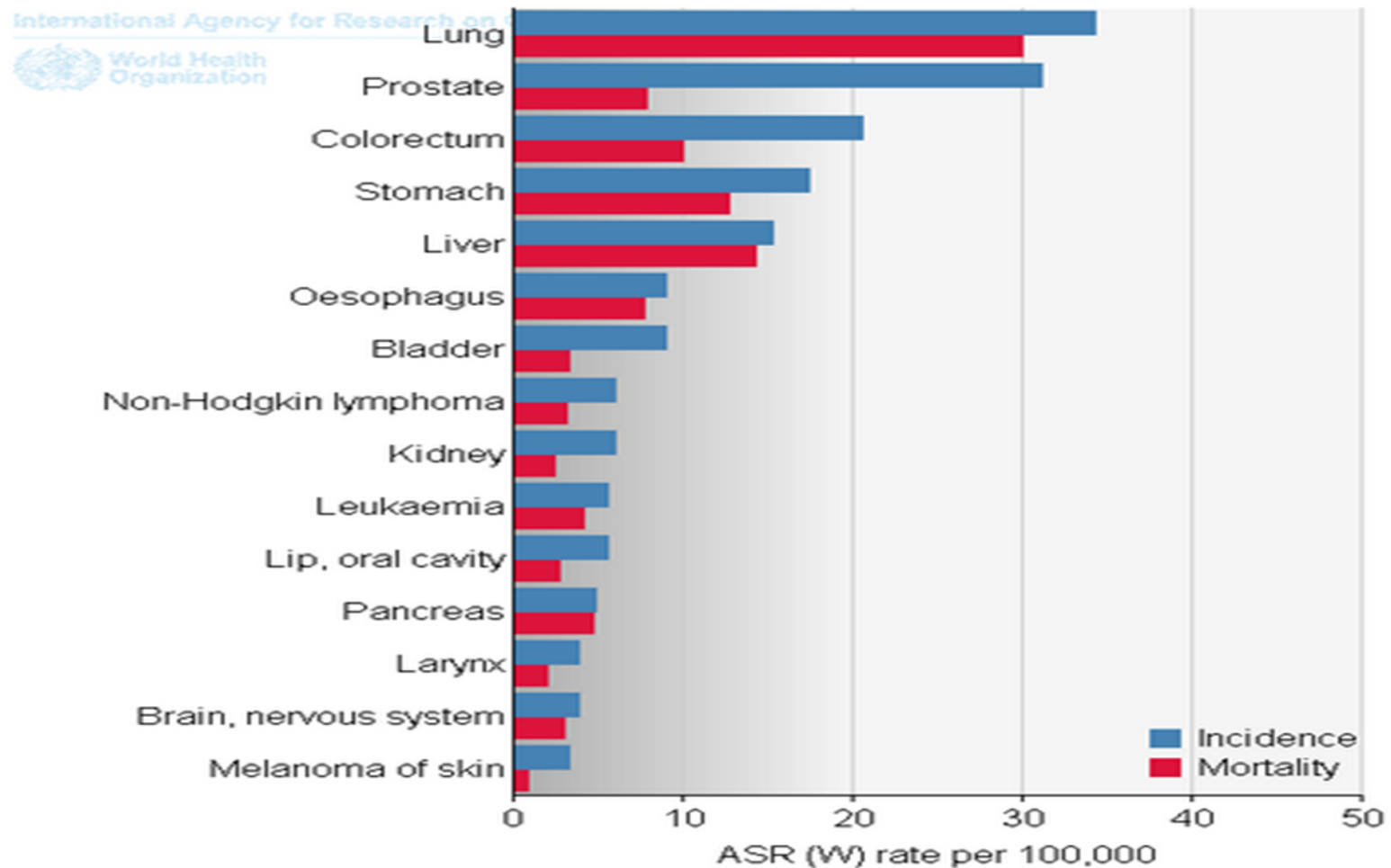
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Introduction

- Cancer is one of the leading causes of morbidity and mortality worldwide, with approximately 14 million new cases in 2012
- Was responsible for 8.8 million deaths in 2015
- Nearly 1 in 6 deaths is due to cancer

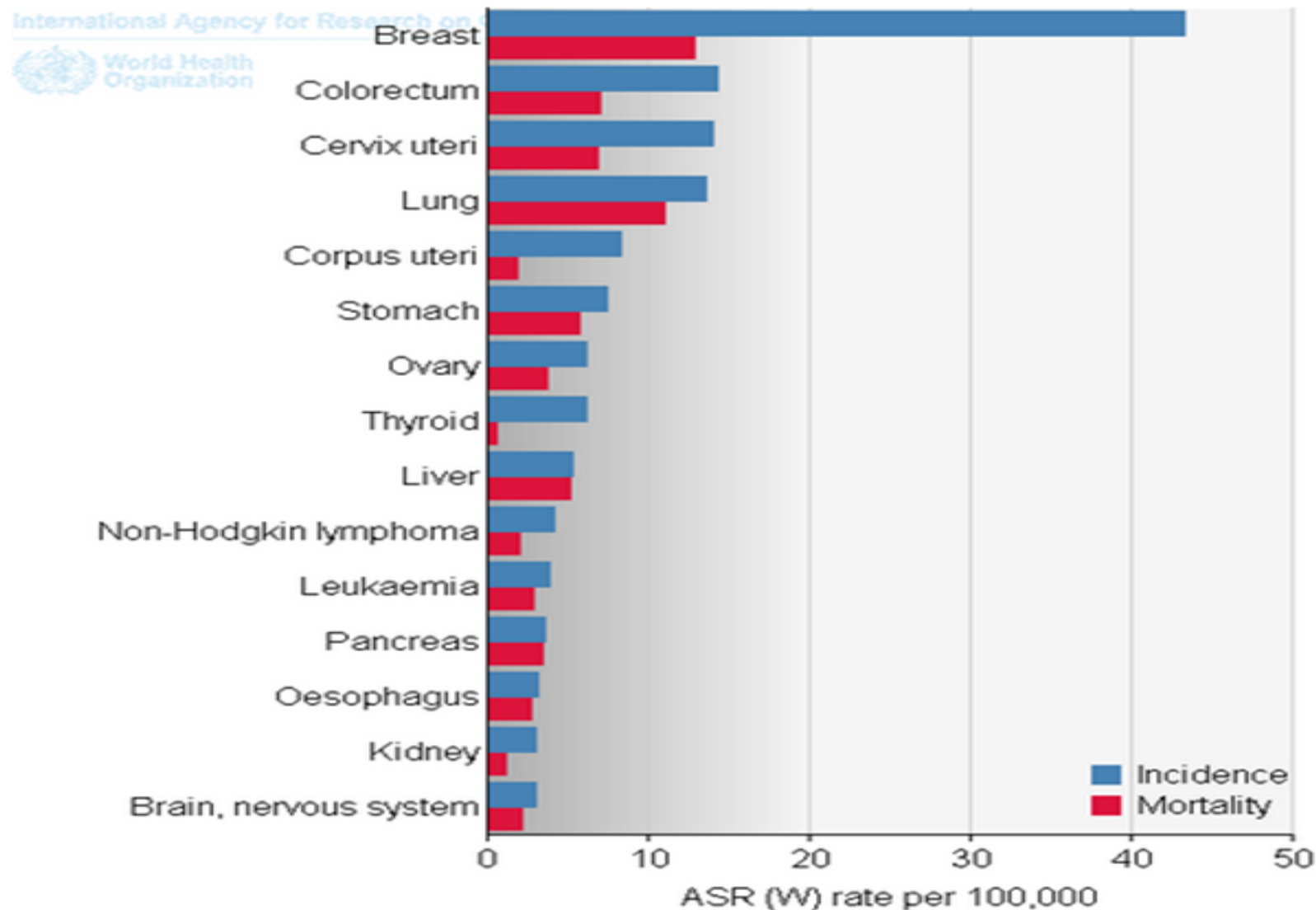
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Estimated age-standardised incidence and mortality rates: men



Contd

Estimated age-standardised incidence and mortality rates: women



Contd

- Approximately 70% of cancer deaths occur in low- and middle-income countries
- Tobacco use is the most important risk factor for cancer and is responsible for approximately 22% of cancer deaths
- Cancer causing infections, such as hepatitis and human papilloma virus (HPV), are responsible for up to 25% of cancer cases in low- and middle-income countries

Cond



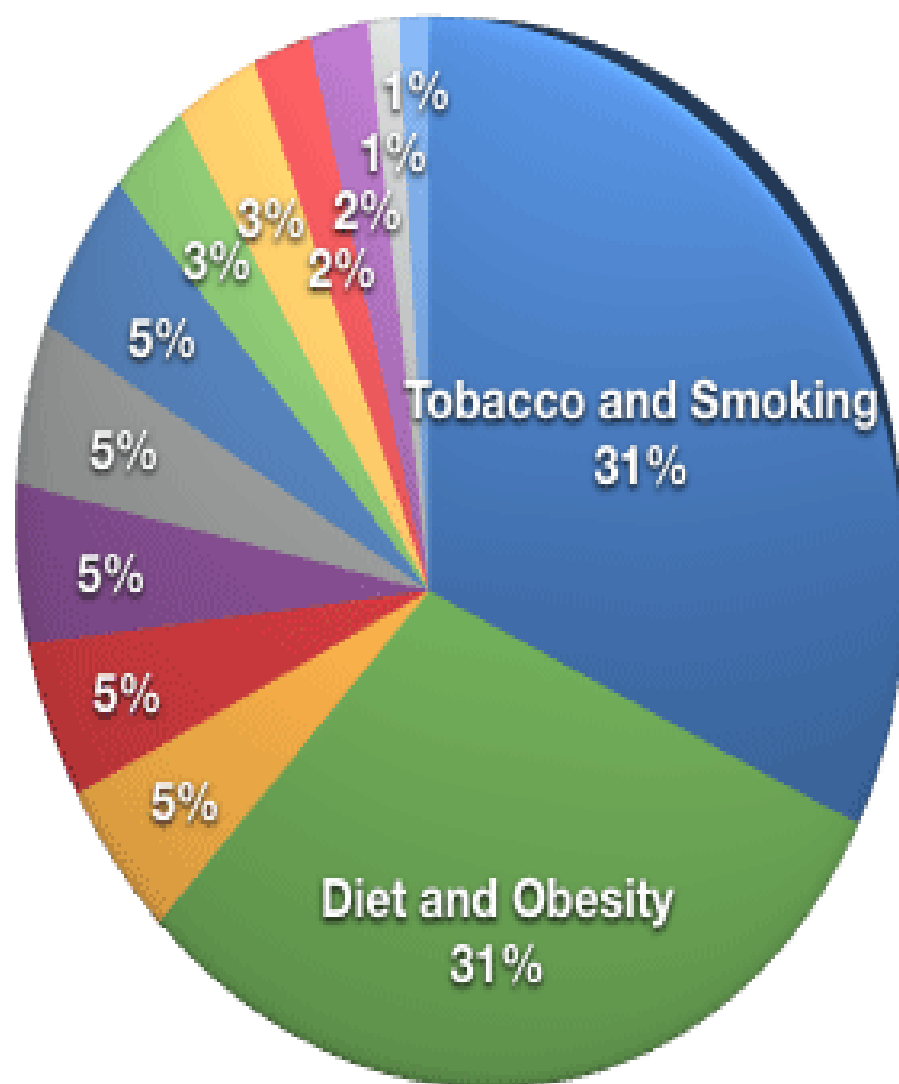
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- Although Bangladesh has no population Based cancer registry, an estimated 122,715 new cases of cancer developed in 2012 which increased to 136,719 in 2015 (GLOBOCAN,2012)
- Lung cancer and mouth/oropharynx cancer rank as the top two prevalent cancers for men and cancer cervix uteri and breast cancer for women (Hussain,2013)

Contd

- The cancer registry maintained by the National Institute of Cancer Research and Hospital (NICRH), Dhaka, showed lung cancer to be the leading cancer (17%), followed by cancers of breast (12%), lymph nodes and lymphatics (8%) and cervix (8%) for sexes combined among all ages
- In malignant hematological disorders more male (69%) are affected than females (31%) and acute myeloid leukemia is the most common condition among both the gender (Hossain et al., 2014b)

Risk Factors for Cancer



- Tobacco and Smoking
- Diet and Obesity
- Sedentary Lifestyle
- Occupational Exposure
- Family History
- Viruses
- Perinatal Factors/Growth
- Alcohol
- Socioeconomic Status
- Pollution
- UV radiation
- Drugs & Medical Procedures
- Salt, Food Additives & Contaminants

Preventable risks

- Around one third of deaths from cancer are due to the 5 leading behavioral and dietary risks:
 - high body mass index
 - low fruit and vegetable intake
 - lack of physical activity
 - tobacco use and
 - alcohol use

- According to Cancer Fact & Figures 2017, by American Cancer Society
- About 16,68780 new cancer cases are expected to be diagnosed in 2017
- About 6,00920 Americans are expected to die of cancer in 2017, about 1650 people per day

- So cancer causes death, but still there is some hope
- Some cancers have good percentage of five year relative survival rates
- Relative survival is the percentage of people who are alive a designated time period (usually 5 years) after a cancer diagnosis divided by the percentage of people expected to be alive in the absence of cancer based on normal life expectancy

Table 8. Five-year Relative Survival Rates* (%) by Stage at Diagnosis, US, 2006-2012

	All stages	Local	Regional	Distant		All stages	Local	Regional	Distant
Breast (female)	90	99	85	26	Ovary	46	92	73	29
Colon & rectum	65	90	71	14	Pancreas	8	29	11	3
Esophagus	18	41	23	5	Prostate	99	>99	>99	29
Kidney†	74	93	66	12	Stomach	30	67	31	5
Larynx	61	76	45	35	Testis	95	99	96	74
Liver‡	18	31	11	3	Thyroid	98	>99	98	55
Lung & bronchus	18	55	28	4	Urinary bladder§	78	70	35	5
Melanoma of the skin	92	98	62	18	Uterine cervix	68	91	57	17
Oral cavity & pharynx	64	83	63	38	Uterine corpus	82	95	69	17

*Rates are adjusted for normal life expectancy and are based on cases diagnosed in the SEER 18 areas from 2006-2012, all followed through 2013. †Includes renal pelvis.

‡Includes intrahepatic bile duct. §Rate for in situ cases is 96%.

Local: an invasive malignant cancer confined entirely to the organ of origin. **Regional:** a malignant cancer that 1) has extended beyond the limits of the organ of origin directly into surrounding organs or tissues; 2) involves regional lymph nodes; or 3) has both regional extension and involvement of regional lymph nodes. **Distant:** a malignant cancer that has spread to parts of the body remote from the primary tumor either by direct extension or by discontinuous metastasis to distant organs, tissues, or via the lymphatic system to distant lymph nodes.

Source: Howlader N, Noone AM, Krapcho M, et al. (eds). *SEER Cancer Statistics Review, 1975-2013*, National Cancer Institute, Bethesda, MD, http://seer.cancer.gov/csr/1975_2013/, based on November 2015 SEER data submission, posted to the SEER website April 2016.

Table 7. Trends in 5-year Relative Survival Rates* (%) by Race, US, 1975-2012

	All races			White			Black		
	1975-77	1987-89	2006-12	1975-77	1987-89	2006-12	1975-77	1987-89	2006-12
Brain & other nervous system	22	29	35	22	28	33	25	32	44
Breast (female)	75	84	91	76	85	92	62	71	82
Colon & rectum	50	60	66	50	60	67	45	52	59
Esophagus	5	9	21	6	11	22	4	7	13
Hodgkin lymphoma	72	79	89	72	80	89	70	72	86
Kidney & renal pelvis	50	57	75	50	57	75	49	55	75
Larynx	66	66	62	67	67	64	58	56	52
Leukemia	34	43	63	35	44	64	33	35	58
Liver & intrahepatic bile duct	3	5	18	3	6	18	2	3	13
Lung & bronchus	12	13	19	12	13	19	11	11	16
Melanoma of the skin	82	88	93	82	88	93	57†	79†	69
Myeloma	25	27	50	24	27	50	29	30	52
Non-Hodgkin lymphoma	47	51	73	47	51	74	49	46	65
Oral cavity & pharynx	53	54	67	54	56	69	36	34	47
Ovary	36	38	46	35	38	46	42	34	38
Pancreas	3	4	9	3	3	9	2	6	8
Prostate	68	83	99	69	84	>99	61	71	97
Stomach	15	20	31	14	18	30	16	19	30
Testis	83	95	97	83	95	97	73†‡	88	90
Thyroid	92	94	98	92	94	99	90	92	97
Urinary bladder	72	79	79	73	80	79	50	63	66
Uterine cervix	69	70	69	70	73	71	65	57	58
Uterine corpus	87	82	83	88	84	86	60	57	66

*Rates are adjusted for normal life expectancy and are based on cases diagnosed in the SEER 9 areas from 1975 to 77, 1987 to 89, and 2006 to 2012, all followed through 2013. †The standard error is between 5 and 10 percentage points. ‡Survival rate is for cases diagnosed from 1978 to 1980.

Source: Howlader N, Noone AM, Krapcho M, et al. (eds). *SEER Cancer Statistics Review, 1975-2013*, National Cancer Institute, Bethesda, MD, www.seer.cancer.gov/csr/1975_2013/, based on November 2015 SEER data submission, posted to the SEER website April 2016.

- With the advent of new knowledge regarding cancer pathogenesis & new diagnostic approaches
- Early detection of cancer is possible & many targeted therapy is available
- So some cancers are curable. Cure is a statistical term that applies to groups of cancer patients rather than to individual patients

- Cure implies those who are rendered clinically free of detectable cancer and who have the same survival expectancy as a healthy age matched control group
- A cure does not guarantee that the particular patient meeting this criteria will not eventually die from the original cancer
- So there is no cancer curable in reality
- May recur after cure

Curable cancer

- For a cancer to be curable there are some factors:
 - Type of cancer(Tissue type)
 - The stage of the cancer
 - Presence of distant spread
 - Co-morbid condition
 - Functional status
 - Treatment response

Curable Cancer

- Early screening & diagnosis
- Newer radiation technique
 - 3 dimensional conformal therapy (3D CRT)
 - Intensity Modulated Radiation Therapy(IMRT)
 - IGRT & Gated radiotherapy
 - Brachytherapy
 - Intra operative radiotherapy

Curable Cancer

- Development of newer Chemotherapy
- Hormonal therapy
- Targeted therapy

Tumor marker

MARKERS	ASSOCIATED CANCERS
A) HORMONES	
*Human Chorionic gonadotropin	Trophoblastic tumors, non seminomatous testicular tumors
*Calcitonin	Medullary carcinoma of thyroid
*Catecholamines and metabolites	Pheochromocytomas and related tumors
*Ectopic Hormones	Paraneoplastic syndromes
B) ONCOFETAL ANTIGENS	
*Alpha fetoprotein	Hepatocellular carcinomas, non seminomatous germ cell tumors of testis
*Carcinoembryonic antigen	Carcinomas of the colon, pancreas, lung, stomach and heart
C) ISOENZYMES	
*Prostatic acid phosphatase	Prostate Cancer
*Neuron specific enolase	Small cell cancer, Neuroblastoma

Tumor marker

D) SPECIFIC PROTEINS	
*Immunoglobulins	Multiple Myeloma and other gammopathies
*Prostate-specific antigen and prostate - specific membrane antigen	Prostate Cancer
E) MUCINS and other glycoproteins	
*CA-125	Ovarian cancer
*CA-19-9	Colon Cancer, Pancreatic Cancer
*CA-15-3	Breast Cancer
F) NEW MOLECULAR MARKERS	
*p53, APC, RAS mutations in stool and serum	Colon Cancer
*p53 and RAS mutations in stool and serum	Pancreatic Cancer
*p53 and RAS mutations in sputum and serum	Lung Cancer
*p53 mutations in urine	Bladder Cancer

Tumor marker: detection

S.N.	SEROLOGY	ENZYME ASSAYS
1)	Immunological	Immunohistochemistry
		Radio-Immunoassay
		Enzyme Linked Immunosorbent Assay
2)	Flow Cytometry	
3)	Cytogenetic analysis	Fluorescent in-situ hybridization
		Spectral Karyotyping
		Comparative genomic hybridization
4)	Genetic analysis	Sequencing (automated)
		Reverse transcription
		Gel electrophoresis
		DNA microarray analysis
5)	Proteins	Surface enhanced laser desorption / Ionization

Curable cancer-Prostate

- Many prostate tumors grow slowly or not at all. They aren't harmful enough to need treatment. Many men with these types of tumors can live for years without problems
- Metastatic prostate cancer difficult to treat. A small percentage of prostate cancers metastasize,(28% of men live 5 years)
- Screening- Digital rectal examination, PSA

Curable cancer-Breast

- The commonest cancer in women
- 5% is due to inheritance of a mutated copy of either BRCA1 or BRCA2
- Common type ductal cell carcinoma
- Screening – breast lump, mammogram
- Modalities of treatment Surgery, Radiotherapy adjuvant and neoadjuvant chemotherapy , Hormonal therapy (tamoxifen, letrozole), MTT (HER2 inhibitor, mTOR inhibitor, Angiogenesis inhibitor, PARP inhibitor)

Curable cancer-Thyroid

- The most common type of thyroid cancer, papillary, grows slowly
- Surgery- Thyroidectomy
- Hormone replacement
- Anaplastic thyroid cancer has a 5-year survival rate of only 7%
- Screening- Thyroid lump or swelling, Thyroid ultrasound

Curable cancer-Testicular cancer

- In its early stages it is curable with surgery to remove one or both testicles that have a tumor
- For later-stage cancers, surgery and radiation or chemotherapy often work well
- No specific screening test, visible testicular swelling

Curable cancer-Melanoma

- Can usually spot melanoma skin cancer with the naked eye while it is still in its early stages
- If it hasn't spread beyond the surface of the skin, cure may possible with surgery
- Metastatic Melanoma (Only 15%-20% got 5 year survival)
- Examine skin for large, dark, oddly shaped, or raised blotches at back and scalp, scrotum, and in between toes
- Positive family history

Curable cancer- Hematological

CML- Use of Imatinib, a BCR-ABL tyrosin kinase inhibitor

- More potent 2nd generation BCR-ABL inhibitors

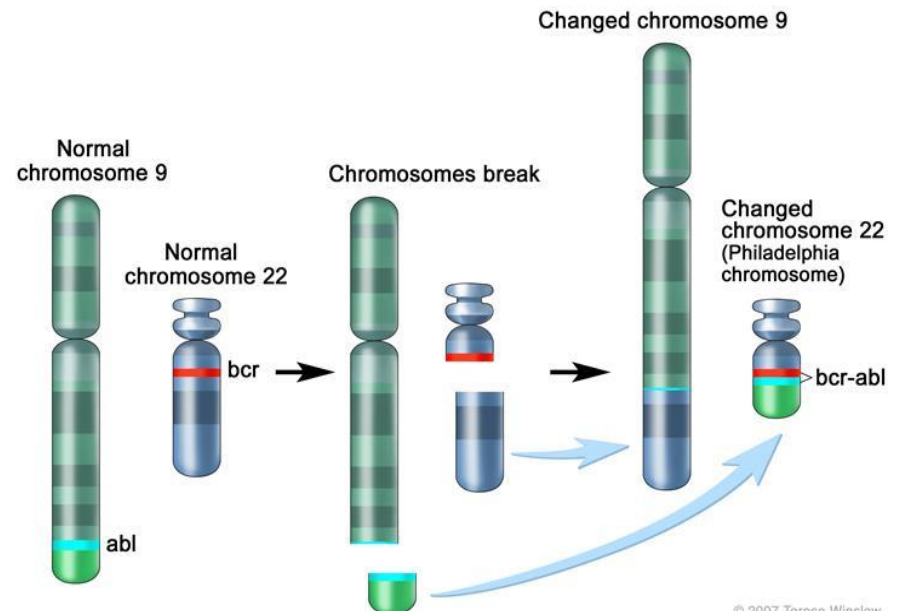
- Dasatinib

- Nilotinib

- Bosutinib

- Ponatinib

- Stem cell transplantation

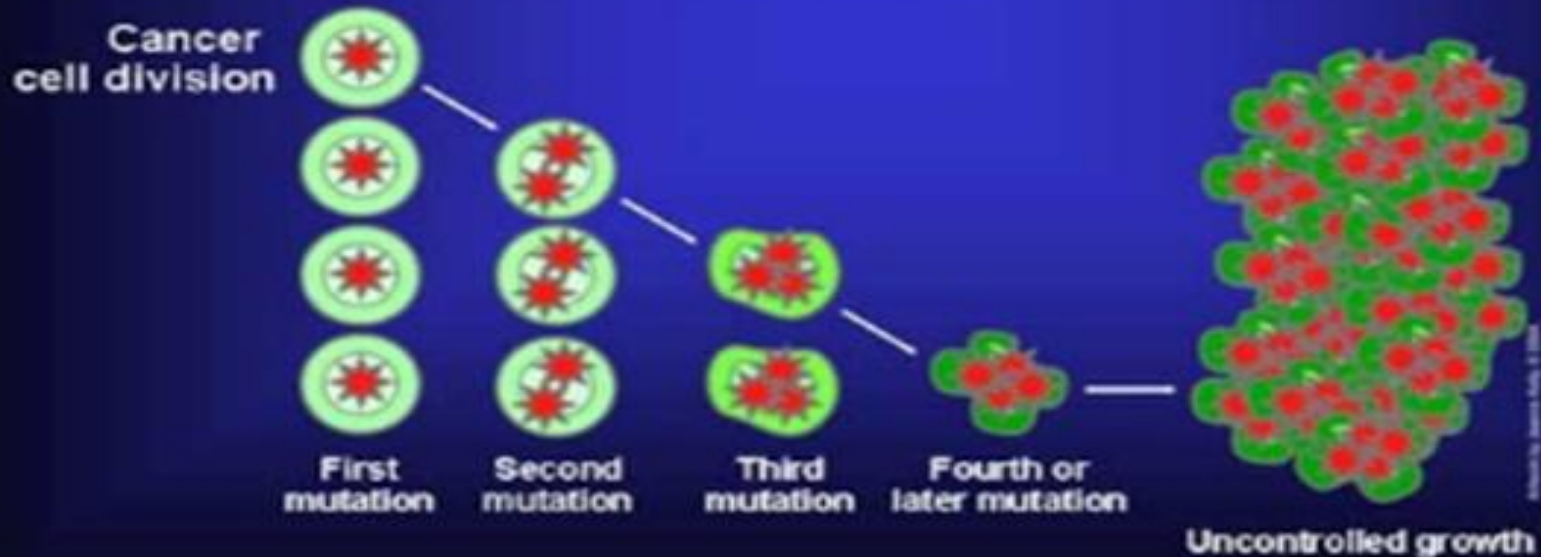
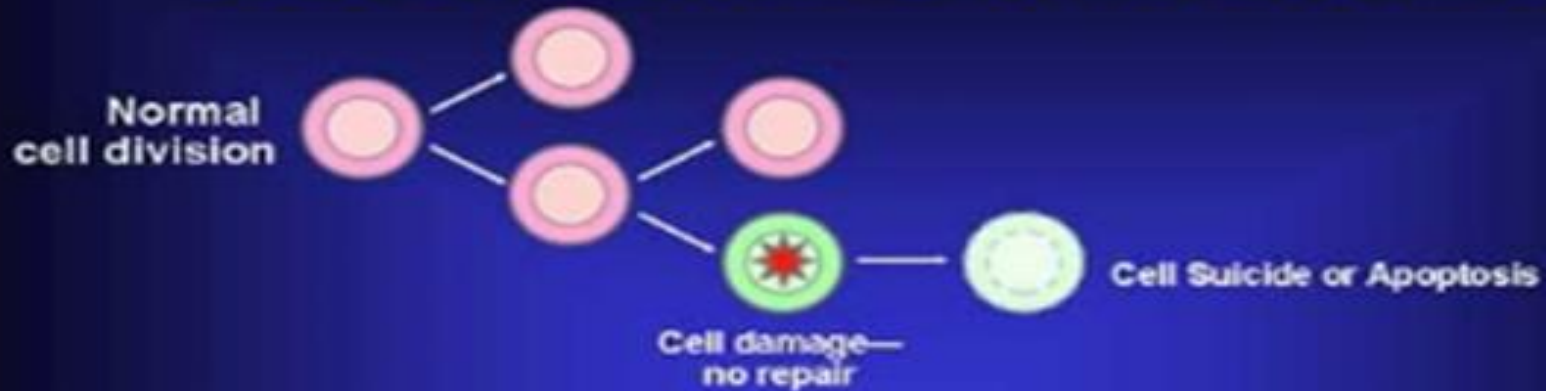


Curable cancer- Hematological

- CLL- Fludarabin+rituximab+cyclophosphamide is 1st line
- Ibrutinib, bendamustine, ofatumumab all have role
- Stem cell transplantation
- In NHL use of rituximab kills CD20 +Ve cells by antibody directed cytotoxicities, apoptosis induction and sensitizes cells to CHOP therapy

Cancer Pathogenesis

Loss of Normal Growth Control



Adapted by Science Today, 4/2004

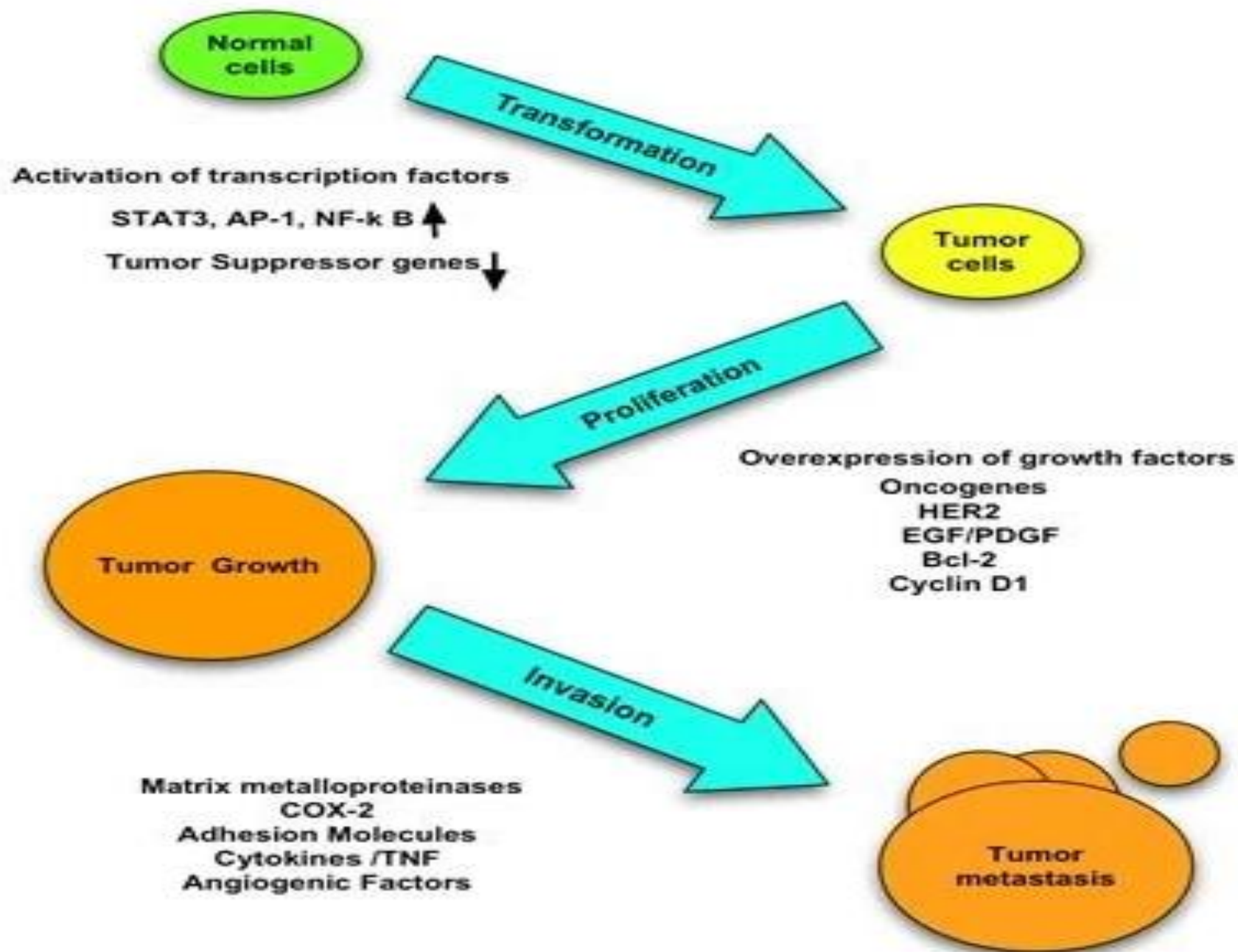


Table 4.1 Examples of oncogenes and tumour suppressor genes frequently mutated in cancer

Gene	Associated disease
Oncogenes	
ABL	CML, ALL
AKT	Ovarian, pancreatic cancers
BRAF	Melanoma, colorectal, thyroid, borderline ovarian cancers, NSCLC
CCND1 (Cyclin D1)	CLL, B-ALL, breast cancer
CDK4	Melanoma, familial malignant melanoma
EGFR	Glioma
HRAS	Infrequent sarcomas, rare other types
KRAS	Pancreatic, colorectal, lung, thyroid cancers, AML, others
MYC	Burkitt lymphoma, B-CLL, others
NRAS	Melanoma, MM, AML, thyroid cancer
PDGFR	GIST, AML, CML

Tumour suppressors	
ATM	T-PLL, leukaemia, lymphoma, ataxia telangiectasia
BCL2	NHL, CLL
BLM	Leukaemia, lymphoma, skin squamous cell, Bloom syndrome
BRCA1	Ovarian cancer, breast cancer, inherited ovarian and breast cancer
CDKN2A (p16INK4A)	Melanoma, pancreatic cancer, multiple other
NBS1	Glioma, medulloblastoma, Nijmegen breakage syndrome
PTEN	Glioma, prostatic, endometrial cancers, Cowden syndrome
RB1 (pRb)	Retinoblastoma, sarcoma, breast, small-cell lung cancer
TP53 (p53)	Breast, colorectal, lung, adrenocortical cancer, glioma, sarcoma, many others, Li–Fraumeni syndrome

ALL, acute lymphocytic leukaemia; AML, acute myelogenous leukaemia; B-ALL, B-cell acute lymphocytic leukaemia; B-CLL, B-cell lymphocytic leukaemia; CLL, chronic lymphocytic leukaemia; CML, chronic myeloid leukaemia; GIST, gastrointestinal stromal tumour; MM, multiple myeloma; NHL, non-Hodgkin lymphoma; NSCLC, non-small-cell lung cancer; T-PLL, T-cell prolymphocytic leukaemia.

The hallmarks of cancer: necessary functional capabilities

- In the current conceptualization, there are eight hallmarks—acquired capabilities—that are common to many forms of human cancer
- Each capability serves a distinct role in supporting the development, progression, and persistence of tumors and their constituent cells

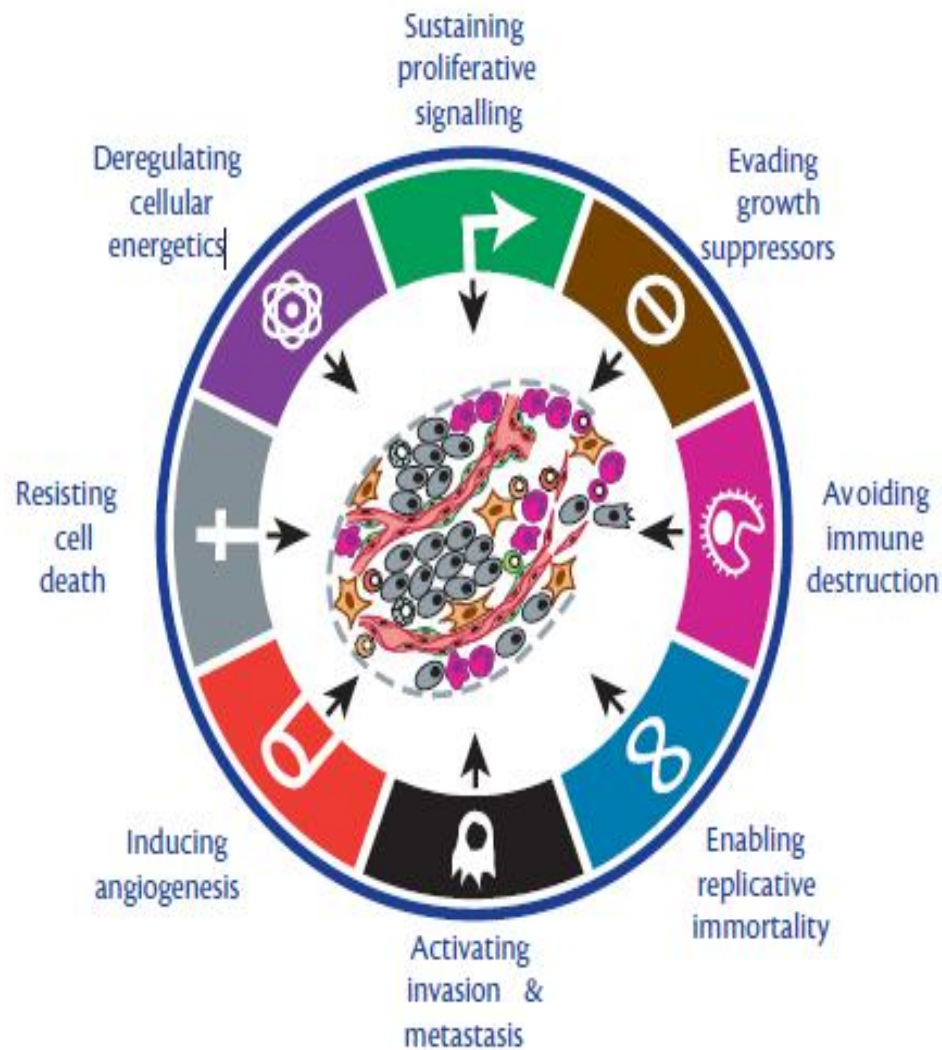


Fig. 1.1 The hallmarks of cancer. Eight distinctive functional capabilities—the hallmarks of cancer—are thought to be necessarily acquired during the multistep pathogenesis pathways leading to most forms of human cancer. Certain forms of cancer may be less dependent on one hallmark or another. Thus, adenomatous tumours evidently lack the capability for invasion and metastasis. Leukaemias may not require angiogenesis or invasive capabilities, although progression to lymphoma almost certainly requires both. And, the necessity for metabolic reprogramming or evading tumour immunity may be less pronounced in certain cancers.

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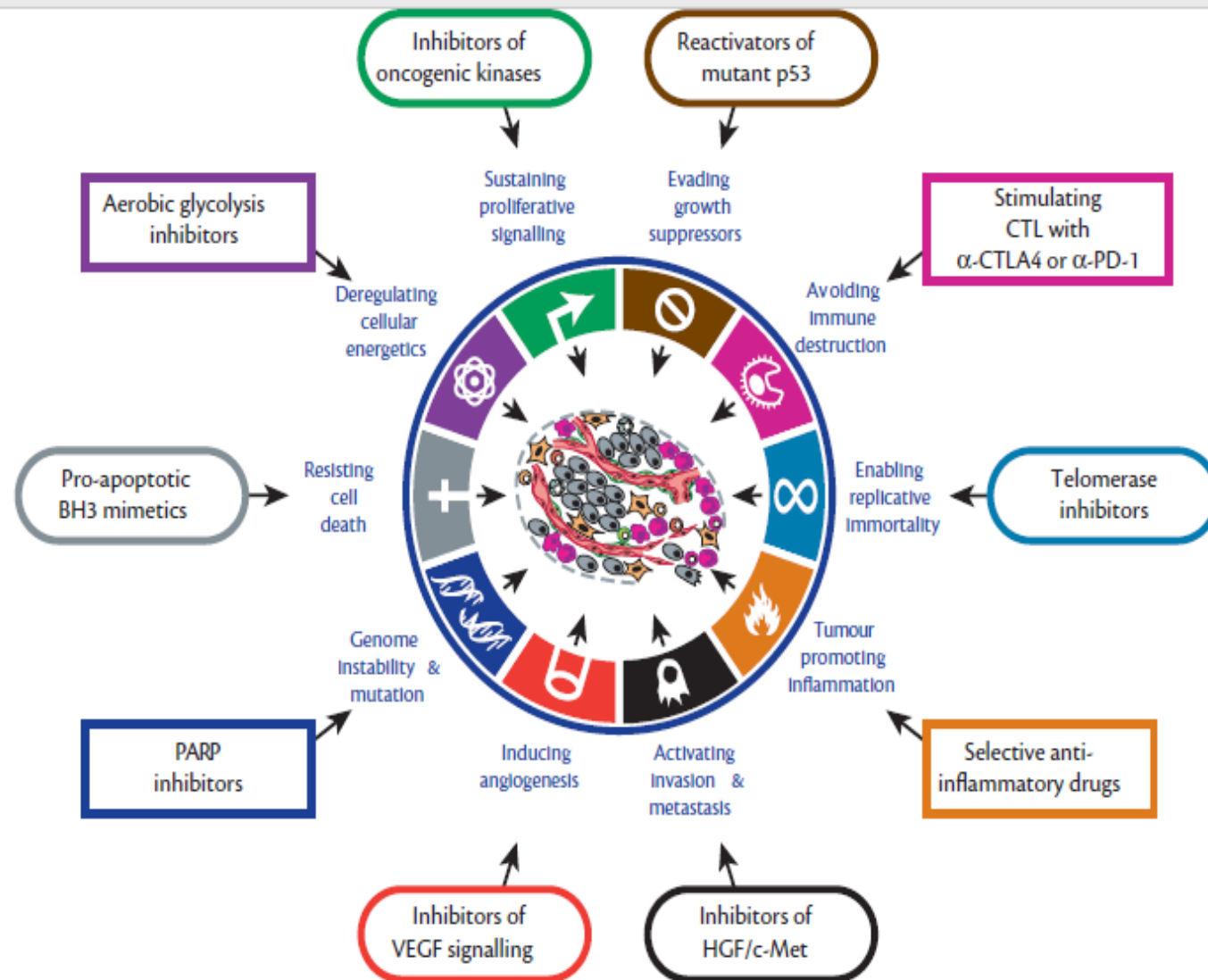


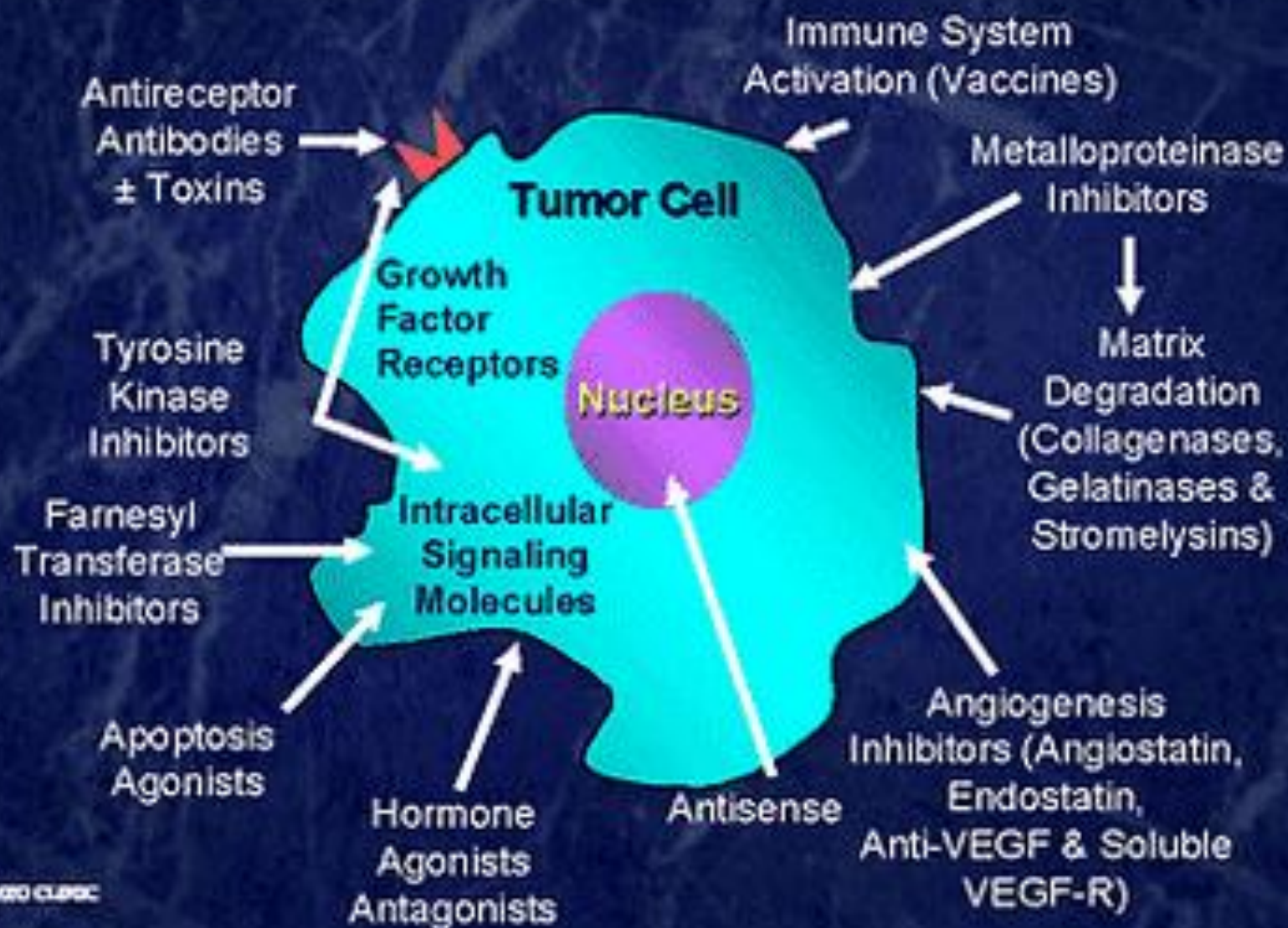
Fig. 1.2 Therapeutic targeting of the hallmarks of cancer. Drugs have been developed that disrupt or interfere with all eight of the hallmark capabilities, and with the two enabling facilitators (genome instability and tumour-promoting inflammation). Some of these hallmark-targeting drugs are approved for clinical use, while others are being tested in late-stage clinical trials; moreover, there is a pipeline full of new hallmark-targeting drugs that are in development and preclinical evaluation. Recognizing that eventual adaptive resistance during therapeutic treatment is apparent for virtually all of these hallmark-targeting drugs, a hypothesis has emerged: perhaps, by co-targeting multiple independent hallmarks, it will be possible to limit or even prevent the emergence of simultaneous adaptive resistance to independent hallmark-targeting drugs; clinical and preclinical trials are beginning to assess the possibilities.

Reprinted from *Cell*, Volume 144, Issue 5, Hanahan D, Weinberg RA, Hallmarks of cancer: the next generation, pp. 646–674, Copyright © 2011, with permission from Elsevier, <http://www.sciencedirect.com/science/journal/00928674>

A photograph showing several hands of different skin tones reaching up from the bottom and down from the top to form a circular ring. The hands are positioned with palms facing inward, creating a sense of unity and collective effort. The background is a plain, light color.

**SHOW THE WORLD
HOW TO FIGHT AGAINST CANCER**

Targeted Cancer Therapies



Molecular targeted therapies

- Drugs or substances are targeted at pathways, processes and physiology that disrupts cancer cells receptors, gene, angiogenesis and tumor PH
- MTT drugs that inhibit a more specific target in cells, mixture of cytostatic and cytotoxic, toxicity target or molecule related
- There are two targeting strategies, functional directed and phenotype directed

Target molecules

☐ Proteins on the cancer cell surface

- EGFR 1
 - HER2/Neu receptor
 - IGFR
 - VEGFR
 - CD molecules
-
- Mutant (altered) proteins
 - Mutant BRAF protein in malignant melanoma
 - Fusion Protein
 - BCR-ABL fusion protein in leukemia

Classification of MTT

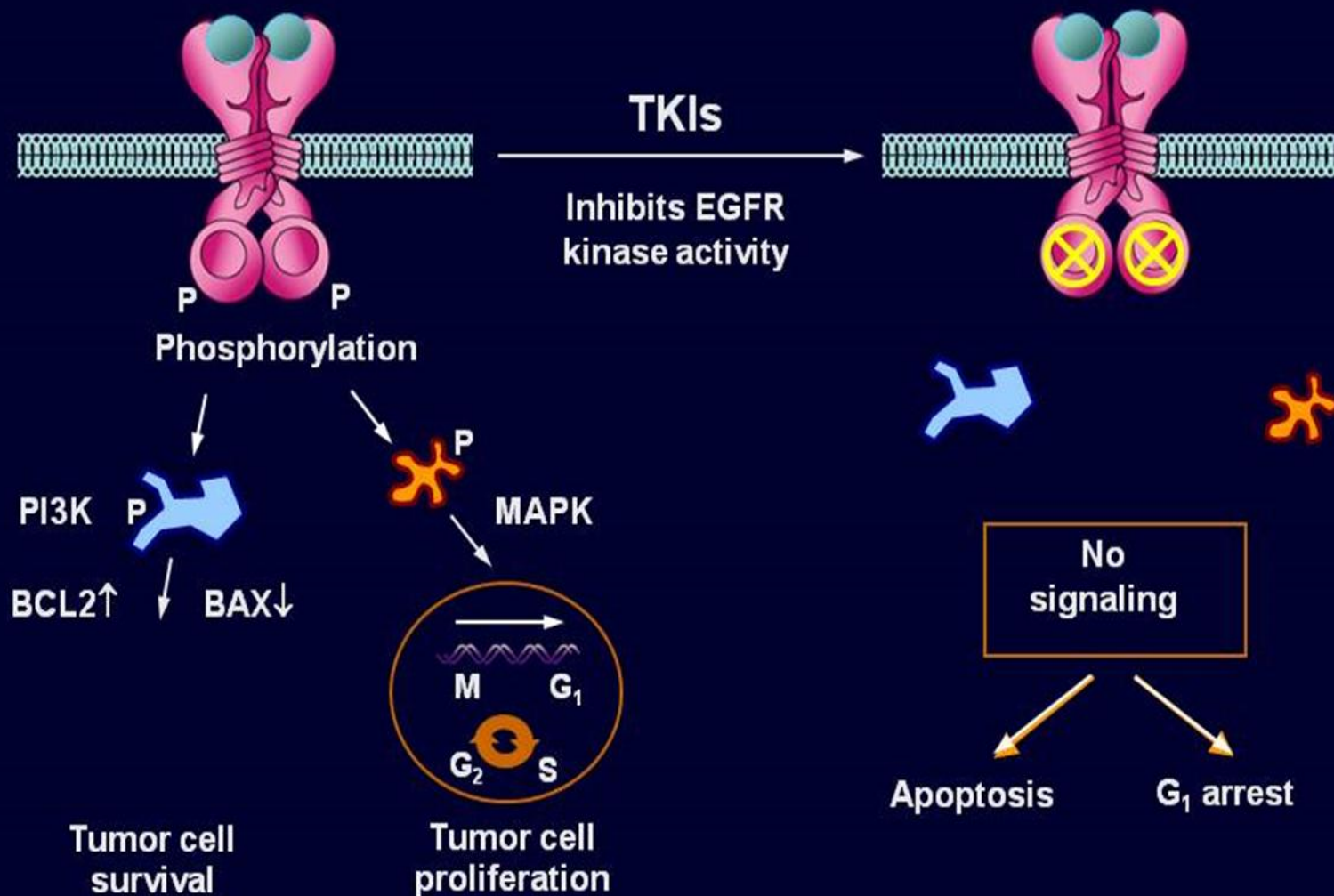
- Tyrosine kinase inhibitors, multikinase inhibitors
- Monoclonal antibodies
- mTOR kinase inhibitor
- Proteasome inhibitor
- Cyclin dependent kinase inhibitor
- PARP1 inhibitor
- Immune check point inhibitor

- Interleukin 2 receptor toxin
- Gene expression modulator
- Hedgehog pathway inhibitor
- Histone deacetylase inhibitor
- Retinoic acid receptor expression modification
- Non specific immunomodulator

Tyrosine kinase inhibitor, multi-kinase inhibitor, other kinase inhibitor

- Tyrosine kinase is an enzyme which phosphorylates mediators which are responsible for the intracellular signaling cascade
- Examples:
 - EGFR
 - HER2/Neu
 - PDGFR
 - VEGFR
 - C-Kit

Proposed Mechanism of Action of EGFR-Targeted Tyrosine Kinase Inhibitors



1. BCR-ABL Tyrosine Kinase Inhibitors(TKI)

Imatinib Mesylate,
Dasatinib,
Nilotinib,
Bosutinib
Ponatinib

2. Epidermal Growth Factor Receptor - TKI

Gefitinib,
Lapatinib,
Erlotinib

3. Vascular Endothelial Growth Factor – TKI

Vatalanib,
Sunitinib,
Sorafenib,
Pazopanib

Table 1: Current FDA-Approved Tyrosine Kinase Inhibitors

Drug	Indication(s)	Tyrosine Kinase Target(s)	Approval Date
Lapatinib	Breast cancer (in combination with capecitabine)	EGFR2 (HER2 or ERBB2)	March 2007
Erlotinib	NSCLC, pancreatic cancer (in combination with gemcitabine)	EGFR1 (ERBB1)	November 2004
Gefitinib ^a	NSCLC	EGFR1 (ERBB1)	May 2003 (new labeling June 2005)
Imatinib	CML, GIST	BCR-ABL, c-KIT	May 2001
Dasatinib	CML (refractory to imatinib)	BCR-ABL, c-KIT	June 2006
Nilotinib	CML (refractory to imatinib)	BCR-ABL, c-KIT	October 2007
Sunitinib	Renal cell carcinoma, GIST (refractory to imatinib)	VEGF, PDGF, c-KIT, FLT3	January 2006

^a Use is limited to patients who have previously taken gefitinib and are benefiting or have benefited from it.

EGFR: epidermal growth factor receptor; HER/ERBB: human epidermal growth factor receptor; NSCLC: non-small cell lung cancer; CML: chronic myelogenous leukemia; GIST: gastrointestinal stromal tumor; BCR-ABL: breakpoint cluster region/Abelson oncogene; VEGF: vascular endothelial growth factor; PDGF: platelet-derived growth factor; c-KIT: stem cell factor receptor; FLT3: FMS-like tyrosine kinase-3 receptor.

Source: References 18-24.

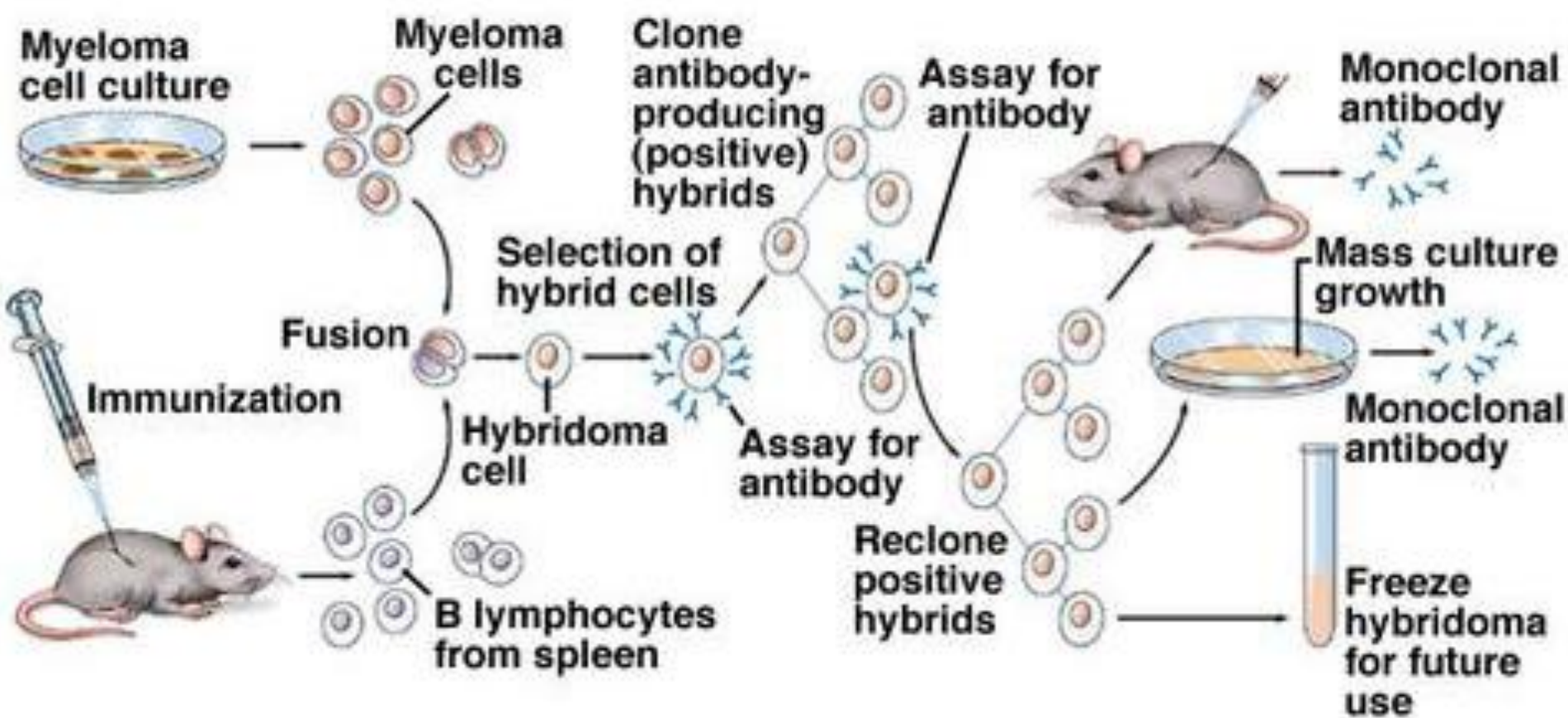
Advantages of Tyrosine Kinase Inhibitors

- Orally effective
- Better quality of life
- Can be used as monotherapy
- No need for premedication or dose monitoring
- No hematological toxicity(EGFR inhibitor)
- Potential for long-term treatment

Monoclonal Antibody

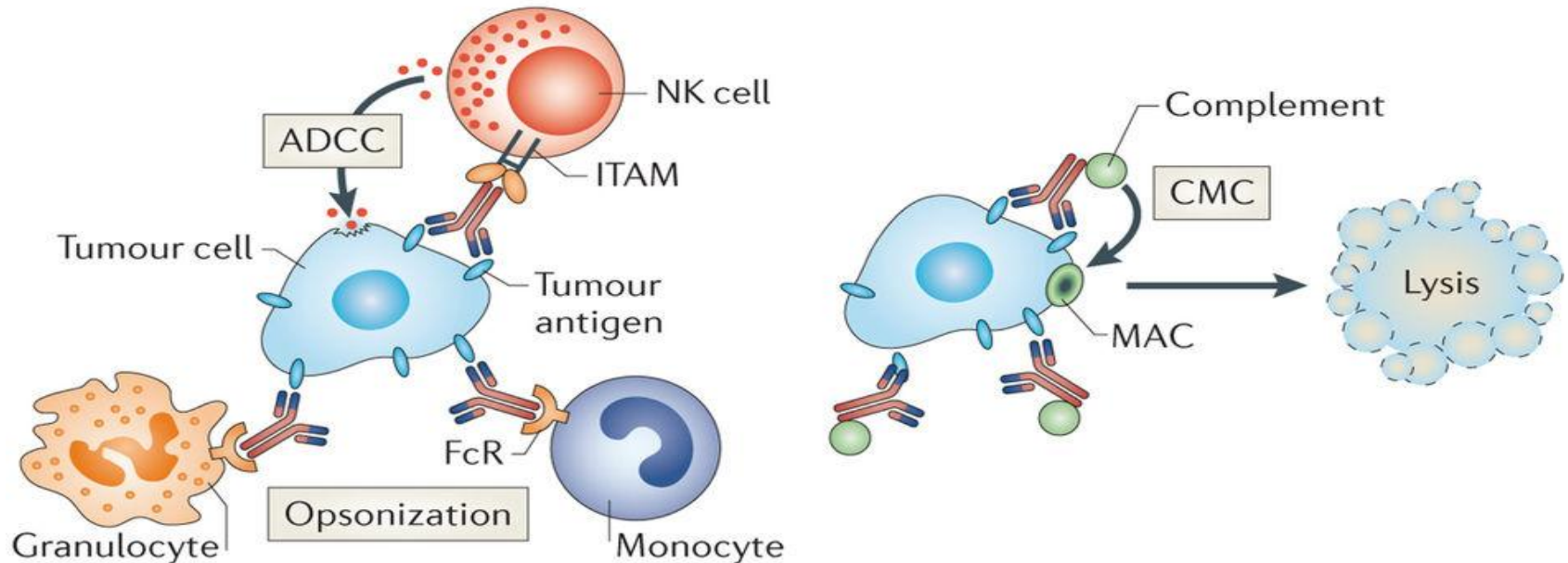
- Definition
 - Monoclonal antibodies are laboratory produced antibodies that can bind to substances in the body including cancer cells to stop proliferation, differentiation and progression of cancer cells
- Types
 - Unconjugated
 - Conjugated (with toxin or radioactive substances)

Monoclonal Antibody Production

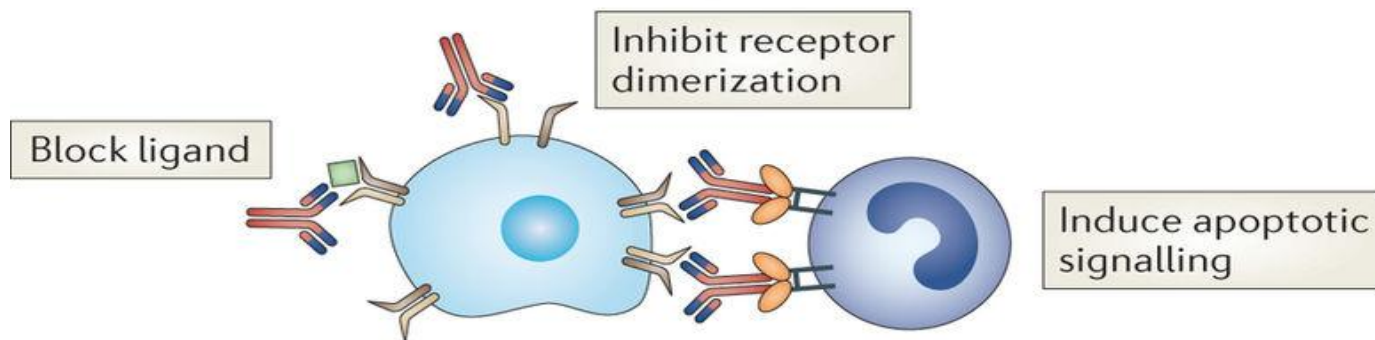


Mechanism of action

a Immune-mediated effects of tumour-specific IgG



b Direct effects of tumour-specific IgG



Monoclonal Antibody

Agent	Target	Indication
Rituximab	CD 20	<ul style="list-style-type: none">• Diffuse, large B-cell NHL
Alemtuzumab	CD 52	<ul style="list-style-type: none">• B-cell CLL
Ofatumumab	CD 20	<ul style="list-style-type: none">• CLL
Gemtuzumab	CD 33	<ul style="list-style-type: none">• Myeloid leukemia
Ibritumomab	CD 20	<ul style="list-style-type: none">• B-cell follicular NHL
Tositumomab	CD 20	<ul style="list-style-type: none">• Low grade NHL

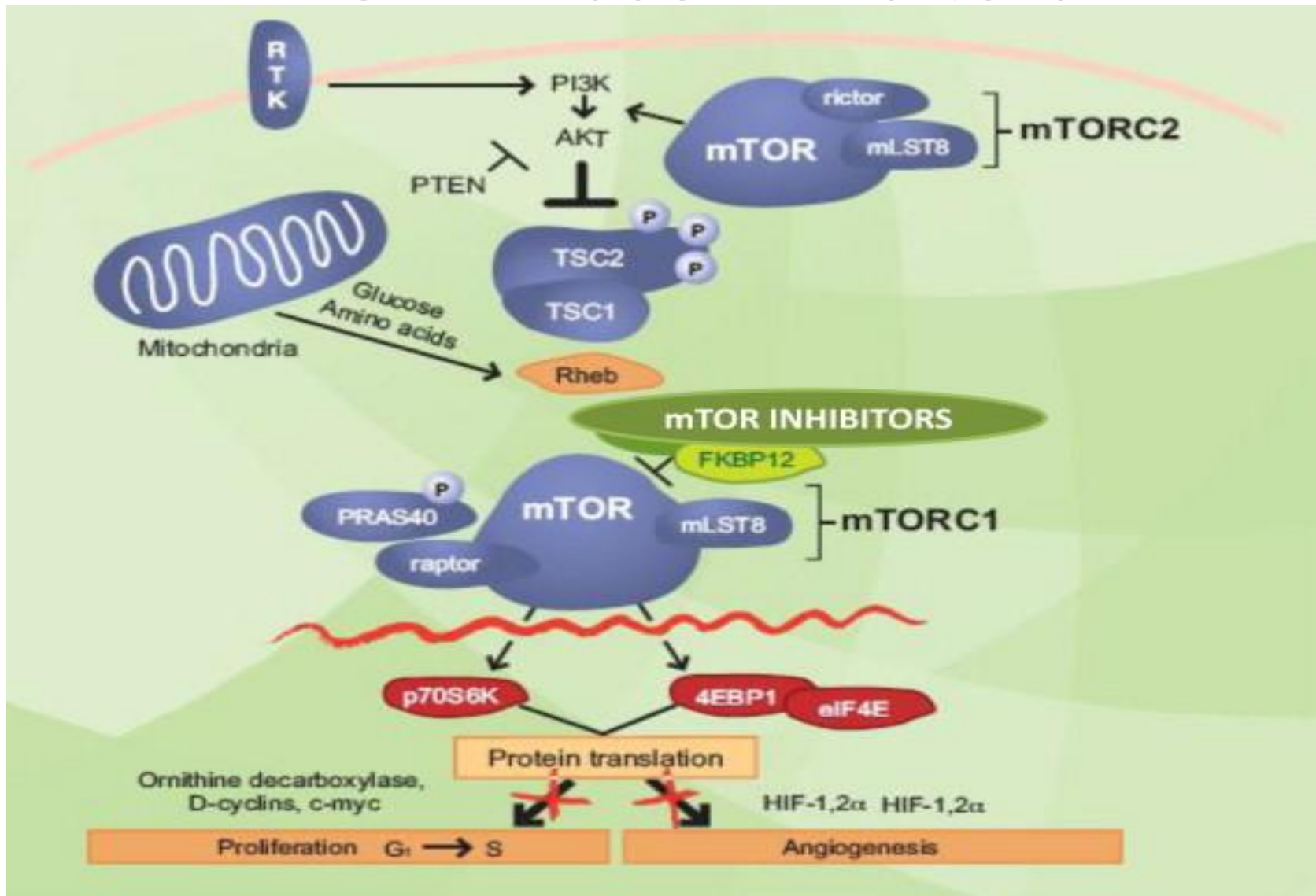
Monoclonal Antibody

Agent	Target	Indication
Cetuximab	EGFR1	<ul style="list-style-type: none">• Metastatic Ca colon• Metastatic head and neck cancer
Panitumumab	EGFR1	<ul style="list-style-type: none">• Metastatic Ca colon
Trastuzumab	HER2	<ul style="list-style-type: none">• Ca Breast• Metastatic adenocarcinoma GEJ
Bevacizumab	VEGFR	<ul style="list-style-type: none">• Metastatic Ca colon• RCC• Glioblastoma• NSCLC
Denosumab	RANKL	Bone mets GCT of bone

Monoclonal Antibody

Agent	Target	Indication
Gemtuzumab ozogamicin	CD 33	<ul style="list-style-type: none">• Diffuse, large B-cell NHL• Myeloid leukemia
Ibritumomab Tiuxetan	CD 20	<ul style="list-style-type: none">• B-cell follicular NHL (refractory)
¹³¹ I - Tositumomab	CD 20	<ul style="list-style-type: none">• NHL (refractory)

mTOR kinase inhibitors

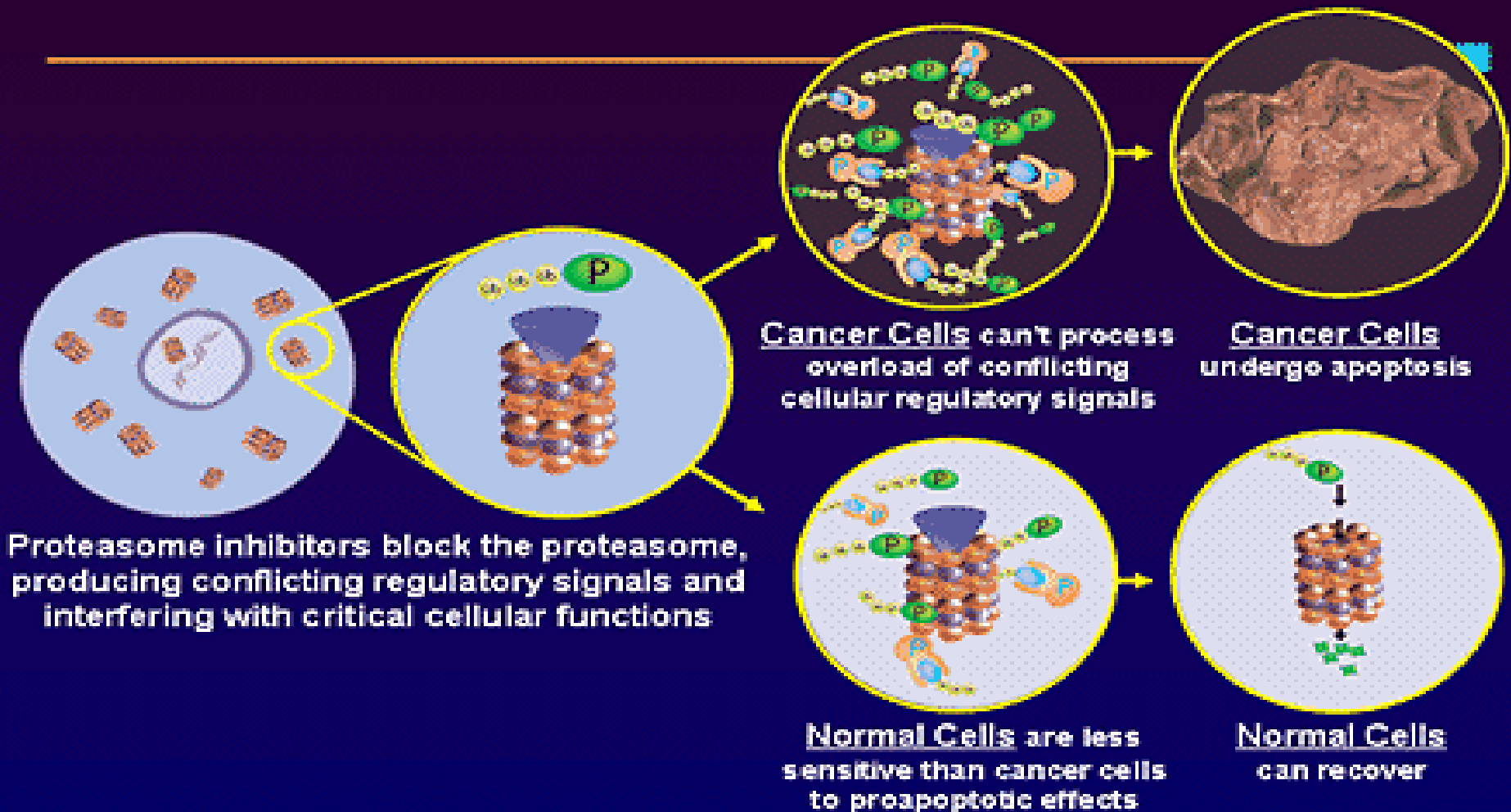


mTOR kinase inhibitors

Agent	Target	Indication
Temsirolimus	mTOR	• Advanced RCC
Everolimus	mTOR	• Advanced RCC , breast cancer

Proteasome Inhibitor

How Proteasome Inhibition Works



Proteasome Inhibitor

Agent	Target	Indication
Bortizomib	26S Proteasome	<ul style="list-style-type: none">• Multiple myeloma• Mantle cell lymphoma
Carfilzomib	26S Proteasome	<ul style="list-style-type: none">• Multiple myeloma

Others

- Cyclin dependent kinase inhibitor
Flavopiridol used in CLL
- PARP1 inhibitor
Olaparib: Metastatic Ca breast with BRCA mutation,
Iniparib: triple negative metastatic Ca breast
- Interleukin 2 receptor toxin
Denileukin diftitox: Cutaneous T-cell lymphoma
- Gene expression modulator
Retinoids: Leukemia
Rexinoids: Leukemia
Romidepsin: Cutaneous T-cell lymphoma

- Hedgehog pathway inhibitor
 - Vismodegib: Basal cell carcinoma
 - Sonidegib: Basal cell carcinoma
- Histone deacetylase inhibitor
 - Belinostat: Peripheral T-cell lymphoma
 - Panobinostat: Multiple myeloma
- Retinoic acid receptor expression modification
 - Tretinoin: acute promyelocytic leukemia

Limitations of MTT

- Development of resistance to MTT
- Target itself changes through mutation
- Tumor finds a new pathway to achieve tumor growth
- Difficulties of drug development against some identified targets

Gene therapy and genetic immunotherapy

- Strategies-
 - Somatic correction of gene defects
 - Expression of tumor suppressor gene
 - Antisense oligonucleotide for mutant oncogene
 - Genetic pro-drug activation
 - Genetic immunomodulation
 - Immunotherapy

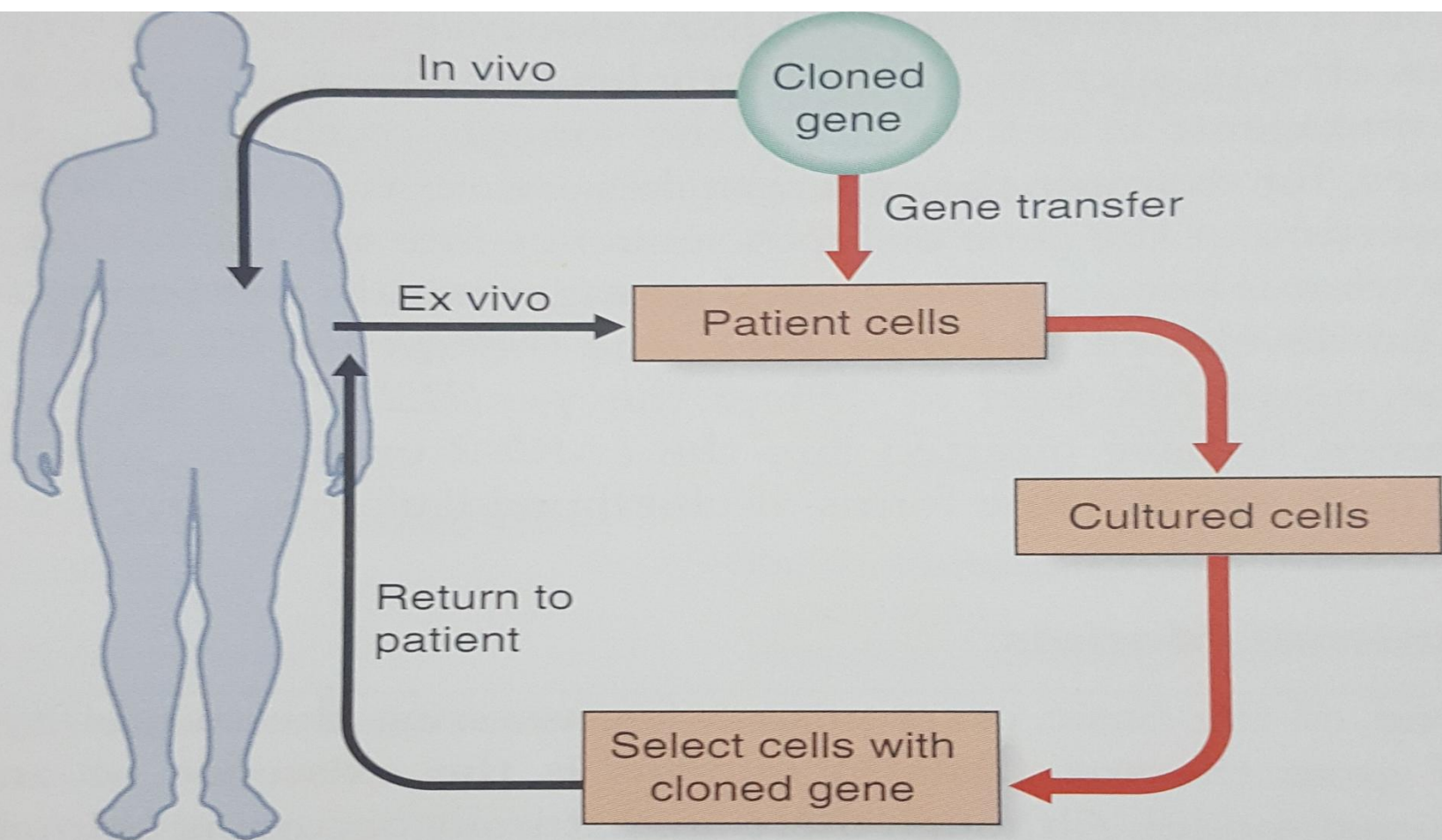


FIGURE 23.1 In vivo and ex vivo gene therapy. In vivo gene therapy delivers genetically modified cells directly to the patient. An example is *CFTR* gene therapy using liposomes or adenovirus via nasal sprays. Ex vivo gene therapy removes cells from the patient, modifies them in vitro and then returns them to the patient. An example is the treatment of fibroblasts from patients with hemophilia B by the addition of the factor IX gene. Modified fibroblasts are then injected into the stomach cavity.

Expression of tumor suppressor gene

- Gendicine- recombinant adenovirus expressing P53, approved for use in China for head neck cancer
- Sequential use of intratumoral injection of retroviral vector with P53 in NSCLC and chemotherapy Cisplatin may be synergistic.(on Phase II trial)

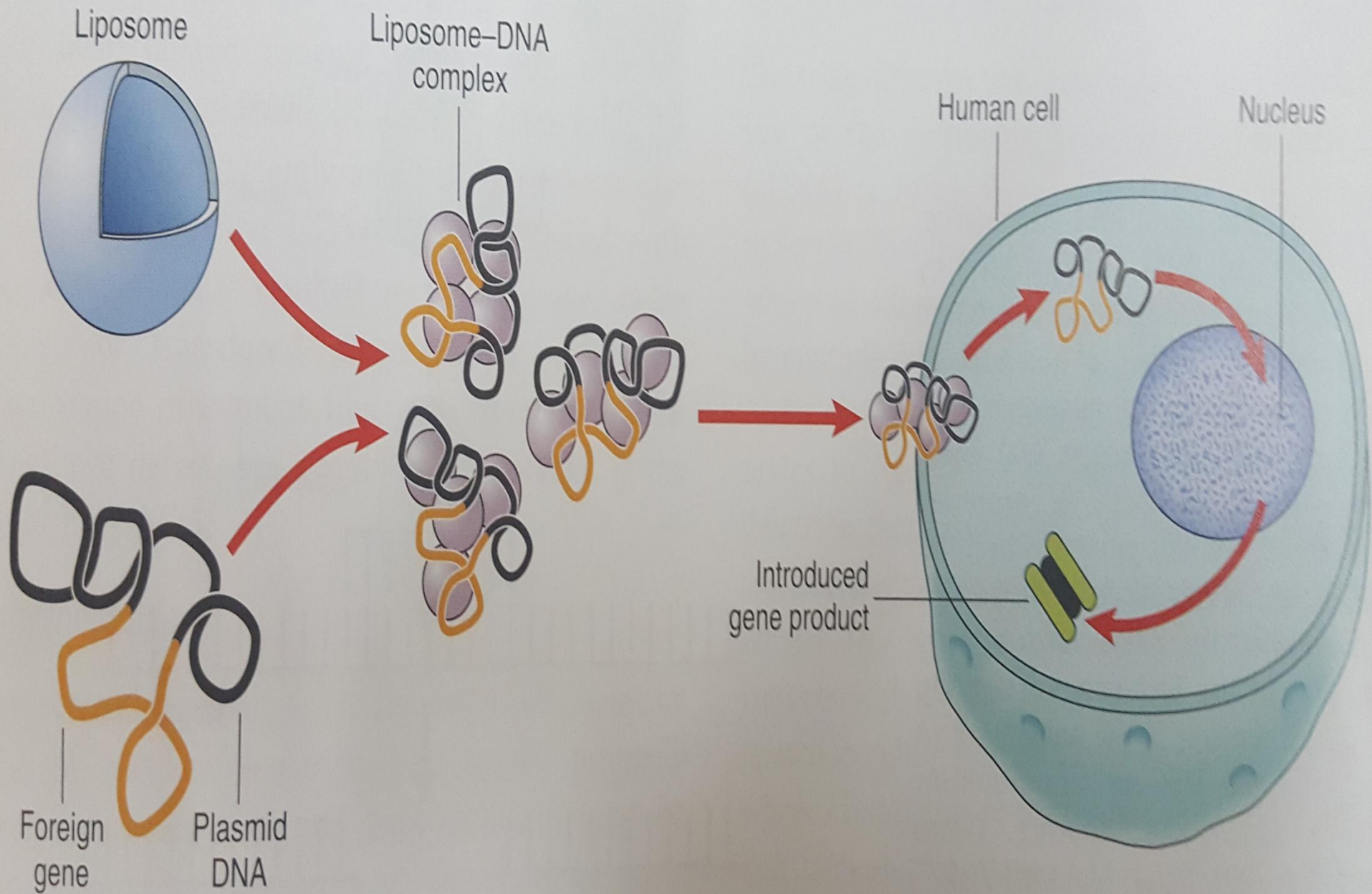
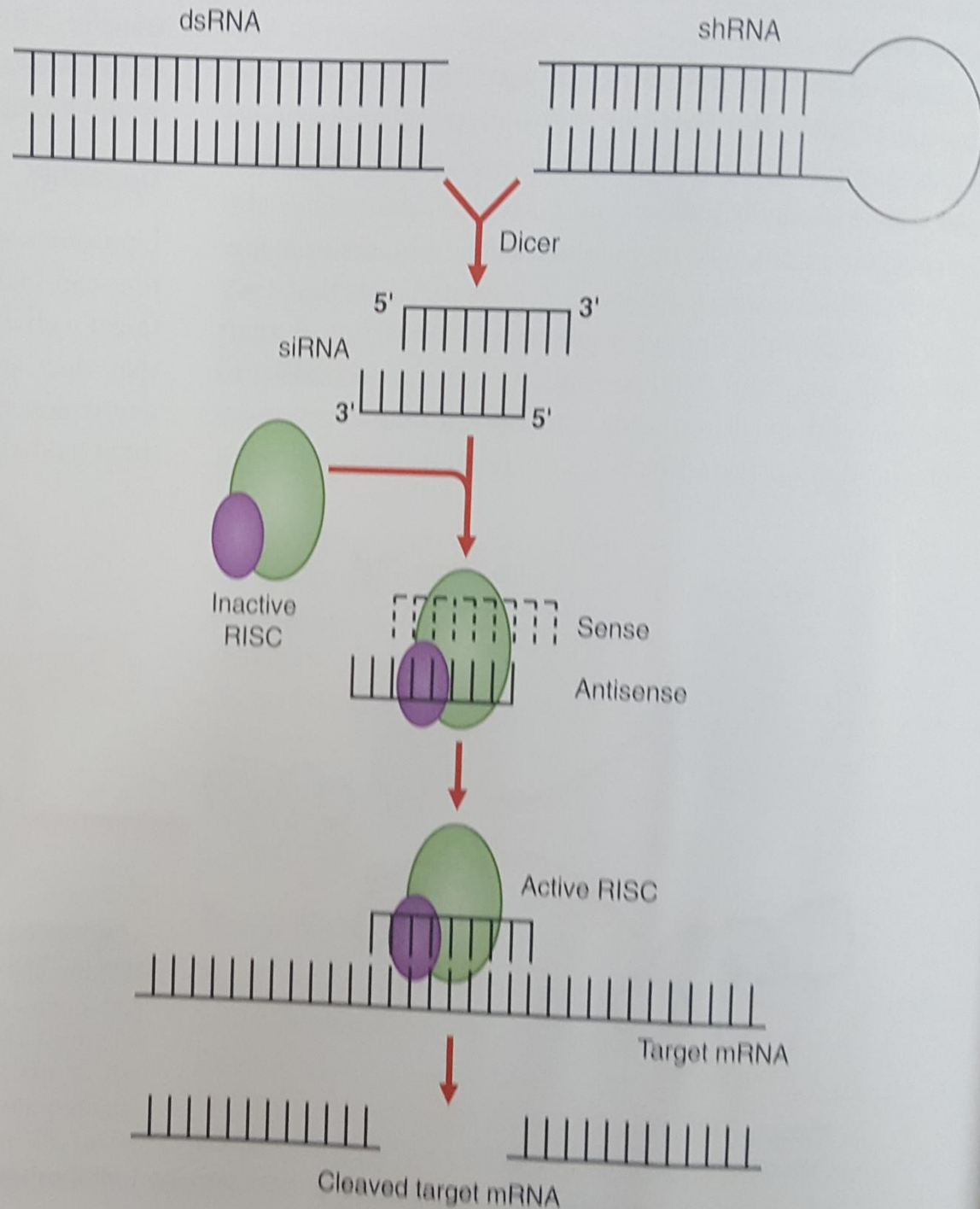


FIGURE 23.2 Diagrammatic representation of liposome-mediated gene therapy.

Correction of Mutant Oncogene

- Antisense DNA oligonucleotide inhibit transcription into mRNA or translation of mRNA into protein
- G3139 (Oblimersan) is an antisense DNA oligonucleotide targeting the initiation codon region, BCL2 messenger RNA
- Clinical trials in many malignancies including advanced prostate cancer, melanoma, lymphoma, leukaemia

FIGURE 23.3 Mechanism of RNA interference. Double-stranded (ds) RNAs are processed by Dicer, in an ATP-dependent process, to produce small interfering RNAs (siRNA) of about 21–23 nucleotides in length with two-nucleotide overhangs at each end. Short hairpin (sh) RNAs, either produced endogenously or expressed from viral vectors, are also processed by Dicer into siRNA. An ATP-dependent helicase is required to unwind the dsRNA, allowing one strand to bind to the RNA-induced silencing complex (RISC). Binding of the antisense RNA strand activates the RISC to cleave mRNAs containing a homologous sequence. (From Lieberman, et al 2003 Trends Mol Med 9:397–403, with permission.)





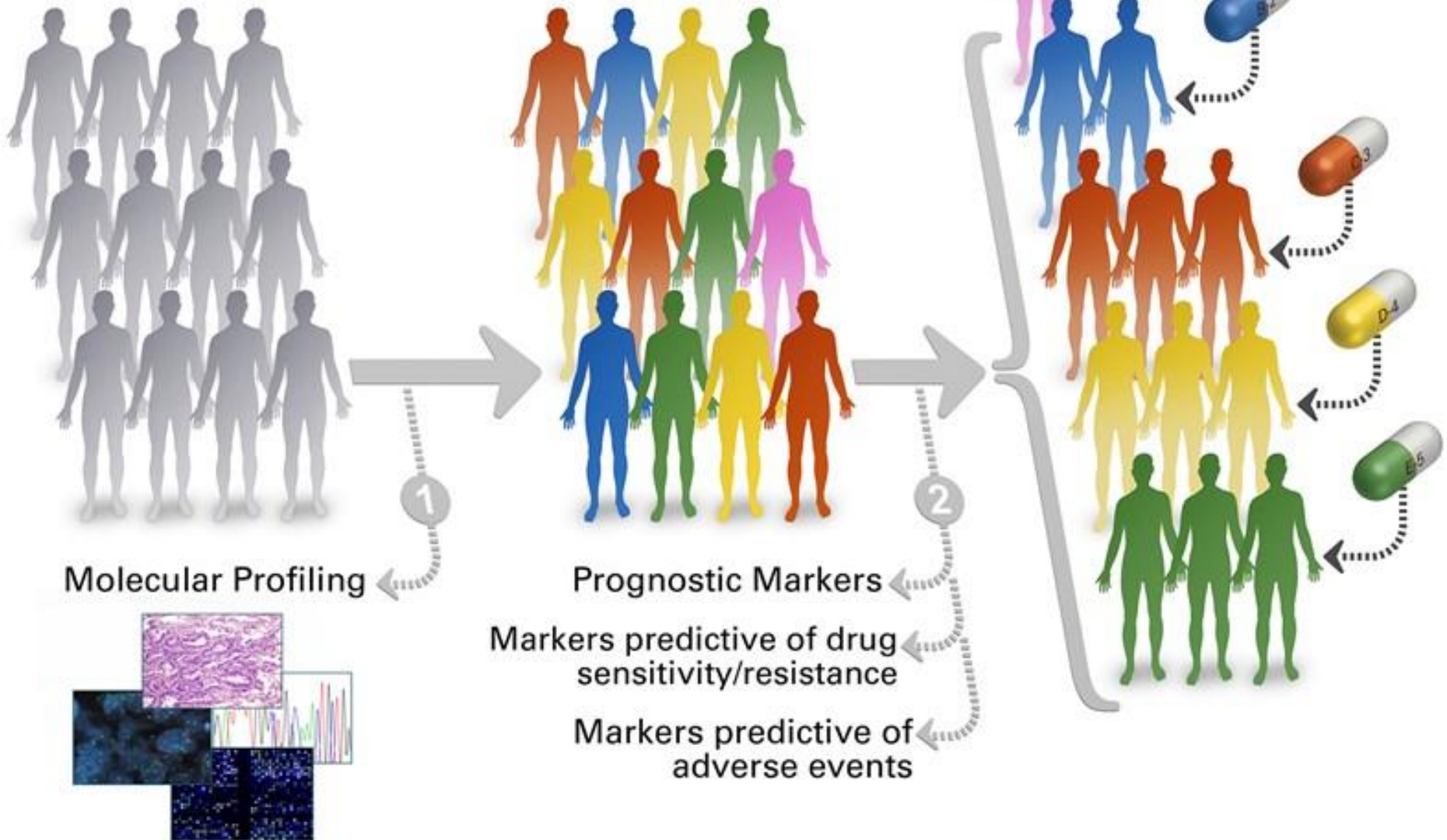
As seen in
the June
2015 issue of
David LIFE
Magazine

Precision Medicine & the Future of Cancer Care

Precision medicine

- Precision medicine is a method of treatment which a patient's cancer will be extensively characterized for mutations and other molecular abnormalities, and treatment will be based mainly on the identified molecular changes instead of the type of cancer

Personalized Cancer Therapy



WITHOUT
PRECISION MEDICINE

PATIENT



SAME THERAPY



SOME BENEFIT,
OTHERS DO NOT

BENEFIT



NO BENEFIT



ADVERSE EFFECTS



WITH
PRECISION MEDICINE

EACH PATIENT BENEFITS



DNA TESTS

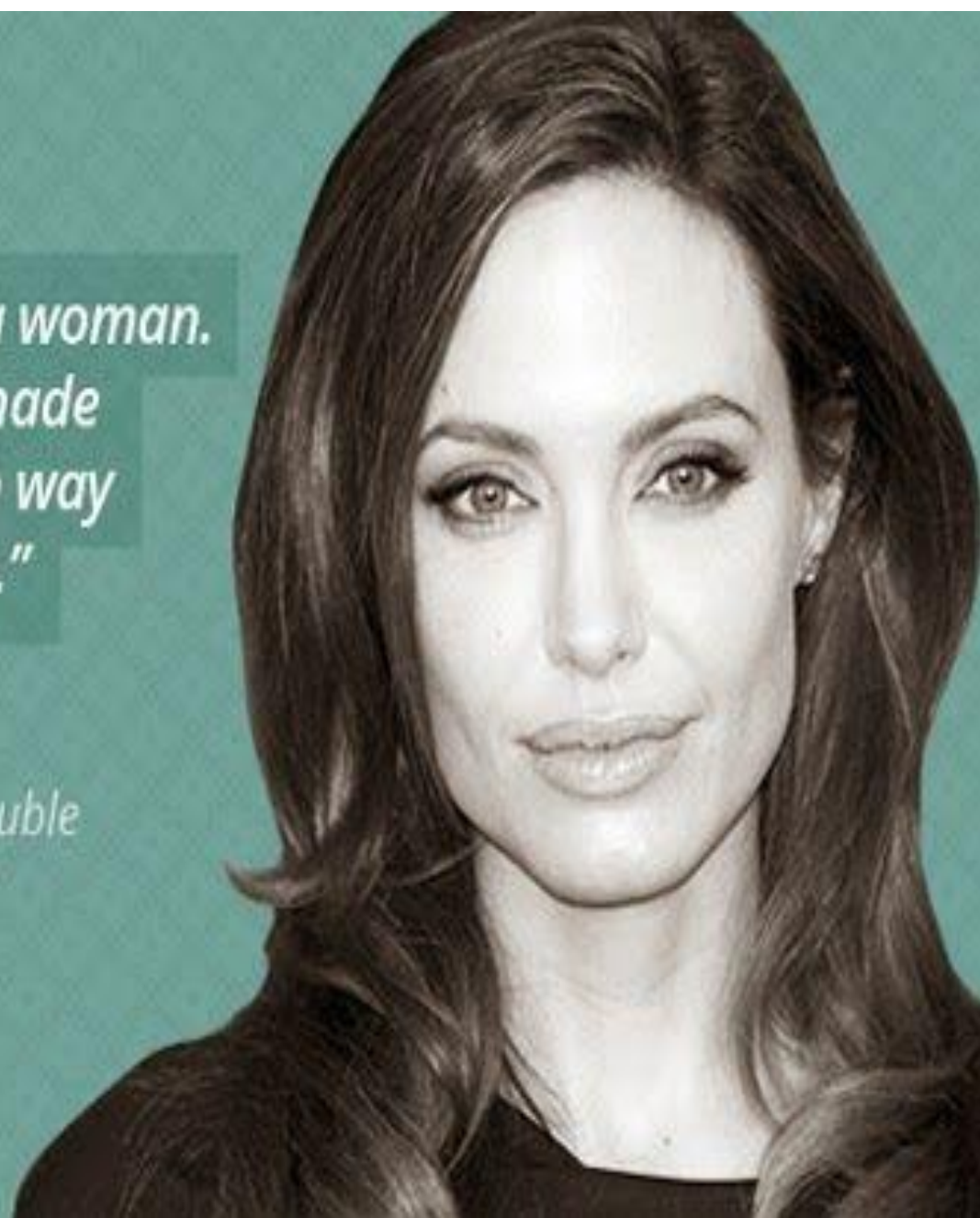


TAILORED
THERAPY



*"I do not feel any less of a woman.
I feel empowered that I made
a strong choice that in no way
diminishes my femininity."*

*- Angelina Jolie on getting a double
mastectomy*



16 December

Great Victory Day



Thank You All



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4. Manual of clinical oncology, by Dennis A Casciato
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6. Internet content
7. Different PowerPoint presentations from my students